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**Journal of Global Health (JoGH)** is a peer-review general medical journal focusing on issues relevant for global health. The mission of the journal is to serve the community of researchers, funding agencies, international organizations, policy-makers and other stakeholders by providing an independent critical assessment of the key issues that dominated the global health community.

JoGH publishes original articles, viewpoints, research protocols and other publication items, making them available in full text online as soon as they are ready for publication. The articles are collected in two annual print issues, at the end of June and December. All submissions and editorial inquiries should be directed to editor[at]jogh.org.

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The *Journal of Global Health* is a peer-reviewed journal published by the Edinburgh University Global Health Society, a not-for-profit organisation registered in the UK. The *Journal* publishes editorials, news, viewpoints, original research and review articles in two issues per year.

The *Journal's* mission is to serve the community of researchers, funding agencies, international organizations, policy-makers and other stakeholders in the field of international health by:

- presenting important news from all world regions, key organizations and resources for global health and development;
- providing an independent assessment of the key issues that dominated the previous semester in the field of global health and development;
- publishing high-quality peer-reviewed original research and providing objective reviews of global health and development issues;
- allowing independent authors and stakeholders to voice their personal opinions on issues in global health.

Each issue is dedicated to a specific theme, which is introduced in the editorial and in one or more viewpoints and related articles. The news section brings up to five news items, selected by the *Journal's* editorial team, relevant to seven regions of the world, seven international agencies and seven key resources important to human population health and development.

We particularly welcome submissions addressing persisting inequities in human health and development globally and within regions. We encourage content that could assist international organizations to align their investments in health research and development with objective measurements or estimates the disease burden or health problems that they aim to address. Finally, we promote submissions that highlight or analyse particularly successful or harmful practices in management of the key resources important for human population health and development.

All editors and editorial board members of the *Journal* are independent health professionals based at academic institutions or international public organisations and so are well placed to provide objective professional evaluation of key topics and ongoing activities and programs. We aim to stay true to principles of not-for-profit work, open knowledge and free publishing, and independence of academic thought from commercial or political constraints and influences. Join us in this publishing effort to provide evidence base for global health!

March 7, 2011

The Editors, *Journal of Global Health*



Child health is at the heart of Millennium Development Goals and great progress has been made to improve global child survival. The recent estimates from China demonstrate a 37% decrease under-five mortality rates from 2009 to 2015. The leading causes of death remain birth complications, congenital abnormalities, accidents and pneumonia, with the latter still predominating in poorer provinces.

Photo: courtesy of Prof. Kit Chan, Usher Institute of Population Health Sciences and Informatics, Centre for Global Health Research, University of Edinburgh.

# Reporting guidelines in global health research

Ana Marušić, Harry Campbell

Editors in Chief, *Journal of Global Health*

Reporting guidelines have become important tools in health research. They improve the accuracy, completeness and transparency of reporting most important aspects of research studies [1]. This is particularly important not only for accurate evaluation of the methodological quality of research and validity of the results, but also increases the quality of evidence synthesis from health research for practical application [2]. Research that is not clearly reported leads to waste in research, distorts existing evidence and compromises the replication of research findings. It has been well demonstrated that the endorsement of the CONSORT – the first reporting guideline, developed for randomized controlled trials – increases the completeness of completeness of trial reporting in medical journals [2].

The central part of a reporting guideline is a checklist which lists minimum information that must be provided in a published article. Checklists made their way into health research reporting from industry, where they, just as in medicine, serve as quality and safety assurance of processes and products, particularly those involving high risk [3]. A good example of a medical checklist is the WHO Surgical Safety Checklist, which clearly demonstrated a highly significant reduction in complication or death rates after surgery [4,5].

There are currently more than 300 reporting guidelines for different study designs and health research disciplines – the most comprehensive source of information is the EQUATOR Network [6]. The *Journal of Global Health (JOGH)* requires from its authors to follow relevant reporting guidelines when submitting their manuscript [7].

We would like to draw your attention to newly published reporting guidelines that are relevant for global health.

The reporting guideline “Strengthening the Reporting of Observational Studies in Epidemiology for Newborn Infection” or STROBE-NI is an extension of the STROBE statement for neonatal infection research. It was recently published in *Lancet Infectious Diseases* [8] and is also available at the EQUATOR Network site [9]. Neonatal infections ac-

count for about one quarter of the 2.8 million neonatal deaths globally each year [10] and there is an urgent need for research investment to define new approaches to tackle this problem. As noted by the authors, the guideline seeks to “optimise reliability, clarity and comparability of scientific reporting of neonatal infections in observational studies and relevant trials, especially aetiological (bacterial, viral and fungal) data, to maximise their utility and impact.” This fills an important gap in this important topic and will complement existing guidelines related to child health trials and systematic reviews and meta-analyses. The SPRING checklist follows the STROBE format and focuses on key issues important to the design and reporting of neonatal infection research. Importantly, the SPRING group included substantial expertise from researchers from low and middle income countries to ensure they are relevant to these high burden settings.

The Guidelines for Accurate and Transparent Health Estimates Reporting or GATHER statement was first published in the *Lancet* [11] and *PLoS Medicine* [12]. It is also available at the site of the GATHER statement [13], as well as the EQUATOR Network [14]. Due to very incomplete data in most countries globally statistical or mathematical models are often used to estimate key health indicators. These are then used to inform global and national decision-making and priority setting. It is important, therefore, that we can have confidence in the estimates and are able to understand how they were derived and what the uncertainty bounds are surrounding the estimates. In order to promote accurate interpretation and responsible use of these data, World Health Organization (WHO) convened a number of expert consultations to prepare a set of standard reporting guidelines – Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) [11,12]. The guideline comprises a checklist of 18 essential items for best reporting practice. An important aspect of GATHER is that the data underlying the modeled estimates are made accessible online. Given the importance of these principles in promoting best practice in studies generating data to underpin evidence-based policy making, we strongly support this

initiative. We hope that medical and public health journals will ensure that burden of disease studies that fall within the ambit of these guidelines will be required to implement these guidelines before accepted for publication.

Finally, the newest reporting guideline addresses the translation of evidence to practice by providing a reporting guideline for health care practice guidelines. The guideline is published in the *Annals of Internal Medicine* [15], and is also available at the EQUATOR Network [16] and the web-site of the RIGHT statement [17]. This guideline is the results of a working group which addressed the problem of often poor reporting of health care practice guidelines despite their importance and popularity as a tool to improve the quality of health care. The reporting guideline was developed as a joint effort from expert and consumer representatives, including

internationally recognized organizations such as Guidelines International Network, Cochrane Collaboration, AGREE Collaboration, GRADE working group, International Society for Evidence-Based Health Care, EQUATOR Network, and National Guideline Clearinghouse [15,17]. The guideline comprises a checklist with 22 items and a flow diagram, as well as an explanation and elaboration paper.

In addition to the requirement to use a relevant reporting guideline when submitting their *manuscript* to the *Journal of Global Health*, we encourage our authors and readers with an interest in the fields covered by the three reporting guidelines to help disseminate the guidelines and promote their use. Also, contact guideline developers with comments and suggestions about improving and further developing these reporting guidelines.

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## ▶ Africa

▶▶ A Department of Basic Education (DBE) report estimates that nearly 600 000 of South Africa's disabled children do not attend school, with an estimated 5552 pupils on waiting lists for a place at a special school. A Human Rights Watch report (*Complicit in Exclusion*) published in August 2015 highlighted these problems, and calls for waiting lists to be dealt with. One of the report's researchers, Elin Martinez, suspects that the number of children on waiting lists is underestimated, and the government does not have accurate statistics on children with disabilities who do not attend school. The system of special schools for children with severe or multiple disabilities is further strained as students with mild or moderate disabilities are referred to them rather than being accommodated in mainstream schools. This is exacerbated by the lack of support in mainstream schools, and teachers can find it very difficult to support students with disabilities due to large class sizes. Children on a waiting list for a special school will remain in their mainstream school until they are admitted, but children on a waiting list who are not already in school can find themselves excluded from both mainstream and special education, and can face lengthy waits. Disabled children can be further excluded from special schools by the inability of their parents to pay transport costs for distant schools, even if they are exempt from school fees due to low income. (*Daily Maverick*, 15 June 2016)

▶▶ Today's people in Vietnam have approximately the same wealth level as Americans in the 1880s, but the same life expectancy as Americans in the 1980s. Vietnam has gained 100 years in health development, and highlights how low-income countries can convert economic growth into health improvements. It serves as an example to Africa, where many countries have lagged behind in translating economic growth into improved health. Previously Africa has been hindered by poor institutions, shoddy infrastructure and the devastating impact of HIV/AIDS. However, African countries are beginning to close the gap, and the two most basic health indicators – life expectancy and infant mortality – are improving. Prof Hans Rosling, a public health expert and co-founder of Gapminder says “it's very clear that Africa is catching up with Europe in health ... in spite of the fact that the poorest in Africa are not moving.” His research suggests that health improvements lead to lower birth rates which enable more women to work outside the home, and more resources devoted to each child – further promoting economic growth. This feedback loop is more effective if countries are well-governed, and governments invest in schools, sanitation and basic health rather than

conflict. His message to African governments is that, with the right policies, health gains can be consolidated, fueling economic growth and leading Africa toward prosperity. (*Financial Times*, 8 June 2016)

▶▶ Following Sanofi–Pasteur's decision to halt production of Fav–Afrique, stocks of Africa's most effective anti-venom treatment for snake bites will expire at the end of June 2016. Each year, 30 000 African people die from snake-bites, and although other treatments are available, none are as effective as Fav–Afrique which treats bites from 10 types of snake. Sanofi–Pasteur decided to discontinue production in 2010, offering to share the technology with anyone who wanted to resume its production – to date, no-one has taken up this offer. Fav–Afrique is complicated and time-consuming to produce, expensive (at an average cost of US\$ 500 per patient) and requires refrigeration – difficult for rural African clinics. The demise of Fav–Afrique reflects a wider market failure in the pharmaceutical industry; companies like Sanofi–Pasteur claim they are not making a fair rate of return on investments and call for donors, governments and other organisations to fund essential drugs like vaccines and anti-venoms. (*Voice of America*, 24 June 2016)

▶▶ Stigma is one of the biggest obstacles in ending South Africa's HIV/AIDS epidemic. The HIV prevalence rate among sex workers – one of the most at-risk groups – and their clients in Durban was 53%, compared to the national average adult rate of 19.2%. Sex workers report being humiliated and dismissed by staff in health clinics, and Dr Luiz Loures, the deputy executive director of UNAIDS believes that discrimination against key populations such as sex workers and gay men means that AIDS is selectively returning despite medical advances in life-saving HIV drugs. Durban recently hosted the 16th International AIDS Conference, and campaigners who had previously fought to break the silence around AIDS are now alarmed over unequal access to HIV treatment. South Africa saw 380 000 new HIV infections and 180 000 deaths from AIDS in 2015. Mark Heywood, a leading activist from the Section 27 rights group marched to “wake up the world again”, saying that “people with HIV are mostly poor, they're mostly marginalised.” This is a backdrop of falling international AIDS funding and only 17 million of the world's 36.7 million HIV-positive people having access to HIV treatment. (*Reuters*, 18 August 2016)

▶▶ According to the WHO, more than 120 000 people die each year in Africa from fake anti-malarial drugs, which

can be sub-standard or contain no active ingredients. Sub-standard drugs, with insufficient quantities of active ingredients, can also lead to drug resistance – particularly dangerous for diseases like malaria and tuberculosis. By some estimates, one-third of all anti-malarial drugs in sub-Saharan Africa are fake. However, some small companies are using technology to tackle the problem. For example, Sproxil, led by Dr Ashifi Gogo, offers scratch-panel stickers with an authentication code for consumers to text to Sproxil for verification. Sproxil spokesman Tolulope Gbamolayun says that 29 million verifications have taken place since the scheme launched in 2009. Bright Simons set up a similar “verify-by-mobile” system (mPedigree Net-

work), where printed barcodes and scratch-off stickers – developed in partnership with Hewlett-Packard – help customers verify drugs. In Nigeria, the technology is helping regulators track down fraudsters. The pharmaceutical industry has also introduced a number of technologies to detect fake drugs, and the US Pharmacopeial Convention has set up a center for pharmaceutical training to train African pharmacists in screening for substandard and fake drugs. However, such initiatives have to deal with the massive scale of fake medicines, government corruption, lack of accountability, inaction from multinational pharmaceutical companies, and under-resourced drug regulatory bodies. (*BBC*, 28 September 2016)

## ▶ Asia

▶▶ In June, Tibetan female farm-workers marched on the capital Lhasa against the confiscation of their farmland to make way for new urban developments. According to an anonymous source, the protest was confined to women, out of fears that the Chinese police would crack down on any men taking part. The Chinese authorities had promised to compensate the farmers at a rate of US\$ 30 352 per *mu* [approx. 0.16 acres] of land, but farmers claim that they have only received US\$ 3035 per *mu*, and are demanding US\$ 27 316 per *mu*. The farmers claim that confiscating their land at such low rates of compensation will drive them into poverty for generations. Other sources say that traditional Tibetan homes in the Lhandrub region are being destroyed and replaced by Chinese-style dwellings, without the consent of the citizens. (*Radio Free Asia*, 10 June 2016)

▶▶ Northern Myanmar's jade mines employ an estimated 300 000 migrant workers, drawing people from across the country. Scavenging through mine waste to find jade stones is potentially lucrative, but living conditions are harsh and dangerous landslides are common. Despite the dangerous conditions, drug addiction is a bigger threat to miners' health. There are no official statistics, but according to local activists up to 50% of miners are drug users in some areas. The miners are drawn to drugs and alcohol to ease physical pain and help with relaxation after intense manual labor. Opium, heroin and methamphetamine are readily available in many mining areas, produced by ethnic rebel groups, militias and criminal gangs. Drug users who share needles are at risk of HIV infection, and there is some provision of harm reduction services such as clean needles, methadone, HIV testing, counselling and antiretroviral drugs. However, Myanmar's Drug Advocacy Group has called on the new NLD government to scale-up services

and adopt a rights- and health care approach to the drugs problem. And despite the existence of – albeit limited – harm reduction services, law enforcement against dealers is almost non-existent, compounded by buying-off local officials, police and military officers. (*Irrawaddy*, 20 June 2016)

▶▶ The Association of Southeast Asian Nations (ASEAN) fully ratified its Open Skies policy in May 2016 following Indonesia and Laos sanctioning it. It means that airlines from its 10 member states can fly freely in the region. The increased connectivity and reduced prices should boost tourism – 12% of the region's GDP – but is less helpful to dengue control. Dengue is set to join the list of diseases spread by air travel, which includes measles, influenza and SARS. With 70% of the global dengue burden, the open skies policy will probably lead to the wider spread of the disease. Severe dengue outbreaks would cause heavy losses in tourism revenue – it is estimated that Thailand alone could lose US\$ 363 million if tourism from non-epidemic countries fell by a mere 4%. It is imperative that governments rely less on sporadic and individual vector control, but focus on efforts to limit transmission risk, introduce dengue vaccination programmes, and to keep a high level of public awareness to minimise the spread of dengue. (*The Diplomat*, 15 June 2016)

▶▶ The recent arrest of the rapper Namewee, whose video depicted religious leaders dancing in a mosque, highlights how Malaysian Islam is gradually becoming more conservative. The government, led by Mr Najib Razak, appears to be less autonomous on religious policy, more reliant on Islamic advisers, and less likely to rein in Islamic firebrands. This may be an attempt by Mr Razak and his ruling party, which nearly lost the 2013 general election, to bolster sup-

port among the Islamic opposition and distract attention from a scandal whereby billions of dollars went missing from a state-owned investment company and Mr Najib was implicated in receiving some of the money. The ruling party has fast-tracked the reading of a bill from the Pan-Malaysian Islamic Party (PAS), which would increase the punishments that Islamic courts can impose on Muslims convicted of religious offenses (currently fines, six strokes from a cane or three years in jail) – and some in PAS think that Muslims who drink alcohol should receive up to 80 lashes, and those who have sex outside marriage up to 100 lashes. This may exacerbate Malaysia's exodus of young people, including moderate Muslims, and a rise in such rhetoric could encourage radicals. Indeed, almost 70 Malaysians have had their passports cancelled after attempting to join Islamic State, three people have been arrested after allegedly plotting attacks on nightspots and a Hindu temple, and 11% of Malaysians have a favorable view of Islam-

ic State, compared to 4% in Indonesia. This is all much more worrying than Namewee's videos. (*The Economist*, 24 September 2016)

▶▶ The number of confirmed Zika cases in Vietnam has doubled to 23 over the past 3 days, with a dozen new infections confirmed in Ho Chi Minh City. Zika has been spreading in Southeast Asia after outbreaks in the Americas, and Thailand reported the region's first confirmed case of the birth defect microcephaly. Vietnam also reported a microcephaly case that is probably linked to Zika. In October, Vietnam raised the alert level for Zika, and stepped up the monitoring of pregnant women. There is no vaccine or treatment for Zika, and an estimated 80% of those infected report no symptoms, making it difficult for pregnant women to know whether they have been infected. As well as microcephaly, Zika has also been linked to other neurological disorders, including Guillian-Barre. (*Voice of America*, 2 November 2016)

## ▶ Australia and Western Pacific

▶▶ Mr Masamitsu Yamamoto, a 58-year old man, is on trial at the Tokyo District Court over his alleged violation of Japan's Cannabis Control Law. Mr Yamamoto has terminal liver cancer, and maintains that he uses cannabis as pain relief after exhausting all other options and failing to get access to legal cannabis treatment. Some European countries, US states and Canadian provinces allow the medical use of cannabis, but Japan's Article 4 of the Cannabis Control Law specifically bans the use or prescription of medicines derived from cannabis – and violators face up to 5 years in prison. Mr Yamamoto is campaigning for the "compassionate use" of medical marijuana. Dr Kazunori Fukuda, a former cancer researcher at the National Cancer Center Research Institute, argues that cancer patients suffer from appetite loss and depression, which can be alleviated by cannabis. However, an official from Japan's Health, Labor and Welfare Ministry states that the WHO has not given clear guidance on the use of medical marijuana, and that cannabis, a controlled substance under international treaties, is potentially a "gateway drug" to other drugs. "We need to weigh the risks of abuse against the wishes of a few people who want to use marijuana," the official said. (*Japan Times*, 26 June 2016)

▶▶ Mr Ashley Peacock, a New Zealand citizen, suffers from severe autism and psychotic episodes, and spends most of his time in an isolated mental health unit despite posing no risk to the wider public. He lives in a 3m x 4m room with

a mattress on the floor and no toilet facilities, and is allowed outside for 90 minutes each day. Autism Action NZ have campaigned for his release, and argue that his case highlights shortfalls in the care of people with severe autism in New Zealand. They call for crisis teams that specialise in autism, with an awareness of autism's co-morbidities with mental health issues, and for residential care facilities that can meet the needs of people like Mr Peacock. Without this support, people with autism either "fall through the cracks" or end up in the mental health system which cannot meet their needs, according to Kim Hall of Autism Action NZ. (*radionz.co.nz*, 8 June 2016)

▶▶ Australia has joined a handful of countries where AIDS is no longer a public health issue. At the peak of the Australian AIDS epidemic in the 1990s, 1000 people died each year from the illness. However, since the introduction of antiretroviral drugs in the mid-1990s, the number of Australians dying each year from AIDS is so low that numbers are not recorded. However, researchers point out that ending the AIDS epidemic does not mean that the end of HIV infections – each year, 1000 Australians are infected with HIV. There are concerns that some young people who did not witness the AIDS epidemic in the 1980s and 1990s may be complacent about the risks of HIV infection. Don Baxter, from the Australian Federation of AIDS Organisations, calls for Australia to continue to support other countries who are still dealing with the AIDS epidemic, and for



the country to increase its financial support to the Global Fund to target HIV and AIDS internationally. (*ABC*, 10 July 2016)

▶▶ Australia and Papua New Guinea have agreed to close the controversial detention camp for asylum seekers on Manus Island, off Papua New Guinea. Asylum seekers attempting to reach Australia are sent to either Manus or Nauru, and are ineligible to be settled in Australia. These camps have faced criticism from the UN and various human rights groups, and there are reports of abuse, assault, inadequate medical care and dirty, cramped conditions. Australia has defended its use of the camps and asylum policy, saying it is necessary to prevent people dying on the dangerous crossing from Indonesia to Australia – hundreds of people have already died attempting it. Mr Peter Dutton, Australia's immigration minister, confirmed that Australia would not accept any of the refugees held in Manus, who face either being resettled in Papua New Guinea or returned to their home country. Some asylum-seekers have spent years in the camp, and furthermore there are reports of refugees being attacked in Papua New Guinea. (*Al Jazeera*, 17 August 2016)

▶▶ Although Japan's care for pregnant women is aligning with practices in other developed countries, it differs in the provision of pain relief during labour. Women are generally treated as fragile during their pregnancy, but little pain-relief is offered during labour, and Japan's Buddhist tradition teaches that women should embrace the pain of labour to prepare for motherhood and promote bonding with their baby. Many women are keen to have an epidural anesthetic during childbirth, but few obstetric centres or hospitals provide them – and almost never outside normal working hours. The national health-insurance scheme's contribution toward childbirth (US\$ 4053) does not generally cover the cost of an epidural. Japan's government is keen increase the country's fertility rate from the current 1.5 children per woman to 1.8 to slow population shrinkage, and making childbirth a less painful experience may help. Another worrying trend is Japan's high and rising proportion of underweight babies (2.5 kg or less at birth) – in 2015, 9% of babies were underweight. One reason is that women do not gain enough weight during pregnancy – doctors advise women to gain no more than 6–10 kg, compared to 11–16 kg in the UK. (*Economist*, 22 October 2016)

## ▶ China

▶▶ The town of Wukan (widely regarded as an incubator for grass-roots democracy in China following its residents' eviction of local Communist officials and police in 2011 over alleged corruption) has been locked down by riot police and Secretary Lin Zulian – its chief – arrested after he called for renewed protests against corruption and land-grabs. According to the police, Secretary Lin was detained because prosecutors suspect him of having received bribes, but residents took to the streets to protest his arrest, and to call attention to the land disputes. According to one resident, the town's residents fully believe that Secretary Lin's arrest is the work of higher authorities who wish to suppress the [land] issue. In a draft speech circulated online to residents before his arrest, Mr Lin called for renewed protests against land corruption and for residents to sign a petition. He also called for loyalty to the Communist Party, collective democracy under the rule of law, and stated that “first, cursing and hitting people is not allowed. Second, destroying public order is not allowed. Third, smashing things is not allowed and violators will be severely punished.” The town was patrolled by several hundred riot police with shields and batons following his arrest. (*Financial Times*, 19 June 2016)

▶▶ According to a report from the World Bank Group, the World Health Organization and Chinese government agencies, structural reform to China's health-care system could save up to 3% of its GDP. China needs to slow down its main drivers of health-care costs (an aging population, and soaring incidence of cancer, diabetes and heart disease), and avoid the creation of “high cost, low-value” health care. The report recommends measures such as bolstering China's primary care system and allowing private-sector providers greater access to the public sector. The World Bank estimates that health expenditure in China will increase from US\$ 529 billion in 2015 to US\$ 2.35 trillion in 2035 – which is 5.6% and 9.1% of GDP respectively – without reform. China has made progress in improving health-care access, with almost its entire population covered by some form of health insurance, but the country's public hospitals are overwhelmed, and rely on medicine sales for revenue which creates skewed incentives for doctors to over-prescribe. “We're confident that these reforms will help China build a strong foundation to create a healthier population, which will be an engine for job creation and sustainable economic growth,” says Jim Yong Kim, the president of the World Bank Group. (*Bloomberg*, 22 July 2016)

▶▶ Mr Tan Jingsong, a partially-sighted law graduate, was rejected for a government job he applied for in Yueyang, Hunan province – despite receiving top marks in the written exam undertaken by all the candidates. The job did not specify any physical requirements, but Yueyang's Human Resources Bureau rejected Tan's application because the General Standard for the Physical Examination of Civil Servants specifies a minimum vision threshold of 0.8 in both eyes – Tan is completely blind in one eye, and has a corrected vision of 0.3 in the other. The Disabled Persons' Federation point out that the State Council and Hunan Province have stated that disabled people should make up at least 1.5% of employees in public institutions. Chao Xiangyang, the Federation's deputy director, says that the General Standard fails to take disabled people into account, and almost invalidates any other legal employment protections. Associate Prof. Liu Xiaonan of China University of Political Science and Law believes that the General Standard is not sufficiently job-specific, and may lead to institutional discrimination. "Disabled people in public service can better reflect the civilisation and equality of a country," Liu says. (*People's Daily Online*, 18 August 2016)

▶▶ Following a recent survey, China's State Food and Drug Administration (SFDA) regulator found fraudulent practice on a massive scale, with more than 80% of clinical data being "fabricated". It looked at data from 1622 clinical trial programmes of new drugs awaiting regulatory approval for mass production, and discovered that much of the data gathered during these trials was incomplete, failed to meet analysis requirements or was untraceable. This exposé was published in the *Economic Information Daily* newspaper, which also cited a source claiming that

some companies were suspected of deliberately hiding or deleting records of adverse effects, and tampering with data that did not meet expectations. As a result, more than 80% of mass-production applications for new drugs have been cancelled, and further evidence of malpractice may emerge. According to a health care insider, China's generic drugs industry is plagued with quality problems, and many "new" drugs are merely combination of existing drugs while clinical trial outcomes are written beforehand with the data massaged to fit in. Another source claimed that national standards on clinical trials are not widely implemented. The regulatory problems around China's pharmaceuticals industry is shown elsewhere, reflected in the Chinese public's bulk-buying of items such as infant milk formula produced overseas. (*Radio Free Asia*, 22 September 2016)

▶▶ China's State Council outlined plans to increase its citizens' average life expectancy to 79 years by 2030, from its current level of 76.34 years. Its "Healthy China 2030" blueprint outlined plans to invest in areas such as elderly care, medical equipment and data, and food safety, and to increase expenditure on health care to US\$ 2.37 trillion a year, from its current US\$ 0.66 trillion. The government plans to have three doctors per 1000 people, and to reduce infant mortality, traffic deaths, deaths from chronic diseases, improve psychological interventions, and reduce smoking and alcohol abuse. It also intends to improve cancer survival rates, increase physical activity and introduce a national monitoring system for food safety and food-borne diseases. The blueprint also commits to tackling China's gender imbalance by setting up birth monitoring systems. (*Asia Times*, 26 October 2016)

## ▶ Europe

▶▶ Most European countries have strict laws on drug-taking, but over the past few years most have relaxed their enforcement, with recreational users being fined or warned rather than jailed. This is led by the Netherlands with its tolerance policy on the possession of cannabis, the Czech Republic which decriminalised the possession of small quantities of drugs, and Portugal which decriminalised the possession of all drugs for personal use. However, more recently the trend toward relaxation has halted, despite the Netherlands, the Czech Republic and Portugal highlighting the success of these policies. These countries illustrate that decriminalisation does not lead to higher consumption or act as a gateway to harder drugs, and that it is linked to lower HIV infections. Their drug-related fatalities also ap-

pear to be lower than other countries with stricter laws. However, even these three trail-blazing countries are tightening their approach, due in part to squeezed public finances (less money for harm-reduction services), complacency (the success of the policies means that politicians may think the problem is solved), and public backlash against liberal drugs policies. The timing of Europe's tightening policy on drugs is unfortunate, as there are some worrying signs that the USA's epidemic of opioid consumption may spread to Europe. (*Economist*, 18 June 2016)

▶▶ The High Court in England ruled that the NHS is able to fund pre-exposure prophylaxis drugs ("PrEP"), which are highly effective in preventing HIV infection following transmission. When taken consistently, it reduces the risk

of HIV infection by more than 90%. NHS England claimed it did not have the power to fund preventative treatments, and the National AIDS Trust (NAT) challenged this decision in court. Mr Justice Green ruled that NHS England “has erred in deciding that it has no power or duty to commission the preventative drugs in issue.” The NAT are now calling for the NHS to make PrEP immediately available, pointing out that over 4000 people each year are infected with HIV in the UK, and that further prevention options are desperately needed to supplement condom use. The British Medical Association welcomed the court’s ruling, saying that PrEP could “help save many lives”. However, NHS England intends to appeal the ruling, saying Mr Justice Green’s interpretation of legislation was inconsistent with Parliament’s intent. (*The Independent*, 2 August 2016)

▶▶ According to the National Records of Scotland, drugs-related deaths reached a record high in Scotland, with a total of 706 people dying in 2015 from drug abuse. This is a 15% increase from 2014, when 613 people died, and the number of drugs deaths in Scotland has been steadily increasing since 1995, when 426 deaths were recorded. Deaths were particularly high among older users, with 73% of deaths occurring in people aged over 35 years, while deaths among younger users (aged under 24) fell. Heroin and morphine were involved in 49% of deaths – the highest-ever level. Aileen Campbell, the minister for public health stated that drug use is falling overall in Scotland, and that the health problems of older drug-users is a legacy of historical drug abuse. However, the group Addaction Scotland highlighted falling numbers of fixed-site needle exchanges – often users’ entry points for treatment – and cuts in treatment services. Other health professionals and drug charities have called for supervised heroin consumption to enable users to receive drugs more safely. This could also reduce the number of new HIV infections; in Glasgow drug-related HIV infections rose to 47 in 2015 from an average of 10 per year, with public injecting posing further risks. (*BBC*, 27 August 2016)

▶▶ The latest European Social Survey (ESS), based on a survey of 40 000 people across 21 European countries, found

that a large number of European people are affected by physical and mental health conditions. It uncovered large gender discrepancies in depression and severe headaches, as across Europe women are much more likely to report these conditions. Men are much more likely to smoke compared to women, with smoking rates much lower in northern Europe, the UK and Ireland; and considerably higher in central and eastern Europe. Overall, Sweden has the least number of smokers – 15% – a huge fall compared to its earlier rates of 77.8% and 76.2% for men and women. Men are more likely to report being overweight than women in all countries, and the highest rates are in central and eastern Europe, and the lowest rates in Switzerland, Austria and Denmark. Binge drinking is particularly common in the UK and Portugal, but rarer in Nordic countries and among women in central and eastern Europe. Across all 21 countries, men consume almost twice as many units as women, and overall drinking rates are particularly high in Ireland. (*Science Daily*, 23 October 2016)

▶▶ Worldwide, stock markets fell as Donald Trump was elected as the next President of the USA. However, share prices in many European pharmaceutical companies rose sharply, with Hikma Pharmaceuticals rising 6%, Roche and Novartis rising by more than 4%, and GlaxoSmithKline rose 1.8%. These rises were driven by market expectations that a Trump presidency would end new rules controlling the price of pharmaceuticals, which had followed an earlier public outcry over drug prices (eg, Retrophin’s announcement that it was increasing the price of an anti-parasitic drug from US\$ 13.50 to US\$ 750 per dose). The European pharmaceutical market has traditionally performed well in periods of uncertainty and a strong US dollar. Barclay equity strategists included four pharmaceutical and health care companies in their list of the 10 European countries most likely to benefit from a Trump victory, namely Actelion, Hikma Pharmaceuticals, UCB SA and H Lundbeck. Furthermore, the election of a Republican Senate could provide a further boost to the European health care sector. (*Business Insider*, 9 November 2016)

## ▶ India

▶▶ Médecins Sans Frontières (MSF) has warned that India will not remain “the pharmacy of the world” if proposals under the Regional Comprehensive Economic Partnership (RCEP) agreement between the 10 ASEAN countries are adopted. Currently, developing countries are exempt from “Data Exclusivity” and “Patent Term Extensions” (which offers legal protection for a drug beyond the normal patent

rules and duration), but leaked proposals from the RCEP trade talks show that some countries are proposing to halt these exemptions. If implemented, India would be prohibited from registering more affordable versions of a drug while the exclusivity is in force over the clinical trial data. “We appeal to India’s IP [intellectual property] negotiators in particular to stand by the promises made last week by

Health Minister JP Nadda at the UN High Level Meeting on HIV/AIDS that ‘India is committed to maintaining TRIPS [Trade Related Aspects of Intellectual Property Rights] flexibilities to ensure access to affordable medicines,’ said Leena Menghaney, South Asia Head of MSF’s Access Campaign. (*The Hindu*, 19 June 2016)

▶▶ The Punjab is suffering a hidden epidemic of drug abuse, with nearly 20% of young men in the state using opioids. Within the past 5 years, Punjab’s drug users have increasingly switched from the traditional poppy husks toward injectable heroin. The levels of drug misuse in the Punjab are particularly acute, and may be caused by falling agricultural employment not being off-set by job-creation in the cities. Gursharan Singh Kainth, an economist, calls for an “agro-industrial revolution” to provide better jobs for young men. Punjab’s plight is revealed in a new film, *Udta Punjab*, which draws a parallel with a real-life case of a convicted drug lord who named a leading politician’s brother-in-law as his accomplice. The film nearly missed its release date due to India’s film board demanding 89 cuts, including every reference to Punjab, but thanks to an intervention by the Bombay High Court, the censors were over-ruled. (*The Economist*, 25 June 2016)

▶▶ The *Bangalore Mirror* newspaper reports that an estimated 199 060 people are living with HIV in the state of Karnataka, but only 128 399 people are receiving antiretroviral treatment (ART). In addition, despite having the second-highest number of ART centers in India, Karnataka faces problems of staff shortages. The WHO recommends that treatment begins as soon as possible after diagnosis, regardless of the CD4 white cell count, but across India, ART begins when the cell count falls below 350. Even at this level, there are an estimated 1 345 678 people with CD4 counts of less than 350, but 940 000 receive treatment, giving a coverage rate of 70%. Dr Anesha Ahluwalia, a health expert, calls for the Indian government to follow the WHO’s guidelines on ART, noting that people are less likely to come back for follow-up appointments and the difficulties in tracking the incidence of HIV under the current system. (*The Bangalore Mirror*, 19 September 2016)

▶▶ The Liver Foundation, a Kolkata-based charity, is training unqualified medics in primary medical care. India has one of the worst doctor-to-patient ratios in the world, which gives rise to self-trained practitioners – and recently, several children died in the Tamil Nadu state after reportedly being treated by unqualified medics. However, the Liver Foundation believes that unqualified medics should be used for health care to help bridge the serious staffing shortfall which is especially prevalent in rural areas, and a study published in *Science* aimed to assess the effectiveness of the foundation’s training program. Some unqualified practitioners reported being more confident in their roles, and overall they were more likely to adhere to checklists and provide correct treatments. However, although the rates of unnecessary drug prescriptions were unaffected by training, they did not differ significantly from publicly-trained doctors who are often poorly trained and lack incentives to provide good care. This suggests that training unqualified practitioners (who are then designated as village health workers rather than doctors) can improve their practice to match those of public sector doctors. Training is already expected to be scaled-up in Tamil Nadu, and offered to thousands more informal practitioners. This move is likely to be resisted, and previously the Indian Medical Association has taken legal action to block similar schemes. (*BBC*, 11 October 2016)

▶▶ India launched a new scheme to provide free health check-ups to pregnant women at government health centers and hospitals, and women living in under-served, semi-urban, poor or rural areas will be targeted. Prime Minister Modi appealed to doctors to contribute 12 days each year to save mothers and newborns’ lives in India, where 45 000 pregnant woman die each year – of which, only 19.7% benefited from pre-natal health checks. So far, 15 000 gynecologists and obstetricians have volunteered to participate, and the government is keen to introduce techniques from the private sector – where death rates are lower – into the screening program. Women will be tested for anemia, blood pressure, high blood glucose, hormonal disorders and other pregnancy-related problems, and will be provided with free ultrasounds to track their unborn baby’s health and development. (*Hindustan Times*, 4 November 2016)

## ▶ The Americas

▶▶ A survey published in the *Journal of the American Medical Association* has found some improvements in the US diet from 1999 to 2012. The percentage of people eating poor diets has fallen from 56% to a still-high 46%, and the majority of citizen still don’t eat an optimal diet. The big-

gest changes are in the number of people reporting higher grain consumption, and slightly higher consumption of nuts, seeds and yoghurt, and less sugary drinks, white potatoes and refined grains. However, the amount of fruit and vegetables consumed has not changed, and people are still

consuming the same levels of meat, processed meat and sodium. The picture is starker when the diets of various groups are considered: white Americans improved their diets the most, while improvements among poorer people and minority groups were smaller. These groups are often the targets of aggressive marketing campaigns for junk food. Improving the country's diet is essential for improving its overall health, and one of the study authors, Dr Darius Mozaffarian calls for the US to address its food issues. "We have strong policies about safety for cars, about safety for toys, about safety for workplaces and offices we come to, about car seats, about seat belts. And yet we have very little strong government policy about overall healthy foods," he says. (*Time*, 21 June 2016)

▶▶ Venezuela was certified free of malaria in 1961, nine years ahead of the USA. However, there has been a 356% increase in malaria cases since the 1990s, and Venezuela may have 200 000 cases in 2016. According to unofficial figures compiled by doctors, Venezuela has had 125 158 infections to date in 2016, compared to 136 402 for the whole of 2015 – which was itself a 75-year high. Venezuela's malaria outbreak also threatens neighboring Brazil and Colombia. According to the Health Ministry, only 300 mosquito nets were distributed in 2014, despite 800 000 people living in high-risk areas, and the country spends less than US \$1 per person on malaria control – the second-lowest figure in Latin America. This means that the situation is likely to deteriorate; it is already compounded by drugs shortages arising from the country's economic crisis, and people flocking to gold-mines for employment – located in malaria-prone areas – and spreading the disease when they return home. (*Fox News*, 17 August 2016)

▶▶ The Colombian president, Juan Manuel Santos, was awarded the 2016 Nobel Peace Prize for his "resolute efforts to bring the country's more than 50-year-long civil war to an end." The Colombian civil war has killed more than 220 000 people and displaced millions. The prize was awarded despite the country's voters rejecting the peace deal between the government and the FARC rebels in a referendum shortly after the announcement. The committee states that this setback does not necessarily mean the end of the peace process, as it was a rejection of a specific peace agreement and not the desire for peace. Mr Santos pledged to continue to search for peace until the end of his mandate. "I accept it not on my behalf, but on behalf of all Colombians, especially the millions of victims of this conflict

which we have suffered for more than 50 years," said Mr Santos. (*NPR*, 7 October 2016)

▶▶ Following on from the legislative and technical difficulties behind the Affordable Care Act ("Obamacare"), health care reform in the USA has hit another problem, as premiums on covered plans have increased by 20%. While this appears to be a major setback for health care reform, the spike in premiums only affects the plans traded on the "exchanges" insurance market system, for people who are not covered by their employers or government programs such as Medicare. The main driver for this increase is insufficient healthy people signing up for Obamacare in many states, which has affected insurers' risk calculations. However, most people who buy health insurance on the exchanges system are eligible for subsidies, which offers some protection and are therefore less likely to withdraw from Obamacare. Moreover, despite these setbacks, Obamacare has succeeded in reducing the number of US citizens without health insurance – now at its lowest level – and in reining in the growth of health care costs. (*Seattle Times*, 30 October 2016)

▶▶ Haiti has been devastated by Hurricane Matthew, the fiercest storm to hit the country in 50 years, and the latest catastrophe to hit the country which has still not recovered from the 2010 earthquake which killed 200 000 people and caused damages of US\$ 8 billion – 120% of GDP. Hurricane Matthew wiped out livestock and crops such as rice, bananas and coconuts on which most people depend. Haiti is already the poorest country in the western hemisphere, and relies on US\$ 2.2 billion of annual remittances from its diaspora, and more than 20% of the government's annual budget comes from foreign aid or direct budget support. As post-hurricane efforts get under way, some people, including Maarten Boute, a prominent businessman in Haiti, are calling for a new approach to reconstruction following on from mistakes in the post-earthquake reconstruction. Mr Boute argues that the best way to help Haiti is to source relief locally, buy Haitian exports, and generate investment and tourism; and there must be a sharper focus on productive projects with Haitian partners. This is illustrated by the Caracol industrial park – intended to boost the clothing industry after 2010 – which has fallen short of its job-creation goals, and farmers who lost their land for the project complain that they were not properly compensated. "This is a long-term job. We're not just rebuilding the hurricane damage, we're laying the foundations for the future," says Mr Boute. (*Financial Times*, 2 November 2016)

## ► The Bill and Melinda Gates Foundation

►► Bill Gates expressed support for the potential of genetic engineering to eliminate the species of mosquitoes which spread malaria and dengue fever. The CRISPR/Cas9 gene from bacteria could be used to edit the mosquitoes' DNA to prevent them from reproducing, causing that particular species to become extinct. Bill Gates noted that the malaria- and dengue-carrying mosquito species are a small percentage of mosquitoes, and eliminating them would not endanger the environment or harm people. In April, he called these mosquitoes "the most dangerous animal in the world", and does not share the belief that the technology could be a "weapon of mass destruction". (*Forbes*, 10 June 2016)

►► In a blog post, Bill Gates highlighted how raising chickens is an easy and cheap way to ensure a food supply and earn an income for poor people with access to land. Chickens are cheap to maintain, as they can often live on food they find themselves, and only need basic shelters to protect their nests and eggs. Chickens stay close to home, making them easier to look after. A farmer with 5 hens which are fertilised with a neighbor's rooster can produce 40 chicks within three months. In West Africa, these chicks can sell for US\$ 5 apiece, generating up to US\$ 1000 a year. This is a small but significant step-up from the absolute poverty-line of US\$ 700 a year. Lastly, eggs are also a protein-rich foodstuff. (*Fortune*, 8 June 2016)

►► Through a project financed by the BMGF among other partners, Uganda is planting five new bean varieties, which are both high in iron and drought-resilient. The beans – a cheap source of nutrition for poorer communities – are part of a wider effort to reduce malnutrition and reduce anemia, particularly among children and pregnant women. Iron deficiency is a major nutritional problem affecting 2 billion people worldwide which can impair children's cognitive and physical development, and anemia makes pregnancy and childbirth more dangerous to women. The beans were co-developed with the Rwandan Agricultural Board through the HarvestPlus program, using iron sources with locally-adapted germplasm in Uganda. The improved yields will also boost farmers' incomes, and the beans' drought resilience is vital for small-scale farmers and communities. (*Thomson Reuters Foundation*, 10 August 2016)

►► The BMGF has supported new research into the causes of childhood diarrhea, which kills 500 000 children each

year. The study, led by the University of Virginia School of Medicine (Division of Infectious Diseases and International Health), looked at diarrhea cases in Bangladesh, India, Pakistan, the Gambia, Kenya, Mali and Mozambique. The researchers re-analyzed more than 10 000 archived samples from the Global Enteric Multicenter Study (GEMS), and found two more causes of diarrhea: *C. jejuni* and adenovirus, and that the number of cases caused by *Shigella*, adenovirus, *Campylobacter* and *E coli* was significantly underestimated. This means that many unexplained diarrhea cases are caused by a known rather than an unknown pathogen, thus giving a roadmap for treating childhood diarrhea as it is more feasible to develop vaccines and treatments for a smaller number of known pathogens. "For the first time in history, we can identify almost all of the pathogens that cause diarrhoea, thanks to the GEMS re-analysis study. And now that we know more, we can more precisely target our efforts to make sure every child has the opportunity to live a healthy and productive life," said Anita Zaidi, director of the BMGF's Enteric and Diarrheal Diseases team. (*Medical Xpress*, 27 September 2016)

►► The BMGF is working to provide more phones and financial services to women around the world, highlighting that 1.7 billion women in low- and middle-income countries don't have access to mobile phones – more than 400 million fewer women than men in these countries. Mobile phones are bringing down the cost of providing basic financial services, but the technological gender gap means that those outside the formal banking system who would benefit most from easier access to savings, small loans and money-transfer facilities can't be reached if they don't have mobile phones. More than 50% of this gender gap occurs in India, where women are often prevented from accessing technology by fathers and husbands, and only 30% of internet uses in India are female. Financial inclusion in developing countries like India is particularly important, as women are more likely than men to use financial services and more likely to use them in a way that will benefit their families. The BMGF is working with mobile operators and the GMSA [a global association of mobile phone providers] Mobile Money Programme, to bring more mobile money services to those outside the formal banking system. (*Wall Street Journal*, 26 October 2016)

## ▶ The GAVI Alliance

▶▶ Diarrhea caused by rotavirus is responsible for 33% of hospitalisation among Myanmar's children. In response, health officials are calling for the rotavirus vaccine to be added to the country's National Immunisation Program. They acknowledge that the government cannot afford to include it, but are campaigning for an application to GAVI to support its introduction, which is currently only available privately. GAVI currently supports 5 vaccine programs in Myanmar, including measles and pneumococcal immunisations. Children who are malnourished, or with impaired immunity are more vulnerable to the virus. A spokesperson for Myanmar's Ministry of Health and Sports confirmed that they plan to implement the rotavirus vaccine with support from GAVI and UNICEF. (*Myanmar Times*, 22 June 2016)

▶▶ GAVI has pledged US\$27.5 million to a WHO pilot project on the introduction of the malaria candidate vaccine RTS,S in sub-Saharan Africa. GlaxoSmithKline, the vaccine developer, and PATH will donate vaccine doses in the pilot areas. In addition to GAVI funding, the WHO will provide US\$ 17 million and PATH has received US\$ 8 million from the BMGF for the project. GAVI funding is conditional upon the WHO securing additional funding to cover the remaining shortfall – an estimated US\$ 27.5 million. RTS,S was developed as a “not-for-profit” vaccine with shared costs, and GlaxoSmithKline has invested more than US\$ 350 million in its development. David Kaslow, the Head of PATH's Center for Vaccine Innovation and Access, said that the results from the Phase 3 studies showed the potential benefit of RTS,S, when used alongside bed-nets and other malaria control interventions. (*Regulatory Affairs Professional Society*, 23 June 2016)

▶▶ GAVI and health technology company Royal Philips have signed a letter of intent to jointly develop scalable digital transformation plans to improve the quality of immunisation data, and its collection in primary and community care. This will help countries improve the planning, coverage and impact of their immunisation programmes, by identifying children who miss out on vaccination. “We are convinced that partnerships, such as this one with GAVI, are paramount to realising the goal of universal health coverage for all, especially among children. Thanks to the digital revolution, we can now start doing what was previously unthinkable: enable access to care, improve patient outcomes and lower healthcare costs,” says Jeroen Tas, CEO of Connected Care and Health Informatics at Phillips. This partnership is one example of how GAVI aims to step up its data-strengthen-

ing activities and address some of the fundamental weaknesses in data collection systems in the countries which it supports. (*ReliefWeb*, 21 September 2016)

▶▶ Médecins Sans Frontières (MSF) has declined a donation from Pfizer of 1 million pneumonia vaccines which would protect against a leading killer of children. Instead, MSF argues that the donation would harm the long-term aim of lower prices for vaccines, and that accepting it – which would save lives – involves a trade-off by reducing access to affordable vaccines and medicines. GlaxoSmithKline, the only other producer of the pneumonia vaccine, recently lowered its price to US\$ 3.05 per dose for humanitarian organisations, but Pfizer only offers discounted prices to GAVI while offering free donations to humanitarian organisations. Vaccine prices are increasing, and it is now 68 times more expensive for MSF to fully vaccinate a child in 2016 compared to 2001, and 45% of the cost is attributable to pneumonia vaccines – leading to MSF to call for the price of pneumonia vaccines to be reduced to US\$ 5 per child. MSF argue that countries currently eligible for GAVI support will start losing it in 2016, citing Angola which will shortly have to buy pneumonia vaccines itself, leading to a 1500% price increase per dose; and Bolivia and Indonesia will also see massive price increases. Pfizer made US\$ 13.1 billion in profits in 2015, and sales of pneumonia vaccine in developed countries forms a large chunk of its profits, so offering cheaper prices to humanitarian organization and developing countries may not significantly reduce its profits. Pfizer believes that donations have a crucial role in addressing humanitarian crises, but MSF argue that donations remove incentives for new manufacturers to enter a market, thereby reducing competition and keeping prices higher. (*Humanosphere*, 25 October 2016)

▶▶ In the wake of Hurricane Matthew, large teams are being mobilised by the Haitian Ministry of Health and Population to vaccinate 800 000 people in the worst-affected areas against cholera. This initiative is being supported by the PAHO and WHO, with vaccines supplied by GAVI. It aims to reduce morbidity and mortality from cholera, and to prevent its spread to other areas of the country. Vaccination will offer protection against 60–70% of severe cases, but other measures, such as daily chlorination of water, hand-washing, food hygiene, drinking potable water, and rehydration and treatment for diarrhea are also vital. Since Hurricane Matthew struck Haiti on 4 October 2016, there has been a significant increase in the number of suspected cases and deaths from cholera. (*ReliefWeb*, 9 November 2016)

## ► The World Bank

►► The World Bank has approved a loan of US\$ 310 million to help build climate resilience in Vietnam and ensure sustainable livelihoods for 1.2 million people in the Mekong Delta region. The Mekong Delta supports 50% of Vietnam's rice production, 70% of its aquaculture and 30% of GDP. However, recent extreme weather in this area, including drought and salinity intrusion, is having an adverse impact on the many poor farmers living in the area, and it is extremely vulnerable to climate change as well as upstream development. The funding will help farmers adapt agriculture and aquaculture to climate change, including better planning, and land and water management. The World Bank will work in partnership with the government to deliver the project, plus other key development partners. ([thanhniennews.com](http://thanhniennews.com), 13 June 2016)

►► The World Bank has approved funding of US\$ 200 million toward social safety programmes implemented by the Tanzania Social Action Fund (TASAF) – more than 6.6 million Tanzanian citizens (15% of the country's population) who live in extreme poverty or food security will benefit. Tanzania's Productive Social Safety Nets (PSSN) project, which funds TASAF, will support the government's recent scaling-up of conditional cash transfers and the increased participation of key beneficiaries in new programmes of public infrastructure, savings and investments. The PSSN has already reached the poorest 15% of Tanzania's population, and the additional funding will consolidate its impact. PSSN is part of a wider World Bank Group project, which targets people living in extreme poverty to create human capital to reduce poverty and inequality. ([allafrica.com](http://allafrica.com), 18 June 2016)

►► The World Bank and Global Fund have committed to invest US\$ 24 billion in Africa over the next 3–5 years to support universal health care, and to help countries put surveillance systems in place for early disease detection. At the same time, Kenya pledged to increase its Global Fund contribution from US\$ 2 million to US\$ 5 million. According to the WHO, each year 100 million fall into poverty because of health care expenses, and 1 billion people cannot access health care. "African countries can become more competitive in the global economy by making several strategic investments, including investing more in people, their more prized resource. A critical part of this commitment is to accelerate progress on universal health coverage – ensuring that everyone, everywhere has the opportunity to live a healthy and productive life," says Mr Jim Young Kim, President of the World Bank Group. ([Daily Nation](http://DailyNation), 27 August 2016)

►► According to the World Bank study *Poverty and Shared Prosperity*, the number of people living in extreme poverty

continues to fall despite the 2008–09 financial crisis and slowing global economic growth. It shows that in 2013, fewer than 800 million people lived on less than US\$ 1.90/day; this is 11% of the world's population, compared to 35% in 1990 and means that 1.1 billion people have moved out of extreme poverty. Wages rose for the poorest 40% of people in 60 out of 83 countries studied between 2008 and 2013. The World Bank links future poverty reductions with falling inequality, noting that inequality has fallen in many countries over the past 10 years. Among countries which have reduced inequalities in recent years (eg, Brazil, Cambodia, Mali, Peru, Tanzania etc), the World Bank identified the importance of early childhood development and nutrition; universal health coverage; universal access to quality education; cash transfers to poor families; improved rural infrastructure; and progressive taxation. The main drivers in poverty reduction have been countries in East Asia and the Pacific, but as their poverty levels continue to fall, their contributions to poverty reduction will fall too. It also means that 50% of extremely poor people now live in sub-Saharan Africa, and that the remaining pockets of poverty will become harder to reach and address. ([NPR](http://NPR), 3 October 2016)

►► The remits of multilateral development banks (MDB) – including the World Bank – have not changed in line with challenges presented by the 21st century, according to a report published by the Center for Global Development. These challenges include: climate change, which will require more investment, especially global private capital, in greener infrastructure; the health risks posed by growing resistance to antibiotics and the possibility of pandemics; and helping the millions of refugees from conflicts such as the Syrian and South Sudan civil wars require investment in education and jobs for the displaced people. However, MDBs rely heavily on country-based loans to achieve these aims, which can be an inflexible and often inappropriate instrument in today's climate. MDBs can be held up by unfulfilled donor pledges and debates on what constitutes a poor country; but to respond quickly to a pandemic or refugee crisis they need dedicated contingency funds and more innovative financing. Currently, these are addressed through small special funds and one-off budgetary set-asides. The MDBs not only need more resources, but should unlock their existing assets and capital resources and use them more flexibly, and developing countries – now over 50% of the global economy – should be adequately represented in decisions about investment and sustainability. ([Bloomberg View](http://BloombergView), 6 October 2016)



## ▶ United Nations (UN)

▶▶ The UN Security Council adopted a resolution that allowed the interception of ships at sea destined for Libya, in an effort to target the flow of weapons into the country, where Islamic State is gaining ground. It authorises military intervention to inspect vessels going to or from Libya, and seizing any weapons on board. Arms embargoes have been in place since 2011, but are ineffective in blocking weapons from countries such as Egypt, Turkey and the United Arab Emirates. Libya has been in disarray since the fall of Moammar Gadhafi, and the lack of a strong government and state institutions have created a breeding-ground for terrorist networks like Islamic State and Al Qaeda. The UN-brokered national unity government (the Government of National Accord) is struggling to gain control, and the continued instability is a major factor behind the high numbers of people fleeing to Europe across the Mediterranean Sea. France's ambassador, François Delattre, said that the resolution was a "game-changer" as it finally gives the UN and EU the means to enforce the arms embargo, and be strengthened in the fight against Islamic State. (*Wall Street Journal*, 14 June 2016)

▶▶ A UN report on poverty in Latin America found that the region grew more equal, with nearly 50% of its population enjoying increased income and 25% joining the middle class between 2003 and 2013. This is coupled with only 1% moving into a lower-income group, and the share of people living on less than US\$ 2.50 a day fell by half, to 11.5%. This has led to Latin America's Gini coefficient [an indicator of inequality] falling from 0.55 in 1994 to 0.49 in 2013. However, less favorable economic conditions due to the end of the global commodity boom have caused the region's GDP growth to falter at 0.6% per annum. Income growth among poorer people is especially vulnerable to economic shocks, and the report states that without robust economic growth, poverty reduction programmes (eg, cash transfers) may be insufficient to prevent people falling back into poverty. Downward mobility can be cushioned by more secure jobs with benefits, assets, help with caring for dependents, and formal safety nets such as unemployment payments and pensions, but these indicators all appear troubling for Latin America, and its success in poverty reduction may be as fleeting as the commodity boom which made it possible. (*Economist*, 18 June 2016)

▶▶ The UN may admit a role in the outbreak of cholera in Haiti [following the 2010 earthquake] which killed at least 10 000 people and sickened hundreds of thousands of others. Although the potential admission stops short of admit-

ting that the UN caused the epidemic, and does not indicate any changes to its immunity from legal actions, it nonetheless represents a significant shift in the UN's position after five years of denial of any responsibility. The outbreak appears to have originated from a base housing UN peacekeepers recently returned from Nepal, where a cholera outbreak was under way – the base's effluence was discharged into a nearby river. Mr Philip Alston, a UN special rapporteur who wrote a confidential report which states that "the epidemic would not have broken out but for the actions of the United Nations", has criticised the UN's avoidance of acknowledging the outbreak's source, and states that the UN's overall credibility and integrity is undermined by its actions. He also criticises the UN's cholera eradication program in Haiti, claiming it has failed – infection rates have risen since 2014 and the UN has struggled to raise the US\$ 2.27 billion needed to eradicate cholera in Haiti. No major water or sanitation projects have been completed, and two pilot projects were closed due to a shortage of funds. A separate UN report shows that 25% of UN sites in Haiti were still discharging waste into public canals as late as 2014. The Second Circuit Court of Appeals in New York is considering a decision on a case against the UN brought by families affected by the cholera outbreak – the UN has previously claimed diplomatic immunity. (*New York Times*, 17 August 2016)

▶▶ In an unusual move, the UN General Assembly, which rarely discusses health-related issues outwith crises, will debate the growing threat of bacteria which are resistant to antibiotics. This is a recognition that antimicrobial resistance (AMR) must be addressed by world leaders, and a UK government report has estimated that deaths from AMR could rise from 700 000 a year to 10 million a year by 2050, costing US\$ 1 trillion in lost production. AMR is caused by a number of factors, such as people taking antibiotics incorrectly or stopping them too soon, and the massive and often inappropriate use of antibiotics in agriculture, where antibiotics are used to promote growth and deal with infections among farm livestock. Countries will need to develop action plans to deal with AMR, although many member states have failed to deliver on promises to tackle AMR. (*Business Insider*, 19 September 2016)

▶▶ According to UN envoy Staffan de Mistura, rebel-held eastern parts of the Syrian city of Aleppo may face "total destruction" within two months, with thousands of deaths. The city of 275 000 people has been besieged for a month, as Russian and Syrian forces attack the jihadist group Jabhat Fateh al-Sham following the breakdown of a ceasefire

in September 2016. At least 200 wounded civilians are in need of evacuation to save their lives, and at least 376 people have been killed and 1266 wounded over the past 2 weeks. Mr de Mistura offered to personally accompany jihadists linked to al-Qaeda out of the city if it would stop

the fighting, and appealed to Russia and Syria's government not to destroy the city in order to eliminate rebels, warning that history would judge them if they used the presence of jihadists in Aleppo as "an alibi perhaps for destroying the whole city." (*BBC*, 6 October 2016)

## ▶ UN AIDS and The Global Fund

▶▶ UNAIDS announced that from 2010 to 2015, the number of HIV-positive people taking antiretroviral therapy (ART) has more than doubled to 17 million people, with 2 million people gaining access to treatment in 2015 alone. Global ART coverage has reached 46%, and coverage in eastern and southern Africa – the areas most affected by HIV – increased from 24% to 54%, reaching 10.3 million people. The ART scale-up has reduced AIDS-related deaths from 1.5 million in 2010 to 1.1 million in 2015. However, these figures mask regional disparities, and falling rates of new HIV infections in young adults have begun to slow, with the estimated number of new infections almost static. The world must continue this momentum in order to reach the 90–90–90 goal (90% of HIV-positive people know their status, 90% receive treatment, and 90% of people on treatment have viral suppression) by 2020, and to be on track to end the AIDS epidemic by 2030. (*al-lafrika.com*, 1 June 2016)

▶▶ At a workshop in Thimphu, Bhutan, the health secretary Dr Dorji Wangchuk highlighted how Global Fund support for dealing with HIV, tuberculosis (TB) and malaria has enabled Bhutan to work toward meeting the Millennium Development Goals. To date, the Global Fund has allocated more than US\$ 13 million (US\$ 4.1 million for HIV/AIDS, US\$ 3.6 million for TB and US\$ 5.4 million for malaria). Bhutan has moved from the "least development category", and some donors have begun to phase out support. Although the Global Fund has placed Bhutan in the "pre-elimination" phase, it is still eligible for funding after the end of the New Funding Model in 2018, but despite this continuation overall external support is decreasing from 30% of expenditure in the 1990s to 12% today. This means that alternative mechanisms, such as the Bhutan Health Trust Fund (BHTF) are needed, to provide co-financing for sustaining public-health programmes. Bhutan's successes in treating these conditions are illustrated by 160 people with HIV accessing antiretroviral treatment, 4200 TB cases have been diagnosed and treated, and 362 000 insecticide-treated bed-nets. (*kuenselonline.com*, 9 June 2016)

▶▶ Jamaica has seen real gains in the fight against HIV/AIDS, such as a mother-to-child transmission rate of less

than 2%, and sharp falls in the prevalence rate, including among children and sex workers. However, there are concerns that these gains could be reversed as the Global Fund transitions its support to Jamaica in 2018, due to its attaining middle-income status. In 2010, the Global Fund awarded Jamaica US\$ 40 million, but in 2015 this fell to US\$ 15 million, and the funding cycle moved from 5 to 3 years. It is anticipated that Jamaica may transition out of receiving Global Fund support after this current funding round. With reduced support, Jamaica is focusing on key populations, eg, people living with HIV, men who have sex with men, transgender people and sex workers. There are concerns that the Jamaican government will not be able to cover the funding shortfall following the withdrawal of Global Fund support. This may compromise the recent government's declaration to fast-track efforts on the fight against HIV/AIDS, and to end the AIDS epidemic by 2030. "Civil societies are now looking at their own transition plan. We are praying that it [Global Fund] doesn't go. We are advocating that it doesn't go," says Kandasi Levermore of the Jamaica AIDS Support for Life organization. (*Jamaica Gleaner*, 26 June 2016)

▶▶ Global Fund supporters, including governments, the private sector and civil society partners, have pledged US\$ 12.9 billion for the 5th Voluntary Replenishment of the Global Fund to Fight AIDS, Tuberculosis and Malaria. However, the Global Fund's investment case states that this falls short of the amount needed to meet the 2030 global targets for these diseases; and that US\$ 13 billion is 80% of the amount needed to achieve the 2030 targets for these diseases. The shortfall is expected to be met by partner countries, but despite growing health expenditure, it is insufficient to bridge the gap. If the world meets the global 2020 target of mobilizing US\$ 26 billion per year for the HIV/AIDS response in low- and middle-income countries, it will achieve a 15-fold return on investment, and in the long-term it will save money by preventing 21 million AIDS-related deaths and 28 million new HIV infections. (*ReliefWeb*, 21 October 2016)

▶▶ The Global Fund and partners are working together to support countries which are experiencing problems in im-

plementing grants. These problems can include grants starting late, falling behind schedule, and difficulty absorbing all the financing they have been awarded. This initiative, known as Implementation Through Partnership (ITP) aims to alleviate bottlenecks, increase efficiency and effectiveness, and thereby maximising impact. It is focusing on the 20 countries which received more than US\$ 150 million in Global Fund allocations, but have expenditure vs budget rates of under 70%, or require 50% or

more of expenditure scale-up, or have more than 20% of their grant allocations forecast to be undispersed. These countries, which include Benin, Ghana, DR Congo, India and Pakistan, will receive technical support, leadership and advocacy to launch projects, and evolve from “implementation” to “impact”. Post ITP, the Global Fund plans to learn from what worked well and integrate them into a sustainable model for future grants. (*aidspace*, 1 November 2016)

## ▶ UNICEF

▶▶ According to UNICEF, 90% of the children who arrive in Italy from North Africa are not accompanied by adults, and 7009 unaccompanied children made the journey in the first 5 months of 2016 – twice the 2015 level. There are currently 235 000 refugees and migrants in Libya and 956 000 in the Sahel countries, and many, if not most, of these people will hope to cross to Europe. UNICEF is concerned about the number of children who do not register themselves when they arrive in Europe, but continue onwards and become vulnerable to criminal gangs. Italian social workers have found that boys and girls were sexually assaulted and forced into prostitution in Libya, and that some girls were pregnant on arrival, after being raped. Aimamo, a 16-year old boy, reported conditions of near-slavery on the farm in Libya where he and his brother worked to pay the people-smugglers. Marie-Pierre Poirier, UNICEF’s special co-ordinator for the European migrant crisis, says that these children have “endured war, persecution, deprivation and terrible journeys,” and that “even when they have reached the relative safety of their destination, they still need protection, education, healthcare and counselling. We must be on their side.” (*Al Jazeera*, 14 June 2016)

▶▶ UNICEF’s latest *State of the World’s Children* report shows that more than 69 million children will die from mostly-preventable diseases by 2030, and 167 million will be living in extreme poverty, unless world leaders take decisive action. 2030 is the target date for achieving the Sustainable Development Goals. Nearly 50% of these child deaths will be sub-Saharan Africa, where at least 247 million children – nearly 2-in-3 children – lack the necessary resources to survive and develop. UNICEF’s executive director, Anthony Lake, says that these children are mostly reachable, but there are political and resource constraints. Although the world has made huge progress in tackling child mortality, school enrolment and poverty reduction, the report highlights that the world’s most disadvantaged people are still missing out, as the poorest children are still twice as likely to die before their 5th birthday and suffer from chronic

malnourishment, compared to their richer peers. This picture is even worse in sub-Saharan Africa, where children are 10 times more likely to die before their 5th birthday compared to children in richer countries, and by 2030 it will have 90% of the world’s poor children, and over 50% of the 60 million children who are not in school. One of the report’s authors, Kevin Watkins, says attention must be shifted to tackling child labour and early or forced marriage to improve schooling rates, and onto the needs of refugee children who are displaced and forced into poorly-paid jobs to support their families. The report calls for cash transfers to support children in school, among other measures. (*The Guardian*, 28 June 2016)

▶▶ UNICEF has confirmed that 145 child soldiers have been released following negotiations with two rebel groups – the Cobra Faction and the main SPLA/IO group – in South Sudan. Their liberation including disarming them, providing them with civilian clothes and enrolling them into a re-integration programmes, where they receive counselling and support with re-connecting with their families. UNICEF notes that at least 16 000 children remain fighting in the frontlines or working as porters with both armed militia and the national army, with 8000 children being recruited this year alone. The three-year conflict in South Sudan has killed thousands of people, and driven more than 2.5 million people from their homes, and the UN has called for an arms embargo to prevent further violence. UNICEF hopes that the latest release of these children will be followed by others, and UNICEF’s head in South Sudan, Mahimbo Mdoe, called on all parties to abide by international law, end the recruitment of child soldiers, and to release children who are currently serving. “Children in South Sudan need safety, protection and opportunities,” he said. (*New Arab*, 26 October 2016)

▶▶ Anthony Lake, the Executive Director of UNICEF, has classed the airstrikes on a Syrian school which killed an estimated 22 children and 6 teachers, as a “war crime”, if

they were deliberate. He noted that they may be the deadliest attack on a school since the beginning of the war. The airstrikes took place in the rebel-held province of Idlib, which is the main Syrian opposition stronghold although radical militant groups also have a major presence. An eye-witness said that as many as 10 airstrikes may have hit the residential area where the school is located. Across Syria, UNICEF confirms that 591 children were killed in 2015 as a result of the civil war, 1.7 million children did not attend school, and another 2.1 million children are at risk of dropping out of school. In the besieged city of Aleppo, teachers and volunteers have set up some schools underground to ensure that some teaching can continue amidst the airstrikes. (*Sky News*, 27 October 2016)

▶▶ UNICEF has announced innovation seed funding of US\$ 9 million, to enable 5 start-up companies to create affordable mobile connectivity, blockchain [a distributed database that maintains a continuously-growing list of records] in childhood development, data collection in maternal care, and technology to help improve literacy skills. This is the first time that UNICEF has funded start-up companies, and the 5 companies (SayCel, mPower Social Enterprises, 9 Needs Pvt, Innovations for Poverty Alleviation, and Chatterbox Dating Mobile), were chosen because they are building solutions to the “world’s most pressing problems”, accord to Chris Fabian of UNICEF’s Innovation Unit. The intellectual property of each company’s work will be made available under open source – one of UNICEF’s requirements for funding these companies. (*Wired*, 15 November 2016)

## ▶ World Health Organization (WHO)

▶▶ Amid a global vaccine shortage, the WHO has recommended cutting the standard dose of yellow fever vaccine by 80% (“fractional dosing”) in emergencies. Emergency stocks have been depleted by a mass immunisation drive in Angola, where more than 300 people have died from the disease since December 2015, and there has been a surge of cases in the DR Congo. The DR Congo has reported 1044 suspected cases of yellow fever since March 2016 and 71 deaths. The WHO cautioned that fractional dosing is a short-term measure for emergency situations where a shortage exists. The WHO maintains that its current vaccine levels are adequate, but an outbreak in the DR Congo’s capital city, Kinshasa, meant that fractional dosing is being seriously considered to “prevent transmission through large-scale vaccination campaigns.” Fractional dosing provide immunity for at least 12 months in healthy adults, although it is unclear if they are effective for young children. (*BBC*, 17 June 2016)

▶▶ The WHO announced that Thailand is the first country in Asia to eliminate the mother-to-child transmission of HIV and syphilis. Elimination means the reduction of transmission to such a low level that it is no longer a public health problem, and in Thailand this fell from 1000 children in 2000 to 85 children in 2015. Although Cuba is the first WHO-validated country to eliminate mother-to-child HIV transmission, Thailand – with 450 000 people living with HIV – is the first country with an HIV epidemic to do so. Thailand was affected by a massive HIV epidemic in the 1980s and 1990s, and had responded with awareness and condom campaigns and free antiretroviral treatment, which have cut the number of new infections from 143 000 in

1991 to 8100 in 2013. Thailand also provided all pregnant women – including undocumented migrant workers – free antenatal care, delivery and services for HIV and syphilis, which combined with scaled-up coverage rates has led to this success. According to Dr Poonam Khetrupal Singh, WHO’s regional head for Southeast Asia, “this is a remarkable achievement for a country where thousands of people live with HIV. Thailand has demonstrated to the world that HIV can be defeated.” (*Reuters*, 7 June 2016)

▶▶ The WHO says its staff have been obstructed from doing their work in South Sudan’s capital and expressed concern about the conflict’s likely impact on health care services. A WHO spokesman, Tarik Jašarević, said “the movement of WHO staff in Juba was being restricted by military forces”, but also that the WHO had supplied the Juba Teaching Hospital with essential medicine and body bags. “Medical kits would be distributed to partners on protection of civilians sites, and the WHO was mobilizing additional human and financial resources,” he said. Mr Jašarević also pointed out that even before the latest fighting the health care sector faced funding shortfalls this year. “Out of the US\$ 7.5 million which the WHO needed for health interventions in South Sudan, only US\$ 4.3 million had been received thus far. The health cluster as a whole was only 28 percent funded,” he said. (*Radio Tamazuj*, 13 July 2016)

▶▶ According to the WHO, a global shortage of HIV testing could undermine efforts to diagnose and treat people infected with HIV. There are worrying gaps in the provision of these tests, which check HIV status and health, and the WHO warns that it could lead to UN targets on ending HIV

being missed. Reasons for the gap include lack of reagents, equipment not being properly installed or maintained, and inadequate staff training. Some programmes may have overly-focused on buying equipment without planning for its optimal use. For example, in Zimbabwe, only 5.6% of patients on HIV treatment in 2015 received regular blood checks to monitor their viral load – the target is 21% – and this was largely due to problems with resource mobilisation, specimen transport and equipment procurement. HIV experts Peter Kilmarx and Raiva Simbi highlight that “strong leadership, resources, planning and management are needed to scale-up laboratory services.” (*BBC*, 25 August 2016)

▶▶ Douglas Henderson, epidemiologist, died on 19 August 2016, and he will be chiefly remembered for leading the WHO’s smallpox eradication campaign. When he began the campaign, the funds allocated for global eradication – US\$

2.7 million – were not enough to purchase vaccines. However, Dr Henderson realised the futility of attempting to vaccinate everyone against smallpox, and focused on surveillance and containment. Whenever a case of smallpox was identified, a team was dispatched to identify and vaccinate everyone whom that person had been in contact with, and their contacts. He also insisted that policy could only be set by people actively engaged in smallpox fieldwork. Dr Henderson believed that his greatest achievement was the WHO’s expanded program on immunisation, which aimed to provide universal access to necessary immunisations. “I believe that the important, longer-term contribution of smallpox eradication . . . was its demonstration of how much could be accomplished with how little in the control of infectious diseases through community-wide vaccination programmes,” he wrote in his 2009 autobiography *Small-pox – the Death of a Disease*. (*Guardian*, 7 September 2016)

## ► Demography

►► New figures from the US federal government shows a decline in the US birth rate and an increase in the death rate, which could lead to downwards pressure on the country's population growth. In 2015, there were 3.98 million births in the US, a 0.3% reduction from 2014 and reversing previous gains. Despite the sharp fall in births among women aged 15–19 years, some demographers are concerned that the birth figures are lower than expected, and that the US is still to recover from the slowdown in its birth-rate arising from the 2007 recession. The rise in the country's death rate (from 729.5 deaths per 100 000 people in 2015, from 723.2 in 2014) is partly due to increases in deaths from heart disease, stroke and Alzheimer disease; and although the statistics on deaths from suicide and drug use are not yet available they are also likely to show an increase. According to Jeffrey Passel, a senior demographer at the Pew Research Center, "to keep the labour force growing, we're going to need to have pretty healthy levels of immigration." (*Wall Street Journal*, 15 June 2016)

►► India is placed last on an annual retirement security index, which ranks 43 countries, including the BRICS nations, on retirement security factors including quality-of-life, health and finances. India was the poorest–scoring BRICS country in health care, mainly caused by its low expenditure on health care, high non-insured health expenses, and inadequate basic health care in rural areas. India also fared badly in the quality-of-life category, due to factors like air quality, happiness and environmental pollution. Another report from HSBC shows that 47% of working people in India have not begun to save for their retirement, or face difficulties in saving for their retirement. This is coupled with high expenses during retirement – 68% of retired people in India report borrowing or supporting other people financially, compared to 50% globally – which suggests that people aren't saving enough for retirement. About 8.6% of India's population is aged over 60, and the elderly population is expected to increase by 20% by 2021. (*Huffington Post India*, 20 July 2016)

►► Almost 15% of US citizens are poor – including 20% of all children – and almost one-third of all households is headed by a single mother. These levels are higher than most other developed countries, and have proven stubbornly high even during strong economic growth. Bill Clinton enacted the last major reforms to US welfare in 1996, which capped welfare at US\$ 16.5 billion a year, and put the states in charge of implementing it. Labelling it Temporary Assistance for Needy Families, he intended to make "welfare a second chance, not a way of life", with payments

conditional on the recipient looking for work, and limiting their receipt to 5 years in total. On some measures, the policy has been successful, as spending on welfare fell to US\$ 11.1 billion a year (although non-cash benefits like food and housing vouchers covered any shortfalls), and fewer Americans claim welfare. However, the tough economic conditions of the past 10 years have highlighted its shortcomings for the millions still stuck in poverty. First, Mr Clinton promised guaranteed public-sector jobs to claimants, which did not materialise, and many individual states have provided inadequate training. The move toward low-grade service jobs across the US economy means that many people are stuck close to the poverty line; and even among those who fare better, the sharp withdrawal of tax credits (in effect, up to a 60% tax rate) disincentivises progress. Falling cash payments has led to a new, cash-poor, group of people who rely on vouchers rather than cash, leaving them unable to pay a phone bill or afford a haircut. Improving their outlook could mean increasing the amount of welfare paid in cash, and ensuring that states cannot plunder welfare payments. (*Economist*, 20 August 2016)

►► According to the UK's Overseas Development Institute (ODI), Africa's children will comprise more than 40% of the world's poorest people by 2030 – almost double the current amount – unless education and health care are improved. The ODI estimated that 88% of all children living on US\$ 1.90/d by 2030 will be in sub-Saharan Africa – up from 50% today. The ODI calls for cash transfers, education and health care to reduce poverty, extreme inequality and alter demographic patterns, and notes the central role of education in enabling girls to gain skills, delay marriage and demand better health and reproductive care. Mr Kevin Watkins, the director of ODI, states that Nigeria – Africa's most populous country – has the largest number of children out of school and large gender gaps in education. Unless Nigeria improves, it will distort gains within other countries in sub-Saharan Africa. Sub-Saharan Africa has experienced economic growth and made significant progress in child survival rates, and Mr Watkins calls on African leaders to invest in their young people and end child marriage (more than 10% of girls are married by age 15, and 40% are married by age 18 in sub-Saharan Africa), which prevents young women from exercising choice and realizing their potential. (*Thomson Reuters Foundation*, 24 August 2016)

►► The current Sustainable Development Goals – which aim to end poverty, boost prosperity and promote sustainability – will end in 2030 when the world's population will be 8.5 billion people, and just 20 years ahead in 2050, the

world's population will have increased to nearly 10 billion. For an indication of how the world could look in 35 years' time, it is interesting to track progress from 34 years ago. In the early 1980s, the population was 4.5 billion, of whom 42% lived in extreme poverty. Today, the population has reached 7.5 billion, yet just 10% of the total population live in extreme poverty. This is largely due to China and India, who have succeeded in lifting millions of people out of poverty and improving health outcomes. This was achieved partly by strengthening institutions and promoting strong, relatively inclusive growth; and China look advantage of its "demographic dividend", whereby the labor force grew

faster than the dependent population. Today, 90% of global poverty is concentrated in countries with growing working-age populations – an important opportunity for rapid poverty reduction, provided that productive jobs can be generated. However, several middle-income countries will begin to experience a decline in the relative share of their working-age population, as higher incomes impels households to delay having children. This can be potentially be offset by the accumulated savings of an older generation producing a surge in investment, helped by improving productivity and adapting social-welfare systems. (*Project Syndicate*, 25 October 2016)

## ► Economy

►► A study from Boston University and the Chinese Academy of Social Sciences found that China is a bigger presence in development finance that the major multilateral financial institutions combined, doubling the volume of global development finance over the past 10 years. In 2014, two Chinese policy banks – the China Development Bank (CDB) and the Export-Import Bank of China – have an estimated overseas loan portfolio of US\$ 684 billion which is just below the US\$ 700 billion from the combined western multilateral development institutions (World Bank, Asian Development Bank, Inter-American Development Bank, European Investment Bank, European Bank for Reconstruction and Development, and African Development bank). The CDB has overtaken the World Bank as the single biggest provider of international development finance. However, there are concerns over the environmental and social impacts of China's development assistance, which may lack the stringent loan conditions from western institutions. This is particularly acute in energy projects, with coal projects backed by China having an estimated annual social cost of US\$ 27 billion. (*Financial Times*, 17 May 2016)

►► The East African Community (EAC), comprising 6 countries, is Africa's most integrated trading bloc. It agreed a customs union in 2005, and a common market in 2010. And, according to an analysis from the International Growth Centre, the region is richer and more peaceful as a result. The analysis found that bilateral trade was 213% higher in 2011 than it would otherwise have been, despite the ongoing 51 non-tariff barriers. The authors argue that full implementation would double income gains, but are sceptical of the EAC's aim of creating a common currency by 2024, arguing that it would have little benefit on trade. The IMF found that unless the EAC's economies converge,

a single currency would mean that wage adjustments would be the only way to absorb economic shocks – and Greece can attest to the resultant economic hardship. However, the authors conclude that interdependence reduces the risk of war, and in a continent where national economies are small, regional trade blocs provide more economic clout. (*The Economist*, 11 June 2016)

►► Following the UK's vote in June to leave the European Union ("Brexit"), the value of the British pound (GBP) fell sharply. Among the major repercussions from this fall is a drop in the value of UK overseas aid, which fell by US\$ 1.4 billion in one night. To place this in context, US\$ 1.4 billion is almost equivalent to the National Security Council-led Prosperity Fund's budget of US\$ 1.3 billion, which is earmarked to place 11 million children in school, bring clean water and sanitation to 60 million people, save 1.4 million lives through immunisation, and improve nutrition for 50 million people. Moreover, the UK pledges to spend a fixed proportion of its GDP on development assistance, so if economic growth falters or the UK experiences a recession then the value of UK overseas aid will also decrease. The EU budget for development assistance will also be affected, as the UK channels 2 billion Euros (US\$ 2.2 billion) into its budget for overseas aid, and every US\$ 1 that the UK spends on EU development assistance is matched by US\$ 6 from other EU member states. (*Humanosphere*, 24 June 2016)

►► Despite recent events in Turkey, globally coups have become increasingly rare. This is highlighted by recent research from the University of Kentucky, which shows that attempted coups peaked in the mid-1960s, with two peaks in the mid-1970s and early 1990s (the end of the Cold War). However, this analysis also shows that coups are more likely to succeed, with a record 60% now succeeding, compared to 20% at the start of the 21st century. Sep-

arate research from the Stockholm School of Economics suggests that the economic consequences of coups are particularly dire when democracies are overthrown. These typically lower economic growth by 1–1.3% a year over the following decade. This runs counter to the argument that Chile and Turkey's economic growth is linked to their coups in 1973 and 1980 which brought in economic liberalisation; the research found that post-coup economic growth was lower than pre-coup economic growth, and that growth rates were lower-than-expected. Coups tend to cause increased indebtedness, deteriorating external financial positions, a higher chance of economic crises, and reduced social spending shifts priorities from the wider population to the country's elite, with knock-on effects on health and education. However, coups which successfully overthrow autocratic leaders are often economically beneficial. The economic impact of Turkey's failed coup depends on whether Turkey is considered a democracy; its president Recep Tayyip Erdogan was democratically elected, but subsequently centralised power and made Turkey's

intelligence services accountable to him alone. Turkey's ranking for freedom of expression and beliefs is now more akin to an autocracy, while its press freedom is the lowest of any democracy and is in line with a mid-ranking autocracy. (*Financial Times*, 20 July 2016)

▶▶ China is the world's third-largest economy, accounting for 15% of global output, but its contribution to global economy growth could be yet more significant. It is estimated that China contributes 25–30% to total global economic growth. However, much of this growth will fuel China's own economic growth, raising its citizens' living standards. Globally the benefits will be felt at the margin, as more and higher-value exports from China ensures that world-wide people can access more and better products, while Chinese consumption of imported goods will support employment in other countries. India's economy is growing faster than China's, but this will have less global impact because it is growing from a lower base, and the extra size of its economy each year is very much smaller than China's economy. (*Forbes*, 30 October 2016)

## ▶ Energy

▶▶ The International Energy Authority (IEA) has stated that Middle Eastern oil producers, such as Saudi Arabia and Iraq, have the largest share of world oil markets since the Arab fuel embargoes of the 1970s. The collapse in oil-prices has reduced output from higher-cost producers (eg, Canada, Brazil), leading to a surge in demand for Middle Eastern crude oil. Unlike the 1970s oil crisis, OPEC producers – led by Saudi Arabia and its Gulf allies – decided to maintain their output to defend market share, rather than reducing output to increase prices. This has led to surging demand, and thwarted efforts to reduce greenhouse gas emissions as more consumers buy fuel-guzzling cars. In the USA, more than 2.5 times as many sport utility vehicles (SUVs) are now bought compared to standard cars; this is echoed in China, which is rapidly adopting the US's taste for fuel-heavy cars, with more than 4 times as many SUVs being purchased. China is now the focus in the global growth in oil demand, and in 2015 overtook the USA as the world's biggest oil importer. Mr Fatih Birol, IEA's executive director, has called for stricter fuel efficiency targets to reduce demand, and argues that the rise of shale oil will not reduce the Middle East's dominance of global oil markets. (*Financial Times*, 7 July 2016)

▶▶ On the face of it, energy efficiency is a highly appealing policy, which appears to reduce costs, create jobs and save the planet. However, the UK recently ended its US\$ 316

million energy efficiency loan project, after its National Audit Office concluded that people were not signing up, nor delivering cost-effective energy efficiency measures for those who did. On a similar note, there is no evidence that houses built under California's new building energy codes use less energy than earlier houses. This is partly because of the "rebound" effect, whereby improving energy efficiency can lead to higher energy consumption. According to researchers at the Copenhagen Consensus Center, it would cost US\$ 3.2 trillion to achieve the UN target of doubling the rate of improvement in energy efficiency – the International Energy Agency expects expenditure to be US\$ 550 billion by 2035. An alternative approach to tackling climate change is to develop green technology to the point where it is cheaper than oil, gas or coal. This would be achieved not via subsidies, but by increasing research and development expenditure to make the next generations of wind, solar and biomass energy cheaper and more effective. If 0.2% of global GDP was devoted to green-energy R&D, then the chances of breakthrough are significantly increased. This would have benefits 11 times greater than the amount spent – compared to 2.4–3 times under the current method. (*Project Syndicate*, 20 July 2016)

▶▶ Argentina's Supreme Court has ruled that the government must hold public hearings before cutting energy subsidies and increasing domestic utility rates. Since his election in



November 2015, President Mauricio Macri has cut gas subsidies, which caused a sharp upturn in domestic heating bills – up to 400% – following an unusually cold winter, and the cost of electricity has increased by up to 700%. The court ruled that Argentina's government had violated the law on natural gas which requires that hearings are needed to secure the constitutional right to information, consultation and participation for users and consumers. This will restore residential gas prices to their original levels, and the Macri government must now hold public comment sessions before it can implement further increases on residential gas rates. (*TeleSUR*, 18 August 2016)

▶▶ According to the UK government, Électricité de France (EDF) SA's planned Hinkley Point C nuclear plant will cost British consumers US\$27 billion in subsidies over the lifetime of the French company's contract with the UK. EDF plans to build two nuclear reactors at Hinkley Point, which will generate 7% of the UK's electricity, with China's General Nuclear Power Corporation providing 33% of funding. This project has proved controversial, in part due to concerns over China's involvement, and that the contracted price is more than twice the current wholesale rate. It will add an estimated US\$ 20 to each household's annual electricity costs. However, the government noted that nuclear power stations are an important part of ensuring the UK's

low-carbon energy security, large-scale solar and on-shore wind could not produce the same amount of electricity as Hinkley Point without significant upgrades to the national grid, and relying on gas would endanger the UK's carbon emission targets. (*Business Insider*, 29 September 2016)

▶▶ Saudi Arabia is the world's second-largest producer of oil, which is a major contributor to climate change, but is now turning its attention to green energy generation. This may be prompted by the current oversupply of oil and dwindling demand due to the global economic slow-down and the growth of renewable energy. Khaled al-Faleh, the kingdom's oil minister, confirmed that Saudi Arabia is making major investments in renewables, with the goal of producing 9.5 MW from renewable energy, mainly solar and wind sources. However, these investments are aligned to further investments in hydrocarbons and petrochemicals. The Saudi oil giant, Aramco, confirmed that it intends to play a key role in country's drive to become a top clean-energy producer. Other oil giants, including Aramco, are moving to establish investment funds to develop carbon mitigation technologies in addition to renewable energy. A public announcement of this plan is expected to coincide with the formal launch of the 2015 Paris Agreement to phase out man-made greenhouse gases during this century. (*New Arab*, 2 November 2016)

## ▶ Environment

▶▶ Faced with desiccated pastures in Ethiopia's Somali region in November 2015, many pastoralists traveled to Somaliland (an internationally unrecognised but *de facto* sovereign nation separate from Somalia) – a journey of hundreds of kilometres – in the hope of finding rain and fresh pasture. However, they found insufficient rain and pastures to support the number of arrivals, and thousands of cattle, sheep, goats and camels perished. This drought, named *mulia* (ie, "that which erases everything on the ground") is the most severe for 50 years, although there is no repeat of the 1984 famine, which caused the deaths of more than 1 million people. To date, Ethiopia's effective emergency response has staved off disaster, but faced with climate change and increasingly frequent, severe droughts in the Horn of Africa, lifestyle changes may be unavoidable and the traditional way of life of Ethiopia's pastoralists may be increasingly unsustainable. "In areas affected by climate change, you just can't have the same numbers of people surviving in these conditions – it's beyond the control of the people or the government," says John Graham, Ethiopia country director for Save the Children. This is recognized by the pastoralists themselves, who believe that a

government re-stocking program, or a government re-settlement program to more reliable areas may give them a chance to preserve their way-of-life. (*IRIN*, 3 June 2016)

▶▶ Carbon capture and storage can reduce CO<sub>2</sub> emissions and is part of the battle against climate change, but there are concerns over storing it safely and preventing leaks. The small-scale CarbFix project in Iceland pumped a mixture of CO<sub>2</sub> and water into underground basalt rocks. This caused the acidic mixture to dissolve the rocks' calcium magnesium and turn into limestone, and within two years 95% of CO<sub>2</sub> was captured and successfully converted to limestone – an acceleration of a natural process. The main drawback to this new technology is that it is currently twice as expensive as injecting CO<sub>2</sub> into old wells, although the ocean floor is a promising source of basalt for storage. Ken Caldeira, a climate scientist at the Carnegie Institution for Science, described the possibility of low-cost scale-up of the technology as "very good news". (*Japan Times*, 10 June 2016)

▶▶ Iceland's capital city, Reykjavik, is aiming to become carbon-neutral by 2040. The city already produces all its elec-

tricity through hydroelectric power and houses are heated geothermally, so its greenhouse gas emissions are low in comparison with other cities. This means that other sectors, primarily transport, must be at the forefront of its drive to become carbon-neutral. The city has set out plans to increase public transport usage from 4% to 12%, increase the ratio of pedestrians and cyclists from 19% to over 30% by 2030, increase the use of bicycles and buses as primary transport methods, and increase the availability of charging stations for electric cars. “Achieving carbon neutrality is entirely within the realm of what is possible for cities. It sets an ambitious target, while also recognising that certain steps towards climate neutrality may be easier to attain than others,” said Monika Zimmerman, the Deputy Secretary of Local Government for Sustainability. (*Cities Today*, 21 September 2016)

▶▶ The USA’s Environmental Protection Agency (EPA) has been rebuked over its failure to act swiftly in warning the residents of Flint Michigan that their water was contaminated with lead. Flint’s water supply became contaminated after its water source was switched to the Flint River in 2014, partly to save money. Arthur A Elkins, the Inspector-General for the EPA, noted that EPA officials had enough information and authority to issue an emergency order in June 2015, when officials knew that systems designed to protect drinking water from lead contamination were not in place, residents had reported abnormalities in the water, and some test results showed lead levels above the federal action level. However, the EPA did not issue an

emergency order until January 2016, causing these conditions to persist. However, Gina McCarthy of the EPA told a Congressional committee in March 2016 that the agency had been repeatedly misled by state employees, and was not responsible for creating the initial lead problem, noting that state officials had agreed to add corrosion controls to Flint’s water but delayed in doing so. (*New York Times*, 20 Oct 2016)

▶▶ Middle-class residents are increasingly abandoning New Delhi (India’s third-largest city), as particulate levels reached 30 times the safe limit recommended by the World Health Organization, and Anil Madhav Dave, India’s environment minister, warned of an “emergency situation”. Arvind Kerjriwal, the city’s chief minister, announced some measures to combat pollution, including the temporary closure of construction sites, banning diesel generators for 10 days except for hospitals and emergencies, closing a coal-fired power station etc. An earlier scheme to restrict car usage reduced pollution levels, but its effects were limited by cars only contributing 25% of small particle emissions – another 25% is due to the illegal burning of crops by farmers in other states, which the government has failed to tackle. According to the World Bank, the annual cost of India’s air pollution is more than US\$ 40 billion – or 3% of its GDP – and economists warn that outward migration caused by pollution could cause serious economic damage to New Delhi’s economy. However, one area of the economy is booming – sales of air purifiers. (*Financial Times*, 6 November 2016)

## ▶ Food, Water and Sanitation

▶▶ Recent innovations in farming – so-called “smart farming” – has led to farming becoming more like factories, as tightly-controlled operations which produce reliable products, increasingly independently from the natural world. Improved understanding of DNA makes genetic manipulation of plants and farm animals possible, which may be more palatable to consumers than the shifting of whole genes between species. These new technologies are likely to improve profits by cutting costs and increasing yields, and lower prices will benefit consumers. They may also help answer the challenge of feeding the world’s population as it grows from 7.3 billion to 9.7 billion by 2050. According to the UN’s Food and Agriculture Organisation, this would require a 70% increase in production – which can realistically only be met by higher yields, as most land suitable for farming is already under cultivation. Technologies such as farm-management software, hydroponics and

drones increase yields, fish-farming may be brought inland thanks to artificial ecosystems, while cultivated land can be increased by using old buildings (“vertical farms”) and underground tunnels as farmland. Researchers have also produced laboratory-grown muscle cells which can be developed into meat products, and synthetic egg whites, raising the possibility of increasing meat and egg consumption without increasing livestock production. Rice yields in China could increase if the precision agricultural techniques used in North America’s arable farms could be adapted. Technology could also increase Africa’s agricultural yields, illustrated by the NextGen Cassava Project, which increases the crop’s yields and nutritional value while reducing their susceptibility to disease. (*Economist*, 9 June 2016)

▶▶ In recent years, drought and water shortages have affected animal husbandry in Vietnam’s central region, reducing livestock’s natural food sources and causing many

deaths among cattle. The government's Animal Husbandry department will assess the future of animal breeding during prolonged heatwaves and drought, and include new zones for animal husbandry. The breeding of sheep, ostriches, goats, honeybees and silkworms have helped increase farmers' incomes, and offset crop losses caused by drought and saltwater intrusion. In Khánh Hoà province, officials are working on a plan for agricultural restructuring, with a focus on animal husbandry, especially on breeding animals that can survive drought conditions. (*Việt Nam News*, 11 June 2016)

▶▶ In March, China discontinued its minimum price policy for grain, whereby the government bought grain at above-market rates, thus distorting market prices and leading to expensive grain being hoarded in silos. The end of this policy held down prices and lessened crop acreage, in the expectation that grain would be released from storage. However, grain imports and prices are increasing, causing suspicions that much of the stored grain is unsuitable for use. Demand for corn from China's livestock industry has driven record corn imports in April and May 2016. China and Russia have also pledged to invest US\$ 185 million in grain elevators and a terminal in Russia to support China's future grain purchase – another indicator of China's long-term concerns over its grain supplies. (*Financial Times*, 11 July 2016)

▶▶ A global study of heights over the past century has found that the tallest nations (including Estonia, Denmark, Serbia and the Czech Republic) are all found in Europe. The Netherlands has the highest average height for men (182.5 cm), and Latvia has the highest average height for women (170 cm). The study also found that English-speaking countries – primarily the USA – are falling behind

other high-income countries in Europe and Asia Pacific. The relative decline, coupled with these nations' poor record in obesity, highlights the need for good life-long nutrition. However, the average heights for young men and women have decreased by up to 5 cm in some countries in sub-Saharan Africa, including Sierra Leone, Uganda and Rwanda. "The average height of some nations may even be shrinking while others continue to grow taller ... This confirms we urgently need to address children and adolescents' environment and nutrition on a global scale," says Majid Ezzati, a global health researcher at Imperial College London. (*New Scientist*, 26 July 2016)

▶▶ India's Urban Development Minister, Venkaih Naidu, believes that sanitation will be an election issue, as urban residents are more likely to support candidates with strong policies on hygiene. He is also confident that India's National Democratic Alliance (NDA) government will achieve its "Clean India" mission, including making India open-defecation-free (ODF) by 2019. Prime Minister Modi has issued calls to make the Clean India campaign a national movement, and Mr Naidu stressed that behavior changes toward using toilets and putting waste into litter bins is key to its success. He noted that the campaign is on-track to meet its target on constructing household toilets, and Gujarat and Andhra have already declared themselves ODF in urban areas, and Kerala is set to make a similar announcement. To date, 405 cities have been declared as ODF, and nearly the same amount are expected to be ODF by March 2017. However, he is concerned about the bigger challenge of dealing with India's refuse, but noted that the government plans to tackle it by turned 65 million tonnes of urban refuse into compost and electricity. (*First Post*, 29 October 2016)

## ▶ Peace and Human Rights

▶▶ Today, the USA consumes six times more prescription opioids per person than it did 20 years ago, often for chronic, non-terminal pain. Over-prescription, haphazard clinical practice and spotty oversight have led to addiction and deaths. However, other countries face the opposite problem. *The Lancet* estimates that 40 Russians have committed suicide in a single year because of unbearable pain, and globally opioid shortages are more common than the over-use seen in some countries. Nigeria began importing morphine in 2012, which has improved access, but it is only available from Lagos and smaller hospitals outside the capital struggle to afford the journey to buy it. Palliative care is difficult to access in most developing countries, and fa-

cilities are concentrated in cities, making it much harder for rural patients to receive treatment to alleviate their suffering. This situation is mirrored in Colombia, which produces its own opioid painkillers, but some regional governments cannot afford to buy them, or view them as a low priority. Moreover, the campaigning group Human Rights Watch has highlighted the paucity of training in palliative care, meaning that few doctors know how to prescribe pain-killers safely, and the bureaucracy faced by cancer patients to obtain pain relief in some countries. Opioid drugs are relatively cheap to make, but tariffs, import licenses and high costs for small-scale production means that morphine is twice as expensive in developing countries, while low

profit margins on opioids give little incentive to drug firms to bring them to new markets. And often, pain management is simply not a priority in the developing world, where many governments focus on life-threatening epidemics. (*Economist*, 28 May 2016)

▶▶ Uganda has been a safe haven for many South Sudanese people during the country's 60 years of turmoil. However, the Adjumani district in northern Uganda has seen new arrivals increasing to 250/day from an earlier average of 160/day. There are more than 132 000 refugees in the area – the highest concentration in the country – and overall Uganda is home to 510 000 refugees. Uganda's refugee model avoids traditional camps far from communities, but provides refugees with a basic ration, plots of land and materials with which to build their new lives. This has been celebrated as progressive, forward-looking, building self-sufficiency and integrating refugees into their host community. However, this is being stretched to the limits, as increasing number of refugees mean that land plots are shrinking which increases their reliance on aid – the very thing it was supposed to avoid. Ethnic tensions are also increasing as other communities have been caught up in South Sudan's struggle, and refugees' ability to trade their goods in larger markets outside the settlements is compromised by security concerns, which would lower their incomes. As South Sudan's prospects for peace look increasingly grim, Uganda's model of refugee integration faces further strains. (*IRIN*, 13 June 2016)

▶▶ Syrian teenager Yusra Mardini will become the first member of the Refugee Team to compete in the Rio 2016 Olympic Games, in the women's 100-metre butterfly heats. Speaking in Rio alongside the other athletes from the Refugee Team, Yusra said "a lot of things have happened in our lives, but remember that life will not stop for you." The 10-strong Refugee Team comprises judoka [judo contestants], swimmers and track-and-field athletes. Yusra said that her goal is for everyone to understand that most refugees are normal people who have had to flee their homelands, and that each member of the Refugee Team is very aware of the opportunity to present a positive, inspiring picture of refugees. "They have dreams in their lives, and had to go. Everything is about trying to get a new, better life and by entering the stadium, we are encouraging everybody to follow their dreams," she said. (*Huffington Post*, 8 August 2016)

▶▶ Civilians cannot access medical care in the besieged Afghan city of Lashkar Gah – the capital of Helmand province – and agencies are preparing for a possible Taliban takeover. Recent fighting has displaced 10 000 people, and despite government assurances that the city will not fall to the Taliban, aid agencies are making plans for this eventuality. Médecins Sans Frontières (MSF) has "a massive casualty plan prepared and ready to implement immediately in the case of a further deterioration of the security situation". MSF is in contact with militants, plus government and allied forces, and shares its GPS co-ordinates with all sides to help protect patients and staff. When the Taliban briefly took over Kunduz in 2015, it allowed MSF to treat war-wounded people, until its trauma center was destroyed by a US airstrike. In early August, MSF treated 25 war-wounded people in the province, but noted that fighting makes it extremely difficult to travel to Lashkar Gah for treatment. A 15-year old girl died from meningitis, as road blocks and check-points cause delays in reaching hospital, and other people are also likely to be suffering with, and even dying from, treatable conditions because they can't reach hospital. Aid agencies are distributing food, water and supplies to displaced people in Lashkar Gah, but if the city falls to the Taliban civilians may be trapped, as roads are inaccessible and threaten the delivery of aid. (*IRIN*, 17 August 2016)

▶▶ The European Union confirmed that it will not be introducing a UN resolution condemning Myanmar's human rights record – the first time in 15 years – and praised the country's progress under the leadership of Aung San Suu Kyi. The EU acknowledged the tentative steps toward addressing violence between the majority Buddhists and Muslim Rohingyas in the state of Rakhine. The Rohingyas are often perceived as illegal immigrants from Bangladesh, even though many have lived in Myanmar for decades, most were disenfranchised in the 2015 election, and around 125 000 are confined in temporary camps. The US ambassador to the UN, Samantha Power, lauded Suu Kyi's commitment to stand firm against intolerance and her pledge to grant citizenship to all those entitled to it as "powerful and important". In Suu Kyi's first address to the UN General Assembly, she defended her government's efforts to resolve the Rohingya crisis, and stated that the government would persevere in its efforts to bring peace to Rakhine, and will stand firm "against the forces of prejudice and intolerance." (*Reuters*, 24 September 2016)

## ► Science and Technology

►► The recent Ebola outbreak in West Africa shows the importance of fast and accurate diagnostics, especially in countries with weak health systems. Redemption Hospital in Monrovia, Liberia used one of the first machines – GeneXpert – for Ebola testing, which gave cheap and accurate results within 90 minutes, and was crucial in reducing false Ebola scares and restoring confidence among Monrovia residents. Other portable “point of care” testing kits can be used to screen for other infectious diseases such as tuberculosis, HIV and malaria, and can help measure the effectiveness of health campaigns. Tests can be administered on-site, but diagnoses sometimes take place thousands of miles away, for example local doctors in 19 African health centers are connected online with 100 volunteer specialists in Europe. Portable, user-friendly, low-energy diagnostic kits are especially important in areas with limited access to power or laboratory equipment. The next step for diagnostic technology is to test for multiple causes of a symptom, such as a fever. (*BBC*, 20 September 2016)

►► Vaccine production often involves cultivating vaccine-producing bugs in secure and centralised areas, followed by global distribution. Security is needed to prevent organisms, particularly modified organisms, escaping into the wider environment. This approach works well when they are sent to places that have proper infrastructure to handle vaccines, such as reliable refrigerating equipment to keep them cool (the “cold chain”), but often in areas where they are most needed these facilities are less available. However, if vaccines could be made on site, it would simplify and shorten the distribution chain. James Collins from the Massachusetts Institute of Technology may have resolved this, by devising a vaccine factory that consists of the cellular components needed to synthesize the required molecules, rather than whole cells, in a way that can be freeze-dried for easy transport and storage – with no risk of escaped bugs. Mr Collins and colleagues looked at how solutions containing protein-production machinery responded when given DNA templates that encoded the antigens used to make various vaccines, and found that all were readily activated by the rehydrated cellular machinery. If this approach can be commercialised, it could greatly simplify vaccine manufacturing and distribution. (*Economist*, 24 September 2016)

►► The 2016 Nobel Prize in physiology or medicine was awarded to Japanese biologist Yoshinori Ohsumi, for his work on uncovering how the body’s cells deal with and recycle waste, known as autophagy. Cells use this process to degrade some of their contents and clear them away or recycle them, and Dr Ohsumi identified the first genes required for autophagy in yeast and subsequently contributed to the understanding of this works in humans and animals. This knowledge may help develop treatments for conditions

such as Alzheimer Disease, Parkinson Disease and cancer. Dr Ohsumi said his research was important because it highlights how cells cannot function without “quality control,” and shedding and recycling substances it no longer needs. “We create proteins and destroy them, and again create and destroy, and that’s what makes life exist,” he says. (*Wall Street Journal*, 3 October 2016)

►► More than 1% of US children are diagnosed with an autistic spectrum disorder, and no treatment has been shown to effectively address the core symptoms of autism. However, the Preschool Autism Communications Trial (PACT) enrolled 152 children aged 2–4 years with autism – many with severe symptoms – to test the effectiveness of early interventions, which are believed to have a greater impact as symptoms are less severe and the brain is at an earlier stage of development. PACT taught the parents of these children how to interact more effectively with their children. The results of the trial, published in *The Lancet*, shows that six years after the year-long course the children still showed improved social communication and reduced repetitive behaviors, and fewer were considered to have severe autism in comparison with a control group. John Constantino, a child psychiatrist at Washington University describes this as “monumentally important” as there was previously little evidence that early-stage interventions are beneficial. Despite improving communications skills and decreasing repetitive behavior, the therapy did not lessen children’s anxiety – a key symptom of autism – and underscores the importance of developing higher-impact interventions. (*Nature News*, 25 October 2016)

►► The Ebola virus appears to have mutated in 2014, which made it less likely to infect its traditional host of bats, and more likely to infect humans. The mutation, known as A82V, spread quickly beyond Guinea, where Ebola first broke out, and was involved in the vast majority of cases. However, the research teams who identified the mutation emphasize that it was not directly responsible for Ebola’s spread, which is more closely linked to the movement of infected people in urban areas, and the lack of proper burials. It is also unclear if A82V is more fatal; certainly people infected with the mutant strain were 27% more likely to die, but this may be due to limited access to health care, as the outbreak took hold when infected people were moving to urban areas. Even without the A82V mutation, some strains of Ebola have mutations that make it easier for them to spread from bats to humans. Although Ebola is currently halted, and A28V has disappeared, the research highlights that the next outbreak could include different mutations that make it easier for the virus to spread – constant vigilance, monitoring and rapid response is needed. The A82V mutation could have been prevented if the Ebola outbreak had been stopped earlier. (*The Atlantic*, 3 November 2016)

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## WHO headquarters: my experiences as an intern – by Ariadne L'Heveder



**Photo: Ariadne L'Heveder at the World Health Organisation**

“Under the supervision of the team lead of GISRS (Global Influenza Surveillance and Response Systems) and the overall guidance of the head of the Global Influenza Programme, the intern will support activities that directly relate to the finalization of the RSV (respiratory syncytial virus) surveillance strategy.” A somewhat daunting instruction to read following my elation at having secured an internship at the World Health Organisation (WHO) headquarters for the summer before starting my final year of medicine at the University of Edinburgh. However, what started as an overwhelming amount of paperwork, developed into an unforgettable 6 weeks in Geneva.

One of the main reasons I applied to intern at the WHO was because I wanted to gain a sense of how such a vast organization operates on a day-to-day basis, and see whether I could envisage myself working for the WHO given my key interests in global and public health. I was incredibly fortunate to be offered an internship with the Global Influenza Surveillance and Response Systems (GISRS) network, particularly as I joined the team at a very exciting time when they were on the cusp of launching a new pilot for RSV surveillance based on the GISRS platform. RSV is a major cause of global infant mortality and morbidity, especially in low and middle-income countries. Currently however, there is no standardized global surveillance, unlike for influenza virus, where GISRS has successfully carried out surveillance for over 60 years. Thus, the team was in the preliminary stages of establishing what will hopefully become global RSV surveillance, the first step being planning a RSV surveillance pilot. Following a number of meetings to determine the practicalities, epidemiology and laboratory aspects of piloting RSV surveillance, a further meeting: “WHO Technical Meeting on Piloting RSV Surveillance based on the Global Influenza Surveillance and Response System”, which I would help the team pre-

pare for, was arranged to finalise the RSV surveillance strategy before the roll-out of the pilot in September 2016.

I arrived mid-June 2016 and with the meeting starting on 28th June, it was action stations from the get-go! I was assigned a number of tasks to help with the meeting preparations, such as writing the first draft of slides for the WHO speakers' presentations, and developing a specimen submission form and an accompanying excel data reporting spread-sheet to go into the guidance document for the RSV surveillance pilot. I also became very involved in setting the agenda for the meeting and was amazed by how much my views were respected and helped shape the planning of the meeting; here was a group of people with such a wealth of experience behind them listening to a meagre intern and taking my ideas on board. It must be said that the working environment is very positive at the WHO. While a strict hierarchy inevitably exists, as I've seen in hospitals, there is a much more fluid exchange of ideas between colleagues at all levels with a huge respect for others' opinions which I found very refreshing. Attending the RSV technical meeting was a truly unique opportunity, and I felt so privileged to be surrounded by world experts on RSV, leading and the representatives from 14 different countries to be enrolled in the pilot, as well as the WHO staff from headquarters and other regional offices.

Following the meeting there was a great deal to follow up on. One key task was helping to redraft the surveillance document and specimen submission form taking on board the comments made at the meeting. I also began the process of creating a pamphlet for health care professionals who would be involved in the RSV surveillance pilot at the sentinel sites. Sadly 6 weeks was far too short a time period for an internship, with most interns working for at least 2 months, and I had to leave with some work left unfinished. I will however hopefully continue to be involved with GISRS peripherally from Edinburgh.

A particularly sad part about leaving was having to say bye to all the incredible people I met during my internship. As well as the staff, I met some wonderful people interning at the WHO and other UN organisations in Geneva. Being surrounded by a community of like-minded people with the most inspiring ambitions for their futures was truly electric. From weekend trips around Europe, hiking the Alps, and BBQs by Lake Geneva, to attending meetings and fascinating seminars together at the WHO, I made some unforgettable memories and had my mind-opened to lots of new public and global health concepts.

It was an utterly unique experience to be part of the team working on the preliminary steps that will hopefully lead to global RSV surveillance. This internship has most certainly bolstered my enthusiasm for global health and has provided me with new skills and key knowledge in virus surveillance and pandemic response, as well as some great contacts and lovely memories with new friends. I cannot thank Professor Harry Campbell and Dr Wenqing Zhang's team at the WHO enough for providing me with this opportunity.



**Photo: The 2016 interns (including Ariadne L'Heveder) with Dr Margaret Chan, the WHO Director-General**





# Good medical practice in a time of chronic disease: time to retrace our steps?

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**A**cross the world, a wide range of non-communicable diseases, drug resistant infections and infectious ailments flourish. Yet the ability of doctors to tackle the multiple morbidities of patients is increasingly limited. I believe this is part due to the ill-defined role of doctors in tackling population health issues such as the structural determinants of health which shape the social conditions in which disease thrives. Here I draw on historical examples to put forward the case that medicine needs to re-envisage the role of the doctor and put greater value on preventative measures. I use the example of the National Health Service (NHS) in the United Kingdom to discuss the challenge and opportunities of uniting clinical practice and public health in the common goal of addressing today's greatest health challenges.

In the midst of great technological advances and societal change worldwide, the role of doctors, and health care more broadly, within broader health systems is increasingly unclear. In high- and low-income settings traditional medical approaches are of limited effectiveness in reversing the rise in non-communicable diseases, however, much of the discourse continues to be grounded in the doctor-patient relationship, with little mention of broader population health needs. Doctors through their position as health care providers and role as advocates have great opportunities to address the social determinants of health, however, the precise role and responsibility of doing so remains ill-defined. The nature of modern health care is such that we simultaneously increase prescriptions of costly medications and broaden access to high-tech interventions, yet do little to tackle the social milieu in which disease flourishes. Over

recent years an array of health problems ranging from burgeoning childhood obesity rates to emerging infectious diseases and antimicrobial resistance have developed which a variety of long term consequences with poor prospects for curbing downstream effects.

Reversing such trajectories needs action at all levels, aligning efforts across primary care, secondary care and public health, both within and between nations. At a time when disease is increasingly driven by macro-level determinants (eg, non-communicable diseases) and collective action problems (eg, antimicrobial resistance), there is a growing need for doctors to take greater consideration of, and responsibility for, population health. This is not just a responsibility of public health professionals. Tackling issues such as antimicrobial resistance relies addressing the challenges faced on the individual clinician level as well as the overarching systems which perpetuate the problem. It is

*In contemporary society, a wide range of non-communicable diseases, drug resistance and infectious ailments flourish. Yet the ability of doctors to tackle the multiple morbidities of patients is increasingly limited. This is part due to the ill-defined role of doctors in tackling population health issues such as the structural determinants of health which shape the social conditions in which disease thrives.*



**Photo: Rudolf Ludwig Karl Virchow (1821-1902), a German physician known for his advancement of public health. Photo via Wikimedia Commons from the US National Library of Medicine, who believes this item to be in the public domain.**

clear from the responses of the Royal Colleges to Strategic review of health inequalities in England post-2010 (*Fair Society, Healthy Lives*) that there is overwhelming agreement on the institutional level that action should be taken by doctors, yet little focus on how [1]. Social determinants of health and the inequalities which result must be seen as fundamental to what doctors do, not an insulted occurrence distinct from medicine. Fundamentally this ambition hinges on ensuring medical training is designed to meet today's population health needs. I believe it is time to re-trace our steps and learn from the past in order to address the challenges ahead.

Historically, the close association between health and society was extensively discussed, particularly around the mid-19th century by medical visionaries such as Rudolf Virchow. During his investigation into the typhus epidemic ravaging Upper Silesia, Germany in the late 1840s, Virchow explored the relationship between social conditions, poverty and disease, leading him to the now famous decree: "Don't crowd diseases point everywhere to deficiencies of society?". His prescriptions which focused on addressing the social conditions and resource inequalities of the impoverished population, rather than medical interventions, met with considerable resistance within local government. Whilst this philosophy was not widely welcomed at the

time, across the world prominent physicians such as William Chadwick in the United Kingdom, Louis-René Villermé in France and Charles Hastings in Canada were reaching similar conclusions and transforming the face of medicine. This period ushered in sweeping public health reforms which provided clean water, sanitation systems, improved food standards and better living conditions. Collectively these had a transformative effect on population health, improved social conditions and have left a lasting public health legacy still felt today.

Whilst "social medicine" has a history extending farther back to the Hippocratic Corpus and beyond, the academic discipline was developed during the interwar years. In the United Kingdom, interestingly it was a surgeon—John Ryle—who was one of the movement's pioneering voices. Working alongside other newly appointed professors of social medicine, such as Thomas McKeown, he helped lay down a framework of primary prevention running counter to the prevailing narrative of doctors simply as curers, and health the absence of disease. Contemporaries such as Michael Marmot have since built upon the intellectual foundation of social medicine principles, focusing attention on health inequalities and demanding a reconciliation of social medicine principles with modern medical care. Recognition of the close relationship between health and social circumstance is fundamental to global health discourse and international health practice, however, the implementation of these principles in high-income settings is less commonplace.

For example, in the United Kingdom, the General Medical Council (GMC) which sets the parameters for medical practice (*Good Medical Practice*) [2] continues to rest little weight on public health principles. 'Public health' is mentioned only with regards to the duty to "Respond to requests from organisations monitoring public health"; the overriding focus is on care for the individual patient. *Tomorrow's Doctors* [3], the counterpart guidance on medical education lays considerably more emphasis on the broader responsibilities of the doctor. For example, *Outcome 1 (Doctor as Scholar)* paragraphs nine (*Apply Social Science principles, method and knowledge to medical practice*) and ten (*Apply to medical practice the principles, method and knowledge of population health and the improvement of health and health care*). However, *Outcome 2 (Doctor as Practitioner)* gives no attention to the means or considerations in enacting these principles. This discontinuity reflects the broader lack of guidance for clinical doctors in balancing dual responsibilities to the patient and the population. This deficiency has been particularly challenging for collective action problems such as antimicrobial resistance in which the choices of doctors may have adverse effects for others in the community (ie, spread of resistance), even when done in treating the individual in her best interests.

Over recent decades the role of the doctor has retreated from the forefront of medical ethics into the technical sphere of disease. This transition has contributed to an environment in which the role of clinical doctors in improving population health through their daily practice is culturally undermined. Yet, it is also increasingly recognised that no matter how good clinicians are, once patients reach the hospital, or possibly even primary care facilities, it can be too little too late to cure the individual and a sunk cost for the public purse.

Doctors, politicians and the general public in most settings tends to agree that a good health system requires integration between community and hospital care, and that prevention is preferable to cure. Working together to achieve this objective is imperative; whilst priorities may differ, policy must be guided by evidence rather than be blinded by good intentions. This has clear global relevance—balancing public health and immediate clinical needs is a challenge for any health system but these should be clearly set out. Problems as diverse as the Ebola Virus Disease outbreak in West Africa and the rise in antibiotic resistance highlight the intimate relationship between medicine and social context which impacts on the local, national and global level. During the clinical encounter, today's doctor should of course be wholly committed to the patient in front of them, however, we must face head on the limitations of this approach to effectively improve population health in an era of globalisation and rapid social change.

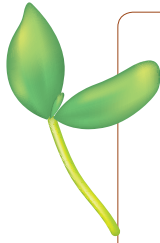
Acting on this sentiment requires interventions at all stages of medical training, underpinned by an ethos which understands and values these ideals. Achieving this change requires that skills are taught in creative and inspiring ways, and values are rooted in a value system which puts injustice and inequality at the heart of medical practice. General practitioners have a particularly important and opportune role in driving this change. Primary care offers the opportunity to implement primary prevention and improve health, not simply treat disease. Doctors ultimately need time to understand the social determinants of health

I draw on historical examples to put forward the case that medicine needs to re-envision the role of the doctor and put greater value on preventative measures. I use the example of the National Health Service (NHS) in the United Kingdom to discuss the challenge and opportunities of uniting clinical practice and public health in the common goal of addressing today's greatest health challenges.

in their communities—local, national or global—in order to build their skills in epidemiology and public health, and finally to take action and effect change. Therefore, this needs a system wide change which gives doctors space during their training and clinical careers to build relationships across health and other agencies, with encouragement to do so, and emboldened vision to make primary health care for all a reality.

At this testing financial time for health services across the globe, additional duties clearly cannot be given to doctors without the means to fulfil them. However, a first step is recognising the importance of this issue. In the United Kingdom, one clear starting point is for the GMC to establish public health as a core duty of doctors in *Good Medical Practice*. The role of the GMC is to “protect patients and improve medical education and practice across the UK” [4]; an overt focus on individual doctor–patient interactions does not maximise this mandate. Incorporating a population health approach into medical practice would help redress the inadvertent adverse effects of the hyper-specialised health care model which modern health systems have increasingly adopted. It could also help ensure medicine is distinguished by an attitude to care for people, not just the ability to diagnose and treat. Addressing the gap between public health practitioners and clinicians in addressing this challenge will thus necessitate a far broader discussion than possible here but should include: the role of nurse–practitioner in primary care and other non–fully trained medical personnel (eg, physician associates) in delivering medical care, the role of the internet and technological innovations in health care provision, and the implications of privatisation on health and social care provision.

John Ryle latterly left a career in surgery to become the world's first Professor of Social Medicine, amongst his extensive writings he argued that “as we direct our students, so in large measure must the outlook and method of each new generation of doctors be determined” [5]. I believe this point must be clearly stated—principles should be enshrined into the work of a doctor, lest the ambition encapsulated in the idea be lost in implementation. This needs a modern re-conceptualised framework of the roles and responsibilities of the doctor which better reflect the multidimensional origins of disease and the greater potential of the medical profession to improve population health. Taking the issues seriously means realising the importance of effective advocacy, and empowering doctors to take on a greater role in protecting and improving the health of populations in an era of chronic disease. Ultimately, by recognising the limitations of clinical medicine to improve the health of our patients and the local populations they are part of, this could nurture an environment in which doctors can take a more prominent role wherever they work to address broader health determinants.



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# The return of the Traditional Birth Attendant

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The World Health Organization has noted much progress towards the realisation of Millennium Development Goals related to maternal and child health. Eighty percent of women in many developing economies now receive at least one visit during pregnancy by a skilled birth attendant (although only 52% had the recommended four visits), and 68% of women across developing regions receive skilled health attendant care (up from 56% in 1990). However, disparities follow regional and urban–rural gaps. Sub-Saharan Africa and Southern Asia lag behind other regions in the provision of antenatal care and skilled attendance at birth (although typically attended by a family member or villager) and over 32 million of the 40 million births not attended by skilled health personnel in 2012 occurred in rural areas. Overall, one-quarter of women in developing nations still birth alone or with a relative to assist them.

While increased numbers of medically-trained midwives and health workers or midwife assistants would increase coverage by up to 40%, these are longer-term solutions. In

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the short term, gross disparities in services in some resource-poor areas have been alleviated by recruiting Traditional Birth Attendants (TBAs) re-trained in emergency obstetric skills to deal with emergency situations and to refer women onto health facilities when necessary. Samoa and Bangladesh are examples. For many women for a range of reasons TBAs are preferable to hospital care. It therefore makes sense to recognise their place within maternity care, to offer basic and ongoing training and to set up registration procedures thus better ensuring the monitoring of outcomes. Incorporating TBAs into the formal health care system would meet both physiological and relational components of birth. In terms of the latter, TBAs would act as cultural brokers between Western and traditional cosmologies and provide women with continuity of care from a known carer; in the West a demonstrably simple but effective intervention promoting physiological safety and reducing the need for higher level medical interventions.

## HUMAN RIGHTS, MILLENNIUM DEVELOPMENT GOALS AND MATERNITY CARE

Despite reiterations of human rights declarations and conventions from 1945 to the present, including revised Millennium Development Goals (MDG) calling for a 75% reductions in Maternal Mortality Rates (MMRs) by 2015, outcomes in some areas remain significantly unchanged leading to a cumulative downward cycle of poor health for offspring, sustained poverty and incremental social disadvantage. MDG3 aims to promote gender equality and empower women, MDG4 calls for reduction of infant mortality by two thirds; and MDG5 calls for improvement to

maternal health. None has been realized to expected levels. Baseline data from 1990 figures showed that over a 15-year period to 2005 maternal deaths decreased by 5.4%; an average of 0.4% per annum although none of the eight regions targeted achieved the goal of 5.5% p.a. reduction. Very little progress was made in sub-Saharan Africa and Southern Asia and although progress was made compared to baseline data the level of skilled birth attendants (SBAs) remained low. Other regions increased their provision of SBAs but failed to catch up to the developed world and fell well below the targeted 80% reduction in MMRs and IMRs. Only 47% of women received four antenatal visits during pregnancy – an unchanged percentage from baseline – although more women (79% up from 64%) received some antenatal care (MDG 5B). Taken as a whole, developing countries increased Skilled Birth Attendance (SBA) from 43% at baseline to 57% but the target of 90% by 2015 has remained an unrealised aspiration and will remain so for the near future [1,2].

According to the World Health Organization (WHO), fresh remedial strategies and pragmatic advice is required around cost-effective interventions to address the major causes of child mortality–pneumonia, diarrhoea, birth asphyxia, pre-term birth/low birth weight and neonatal infections–and maternal mortality–post-partum haemorrhage (PPH) hypertensive disease, obstructed labour and complications associated with unsafe abortion. Although data are approximate only, sources indicate that around 99% of maternal deaths occur in developing countries (and the majority of those in Northern Africa and Southern Asia) [1,3]. There have been substantial advances in many countries during

the past 40 years, viz. Thailand, Malaysia, Sri Lanka and Egypt and Honduras. In rural Bangladesh, where women continue to birth at home without a professional attendant, the MMR declined by 25% over 25 years from 1976 to 2001 due to better access to surgical obstetric care, reduced fertility, lower abortion rates and improved health generally [1]. Progress was also made in eastern and southern Africa where maternal mortality fell from 740 to 410 deaths per 100 000 births. However, advances are slow and most nations in the region failed to realise the MDG5 goal to reduce maternal deaths by three-quarters by 2015. Child mortality is closely related to maternal mortality but no change has occurred in the same region where over half of the births occur at home without skilled assistance or a postnatal visit within 48 hours after birth. Cord care, infection control, management of emergencies, especially postpartum haemorrhage–the leading cause of maternal death–and referral to expert care are obvious remedial measures not made readily available to these women and families.

## THEN WHY BIRTH AT HOME?

Around three-quarters (74%) of maternal deaths are considered to be preventable although women commonly face barriers in accessing facility-based birth. Shiferaw et al confirmed that 78% of lower-income and lower-educated women in Ethiopia chose a TBA; 42% reported it was not necessary to attend a facility (often meaning their husbands considered it unnecessary), 22% attributed the decision to the cost of formal maternity care, 36% said facility birth was not customary and 8% cited long distances or lack of

transport [4]. Other women in Rosen et al's direct observational study of over 2000 births in facilities across fifteen poor-resourced nations found much disrespect and abuse in facility-based care, mostly in the form of abandonment and neglect [5]. The same studies found that appropriately trained TBAs represent a viable solution to the new call by WHO for innovative and pragmatic arrangements to provide all women with a skilled birth attendant.

## REMEDIAL STRATEGIES TO REDUCE MATERNAL MORTALITY RATES AND INFANT MORTALITY RATES

In this regard, health visitor training and training of new entrants to Bachelor of Midwifery programs comprise longer-term interventions given the shortfall in the numbers of females at primary, sec-



Photo: By hdptcar (Flickr User) [CC BY 2.0 (<http://creativecommons.org/licenses/by/2.0>), via Wikimedia Commons]

ondary and tertiary level education especially in sub-Saharan Africa, Oceania, Western Asia and Northern Africa (although females enrolments have increased in Latin America and the Caribbean). More immediate measures include family spacing, contraceptive use and the provision of at least four antenatal visits. UNFPA [3] recommended recruitment of village midwives: a surprising initiative given the joint WHO, UNFPA and Safe Motherhood (Safe Motherhood Initiative (SMI) comprising United Nations, ARROW and the White Ribbon Alliance) statement in the 1990s recommending scaling down Traditional Birth Attendants (TBAs) on the grounds they failed to reduce MMRs and IMRs over the accounting period.

However, as others have noted since, the WHO/UNFPA/SMI decision to deter TBA integration into the formal maternity care system in the early 1990s was hastily conceived [6]. For many years in the 1970s and 80s, TBAs were germane to equity considerations. WHO-sponsored programs had trained them in antenatal, intrapartum and postpartum skills to detect early complications, ensure timely referrals and to reduce infection and postpartum haemorrhage (PPH). By the 1990s, however, WHO declared the TBA initiative had failed and henceforth only medically-trained midwives or nurse practitioners would be installed because only they could identify obstetric risks and be trusted to refer women onto a clinic or hospital [7].

The problem with rescinding TBA endorsement was that WHO had failed to establish a baseline measurement in the 1970s which meant it was impossible to fairly judge TBA performance after a twenty year trial. And accurate recording of birth data remains a significant problem in assessing efficacy of any initiative [8]. The complexity of the problem grows when factoring in the social determinants of health such as poverty, illiteracy, lack of easy access to facilities including impassable roads, lack of transport, poor general health of mothers and the involvement of other community actors, such as family and village elders as causal agents. In summary, developing countries have diverse and complex historical, social, cultural and geographical barriers that need to be inserted into the causal matrix of risk factors accounting for MMRs and IMRs [9]. It also means there is no one strategy that will alleviate the problem although the medical solution generally is a rapid shift towards professionalization of care-givers in the antenatal, intrapartum and postnatal periods [10].

## WHY TBAs?

From the medical perspective, tackling maternal mortality requires upscaling the availability of medically-trained teams of midwives and midwife assistants in health facilities attending mainly to intrapartum care but also to ante-

natal and postpartum care, family planning and safe abortion [11]. Measures to manage PPH are tantamount since it is the single most important risk factor in determining high or low MMRs. But the problem remains in filling the gaps in the interim period between now and accreditation especially when the pool of educated school leavers remains small.

Some nations such as Pakistan, Bangladesh and Samoa not only educate TBAs but are prepared to recognise their tacit skills and knowledge including the use of traditional bush remedies. Further, their embeddedness in traditional cosmologies, cultural rites and social protocols means they act as cultural brokers for women who typically blend medical care with traditional TBA care [12,13] for a range of reasons—social, cultural, financial, and medical.

Some medical commentators are reluctant to endorse the use of other than strictly medically-trained professionals on the grounds they lack academic training, clinical opportunities and a supportive medical environment. However, as UNFPA later realised, TBAs could provide the pragmatic response urgently sought by WHO to meet 2015 Millennial Development Goals and Beyond if trained in the use of medications such as Misoprostol for abortion, medical management of miscarriage, induction of labour, cervical ripening before surgical procedures, and the treatment of postpartum haemorrhage. TBAs could also be trained to use the non-pneumatic AntiShock Garment for postpartum haemorrhage and the haemoglobin colour scale for screening anaemia in pregnancy [14]. Other preventive medications include low dose aspirin and calcium supplementation to reduce the risk of pre-eclampsia. With the addition of other key medical supplies such as antibiotics, magnesium sulphate for eclampsia and safe blood supplies, TBAs could provide greater coverage in areas of greatest deprivation [15,16].

Whilst they could not replicate high level obstetric techniques such as caesarean section or administer an oxytocin drip to arrest PPH or deal with drugs that require refrigeration, other medications available in tablet form, like Misoprostol, could be administered with good effect. The argument is that better coverage in poor resource nations could be achieved by recognising the skills of those already on the ground who, for many women, are currently the carer of choice for a variety of reasons. There is also the point that regardless of whether they are endorsed officially by the health system, or not, women continue to consult them for birth and physical ailments because they often double as village healers using traditional medicines harvested from the bush. In remote areas of Vanuatu, for example, while not endorsed by the health system, rural women typically split their care between the local TBA and the hospital/health post and many of the midwives and

doctors recognised their skills and expertise [13]. In Samoa, TBAs are recognised as valuable adjuncts to the formal maternity care system [12] working collaboratively with staff at Level 1 EmOC facilities (health centres with capacities for administering oxytocin, antibiotics, anticonvulsants, manual removal of the placenta, vaginal delivery and resuscitation) and at Level 2 EmOC facilities (that carry out caesarean section and safe blood transfusion) [17].

## THE RELATIONAL COMPONENTS OF BIRTH

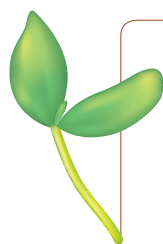
But there is another issue. Whilst the WHO and UNFPA provision of skilled medical care could decrease 79.9% of maternal deaths, medical expertise comprises only one aspect of “a good birth” [3,18]. Quality of care extends to the *relational* components of birth, namely a known and trusted carer (a rare event still in most Western arrangements), respectful dialogue and practices, consensual care, tolerance for informed *dissent* and provision of information and privacy but these aspects of birth have received less attention from policy-makers and providers [19] obviously because of the urgent need to address the physiological aspects of ensuring safe birth. In the case of rural and remote mothers who are either reluctant or unable to attend a health facility (see above), TBAs are ideally placed to act as cultural brokers between Western medical and local, situated knowledges. The utility of relational components (considerations of individual preferences, sacred practices prioritised by the local community and shared cultural values) is affirmed by the success produced by midwifery-led models offering one-to-one care with a known carer [20].

The Department of Health in UK is now committed to providing universal one to one care in labour to promote normality and reduction in intervention such as caesarean section as are Scottish and Welsh governments who found that women preferred continuous one-to-one care from a known carer they trusted (not just a midwife). In Australia,

women assigned to caseload models (continuous care in all phases from a known and trusted midwife, with some backup from others) achieved higher rates of spontaneous vaginal birth, lower CS, epidural, episiotomy rates and babies were less like to be admitted to special care or neonatal intensive unit. Cochrane Collaboration reviews have concluded one-to-one care resulted in spontaneous vaginal birth, shorter labour, less use of analgesia in labour and babies with a low Apgar score at 5 minutes and generally reduced intervention [20]. Although the studies cited were conducted in Western locations, the evidence is convincing that a known carer especially one trained in emergency medical and obstetric techniques not only expedites safe birth but also fulfils human rights criteria, namely choice and interpersonal respect while facilitating ease of birth.

This is because bodies are not just physical entities but cultural resources that bend and move in relation to the social and cultural environment. Birth is an embodied phenomenon rather than a set of isolated physiological processes [15]. Respectful and collaborative practices are not simply “soft” add-ons but translate into better physiological outcomes. The UNFPA revised decision (based upon the Somali review of maternity care and other more recent studies by Sibley et al [16]) found that TBAs were a valuable addition to the maternity care arsenal in developing economies because they enacted a horizontal model of knowledge where no one individual holds a dominant authoritative position and where the body is seen at the intersection of nature and culture.

In summary, given the need for immediate and pragmatic solutions to enduring problems facing remote and resource-poor women, TBAs are ideally placed geographically and culturally to administer basic but potentially life-saving medical and emergency care, to provide antenatal and postpartum care and to refer women with risk factors to formal health facilities. They could be registered and offered regular refresher courses thereby contributing to lower maternal and infant mortality and morbidity rates.



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# Strengthening paper health register systems: strategies from case studies in Ethiopia, Ghana, South Africa and Uganda

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Health information systems (HIS) include a spectrum of data collection tools that support clinical decision-making; facilitate tracking of patients, drug stock, and disease trends; and inform policymaking [1]. As intermediaries between individual patient records and population-level data, health registers occupy a unique space in HIS. Health registers are “a collection of records containing data about aspects of the health of individual persons” [2].

Paper health registers can be books, folders, or forms that include individual-level data for a population. Paper registers are primarily used at the facility level, though they can serve as inputs to higher level reporting. Because they serve health providers, program administrators, and health management decision-makers, registers can sometimes fail to meet all stakeholder identified needs. Studies of paper registers frequently document data quality challenges which compromise efforts to deliver effective care.

Despite the global shift toward digital data collection, there remain low-resource settings that are unable to support the infrastructure required for electronic register systems. For these settings, strengthening paper health register systems can bolster evidence-based decision-making in patient encounters, program planning and policy, and serve as a first step toward improving quality data in HIS as they shift toward electronic systems.

## STRATEGIES FOR IMPROVING PAPER REGISTER SYSTEMS

We developed case studies on innovations in paper health register systems in low-resource settings in Sub-Saharan Africa. The resulting studies were informed by 14 expert interviews (2–4 per study) and 101 documents, including peer-reviewed and non-peer-reviewed literature. Case studies are described in **Table 1**.

This commentary synthesizes lessons learned from these case studies, illuminating four successful strategies for optimizing paper health register systems: support local solutions, align with global standards; collect only essential data elements; foster data use and data quality improvement; and invest in strengthening human resources. Within these strategies we identify specific, actionable recommendations that could be applied by policymakers, facility managers, health workers, or others who are interested in strengthening paper health register systems. While these recommendations may be obvious to those who work in HIS, they are not yet well-documented in the literature.

## SUPPORT LOCAL SOLUTIONS, ALIGN WITH GLOBAL STANDARDS

Many of the challenges with registers occur when these systems are designed and implemented by outside stakeholders

**Table 1.** Summary of case studies\*

	ETHIOPIA'S FAMILY FOLDER	GHANA'S SIMPLIFIED REGISTER	SOUTH AFRICA'S 3-TIERED STRATEGY	UGANDA'S TUBERCULOSIS REGISTERS
Health domain	Primary care	Primary care	HIV/AIDS	Tuberculosis
Innovation	Collects patient and household-level information in a folder system; services provided at the individual level are tracked by a tally system.	Condenses all primary health registers into five SRs.	Collects standard, reduced list of essential data elements from facilities using paper or electronic systems.	Records and reports data elements for 22 TB indicators using WHO standardized registers.
Data collection	Collected by health extension workers in the community and at health posts.	Collected by frontline health workers in the community and at health posts.	Collected from clinical stations by data clerks.	Collected by clinical staff, laboratory staff, and frontline health workers.
Data aggregation	Data aggregated at the primary health unit, which encompasses five to ten health posts.	Data aggregated at the district, regional, and national levels.	Data aggregated at the district, regional, and national levels.	Data aggregated at the district, regional, and national levels.
Integration into national systems	As of February 2014, 75% of health posts in the country use the FF.	MoTeCH implemented the SR in four regions.	Established as national standard for HIV programs in December 2010.	National standard since 1990; TB/HIV collaborative registers since 2005.
Decision-making	Data used to optimize decision-making at the local level and to prioritize doorstep care.	Data informs patient care decision-making and defaulter tracking.	Data used for regional and national decisions; district and facility-level decision-making is slowly growing.	Data used for national decision-making and international monitoring of TB indicators.
Plans for future sustainability (as of 2014)	Scale-up is continuing.	There is not yet a commitment for national adoption of the SR.	All facilities plan to move from paper toward the electronic tiers over the next few years.	TB/HIV collaborative activities will continue to be supported.

ART – Antiretroviral treatment, FF – Family Folder, MoTeCH – Mobile Technology for Community Health, SR – Simplified Register, TB – Tuberculosis, WHO – World Health Organization

\*All case studies are publicly available at: <http://www.technet-21.org/en/discussions/tags/case-studies-on-paper-immunization-registers>.

not aware of the needs and constraints of frontline register users or the HIS that are already in place.

Externally-led efforts can take away a sense of ownership within the health system, result in duplicate data collection, and often increase system fatigue. Frontline health workers may not use registers they find unsatisfactory, and local health authorities may not endorse registers that fail to meet their needs. These case studies demonstrate that register systems inspired by grassroots solutions are often more accepted and more likely to be successfully scaled. Yet global and national standards are essential for consistent measurement and comparability of key health indicators [3,4]. While the data points included in registers should be aligned with global standards, standard registers designed by global organizations may not satisfy local needs. Recommendations include:

- Once a problem with the register is identified, connect with frontline register users who encounter that problem for insight
- Invest in buy-in meetings during planning and implementation to bring multiple stakeholders together
- As the register matures, hold periodic stakeholder workshops to sustain support at all levels

## COLLECT ONLY ESSENTIAL DATA ELEMENTS

Data proliferation is a challenge in all HIS but is magnified in paper registers. Efforts to improve efficiency should

be undertaken with attention to the register's purpose and the broader HIS. An important first step in register design is to explicitly determine whether the register needs to inform clinical decision-making, reporting, or both. While stakeholders may generally accept that non-essential data elements should be trimmed, determining how to judge an element as non-essential requires compromise and can be a major challenge. For some health domains, international guidelines stipulate a minimum data set that can be used as a starting point. Integrating vertical health programs and their registers can consolidate the data points collected in a given register. Recommendations include:

- Consider using registers for either patient care or reporting needs (not both) if their dual purpose is detracting from data quality and use.
- Assess which data elements must be reported; define an essential data set.
- Look to internationally agreed upon case definitions and indicators to design a core set of data elements.
- Design official register systems or updates that complement each other for linked areas of care.
- Minimize indicator duplication across health domains.
- Optimize reporting mechanisms, not just content within reports.
- Use an alternative to traditional registers to link individual to aggregate data.

Client identification, contact and personal information										Immunization & Growth Monitoring History		Immunization and Growth Monitoring															
Reg. Date	Serial #	Reg. #	Project ID #	Name First and Surname	Sex	Date of Birth	Location/ House Address	Telephone #	Mother's Information	Information from previous year or from another health facility or provider	January				February				March				April				
											Dose	Date	Dose	Date	Dose	Date	Dose	Date	Dose	Date	Dose	Date	Dose	Date	Dose	Date	
					M				Mother's Name:	BCG [at birth]		BCG [at birth]		BCG [at birth]		BCG [at birth]		BCG [at birth]		BCG [at birth]		BCG [at birth]		BCG [at birth]			
					F				Mother's Registration #:	OPV 0 1 2 3		OPV 0 1 2 3		OPV 0 1 2 3		OPV 0 1 2 3		OPV 0 1 2 3		OPV 0 1 2 3		OPV 0 1 2 3		OPV 0 1 2 3			
									Mother's Project ID #:	Penta 1 2 3		Penta 1 2 3		Penta 1 2 3		Penta 1 2 3		Penta 1 2 3		Penta 1 2 3		Penta 1 2 3		Penta 1 2 3			
										Rotavirus 1 2 3		Rotavirus 1 2 3		Rotavirus 1 2 3		Rotavirus 1 2 3		Rotavirus 1 2 3		Rotavirus 1 2 3		Rotavirus 1 2 3		Rotavirus 1 2 3			
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										Measles 1 2		Measles 1 2		Measles 1 2		Measles 1 2		Measles 1 2		Measles 1 2		Measles 1 2		Measles 1 2			
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										Vit. A R B		Vit. A R B		Vit. A R B		Vit. A R B		Vit. A R B		Vit. A R B		Vit. A R B		Vit. A R B			
										IPPI 1 2 3		IPPI 1 2 3		IPPI 1 2 3		IPPI 1 2 3		IPPI 1 2 3		IPPI 1 2 3		IPPI 1 2 3		IPPI 1 2 3			
										CSM 1 2		CSM 1 2		CSM 1 2		CSM 1 2		CSM 1 2		CSM 1 2		CSM 1 2		CSM 1 2			
										Dewormer (#)		Dewormer (#)		Dewormer (#)		Dewormer (#)		Dewormer (#)		Dewormer (#)		Dewormer (#)		Dewormer (#)			
										WT (kg)		WT (kg)		WT (kg)		WT (kg)		WT (kg)		WT (kg)		WT (kg)		WT (kg)			
										Growth Mon %		Growth Mon %		Growth Mon %		Growth Mon %		Growth Mon %		Growth Mon %		Growth Mon %		Growth Mon %			
										MUAC (cm)		MUAC (cm)		MUAC (cm)		MUAC (cm)		MUAC (cm)		MUAC (cm)		MUAC (cm)		MUAC (cm)			
										Ht (cm)		Ht (cm)		Ht (cm)		Ht (cm)		Ht (cm)		Ht (cm)		Ht (cm)		Ht (cm)			
										Male Invl. Yes No		Male Invl. Yes No		Male Invl. Yes No		Male Invl. Yes No		Male Invl. Yes No		Male Invl. Yes No		Male Invl. Yes No		Male Invl. Yes No			
										Location F H O S		Location F H O S		Location F H O S		Location F H O S		Location F H O S		Location F H O S		Location F H O S		Location F H O S			
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Image: Page from the Ghana Simplified Health Register. Courtesy of the Upper East Regional Health Directorate, Ghana Health Service and the Heilbrunn Department of Population and Family Health, Columbia

## FOSTER DATA USE AND DATA QUALITY IMPROVEMENT

The need to improve data quality was repeated by experts across all four case studies and is of central importance in strengthening register systems. Commitment to utilizing data for evidence-based decision-making is essential at all levels of a register system. When data are of high quality, it is more likely to be used by stakeholders at every level, and when data are considered to be useful it may be collected and aggregated more carefully. Designing registers to support flexible workflows may improve service delivery, register use, and data quality [5]. Efficient guidelines, trainings, and monitoring systems support the correct use of registers. Recommendations include:

- Format registers to support and inform patient care.
- Consider service delivery patterns, including location of service delivery, in register design.
- Allow for variations in register use to support workflows.
- Skip or abbreviate historical data capture for certain types of patients.
- Field-test the register to understand how the full product will be used.
- Include instructions for data collection and reporting on the register itself.

- Design an internal audit system to standardize data quality monitoring.
- Collect register usability data from frontline register users alongside other ongoing monitoring and evaluation efforts.

## INVEST IN STRENGTHENING HUMAN RESOURCES

People who initiated and sustained improvements within these four case studies had various combinations of passion for data, willingness to mentor, and creativity to think differently about register design. Political support at all levels improves the implementation process and contributes to the sustainability of the register system. Key informants across all four case studies identified human resource constraints as a major challenge to the implementation of health registers. These challenges include both lack of personnel and lack of proper training. Human resource interventions should facilitate engagement with register systems. Recommendations include:

- Use peer-to-peer training models
- Enlist influential public figures for training activities to increase worker buy-in
- Recruit key “change agents” to leadership positions within the register system, and encourage their professional growth

- Design staff positions that can easily task–shift as the register system matures
- Relieve the burden on health providers by allocating activities to data clerks
- Ensure that there is dedicated staff time to support the register system at the district or sub–district level
- Implement a supportive supervision model at the district– and facility–level to encourage decision–making with data from the registers

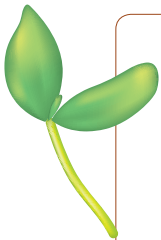
## LIMITATIONS

Efforts were made to include experiences from different geographies, health domains, and stakeholders to best capture the common strengths and challenges faced by paper health registers. The recommendations revealed through these cases are influenced by the particular case studies that were selected and the sources that were most accessible to the researchers. Conclusions may not be generalizable to other contexts.

## THE WAY FORWARD

Paper health registers are important tools in HIS and will continue to occupy a critical role in health service provision, administration, and reporting in many low–resource settings. However, implementing changes to these systems requires commitment of time and resources, and must be approached strategically to avoid system fatigue. Thus, it is important to consider adjustments and updates to multiple aspects of the system. Additional costing studies or operational research could identify efficiencies and reallocate resources toward the most promising solutions. Documenting and sharing lessons learned in other existing HIS can provide additional knowledge to continue to improve these systems.

These cases reveal that there are numerous factors outside of a register's physical attributes that can be addressed to strengthen register systems, including innovative human resource models, policymaking, and implementation strategies. Many stakeholders—including funders, policymakers, public health officials, and health providers—can be a part of strengthening paper register systems to support accurate reporting, evidence–based decision–making, and improved patient care.



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# Emergency medicine and global health policy: history and next steps

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The transformation of global health and the specialty of emergency medicine are both relatively new phenomena. Over the last three decades, they have developed rapidly and in parallel. Utilizing a review of the recent changes of global health policy and practice, and a review of the changing nature and understanding of the global burden of disease and its intersection with emergency medical care, this paper attempts to demonstrate missed opportunities to support the development of emergency medicine on a global scale. This paper also seeks to highlight the need for improved alignment between the global burden of disease, global health policy-setting, and emergency medicine development.

Emergency medicine is a relatively new medical specialty that, when implemented, provides rapid management of acute critical illness and injury. The specialty of emergency

Emergency medicine is a relatively new medical specialty that, when implemented, provides rapid management of acute critical illness and injury. The specialty of emergency medicine allows health care providers to adjust their scope of practice to respond to both the immediate situation and the long-term needs of their community. It supports other branches of medicine by freeing them to practice their own specialized skill set, by providing emergent supportive care, and by serving as a directed gateway to the most appropriate levels of healthcare delivery.

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Regions that have weak or dysfunctional emergency medical services, or have not yet established emergency medicine as a specialty, are at risk for avoidable morbidity and mortality. The resulting impact on individual and population health creates an avoidable social and economic burden. Global burden of disease projections indicate that the developing world should expect more trauma and injury, higher rates of chronic illness, and changes related to urbanization [1]. Yet global health priority setting and funding allocations have failed to address the predicted increased need for emergency medical services. The global community has an opportunity and a responsibility to prioritize emergency medical care through policy changes and investment in education, awareness, and infrastructure to meet the needs of our evolving health care environment.

## RECENT GLOBAL HEALTH POLICY AND PRACTICE AND EMERGENCY MEDICINE

Highlighting some recent developments in global health policy demonstrate disconnect between global health care needs and resource allocation.

The Millennium Development Goals (MDGs) (2000) had potential through global governance to guide funding and policy but has also resulted in unbalanced aid and devel-

opment. MDGs related to emergency medicine include: MDG 1: eradicate extreme poverty and hunger, MDG 3: promote gender equality and empower women, MDG 4: reduce child mortality, MDG 5: improve maternal health, MDG 6: combat HIV/AIDS, malaria and other diseases, MDG 7: ensure environmental sustainability and MDG 8: develop a global partnership for development. However projects and funding have not been allocated in response to burden or need. For example: Concerning MDG 6 an analysis of “official government assistance funding (ODA),” MDG 6 constituted approximately 50% of all health expenditure (1999–2009) with one half of that money going to just 10 countries representing only 21% of the population of least developed countries. In addition, MDG 5, represent only 10% of official development assistance, far below the actual burden of maternal related health expense.

The attention garnered by the millennium development goals, while robust, has removed emphasis from more rational health system development and policy, of which emergency medical care is an integral component. Greater emphasis on burden of disease, population and individual health, and health as a human right would represent more just and appropriate policy and resource utilization.

Elements of emergency care such as trauma and treatment of acute disease have potential to avoid bad outcomes among youth and working age individuals which disproportionately affect societal function. Yet the focus on specific disease outcomes limits needed systemic change, despite some efforts calling for this such as the World Health Assembly (resolution 60.22 in May 2007) supporting emergency medical services [2].

## CHANGING GLOBAL BURDEN OF DISEASE AND IMPACT ON EMERGENCY MEDICINE

As improved epidemiological data collection and modeling contribute to a better understanding of the global burden of disease, it is apparent that there is a changing nature to health needs. In addition there is a clear overlap between expected needs and emergency medicine. However, this has not resulted in expected shifts in support for emergency medicine. Particular areas of concern are: 1) increases in trauma, violence and road traffic injuries—necessitating emergent timely interventions; 2) increases in non-communicable, chronic disease, such as ischemic



Photo: Courtesy of the author

heart disease requiring rapid focused treatment and 3) continued high burden of communicable, maternal, neonatal disease in the world's poorest and medically underserved places.

The authors of the global burden of disease study have called for “evidence-based health care policy” based on their predicted changes; support of emergency medical services is justified [3].

## CURRENT EFFORTS IN EMERGENCY MEDICINE DEVELOPMENT

Countries where emergency medicine is well established have a responsibility to promote worldwide emergency medicine development. Currently global health and emergency medicine overlap in a constellation of entities, which include educational projects and exchanges, specific areas of focus such as trauma and ultrasound, emergency medical services (EMS) development, and humanitarian related activities. The work of international societies of emergency medicine has made great strides in improving training and awareness [4]. Countless educational programs are making concrete improvements through education at the local level [5]. In some cases policy changes such as recognizing the specialty have been achieved, but transformation of the system has been slow and yet to be adopted on a global scale. Given the haphazard nature of global health policy making demonstrated by the historical analysis above, academic emergency medicine should be making a more cogent effort at influencing the agenda. There remains however ambiguity with regard to structural models and implementation as well as a lack of standardization with regard to education.



## EMERGENCY MEDICINE ADVOCACY: THE NEXT STEPS

### Geographic engagement

Working under the guidance of the Paris Declaration on Aid Effectiveness emergency medicine advocates should continue to work with local, national and regional societies to promote development in an ownership driven manner. Focusing as well on alignment and cooperation has been a recurrent failure in attempts to promote the specialty and training activities as evidenced by many programs working in parallel without cooperation. Development in this regard is complicated and at a minimum must involve needs assessment, the use of pre-existing resources including community involvement, local and national ownership, translation of best practices, and systemic and cultural sensitivity.

### Supporting and influencing NGOs

Large and small NGOs represent a large proportion of global health expenditures and in following their own agendas and mandates influence policy and practical delivery of health services. Academic programs and societies of emergency medicine would also benefit from engaging the many emergency medicine NGOs in existence to improve collaborative efforts and support proven models of development. Some NGOs missions overlap well with development of emergency medical services. These NGOs can be influenced though advocacy highlighting the shared goal of improving population level health care.

### The World Health Organization

To date there has been tangential emphasis placed within the WHO on emergency medical services despite several attempts to highlight the needs and opportunities. This may change with the adoption of several programs at the WHO which have strong overlap with emergency medical services. WHO emergency medicine related areas include, trauma care, hospital and health system disaster preparedness and hospital and essential Medicines standards. While these issues fall under the rubric of emergency medicine, codifying it as such will be necessary to take a next step forward in influencing policy toward emergency medicine development.

### Philanthropy

Philanthropy has long held a disproportionate influence on global health policy. Large philanthropic organizations

sway policy not only through simple financial means, but through collaboration with grant recipients and in the extraordinary publicity they garner. Philanthropic foundations are often very closely tied to industry and exist in a complex environment with competing missions and conflicts of interest resulting in less than transparent policy making. Very few organizations have any explicit focus on emergency medical services and vertical programing is still common. However, emergency medicine can and should be appealing to even those in philanthropic positions of power, as they and their staff are often on the ground in settings without any reasonable emergency medical care. Sadly, as is the case in all situations where medical care is not reliable, avoidable medical disasters do occur, even to those visiting for humanitarian reasons. Highlighting the supporting role emergency medical care can provide to any population (obstetrical, pediatric) or disease entity (malaria, HIV) may also gather support.

### Research and public relations

Emergency medicine can do a lot to support its own development with regards to building a clear and well supported message of improved outcomes and cost efficiency. To date, clear evidence of improved population level gains by the institution of comprehensive emergency medical services has not been established, nor has clear cost-effectiveness or a universally successful model of implementation. Citing particular emergency services entities that have proven cost-effective such as defibrillators, so far has not resulted in systemic change [6].

## CONCLUSION

The call for a global movement towards improved emergency medicine services, while not new, has failed to produce the desired results. This, combined with the window of opportunity due to recent focus on global health, makes re-addressing and re-focusing efforts towards a cogent policy a great priority and opportunity.

While best practices and implementation pathways are not clear, collaboration, assessment and needs driven policy, with locally and national involvement and sensitivity are part of best practices. Persuading global level policy makers to accept that provision of emergency medical services is an essential part of health system development should be the highest priority of those working towards emergency medicine development.

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# Assessing the burden of rheumatic heart disease among refugee children: a call to action

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In a recent editorial in *The Lancet*, Langlois and colleagues are adamant in advocating for a better and more universal access to healthcare for refugees landing in Europe [1]. The arguments of equity, social justice and cost-effectiveness are clearly explained in their comment.

Among the different suggestions to improve the refugees' health, the authors invite the policy makers to opt for strategies favoring the "provision of preventive care, including primary and secondary prevention of cardiovascular disease" which "could generate savings for health-care systems by alleviating the burden of stroke, and myocardial infarction".

Their advice, geared towards the betterment of the refugees' adult population, needs to be further complemented by a strong call for providing primary and secondary preventive care for acquired cardiac diseases in refugee children.

While acute rheumatic fever (ARF) has essentially vanished from industrialised countries since the latter half of the 20<sup>th</sup> century, the condition and its major sequel, rheumatic heart disease (RHD) remains an important public health concern in poor, developing and war-torn countries.

Poverty, inadequate and disrupted primary healthcare systems are major contributors to the persistence and resurgence of ARF/RHD in these countries [2].

The estimate of the global burden of RHD has been recently established at 33 million existing cases, which is higher than the previous conservative 15.6 to 19.6 million cases in 2005 [3]. Emerging echocardiographic data following the seminal work of Marijon and colleagues [4], have contributed in revising these data, suggesting for a higher prevalence of subclinical RHD. In particular, according to a recent meta-analysis by Rothenbuler et al [5], among

The current enormous refugee crisis in Europe represents a paradigmatic translational shift: the health systems of the wealthy countries are now called to deal, in a substantial way, with the poor people and their diseases.

children aged below 18 years from 37 pooled countries, the prevalence of clinically silent rheumatic heart disease (21.1 per 1000 people, 95% confidence interval CI 14.1–31.4) would be about seven to eight times higher than that of clinically manifest disease (2.7 per 1000 people, 95% CI 1.6–4.4). South Asia and some African countries have very high prevalence data [5].

Although the significance of subclinical RHD is still not clear, follow up studies indicate that most Subclinical Definite RHD (according to World Heart Federation Criteria) [6] and at least a proportion of Borderline RHD, are likely to be true RHD requiring secondary prophylaxis [7].

To tackle the evolution of RHD, specific control programs based on the concurrent development of disease registers along with the consistent delivering of benzathine penicillin G injections, need to be strengthened by a decentralized echocardi-based active case finding activities, comprehensively integrated into the existing primary health care services.

In this sense, the World Heart Federation's non-communicable disease action plan is calling for a 25% reduction in premature mortality from RHD by the year 2025 ("25 by 25") [6].





**Photo:** Médecins Sans Frontières assists Syrian refugees in Roske, at the Hungary-Serbia border. Among the refugees arriving in Europe, half of them are children. Courtesy of Ana Lemos/MSF (2015).

Unfortunately, this cost-effective strategy has not been routinely implemented in low-income and middle-income countries, because of the structural weaknesses of their health systems.

The current enormous refugee crisis in Europe represents a paradigmatic translational shift: the health systems of the wealthy countries are now called to deal, in a substantial way, with the poor people and their diseases.

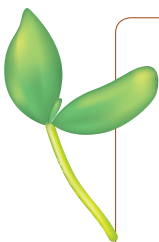
The Syrian children, suffering from more than five years of displacement, have been forced to live in very dire conditions. Being exposed to the effects of the detrimental combination of seasonal harsh cold weather, overcrowding, poverty and very limited access to healthcare [8], they hold the classic risky profile for the development of ARF and subsequent RHD [9].

With an expected echocardiography-based screening detection rate of around 2%, many migrant children landing in Europe (Syrian, Afghan, Eritrean, Bangladeshi, and many others) could be timely identified and placed under prophylactic treatment for RHD. In 2015, more than 1 million asylum seekers arrived in Europe and half of them were children: the figure of 10 000 diagnosed subclinical and clinical RHD could be anticipated. Many more refugees are expected to land in Europe in 2016.

Pilot studies aimed at proving the validity of these assumptions, while assessing the prevalence of RHD among refugee children, are urgently warranted.

Decentralised diagnostic services for ARF/RHD, framed as routine screening through point-of care technologies (echocardiography and antigen tests for the rapid diagnosis of group A streptococcal pharyngitis) should be then considered at migrant/refugee pediatric community level.

In view of the fact that severe RHD is lethal in the absence of surgical treatment, with a death toll of 275 000/year [10], the same arguments of social justice, equity and cost-effectiveness mentioned by Langlois and colleagues should apply here, especially for the silent and marginalized population of refugee and migrant children, often arriving in Europe unaccompanied and defenseless. Europe has the infrastructures, human and financial resources, and knowledge to act accordingly. It must not turn a blind eye to them.



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# Strengthening the evidence base for nutrition and cancer in low and middle income countries

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The rapid changes in nutritional patterns and ways and conditions of life occurring in low- and middle-income countries (LMICs) are likely to be adversely affecting the incidence and survival rates of most cancers. These rapid changes raise challenges and opportunities in research on nutrition and cancer worldwide, and highlight the need for an integrated approach to determine global strategies to better understand, prevent and control the impact these changes are having on the cancer epidemic.

Although awareness of the importance of cancer in LMICs is increasing, there is still the misperception that infectious diseases represent the primary health issue in LMICs, and that cancer risk is not preventable or modifiable, and is not strongly related to nutrition. Historically, infection-related cancers (ie, cancers of the liver, stomach, and cervix) were more common in LMICs. However, the rapid expansion of modern ways of living, dietary patterns and food production observed in LMICs, particularly among the poorest people and communities, is leading to changes in disease

Changing patterns of diet are strong predictors of the increase in cancer and other non-communicable diseases burden in low- and middle-income countries (LMICs). The economic impact of overweight and obesity is as great as that of tobacco use.

patterns and cancer types. Currently, the most frequently diagnosed cancers in LMICs are tumors of the lung, prostate, female breast, stomach, liver, colorectum, cervix, and oesophagus [1]. Taking a global perspective, the number of incident cancers in LMICs reached eight million in 2012 and is expected to continue to rise [1]. While the increase in cancer burden may be partly explained by demographic changes, altered ways of living and dietary factors related to globalization (eg, increased consumption of highly

processed foods, red meat and sugar-sweetened beverages, and increasing sedentary behaviour) are also being increasingly recognized as major contributors to the increase in cancer burden [2].

Traditional diets in LMICs have differed in their quality and quantity, but over the past few decades dietary patterns have been changing rapidly and converging towards a diet high in energy, saturated and *trans* fat, added sugar, processed food products, and generally low in micronutrient-dense foods such as fruits, vegetables, legumes (pulses) and whole grains [2]. While the cancer burden attributable to obesity is still larger in HICs than LMICs, the increasing prevalence of overweight and obesity appears to have a substantial contribution to cancer burden in Latin America, the Middle East, North Africa and parts of Asia [3]. The economic impact of overweight and obesity (US\$ 2 trillion per annum) is now as great globally as that of tobacco, according to a recent analysis from the McKinsey Global Institute [4], affecting all stratum of the societies worldwide, including the most vulnerable population groups (eg, children, low socio-economic groups) contributing to greater social inequalities.

To date, most evidence linking nutrition to cancer comes from HICs, where the combination of risk factors and exposures may differ from those in LMICs. Many LMICs now face a double burden where rates of overweight and obesity and related non-communicable diseases (NCDs) are increasing, while undernutrition persists. A major challenge is to capture and to better understand the interplay between early-life and current dietary exposures that can alter infants' and children's growth patterns, metabolism, risk of obesity and chronic diseases in adulthood.

While the double-burden of malnutrition persists in many LMICs, changes in food systems and the wider socio-ecological determinants of these changes currently unfolding in LMICs, adds to the increased risk of NCDs, but also provides an important window of opportunity to study the impact of these changes on risk of NCDs and cancer in particular. Understanding how local, national, and international food systems shape consumption is important to help guide local policy responses. Food consumption and dietary choices are culturally and economically structured and while food is merely seen in some cultures as a source

Many LMICs are experiencing the double burden of malnutrition (coexistence of macro and micronutrient deficiency) and obesity. These changing patterns of diet, summarized as the nutrition transition provide a window of opportunity to study the impact of these changes as determinants of the risk of cancer and other non-communicable diseases.

of energy for the body, other cultures consider it an element of social bonding and an essential feature of their cultural or religious experiences. To influence positive changes and to protect desirable culinary traditions, it is vital that the link between culture and nutritional choices be acknowledged, understood and addressed for each specific context.

Current UN and international recommendations linked to the prevention and control of NCDs do not adequately reflect the dynamic changes and complexity of exposure in LMICs and may not be appropriate for LMICs. Although urgent action is required, interventions need to be evidence-based and evaluated to ensure that the most critical causes are being addressed.

Key to assessing the impact of current and future nutritional exposures is the capacity to measure these exposures in an appropriate way. This capacity is lacking in many LMICs. Both for research and surveillance LMICs need to strengthen their capacity to collect suitable measures of nutrition-related behaviours. The methods need to provide sufficient detail to allow the determination of food and dietary components and contaminants, to capture their variability and change over time, and to address new and important questions that will arise in the future. The tools and methods employed need to be adaptable to the local circumstances in which they are used while retaining core qualities. Ideally, methods and exposure (and endpoint) measurements should be standardised across countries to enable cross-country comparability and pooling of results so that changing patterns of behaviour can be distinguished from methodological variability and interventions can be appropriately designed by taking into consideration educational levels and culturally sensitive practices of different populations. There is a need to establish where and how biological markers of these exposures can be used or developed, where and how the underlying biological mechanisms can be studied and what the technical requirements are to assure quality in these methods. These are not easy questions to answer, however there is much experience from centres in HICs (such as in Europe, the US, and Canada), without mak-

There is a high priority in building capacity in LMICs to study the nutritional determinants of non-communicable diseases and to undertake high quality research to support government policy.



**Photo: Vegetables, fruit and chicken for sale in a market in Ogbomoso, South-Western Nigeria. Courtesy of Davies Adeloye, personal collection.**

ing assumptions and over-generalising, that can be used to help develop the protocols, train and support staff, and develop the tools and methods required for LMICs. In addition necessary financial resources must be assigned to support research needs in LMICs.

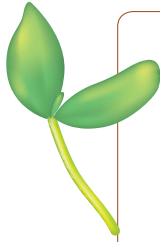
Population surveys, etiologic and intervention studies, as well as implementation research are all important in developing the evidence base to tackle the rise in cancers associated with changing dietary, and physical activity patterns and food production and availability. Repeated transversal evaluation in representative samples will enable the capture of baseline information as well as changes over time at the population level. Prospective epidemiologic cohorts have solidly established their scientific value for evaluating exogenous and endogenous exposures in relation to cancer, with primary advantages being the ability to measure exposures before the onset of disease and to evaluate numerous disease outcomes within a single study. Of the more than 50 epidemiologic cancer cohorts in the US National Cancer Institute's Cohort Consortium, only a handful are from LMICs. Cohort studies conducted in LMICs would be a valuable resource ideally positioned for novel contributions to the understanding of cancer aetiology and survival. Some longitudinal studies have already been initiated in LMICs (such as the ones included in the Consortium of Health-Orientated Research in Transitioning Societies – COHORT [5]), and building on these initiatives may prove very informative and cost-efficient.

With technological advances and the above-mentioned matters being resolved, modern techniques (metabolomics, proteomics, transcriptomics, genome-wide association study [GWAS] and epigenome-wide association study [EWAS]) offer exciting opportunities to enhance our understanding of the dysregulation of cellular metabolism in cancer and the roles of dietary, lifestyle and environmental exposures in modulating cancer processes. Their large-scale application at a population level requires technological (eg, stable high throughput methods, bioinformatics), logistical (eg, appropriate biological samples), and statistical (eg, sufficient study power) resources. In order to facilitate the translation of such methodologies to population studies, priority should be given to the development of standardized technology for appropriate collection and long-term storage of biological samples, particularly blood and DNA, tumor specimens, associated normal tissue, urine and hair. In addition, strategies for implement-

ing the collection, in existing or new cohorts, of stool, saliva, and other relevant biological samples that could allow studying the impact of diet on the microbiome and the latter's role in human metabolism and disease promotion and prevention should be given serious consideration. Staff training is a vital component in the expansion and development of the use of these new technologies around the world.

We have highlighted what is required to better understand the problems and challenges facing LMICs, as well as identified some of the key requirements for solving these problems. Together with the implementation of major public health control programs (eg, tobacco control, limited consumption of sugary drinks, regulation of pesticides use), a high priority is to build capacity in LMICs to undertake high quality research and to provide high quality information to support government policy and action plans. This increased capacity is for better trained staff as well as the provision of suitable infrastructure and technical support. LMICs need the capacity to set their own research priorities and agenda based on their local needs. Building capacity requires a long-term investment, but there are short- and medium-term actions that can build capacity in an incremental way. Different research institutions and UN agencies need to coordinate and harmonize their actions to maximize the impact. A critical step is to have a better understanding of what is already in place, and where the gaps and opportunities are to begin to move forward.





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# Developing the environmental and lifestyle exposure assessment (ELEA) tool for cancer epidemiology research in low resource settings

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Globally, cancer incidence has been predicted to increase by 61% from 2008 to 2030 [1] presenting new health challenges for clinicians, researchers, prevention specialists and policy makers. Moreover, the largest increase is expected in countries with a low human development index, where cancer incidence is predicted to increase by 93% [1], mainly due to demographic shifts and the changing prevalence of risk factors [2]. Existing evidence, mainly from studies in developed and highly resourced countries, indicates that the reduction of known modifiable risk factors associated with cancer, and other non-communicable diseases (NCDs), could lower incidence by approximately 30–50% and is critical to cost-effective cancer control [3]. As a result, efforts are being made to actively reduce the burden of cancer (and associated NCDs) through prevention. However, associations between risk factors and cancer outcomes in low resource settings remain largely theorised [4]. This is largely a result of the lack of high quality local information available to guide cancer control programs. The far richer genetic diversity seen in populations in low resource settings, particularly from the African continent, would render additional findings in this area both novel and insightful [5]. To close this information gap we propose that action is best taken by developing a sound, systematic approach to measuring leading and emerging risk factors to guide future cancer control programs. This would generate local evidence in

Reducing modifiable risk factors could lower cancer incidence by 30-50% but this is largely theorised in low resource settings due to the absence of reliable data. We are encouraged to develop an easy-to-use, cost-effective and systematic process for collecting information on the relative importance of key cancer risk factors.

low resource settings complementing but not replacing targeted research as well as raising awareness and providing information from which appropriate pathways for prevention and care could be developed [2,4].

Here we summarise existing evidence and highlight factors which should be considered in the development of an easy-to-use, cost-effective and standardised data collection process to measure risk factors in low resource settings. Thus, we present an illustrative synthesis of the existing work measuring cancer risk factors in low resource settings to determine how to best facilitate future research. We identified studies covering data harmonisation, standardisation or pooling in cancer epidemiology with a focus on either risk factor measurement or low resource settings.

Our findings confirmed that the ideal method to assess risk factors, even in low resource settings, is a large prospective cohort study despite the significant investment required. Successful cohort studies exploring risk factors produce more robust results ascertaining causation with influential outputs due to their dimension and data richness [6–9], and illustrate the benefit of country-specific data for specialised intervention programs [10]. In low resource settings, India, China and Mexico have succeeded in establishing large scale cohort studies [6–8]. However, several low resource settings have restricted disease diagnostic infrastructure or death notification so the capacity to establish cohort studies is limited. Ideally, large cohort studies should be replicated to provide more definitive answers regarding the geographic heterogeneity of cancer risk factors, but these are often impractical. Rather, cancer risk factor studies in low resource settings are usually single-cancer focused retrospective case-control studies of limited duration or for a single exposure type, for example oesophageal cancer in Iran [11]. Nevertheless these studies often indicate significant heterogeneity regarding known cancer risk factors and sometimes the role of unique risk factors [12].

Significant work using data harmonisation and standardisation principles also exists in cancer epidemiology [13–15]. Key multinational large-scale studies illustrate the process of standardisation and harmonisation on a large scale. For instance the European Prospective Investigation into Cancer and Nutrition Study, a prospective cohort study, includes the development of a standardised dietary method of data collection which has undergone numerous modifications to facilitate standardisation, calibrate results from multiple sites and reduce the potential error [14,15]. On the other hand, the World Health Organization STEPwise approach focuses on collecting consistent data between and within countries with flexibility of use across all settings, including low resource settings, and collected using stan-

By developing a standardised process, and taking advantage of web based flexible technology, the Environmental and Lifestyle Exposure Assessment (ELEA) project proposes to develop a collaborative research platform for the comparative measurement of cancer risk factors, and by doing so, address a gap in knowledge where large cohort studies are impractical.

standardised tools to measure eight behavioural and biological NCD risk factors [9]. In addition, there are a number of multicentre national projects using similar principles of harmonisation and standardisation from which we saw the progression to online project management and increased flexibility in survey content to improve data collection [6–8]. However, large-scale projects are resource intensive and the data collection tools are often lengthy and context specific.

We saw evidence of standardised project management though efficient utilisation of networks, resources and investment in building local research capacity [9,14,16]. Cohort studies rely on a systematic collection of disease outcomes either via hospital admissions, disease registers or death notification. In low resource settings, it was more feasible to systematically collect information from consecutive series of cases and controls from tertiary hospitals or other relevant institutions for retrospective assessment of cancer risk factors [11,12]. However in many cases, regardless of the study design, centralised project management was used to facilitate standardisation and harmonisation by guiding the gathering and checking of data and consistently implementing changes to data collection across sites.

Understandably, centralisation can also introduce a number of complex methodological, cultural, legal, ethical and custodial challenges.

Many multinational large-scale examples are complex prospective studies which require a significant research commitment from both the administering institution and participating local centres. The International Agency for Research on Cancer's cancer registration program, the Global Initiative for Cancer Registry Development (GICR), illustrates a straightforward approach to this type of endeavour in ascertaining basic but essential population based information on cancer [17]. Since the 1960s, cancer registries have enabled the collection of cancer incidence data, also adapted to low resource settings [17,18]. These data have been used to aid political decision making and inform research into cancer control [18]. A key ele-



Photo: IARC / R. Dray

ment to the success of the registries has been the succinct minimalist approach to collecting standardised information. Despite its challenges, the simplicity of the GICR is critical to its worldwide adoption and the availability of comparable data.

Frequently, we saw the use of data pooling, an effective co-ordinated approach that extended the capacity of any individual study to measure effect. The benefits were evidenced in the isolation of an association between smoking and elevated cervical cancer risk following the establishment of human papillomavirus infection as a necessary cause of cervical cancer using various case-control studies [16]. Also, occupational exposure assessment and cancer risk has used this technique as shown in the SYNERGY project which consolidated more than 350 000 exposure measurements to assess lung cancer risk and occupation globally [19]. A challenge when pooling studies is often harmonizing exposure information derived from independent studies. Theoretically if universal indicators are agreed to and utilised consistently, some challenges and study limitations could be overcome.

With this context and existing studies in mind, we can identify the need for an easy-to-use, cost-effective and systematic data collection process for cancer risk factors which could produce regionally compatible and relevant basic information in many locations. This approach is intended to complement the continuation of targeted research and capacity building in such areas and the information obtained would be useful to optimally design further targeted cancer research. We propose the Environmental and Lifestyle Exposure Assessment (ELEA) project as the first step in addressing this need. The tool development and protocol platforms for management and implementation of ELEA are outlined in **Box 1**. These incorporate a number of important issues and experiences drawn from multinational large-scale projects and other relevant studies.

Essential to the ELEA process is ensuring the risk factors and corresponding questions chosen for inclusion are supported by the literature and by experts in the field. It is unrealistic to incorporate an exhaustive list of risk factors, but those included should be priority areas for low resource settings. Additionally, the risk factors should be potentially modifiable or important confounders, most likely to be a leading cause of cancer burden, have the greatest impact, have valid and reliable measurements tested in different populations and high response rates. In this way, the questions could both serve as a collection of retrospective information on behaviour and lifestyle as well as a potential platform for prospective data gathering. We envisage the inclusion of a base set of main questions for use across all settings covering the major cancer risk factors as well as a set of geographically specific questions (and nuanced adjuncts to the main questions, eg, tobacco chewing, specif-

### **Box 1.** Environmental and Lifestyle Exposure Assessment (ELEA) tool development and protocol platforms

**Aim:** to develop an easy-to-use, cost-effective and systematic process for collecting information on the leading and emerging cancer risk factors in low resource settings (ELEA Tool) and protocols for its use (ELEA Protocols).

#### **ELEA tool development method**

1. Identify the key cancer risk factors together with their standardised definitions and measurements relevant to low resource settings.
2. Use a consensus approach with a group of international stakeholders experienced in cancer epidemiology and research in low resource settings to determine the factors and questions for the ELEA Tool
3. Finalise a base set of questions covering cancer risk factors and a smaller set of geographically specific questions as part of an online tool that is practical, brief and easy to administer by a trained interviewer

#### **ELEA protocol platforms**

Administrative platform:

- Project governance (including data access)
- Standard operating procedures
- Online management portal: electronic devices and cloud technology

Repository platform:

- Data management
- Quality control checks
- Harmonisation
- Data treatment

Implementation platform:

- Study administration
- Interviewer training
- Study design
- Study site and fieldwork management

#### **Feasibility testing and next steps**

- Test the feasibility of ELEA through a series of small pilot sites (case-control or case series) to check both the functionality of the ELEA Tool and ELEA Protocols.
- If successful, augment ELEA to incorporate bio-specimen sample collection and storage, and environmental measurements.

ic locally brewed alcohols) to allow for local needs and differences. Universal indicators are critical in measuring these risk factors and reduce many research limitations even though their implementation is challenging. Despite this challenge, the benefits are widely acknowledged and their implementation would facilitate both data collection and comparability of country-specific findings to the international context. That is, the development of comparable cancer risk factor indicators would reduce variation in exposure measurement and permit the potential discovery of previously undetected associations [13]. ELEA strives to

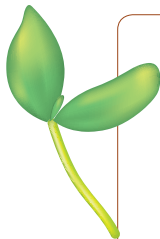
maintain a simple structure, making it applicable where there are limited resources. Potential ways of using ELEA would be to investigate risk factors in exploratory cancer case series studies or hospital based case–control studies. If successful, a biobank component could then be added as a special module depending on local resources.

With the advent of m–Health (mobile health: public health activities supported by mobile devices), many tools have also transitioned from paper based data collection to online platforms to allow for quicker fieldwork and real time feedback. Studies also incorporate the development of online portals as platforms for sharing measurements, frameworks, standards, policies and data sets with positive results. Although internet coverage can be unpredictable, coverage is being proactively enhanced which would aid online project administration. Online methods facilitate real time administration, flexibility and quality control which is integral to ensure consistency and data harmonisation [15]. Additionally, treating data centrally ensures consistent modifications are made. Endeavours of this nature require sophisticated data sharing and governance frameworks as well as common protocols to guide fieldwork.

Moreover, understanding the interplay of lifestyle, environmental and genetic factors is arguably critical to determining the pattern of risk factors to improve cancer control and to prioritising evidence based initiatives especially. Innova-

tive and novel research approaches to overcome the barriers of large scale studies and build on techniques from previous successes are encouraged to advance cancer epidemiology. The first step in research innovation in cancer epidemiology must be the collection of basic but essential descriptive information on risk factor distribution to better guide more complex and complementary techniques. ELEA proposes to develop a strong platform to increase the research capacity of low resource settings and clearly address a gap in knowledge. ELEA could be used as a precursor to large–scale studies, by creating a scientific knowledge base allowing preliminary assessment of the relevance of major cancer risk factors in various settings and populations. By collating a small amount of highly relevant data per subject in a systematic manner across large samples and diverse populations, ELEA would lead to the creation of a Big Data repository, a key resource for cancer epidemiology.

With better epidemiological evidence, local leadership could have an increasing voice in local and international cancer control forums that is supported by evidence. It will function as a catalyst for international collaboration and cooperation with a focus on cancer as a development issue in low resource settings and apply knowledge to complexities of the real world. The extension to existing knowledge of cancer causes from future findings could transform approaches to cancer prevention and treatment.



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# Aligning values and outcomes in priority–setting for health

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Numerous factors and competing interests shape policymaking and budget allocation for health and health systems. In particular, the values and outcomes prioritized by policymakers have important implications for health spending and the impacts they have on populations and countries. Based on Harvard’s Ministerial Leadership Program, this article provides an overarching and integrative framework that policymakers can use to explicitly consider the priorities shaping their decisions, the outcomes that result from their decisions, and processes for making these decisions. The framework includes four key questions: 1) What values underlie the government’s priorities for the country? 2) Based on these values, what goals for the health care system does the government hope to achieve? 3) Based on these goals, where should the government allocate its financial resources for health? 4) How should the government allocate its financial resources for health? The framework also takes into consideration health system, economic, and political outcomes that result from budget allocations.

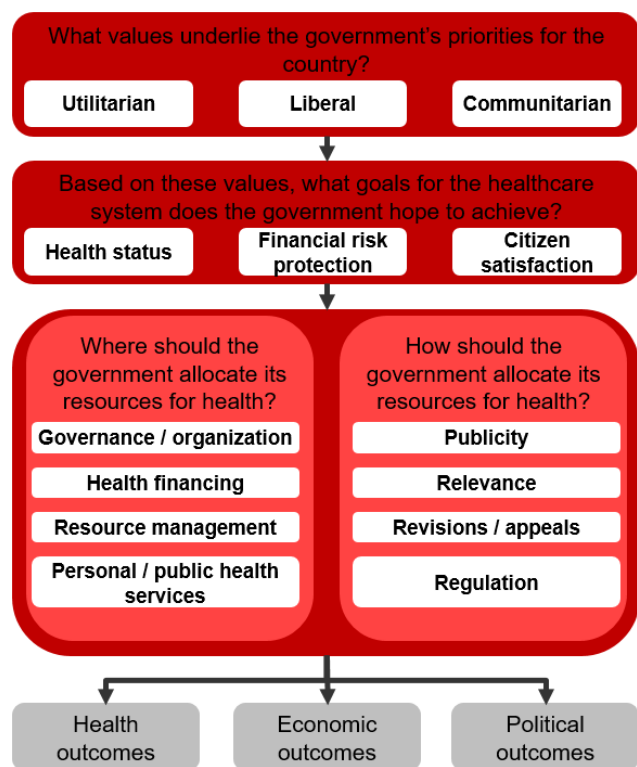
Investments in health and health systems can create value in two distinct but related ways: by generating “value for money” and “value for many” [1]. Policymakers can prioritize budgets to improve efficiency and effectiveness of health expenditures, thereby generating value for money, and target investments to improve equity and responsiveness to users’ needs, thereby achieving value for many.

The size and allocation of the health budget directly and indirectly impact population health. Low- and middle-income countries (LMICs) with similar per capita GDP, health expenditures as a proportion of GDP, and per person health

Numerous factors and competing interests shape policymaking and budget allocation for health and health systems. In particular, the values and outcomes prioritized by policymakers have important implications for health spending and the impacts they have on populations and countries.

expenditure have different outcomes. Investing in health can also bring economic benefits for countries [2–5] and political benefits for policymakers who choose to prioritize health (in countries where citizens have electoral power).

This article presents a framework (**Figure 1**) used at Harvard University’s Ministerial Leadership Program to introduce the roles that values and goals can play in prioritizing health programs and budgets. Based on our experience presenting this framework to several dozen Ministers of Health and Ministers of Finance, we believe it can serve two purposes. First, it can help policymakers explicitly articulate the values and principles that influence their decisions. Values and beliefs already influence decision-making; as discussed later, policymakers should make these values public and transparent to other decision-makers and the public in order to legitimize their decisions and to invite productive debate. Second, the framework explicitly links the way that different values can impact a policymakers’ priorities, which in turn can lead to different health, economic, and political outcomes. In line with the principles



**Figure 1.** Framework for aligning values and outcomes when setting priorities for health.

of systems thinking, we believe that by explicitly stating the “mental models” which guide decision-making, individuals and groups can better test their logic *ex ante* and evaluate the impact of their decisions *post hoc*.

The framework includes four guiding questions:

1. What values underlie the government's priorities for the country?
2. Based on these values, what goals for the healthcare system does the government hope to achieve?
3. Based on these goals, where should the government allocate its financial resources for health?
4. How should the government allocate its financial resources for health?

These questions have direct relevance for all policymakers whose decisions impact health.

## 1. WHAT VALUES UNDERLIE THE GOVERNMENT'S PRIORITIES?

Although a broad range of values can drive the government's approach to resource allocation, these value sets generally fall into three broad categories: utilitarian, liberal, and communitarian [2,6].

Utilitarians typically focus on the value, or utility, that a decision will have. Utilitarians generally believe “the ends justify the means” (assuming “the means” involve ethical and legal decisions). Policy tools such as cost-effectiveness and cost-benefit analysis reflect utilitarian concerns of generating the greatest benefits (utility) using the fewest possible resources. Utilitarians differ in how they choose to measure total utility. Subjective utilitarians argue that individuals must judge happiness for themselves. Objective utilitarians argue that individuals' choices are not always rational and that allocating resources to maximize objective measures of well-being (eg, Disability-Adjusted Life Years [DALYs] and Quality-Adjusted Life Years [QALYs]) will have the greatest benefit.

Liberals take a rights-based approach to allocation of health resources. Liberals believe that humans have the capacity and obligation to display mutual respect, and this respect endows individuals with rights. Some liberals, known as libertarians, focus on negative rights, which guarantee individual freedom. Libertarians might focus on the rights of the individual to buy health insurance or choose their physician. In contrast, egalitarian liberals emphasize positive rights, or a minimum level of resources and services, which guarantee an individual's ability to exercise free choice. Egalitarian liberals tend to favor redistribution of resources to ensure the entire population has access to positive rights. However, egalitarian liberals differ in their views on whether individuals have a right to health services (ie, provision of and access to care) or health status (ie, attaining general well-being).

Communitarians do not focus on the level of the individual in assessing a policy, but on the level of the community or society. They evaluate the merit of a policy based on whether it adheres to a community's value set and whether the policy promotes a society consistent with those values. Communitarians would typically oppose a policy which achieves positive health outcomes using an intervention that defies local norms or values. Communitarians fall into two broad categories: those who believe in a single set of values which would promote a better society (universal communitarians), and those who argue that each society should set its own values based on context-specific factors (relativist communitarians).

These value sets are not mutually exclusive. Policymakers might include both a utilitarian and communitarian perspective in an analysis if they prioritize health interventions based on objective utility but exclude any that defy local norms. Further, governments can modify their ethical values as they learn more about a population's needs and their ability to meet those needs. However, it is important to maintain adequate “coherence and explicitness” when articulating one's values to create transparency for the population [2].



## 2. BASED ON THESE VALUES, WHAT GOALS FOR THE HEALTH CARE SYSTEM DOES THE GOVERNMENT HOPE TO ACHIEVE?

Policymakers must consider which outputs and outcomes to prioritize when allocating resources for health. In this context, *outputs* refers to how well the health system performs its functions, whereas *outcomes* refer to the ultimate goals of the health system. In many cases, strong delivery of health systems outputs is necessary but not sufficient for strong health system outcomes.

A policymaker needs to balance four health system outputs [7]:

- **Equity** refers to the differences in how a policy affects different people. “Vertical equity” evaluates differential impact across different populations, whereas “horizontal equity” evaluates whether the policy treats individuals with the same status the same [2].
- **Efficiency** has many definitions in the fields of policy analysis. For the purposes of health systems analysis, we draw on economic definition of technical efficiency, in which society is producing the most goods and services for the least cost [2].
- **Effectiveness** refers to whether interventions are evidence-based and safe [7]. In other words, an effective intervention will achieve the desired health outcomes.
- **Responsiveness** refers to whether the health system meets the public’s legitimate non-medical expectations. Responsiveness is a highly subjective measure and depends on the perceptions among citizens of a health system’s functioning [8].

Policymakers’ values will influence which health system outputs they prioritize. For example, pure utilitarians will likely care most about efficiency and effectiveness, and they will less likely prioritize equity. They might also disregard the importance of responsiveness as an objective, unless they believe that a health system’s responsiveness generates value for the population. Liberals, who focus on individuals’ rights, will prioritize equity and responsiveness of the system, with libertarians emphasizing the importance of responsiveness (eg, choice of health service providers) and egalitarian liberals emphasizing equity in access to positive rights (eg, basic health services and medicines). Communitarians, who emphasize society’s values, will prioritize the objectives most relevant for achieving the best possible society. Accordingly, they will likely emphasize responsiveness and equity of the system at a societal level, although the emphasis could vary depending on the specific values of the society.

In addition to setting output objectives, policymakers must also pay attention to the health systems outcomes, or the overall goals, of a country’s health system [2,7]:

- **Health status** refers to the health of a population. Measurements of population health status include life expectancy, burden of disease, mortality rates for specific groups, and disease prevalence.
- **Financial risk protection** refers to helping people avoid large and unpredictable payments for health, also known as catastrophic (or impoverishing) expenditures. Mechanisms to provide financial risk protection typically involve insurance schemes or tax-funded health systems.
- **Citizen satisfaction** refers to the degree with which users of the health system rate the system as satisfactory.

As with outputs, health systems outcomes derive directly from values. For example, objective utilitarians might concern themselves most with the population’s average health status, whereas egalitarian liberals might focus most on the distribution or range of health statuses in the population (as a measure of equity). Egalitarian liberals will also emphasize the importance of financial risk protection as a means for ensuring economic opportunities for all. Subjective utilitarians might place a high value on citizen satisfaction, as would libertarians (in the sense that satisfaction relates to individual choice).

## 3. BASED ON THESE GOALS, WHERE SHOULD THE GOVERNMENT ALLOCATE ITS FINANCIAL RESOURCES FOR HEALTH?

Once the government has identified its objectives for the outputs and defined its goals for the health system, it can invest in specific programs or interventions accordingly. A health system has four main functions which a government can prioritize for investment [7]:

- **Governance and organization** encompasses the institutions involved in delivering products and services to citizens such as hospitals and primary care clinics [9]. Investments in this function include improving accountability or transparency of decision-making, updating management policies and processes at the programmatic level, or changing the system’s referral network.
- **Health financing** involves mobilizing, pooling, and allocating financial resources. A government could choose to invest in health financing by creating a new insurance scheme, expanding coverage of existing insurance to new patient populations, or by expanding the range of services covered under existing schemes.
- **Resource management** entails overseeing the inputs, such as human resources and labor, pharmaceuticals,

and medical technologies that produce personal or public health services. The government can invest in the management of resources by purchasing these resources (eg, procuring medicines), improving systems that oversee and deliver resources (eg, budgeting tools, supply chain management), or by investing in infrastructure and human resources to strengthen the health system [10].

- **Personal and public health services** refer to the activities involved in delivering care to patients. Strong health systems enable delivery of these services. Governments also invest in specific services that generate value, such as by investing in primary health care delivery. Several investment cases have been made for disease-specific “good buys” such as those identified by the Lancet Commission on Investing in Health [11]; UNAIDS HIV Investment Framework [12]; STOP TB Strategy [13]; the Global Strategy for Women's and Children's Health spearheaded by the UN Secretary General [14]; interventions identified in the Global Malaria Action Plan [15]; and the Package of Essential Noncommunicable Disease Interventions (also known as WHO-PEN) [16].

Values will influence how policymakers invest across these four functions. For example, a utilitarian might focus on improving resource management to reduce wastage in the system and improve efficiency. Utilitarians might also focus on the “good buy” interventions described above and choose to invest in those that improve population health for the least cost. By contrast, egalitarian liberals might focus on ensuring equitable access to health insurance and effective health services, especially for marginalized patients such as poor and rural populations, even if these programs are more expensive. Communitarians will focus on implementing these functions to coincide with their society's values. For example, a society that emphasizes individual responsibility for health might de-prioritize social support for accessing services, while a society that emphasizes the community's role in promoting health might implement a social health insurance scheme or mobilize the community to raise awareness about disease prevention.

#### 4. HOW SHOULD THE GOVERNMENT ALLOCATE ITS FINANCIAL RESOURCES FOR HEALTH?

There is no formula for determining which health interventions or areas to prioritize, and limiting analyses to comparisons of cost-effectiveness is insufficient for policymaking.

Without universal consensus on the principles for prioritization, governments need to adopt an approach to allocate resources and justify their policies. Accordingly, ethicists

have proposed a framework known as “accountability for reasonableness” (A4R) to guide this decision-making process. A4R, a process grounded in democratic principles aimed at legitimizing decision-making among “‘fair-minded’ people who seek mutually justifiable terms of cooperation,” has four conditions [17]:

1. **Publicity:** Decisions that establish priorities in meeting health needs and their rationales must be publicly accessible.
2. **Relevance:** Policymakers should provide reasonable rationales which appeal to evidence, reasons, and principles accepted as relevant by fair-minded people when justifying their decisions. Rationales should be relevant for a broad range of stakeholders in decision-making.
3. **Revision and appeals:** There must be mechanisms for challenge and dispute and, more broadly, opportunities for revision and improvement of policies in light of new evidence or arguments.
4. **Regulative:** There must be public regulation of the process to ensure that conditions 1, 2, and 3 are met.

A4R does not identify the priorities for government investments; it establishes a transparent process for publicly and legitimately determining these priorities in order to guide investment decisions. These principles have relevance for policymakers and societies that subscribe to all value sets. Indeed, A4R does not promote a specific value set, but rather advocates for explicitly articulating and linking values and principles to decisions and outcomes, which our framework can help put into practice.

The principles of A4R have influenced health priority-setting in several places: UK, where the National Institute for Health and Clinical Excellence (NICE) takes social value judgments into account when recommending coverage for new treatments [18]; Mexico, where decisions about which diseases the public catastrophic insurance should cover involve working groups that evaluate clinical, economic, ethical, and social considerations [19]; and Oregon, where, in 2008, a Health Fund Board made a plan to insure all legal residents of the state involving a wide group of stakeholders and extremely transparent decision-making / information-sharing [20].

#### OUTCOMES FROM HEALTH SPENDING

The decisions described above can have at least three sets of outcomes.

##### **Health system outcomes**

Changes in government health spending can directly impact cause-specific mortality. For example, in low-income

countries a 1% decrease in government health spending is associated with an increase of 18 neonatal deaths for every 100 000 live births and 98 deaths before the age of five [21]. From 1999–2004, a 10% increase in per capita total health expenditure was associated with a 22% reduction in infant mortality rate and 10% increase in per capita public health expenditure was associated with a 21% reduction in infant mortality rate [22]. Globally, a 1% increase in government health spending is also associated with a significant decrease in cerebrovascular deaths [23].

However, simply increasing government (or any) spending on health will not necessarily improve health outcomes, especially if funds are not spent efficiently. Evidence suggests that increasing the efficiency of government health spending, without increasing total budget expenditure, could improve population health outcomes [5]. Increasing health spending efficiency among nations below the regional average to the regional average would result in an increase in health-adjusted life expectancy (HALE) by 1.5 years in Africa, 1 year in Asia/Pacific, and 1.3 years in Middle East / Central Asia. In the most extreme example, increasing health spending efficiency in Sierra Leone to the average for Africa could improve HALE by 5.3 years.

Achieving the health systems goal of financial risk protection through universal health coverage (UHC) can also improve population health status. Countries that currently do not have UHC can improve coverage either by increasing budget allocation to health, or by improving spending efficiency in order to redirect spending to UHC. Cross-country analysis of the influence of insurance coverage on health outcomes suggests that financial coverage has a causal influence on health, especially for low-income individuals, who gain better access to necessary care when they receive coverage [24]. Individual countries' experiences implementing UHC, including Thailand, Turkey, and several countries in Latin America, supports this finding [7,25–27].

### Economic outcomes

Evidence strongly suggests that improved population health has positive economic impacts for a country. Achieving better population health provides a sound “return on investment” in the form of stronger economic output and growth. Evidence for the linkage between health and economic output exists at both the microeconomic and macroeconomic levels.

At the microeconomic level, better health can improve the financial prospects of individuals and households [3]. Malnutrition, frequent illness, and unstimulating home environments can limit the physical and cognitive development of children. Conversely, proper nutrition and health supports adequate physical development and school performance [3]. Interventions targeting specific diseases, such as deworming, nutrition supplements, and malaria preven-

tion can lead to improved education or income outcomes for individuals [4]. Among working individuals, illness can negatively impact income due to impoverishing health expenditures, reduced education opportunities, decreased productivity at work, long-term separation from the work force, and disengagement from other economic activities.

Macroeconomic evidence also supports the idea that investing in health generates positive economic returns [4]. First, *ceteris paribus*, a healthy workforce will have higher labor productivity than an unhealthy workforce due to increased energy and reduced illness-related absenteeism. Second, a healthy population has increased educational opportunities, and education levels have a direct impact on a country's income growth. Third, populations with high life expectancies tend to save more for the future and likely will have more working years. These increased savings can lead to increased investable capital, an important driver of growth. Fourth, health investments that change mortality and fertility can lead to a “demographic dividend,” in which the ratio of working-age to non-working-age people in the country increases and productive capacity increases on a per capita basis. (This demographic dividend accounts for up to one-third of the economic boom that many East Asian countries experienced between 1965 and 1990.)

### Political outcomes

Formulating health policy and allocating resources to health depends on and also impacts a country's politics. For example, the transition toward universal health coverage (UHC) has had distinct positive political benefits in many countries [28]. In addition, health policy in countries such as Turkey, the UK and Brazil has influenced the political landscape and political outcomes.

In Turkey, after a regime change in 2002, the government implemented a Health Transformation Program (HTP) with significant commitment from political leadership. This transformation led to increased levels of public satisfaction with the government [7] and influenced voter intentions in favor of the government [29].



**Photo: Ministers of Health participating in a Roundtable Meeting hosted by the Harvard Ministerial Leadership Program. Photo courtesy of the Harvard Ministerial Program.**

After the re-democratization of the Brazilian government, the 1988 constitution formally defined health as a “citizen’s right and obligation of the state” and established the Unified Health System (SUS), which sought to unify the fragmented care delivery network into a national health system under the MoH [30]. Today, 75% of Brazil’s population, or 195 million people, receive services and coverage from SUS [31].

In the UK, the National Health Service (NHS) receives broad public support, with 89% of the public agreeing with the idea of a tax-funded national health system, which is managed by the government. However, projections show that by 2030, the NHS will have a £65 billion funding gap. Therefore, UK policymakers will have to balance the competing health, financial, and social demands placed on the NHS in order to maintain its relevance going forward.

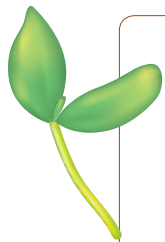
## FRAMEWORK LIMITATIONS

Although we believe that this framework can help policymakers make their values more explicit and link values to decisions and outcomes, it has several limitations. First, it presents decision-making as a linear process, whereas decision-making occurs in the context of complicated pro-

cesses subject to outside forces. Second, the framework does not incorporate decision analysis tools into its approach and cannot and cannot provide a clear-cut answer when making a tradeoff between two different investments. We believe that linking analysis of value-based decision-making with quantitative decision tools is an important next step for study. Finally, because this framework focuses by design on the level of health systems, clinicians cannot use it to make individual care decisions.

## CONCLUSION

This article introduces a framework for policymakers to consider how their values influence priority-setting for health and the impacts that these priorities can have on health systems, economic, and political outcomes. By clearly articulating values and priorities, policymakers can develop a transparent and deliberative process to better discuss and engage their constituents in health systems decisions and to set priorities. These priorities, in turn, can generate value for money by improving efficiency and effectiveness of budget allocation decisions and value for many by enhancing equity and responsiveness in the health system.



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# Universal coverage and economic burden from epidemiological changes of diabetes in Latin America

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Despite the increased coverage schemes of universal health insurance, unresolved challenges still remain in the current health care model. The expected epidemiological changes for chronic diseases in Latin American countries (LACs), will lead, in economic terms, to catastrophic expenditures for the health systems (more than 10% of the health budget) and for patients (more than 30% of the household income). Moreover, the governments, institutions and societies of these countries will have to face strong competition in the allocation of resources to universal coverage for other diseases [1].

Undoubtedly, talking about chronic diseases, diabetes is a global public health problem of great relevance in LACs. In this sense, we will take diabetes as a tracer problem of chronic disease challenges for universal coverage schemes in these countries. The rapid growth of diabetes is a global event with broad challenges for public health systems at a world level. Diabetes and its complications are a great economic challenge for any scheme of universal coverage, particularly when it is present in older people [2]. The chal-

Taking diabetes as a tracer of the problem, evidence was used from epidemiological and economic burden of diabetes on two levels: detailed level, with evidence of the Mexican case; and general level, with evidence of observed and expected trends in 7 countries: Cuba, Venezuela, Chile, Colombia, Argentina, Brazil and Mexico.

lenges increase because in LACs, financial resources for health services are more and more limited, a great part of these is allocated to curing and few resources are used for prevention; on the other hand, a culture of self-care and healthy behaviors is not very present in these countries [3].

We want to highlight the fact that in LACs, just as in other countries, we are also facing a global problem that is generating a high catastrophic expenditure for all of those who are involved. For example, in the case of Mexico, the same methodology of a study conducted in 2004 was used to identify the costs generated in 2015 by diabetes in the national population [4]. Results show the high impact on public health systems, but also on patients' pockets. Indeed, the demand for health care for older adults goes beyond the capacity of the public health system and patients end up financing most of the care for diabetes and its complications [5]. Indeed, of every US\$ 100 spent on diabetes in Mexico in 2015, patients contributed US\$ 54 and the public health system contributed US\$ 46. This evidence has considerable implications in terms of equity and access to public health programs. In this sense, patients' catastrophic expenditures will increase and, above all, the high costs of lost productivity attributable to temporary disability, permanent disability and premature death, generated by diabetes [6].

The main objective of this essay is to highlight that the epidemiological and economic trends reported by several studies in different years (2000, 2010 and 2025), show a constant increase, despite the efforts made by the new universal coverage schemes to reduce the impact of diseases such as diabetes. Also, we highlight the achievements and challenges of universal coverage and how it relates to the

The results suggest that universal coverage schemes with the same old care models based on biomedical approach have certainly expanded access but have not been effective enough to solve population health problems related to chronic diseases. The prevalence, number of cases and economic burden has increased, and will continue to increase.

prevention of diabetes, and finally, we conclude with a list of possible strategies for the solution of this problem in LACs.

## WHAT IS THE PROBLEM?

In the context of universal coverage schemes without substantive changes in the health care model of, diabetes has assumed one of the top trends in morbidity and mortality in most countries of the world, generating great challenges for medicine and public health. The World Atlas of Diabetes registry for 2015, reports 415 million adults with diabetes [7]. This number will continue to increase globally due to an aging population, growth of population size, urbanization and high prevalence of obesity and a sedentary lifestyle.

With respect to the place of diabetes in the epidemiological burden to the Latin American region, a recent study reported diabetes and other chronic diseases as main causes of mortality for all LACs. The relative weight of these diseases on the total burden are in a minimum range of 62% in Costa Rica, with a maximum range of 84% in Chile [8]. With respect to the impact on DALYS for 2011, the main reported causes are major unipolar depression, alcohol consumption, asthma, dental cavities, cardiovascular diseases and diabetes. For example, in the results by country, Brazil had a greater impact, with a total of 37.5 million DALYS, a rate of 232 per one thousand inhabitants.

In Brazil, as in most LACs, diabetes mellitus was in first place, having 5.1% of DALYS, followed by ischemic heart disease (5%), cerebrovascular diseases (4.6%) and depressive disorders and asphyxia at birth (3.8%). In women, diabetes mellitus was in first place (6.9%), depressive disorders in second (6.3%) and cerebrovascular diseases in third place (4.5%). In men, assaults stood out (5.6%), ischemic heart disease (5.6%), cerebrovascular diseases (4.6%) and diabetes (4.4%) [8].

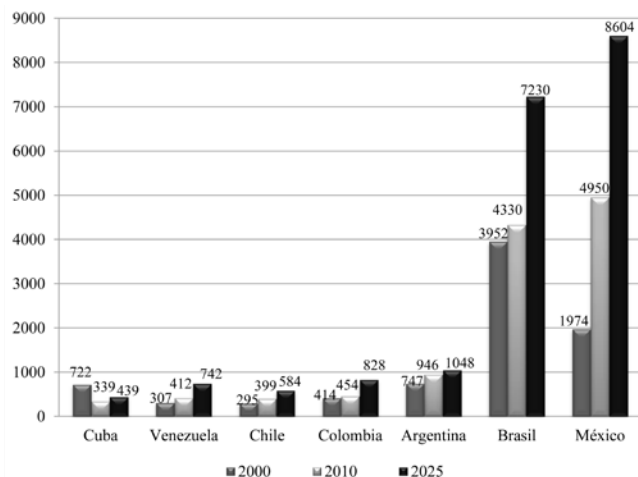
With respect to the epidemiological burden at the global level in 2015, the top ten countries, from greater to lesser

impact, were (millions of adults with diabetes): China (109.6), India (69.3), USA (29.3), Brazil (14.3), Russia (12.1), Mexico (11.5), Indonesia (10.0), Egypt (7.8), Japan (7.2), and Bangladesh (7.1). Evidently, the DALYS with greater impact are also for these 10 countries, led by China and India at the global level, and by Brazil and Mexico at the level of LACs [9].

Moreover, from the perspective of the epidemiological transition, the latest Global Burden of Disease study (GBD) reported that by 2010, diabetes [10], as a tracer of the epidemiological transition in the world, is one of the biggest challenges being faced by health systems and society. The challenges get more complicated, not only in terms of mortality but also by generating growth and diversification in the demand for health care services for resolution, in the framework of the health transition.

With regards to diabetes, contrary to the main purpose of the strategy of universal coverage, the epidemiological transition phenomenon in economic terms, represents a heavy burden in direct costs to the users' pockets, to the health system and society, and indirect costs attributable to premature mortality, temporary disability and permanent disability attributable to the complications of diabetes [11]. Indeed, integrating a database of several published studies, we analyze findings in seven Latin American countries selected under criteria of diabetes prevalence, data on the epidemiological and economic burden of diabetes, and income level: Cuba, Venezuela, Chile, Colombia, Argentina, Brazil and Mexico. The comparative analysis of the 7 countries includes epidemiological and economic trends reported by other studies for the years 2000 and 2010 and expected for 2025 [12]. The costs from epidemiological changes observed in a group of countries selected for this essay, have increasing trends if current epidemiological conditions and current models of care are maintained, mainly in Mexico, Argentina and Brazil (**Figure 1**).

On the other hand, in Latin America and the Caribbean, even with new universal coverage schemes, many people with diabetes have limited access to health care; this means that indirect costs may exceed direct health care costs. In terms of the response of the health system, in recent years, health systems in most LACs have undertaken adjustment, changes or reforms in national health programs trying to meet the goal of universal health insurance. Longer life expectancy and fewer families who are impoverished due to health reasons, are some of the results obtained in recent years following the adoption of universal health insurance in these countries. Indeed, since 2005, the new Health Insurance Program in Argentina has helped introduce historical changes in universal coverage by the health system [13]. In the case of Brazil, the tax-funded Unified Health System modernized the Brazilian health system, creating a



**Figure 1.** Comparative data of economic burden from epidemiological trends (observed 2000, 2010, and expected 2025) in diabetes for selected Latin American countries (millions of US\$). Source: Developed by author with data from references [4,9–11].

national coordinated service that the entire population can access. Investing heavily in a “Family Health” primary care strategy in particular has been the vehicle used to carry out major reforms allowing families greater access to health care through home visits and community activities for better health.

In Chile, the “Social Health Insurance” program ensures nearly universal health coverage for its 17 million inhabitants. From 2005, all Chileans have access to a basic package that guarantees treatment for 80 health problems [14], establishing maximum waiting times for treatment and discretionary spending. In Colombia in 1991, after establishing the right to health in its constitution, 20 years later, access to health services has improved considerably thanks to a national system of subsidized health insurance [15].

In the case of México, covering more than 50 million people, the Popular Health Insurance, with universal coverage strategies, promotes access to health care for all those who lack social security. At the heart of the 2003–2018 health reform, this coverage package includes more than 230 primary and secondary treatments for the entire population, including interventions for diabetes and its major complications [16].

Despite advances in coverage under schemes of “Universal Health Insurance” in all those countries, the epidemiological and economic burdens of problems such as diabetes, far from resolved, continue with constant incremental trends which can be seen in **Figure 1**. Expectations are nothing favorable if major changes are not implemented in the models of care. The problem is that even with more coverage and access to health care, the health care model remains the same as when it began in the 1940s. This mod-

el is based on a fragmented scheme with several institutions providing health care for people in the formal economy (social security institutes) vs institutions for the population in the informal economy (ministries of health) [17]. These institutions, dated from the 1940s, provide health services based on a model of care with a biomedical curative approach. In this sense, most of the national health expenditure goes to curative health programs (90–95% depending on the country) and the results in terms of benefits for chronic diseases such as diabetes, have not been favorable.

Summarizing, we note that aside from interventions from universal coverage programs aimed at diabetes, it is necessary to review and adjust prevention strategies. We already have enough evidence on prevention strategies, costs and effectiveness in all regions of the world. In the case of LACs, this review has defined a list of 10 major prevention strategies (**Table 1**). These strategies consider, from different perspectives, the effects of changes in lifestyle and/or the use of metformin or other drugs used to control blood glucose levels, as the best options.

The challenge for the universal coverage strategy in LACs is the design and implementation of effective prevention strategies. **Table 1** also highlights the main challenges or problems that must be solved for a more effective prevention of diabetes. These challenges are those subsequently taken up for analysis of possible alternative solutions.

## SUGGESTIONS FOR A POSSIBLE SOLUTION

Increased coverage by “Universal Health Insurance” schemes has not been sufficient to meet the challenges of chronic health problems in LACs. In terms of changes in the health system with any scheme of universal coverage, the main adjustment should be related to the transition from one system of care based on a biomedical, curative, fragmented and inequitable model toward a socio–medical model, preventive medicine, which is comprehensive and

Social protection schemes based on universal coverage have not been sufficiently effective to decrease high economic burden on the pocket of users solve these health problems. It may be better to move from a care model based on a biomedical–healing and fragmented approach to models of care based on a socio–medical, preventive and comprehensive approach.



**Table 1.** Diabetes prevention strategies and implementation – challenges in Latin American countries

PREVENTION STRATEGY FROM UNIVERSAL COVERAGE	IMPLEMENTATION CHALLENGES
Institutional intervention for lifestyle changes and/or use of effective pharmacological agents to prevent damage–complications in patients with diabetes or to delay the appearance of the disease in pre–diabetic patients.	Difficulties and inadequacy of international standards in defining lifestyle indicators from a biomedical approach. This leads to high rates of treatment desertion due to problems related to institutional cultural aspects, drug availability and resistance to changes in lifestyle. Pre–diabetes programs are only mentioned but not implemented in practice, mainly due to lack of resources.
Intra–institutional and inter–sectorial programs promoting changes in lifestyle through mass media programs.	Intra–institutional and cultural barriers in the definition, promotion and communication of lifestyle indicators by country or region. Because of the fragmentation of the health system, each institution implements its program according to its resources and organizational culture. When involving inter–sectorial actions that require participation of the health and education sectors there is no agreement or coordination.
Community programs for lifestyle changes centered on eating habits and diet. Directed to 4 age groups: children, adolescents, young adults and older adults	Lack of knowledge and / or limited availability of healthy foods. Conflict between suggested diets and consumption patterns and social and cultural determinants that are difficult to change.
Community programs for changes in lifestyle focusing on physical activity	Lack of time and space for physical activity. Obesogenic environments determined by cultural aspects depending on the country or region.
Programs to eliminate obesogenic environments at macro, meso and micro levels.	No proposal for intervention vs obesogenic environments involving actors from the health–education and environment areas, working together.
Development of an integrated multicenter, multidisciplinary and inter–sectorial approach for prevention of diabetes and its complications.	A biomedical approach continues to dominate, which is fragmented within each institution and without involvement of social science disciplines. In health teams, doctors and other professionals from the health sciences predominate but only rarely involve psychologists, sociologists or anthropologists, despite the large indigenous population that generally does not speak Spanish and with habits and customs that health personnel do not know.
Community prevention programs as part of universal coverage.	Lack of efficiency in the allocation of resources to start a phase of universal coverage strategies. Problems of financial sustainability for consolidation stages of programs focused on diabetes prevention.
National strategies for prevention of diabetes and obesity involving all actors.	Absence or very low participation of key stakeholders of civil society, community leaders and entrepreneurs.
Strategy to impact on the assessment of prevention interventions.	Lack of financial resources, research teams and a culture of accountability at the institutional or national/international levels.
Partnership Program for the Health System and Companies/Institutions working on prevention of complications and to reduce disability from diabetes.	The health system has been unable to build solid partnerships with companies to develop these programs. The social costs of disability attributable to complications continue to grow in all countries.

equitable. This will enable more effective detection and control with a consequent decrease in the effect of complications and treatment desertion. In most LACs, of every 100 patients with diabetes, only 50 are diagnosed and of these 50, only 30 remain in control. With a more effective universal coverage, these indicators should change with new strategies for detection and control.

Effective universal coverage involves approaching diabetes from an interdisciplinary perspective to promote a change in the concept and determinants of diabetes, as well as a change in the social meaning of the disease and greater involvement of users, civil society and businesses. It requires allocating more resources to design, implement and monitor strategies to move from addressing diagnosed patients to strategies for the pre–diabetes population. In all LACs, there is little or no intervention for this population.

Development and validation of new methods are need to evaluate the epidemiological and economic burdens in terms of direct costs of care and indirect costs (temporary disability, permanent disability and premature mortality). For more effective coverage schemes, in all LACs it is necessary to adjust/implement new models of care and health management that can respond to the diversification and quantity of health services that will be generated by the

epidemiological transition in chronic diseases, particularly in patients with diabetes or hypertension.

## WHAT NEEDS TO HAPPEN NEXT?

As part of an effective universal coverage scheme by universal health insurance, the proposed changes in reforms or adjustments in the health system in LACs, should put emphasis on changes in the health care model with a greater focus on the level of primary prevention. The following strategies are highlighted in order of priority:

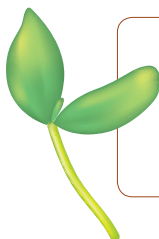
- The current model of care must go through a detailed review, to propose changes in the physical infrastructure and the training of health personnel with a focus on prevention. We must develop infrastructure to expand screening programs, for more detection, prevention and control. We also have to implement changes in the continuing education programs for health personnel to enable a greater focus on primary care (mainly for physicians and nurses). We also suggest integrating social science professionals into health programs (medical anthropologists and medical sociologists) to form part of the health team to implement new strategies for detection, prevention and control of chronic diseases.

- Develop new financing schemes with greater allocation of resources to new programs for screening and prevention in the pre-diabetes population.
- Design and implement systems for epidemiological surveillance and monitoring of the economic burden for a periodic measurement that allows us to know and assess (preferably on an annual or biannual basis) the impact of new strategies on epidemiological trends as indicators of direct and indirect costs.
- Establish patterns of resource allocation to ensure the financial requirements to address diabetes based on expected demand. These patterns must integrate indicators on clinical efficiency (inpatient and outpatient cases), epidemiological efficiency (new cases of diabetes from expected trends in the short term), organizational efficiency (number of cases to be taken care of by level of care) and economic efficiency (average cost of case management by level of care).
- Knowledge of the relative weight of the management of diabetes based on the annual family income, as well as required knowledge of the cost of complications to the users, should be made available through a bulletin sent to patients and their relatives, and to the community as a whole.

- A list of recommendations is needed to promote greater self-care, monitoring of risk factors and the benefits of carrying out these measures, and more importantly to avoid falling into a catastrophic situation because of the costs of diabetes (to avoid an impact of >30% of the family income).
- As a “Regional Observatory Citizen of Diabetes”, social civil organizations could suggest and develop follow-up programmes for the costs of diabetes in different public and private health institutions. The Observatory should function as a checking system that would monitor how much is being spent on managing diabetes and what the money is being spent on.
- With regards to the indirect costs of premature mortality and temporary and permanent disability attributable to diabetes, companies must establish new partnerships and agreements with the health system and workers to have positive gain in economic competitiveness and labor productivity. This will require developing new programs in the workplace for increased detection, prevention, treatment and control of diabetes and its complications.
- In most LACs, the strategy to expand coverage through various schemes of “Universal Health Insurance” presents evidence of benefit and greater access to health care in general but with some limitations in the current shape of the health systems. Indeed, the structure of the health system in which they operate such strategy is the very structure of the past half century, with a focus on curative care.
- The groups of patients with diabetes could collaborate on joint actions with the health system in order to promote universal coverage schemes, new actions based on the perspective of “health behavior” with a vision of diabetes as a “life condition”, more than a health problem.
- All these strategies should place a greater emphasis on actions to move from a model of biomedical care based on curative medicine to one of universal insurance focused on socio-medical health care based on preventive medicine. Like this, LACs can more effectively face the current public health challenges for chronic diseases like diabetes.



**Photo: The difference infrastructure for curative care vs. primary care in Mexico. Courtesy of the author.**



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# Reduction in child mortality in Ethiopia: analysis of data from demographic and health surveys

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**Background** To examine changes in under-5 mortality, coverage of child survival interventions and nutritional status of children in Ethiopia between 2000 and 2011. Using the Lives Saved Tool, the impact of changes in coverage of child survival interventions on under-5 lives saved was estimated.

**Methods** Estimates of child mortality were generated using three Ethiopia Demographic and Health Surveys undertaken between 2000 and 2011. Coverage indicators for high impact child health interventions were calculated and the Lives Saved Tool (LiST) was used to estimate child lives saved in 2011.

**Results** The mortality rate in children younger than 5 years decreased rapidly from 218 child deaths per 1000 live births (95% confidence interval 183 to 252) in the period 1987–1991 to 88 child deaths per 1000 live births in the period 2007–2011 (78 to 98). The prevalence of moderate or severe stunting in children aged 6–35 months also declined significantly. Improvements in the coverage of interventions relevant to child survival in rural areas of Ethiopia between 2000 and 2011 were found for tetanus toxoid, DPT3 and measles vaccination, oral rehydration solution (ORS) and care-seeking for suspected pneumonia. The LiST analysis estimates that there were 60 700 child deaths averted in 2011, primarily attributable to decreases in wasting rates (18%), stunting rates (13%) and water, sanitation and hygiene (WASH) interventions (13%).

**Conclusions** Improvements in the nutritional status of children and increases in coverage of high impact interventions most notably WASH and ORS have contributed to the decline in under-5 mortality in Ethiopia. These proximal determinants however do not fully explain the mortality reduction which is plausibly also due to the synergistic effect of major child health and nutrition policies and delivery strategies.

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Ethiopia has achieved remarkable declines in under-5 mortality. According to the 2015 UN Inter-Agency Group for Child Mortality Estimation (IGME) report, Ethiopia reached its target for Millennium Development Goal 4 for child survival with an estimated under-five mortality rate of 59 per 1000 live births in 2015, a decline from 205 in 1990. This represents an average reduction in mortality of 5% per year; higher than the average for sub-Saharan Africa (2.9%) [1].

Major policy and program activities related to child survival were initiated in Ethiopia between 2003 and 2013 which built on major reforms starting from the 1990s to decentralise and reorganise the health system. An ambitious Health Extension Programme (HEP) was launched in 2003 which aimed to provide universal access to mainly preventive primary health care services [2,3], through more than 34 000 locally recruited, government-salaried mostly female health extension workers (HEWs) who receive one year of training. Two HEWs have been placed in each health post to serve a kebele, the smallest administrative unit of about 5000 people. HEWs split their time between outreach activities and their health post. Outreach activities include: conducting household visits, organizing communities to participate in the expansion of HEP services, educating families to adopt healthy life-styles and serve as 'model families' in their neighborhood. HEWs focus on delivering 16 primary health care (PHC) packages of services including family health promotion, communicable disease prevention and control, hygiene and environmental health and health education and communication services. More recently in 2011, a network of volunteers (Health Development Army), drawn from "model family" households, support the HEWs by providing essential health messages to the community [3,4].

The launch of the HEP in 2003 was followed by the Health Sector Development Programme and the National Child Survival Strategy in 2005. At around the same time there was national scale up of community-based treatment of severe acute malnutrition using ready-to-use therapeutic food [5]. From 2006, when the HEP was fully operational, until the end of 2009, HEWs were involved mainly in preventive and promotive work while their treatment services included the diagnosis and treatment of only malaria, diarrhea (not including low osmolarity ORS) and severe acute malnutrition. A major health policy change occurred in 2009 which enabled HEWs to administer antibiotics (for suspected pneumonia) and zinc (for diarrhea) in the community, while the scale up of integrated community case management (iCCM) only began in 2011.

This paper examines changes in mortality and coverage of child survival interventions in Ethiopia between 2000 and 2011. The impact of changes in coverage of child survival interventions on under-5 lives saved was estimated using the Lives Saved Tool.

## METHODS

### Data sources

We used full birth and death history data collected from women aged 15 to 49 years in nationally representative surveys: namely the 2000 Demographic and Health Survey

(DHS) the first DHS to be undertaken in Ethiopia, 2005 DHS and the 2011 DHS to calculate under-5 mortality. The surveys covered 14 072, 13 721, and 16 702 households respectively.

To assess trends in coverage of child survival interventions and nutritional status we used the same three Ethiopian DHS surveys. The surveys provide detailed information about the health and nutritional status of women and children and coverage of health care services. The analysis included all survey data sets available with full data, including sampling weights, to allow for re-analysis (see Table S1 in the **Online Supplementary Document** for further details on the surveys). To assess coverage of malaria interventions two separate Malaria Indicator Surveys (MIS) were used since these surveys sample specifically from malaria endemic areas. Malaria is seasonal in most parts of Ethiopia, with variable transmission and prevalence patterns affected by the large diversity in altitude, rainfall, and population movement. The MIS from 2007 [6] and 2011 [7] focus on malarious areas defined as <2000m in altitude mapped by global positioning system (GPS); hence these provide a more appropriate estimate of coverage of malaria interventions than the DHS surveys [7]. All of the surveys provided cross-sectional data on intervention coverage in their respective years; however for the MIS, primary data are not available and only point estimates are presented. Definitions and data sources for all indicators can be found in Table S2 in **Online Supplementary Document**.

### Statistical analysis

We used a direct method for estimating under-5 mortality based on the synthetic cohort approach [8,9]. Under this concept, age-specific mortality probabilities for narrow age ranges and defined periods are calculated using death events and exposures. These probabilities are combined to compute the probability that a child has not died before reaching age 5 years [9]. Under-five mortality rates were computed for successive five year periods preceding the 2011 DHS. For the purposes of this analysis, mortality rates were calculated for 5-year periods starting from 1987-1991 up until 2007-2011 (the 5-year period immediately prior to the 2011 DHS). Survival probabilities were calculated over age ranges; 0, 1-2, 3-5, 6-11, 12-23, 24-35, 36-47, 48-59 months as recommended by DHS (Section B in **Online Supplementary Document**) [9]. The standard errors for the computed mortality estimates were obtained using the Jackknife variance estimation, a repeated sampling method [8]. A series of mortality estimates were obtained by deleting and replacing each primary sampling unit; this produced a sample of under-5 estimates, from which the variance was computed in turn. We also estimated the average annual change (AAC) in mortality using mortality estimates for the peri-

ods 1987–1991 and 2007–2011 (Section B in the **Online Supplementary Document**).

We analyzed primary data from three Ethiopia DHS surveys to assess coverage trends for 10 indicators which represent high impact maternal and child health interventions; three additional malaria intervention indicators are presented as point estimates. We re-calculated all coverage indicators using standard indicator definitions [10] for tracking progress toward MDG 4. The sampling design of these DHS surveys, such as clustering at enumeration areas and sampling weights (due to non-proportional sampling), were taken into account. Except for the malaria indicators, coverage estimates for rural areas are presented to reflect the focus of the HEP on universal access. We considered malaria indicators for endemic areas only. The 95% confidence intervals were used to assess whether the changes were significantly different across the three time periods.

We computed anthropometric indicators for stunting (height-for-age) and underweight (weight-for-age) in children younger than three years of age from information on age, height and weight in the surveys applying the WHO child growth standards [11]. Moderate or severe (below minus two standard deviations (SD) from the median) and severe (below minus three standard deviations (SD) from the median) were calculated for both nutritional measures. Infant feeding indicators such as exclusive breastfeeding and micronutrient intake (vitamin A supplementation) were calculated by age of the child. We used Stata (version 13) (Stata Corporation, College Station, Texas, USA) for all mortality and coverage analyses.

We used the Lives Saved Tool (LiST) to estimate the number of deaths averted in 2011 due to changes in coverage since 2000. We compared the changes in mortality produced in LiST with single year estimates from IGME [12] as well as the five-year estimates produced in this analysis using DHS data. LiST uses country-specific or region-specific baseline information on mortality rates and causes of

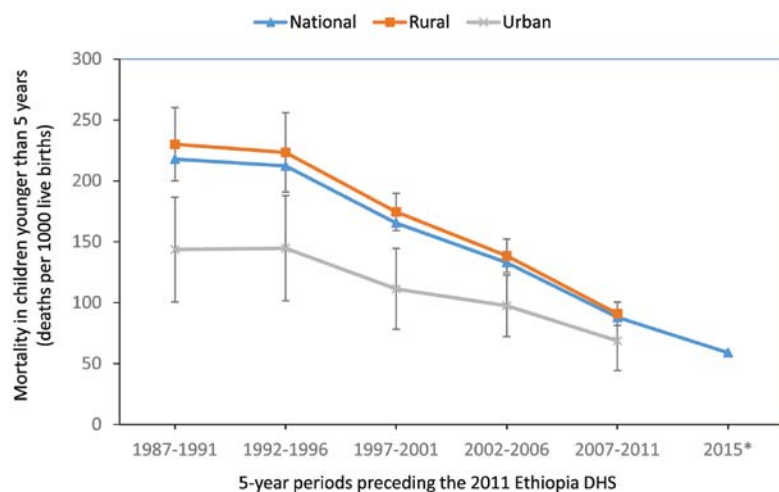
death as well as background variables (fertility, exposure to *Plasmodium falciparum*, stunting rates) and current coverage of more than 60 interventions and their associated effectiveness values [13–16] relative to specific causes of death and risk factors to estimate the deaths averted, overall and by specific interventions. The modeling methods have been widely published including discussion of the limitations [16–18]. We used 2000 as the baseline year and projected forward to 2011 using all available national data on changes in intervention coverage and nutritional status (Section C and Table S5 in the **Online Supplementary Document**).

Specific input values used in this LiST application are available in Table S6 in **Online Supplementary Data**. The analysis was done with the program Spectrum/Lives Saved Tool, version 5.04 (Johns Hopkins University, Baltimore Maryland, USA).

## RESULTS

The national mortality rate in children younger than 5 years decreased rapidly from 218 child deaths per 1000 live births (95% CI 183–252) in the period 1987–1991 to 88 child deaths per 1000 live births in the period 2007–2011 (95% CI 78–98) with an average annual change of –4.5%. The mortality rate was significantly lower in urban areas, compared to rural areas up until the most recent period (2007–2011) where the confidence intervals for the two estimates overlap indicating that the urban mortality estimate was no longer significantly different from the rural estimate (**Figure 1**). Large declines in mortality were also noted in the poorest wealth quintile and among mothers with no education (see Figure S2 and Figure S3 in **Online Supplementary Document**).

Significant improvements in the coverage of interventions relevant to child survival in rural areas of Ethiopia between 2000 and 2011 were noted for all indicators except for vi-



**Figure 1.** Under-5 mortality rates nationally and in urban and rural areas, Ethiopia, 1987–2011. Data are from analysis of the 2011 national Demographic and Health Survey (DHS) in Ethiopia. Vertical lines show 95% confidence intervals for survival probabilities for the rural and urban estimates. Dates on the x-axis represent the 5-year periods preceding the 2011 Ethiopia DHS. \*The 2015 estimate is from the IGME child mortality database (source: UNICEF, [1]).

tamin A coverage, breastfeeding initiation, exclusive breastfeeding, skilled attendance at birth and postnatal care (Figure 2). Coverage of breastfeeding initiation and exclusive breastfeeding remained high (around 50%) throughout the period of analysis, skilled attendance at birth and postnatal care remained low (<5%) and vitamin A supplementation coverage remained at around 50%. Coverage of improved water source and sanitation, DPT3 and ORS achieved greater gains in the 2000–2005 period while coverage of care-seeking for suspected pneumonia and measles vaccination had larger percentage point gains in the 2005 to 2011 period.

With regard to malaria indicators, increases were noted in timely care-seeking for fever and malaria treatment, the largest being for timely care-seeking for fever rising from 16% to 51%. There was little change in coverage of children under-5 sleeping under insecticide-treated nets (ITNs) (41% to 38%) (Figure 3).

Overall, the prevalence of moderate or severe stunting in children aged 6–35 months declined significantly across both survey periods (2000–2005 and 2005–2011) (Figure 4, panel A) with an overall reduction of 13 percentage points (pp). The proportion of children who were moder-

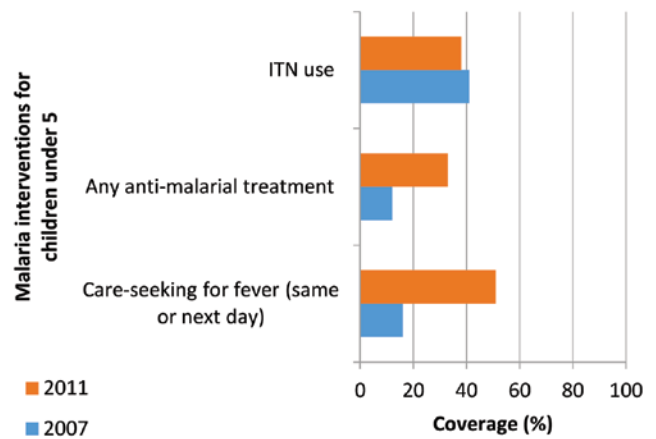


Figure 3. Coverage of malaria interventions in malaria endemic areas of Ethiopia, Malaria Indicator Surveys 2007 and 2011. ITN – insecticide treated nets.

ately or severely underweight also declined significantly among children 6–35 months between 2000 and 2005 (by 11 pp) but did not change significantly between 2005 and 2011. The same trend was seen across all age groups (Figure 4, panel B).

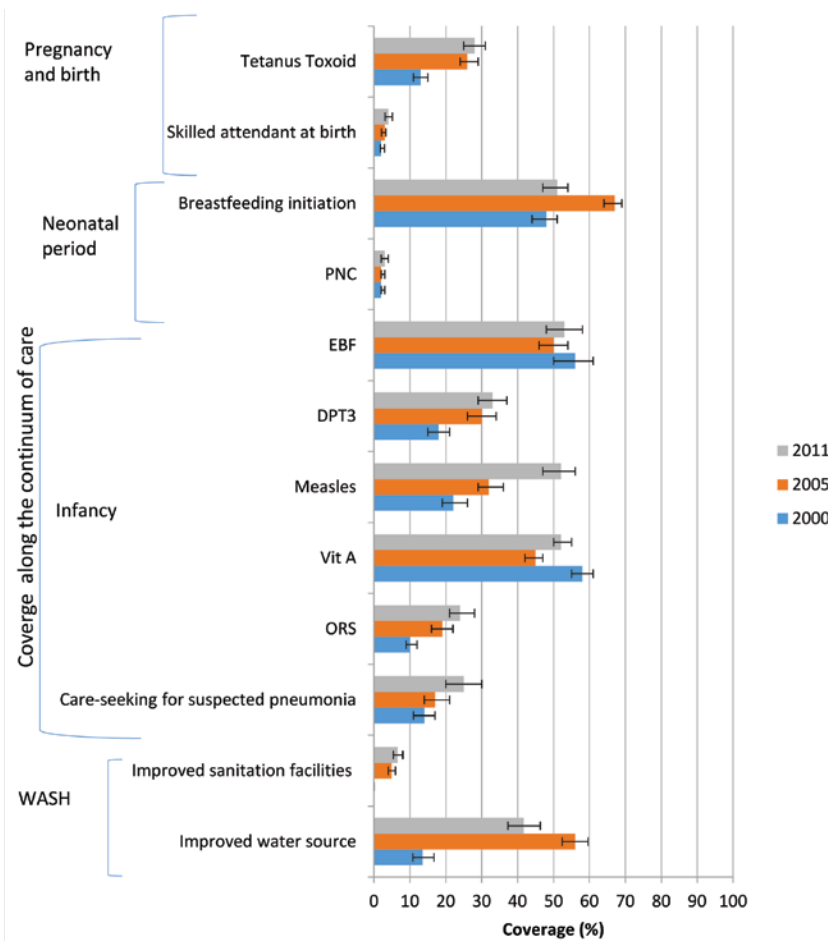


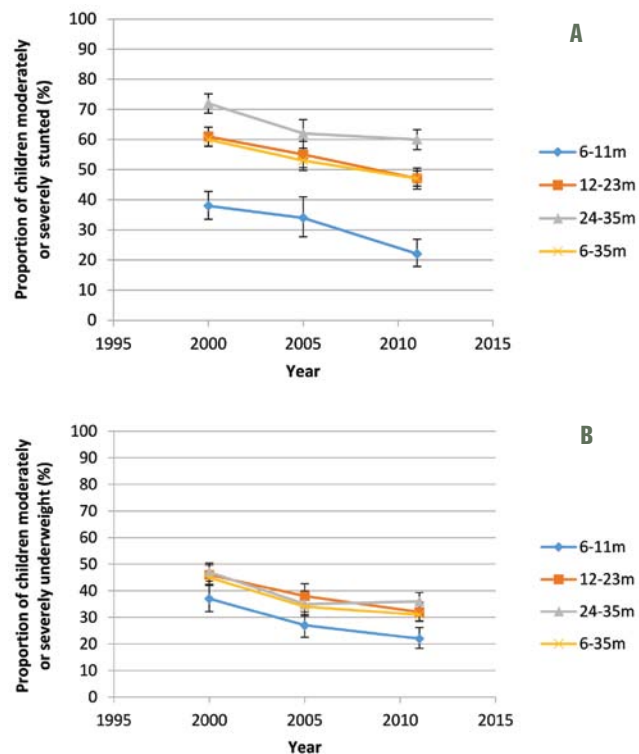
Figure 2. Rural coverage levels for high impact interventions across the continuum of care in Ethiopia as measured in Demographic and Health Surveys (DHS); 2000, 2005 and 2011. Bars represent 95% confidence intervals. DPT3 – three doses of diphtheria, pertussis and tetanus vaccine; ORS – oral rehydration salts; Breastfeeding initiation refers to newborn babies put to the breast within 1 hour of birth; Tetanus Toxoid – percentage of women with a live birth in the last 2 years who received at least 2 doses of tetanus toxoid vaccine during the last pregnancy; PNC – percent of women with live births in the past 2 years who received postnatal care within 2 days after delivery; EBF – exclusive breastfeeding.

Starting at a baseline mortality rate for children younger than 5 years of 146 per 1000 livebirths in 2000 and using available mortality and coverage data up until 2011, LiST predicted under-five mortality to be 119 in 2011, much higher than both the IGME 2011 estimate of 71 (56 to 88) and the 2007–2011 5-year DHS estimate of 88 (78 to 98), and placing it outside the upper confidence range of both estimates.

We calculated the proportion of child lives saved in 2011, by intervention or change in nutritional status, using the LiST estimation of 60 700 deaths averted in 2011 (relative to the situation in 2000) as a denominator. The main factors contributing to the prevention of these deaths in 2011 included nutritional interventions resulting in decreases in wasting rates (18%, 11 400 deaths averted) and stunting rates (13%, 8400 deaths averted), water, sanitation and hygiene (WASH) interventions (13%, 8300 deaths averted), ORS for diarrhea (11%, 7200), and the introduction of the Hib vaccine (10%, 6400 deaths averted) (Figure 5). Decreases in breastfeeding rates between 2005 and 2011 resulted in an additional 2300 deaths.

## DISCUSSION

Ethiopia has achieved a remarkable decline in under-5 mortality which has occurred in both rural and urban areas and among the poorest and least educated mothers. Our



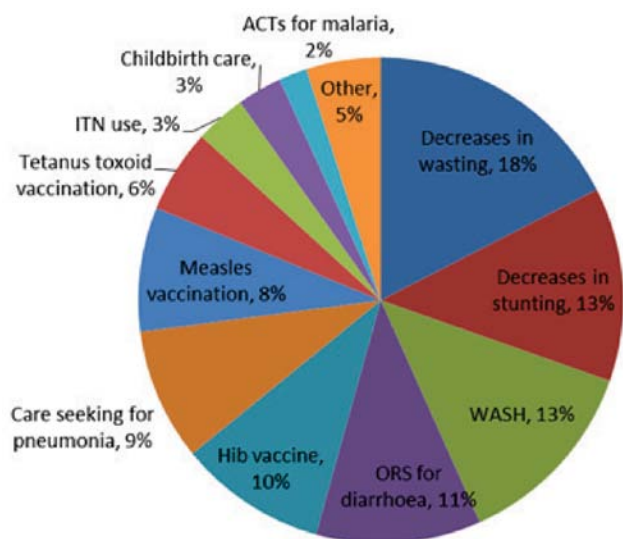
**Figure 4.** Prevalence of stunting (A) and underweight (B) by age in children in Ethiopia in the Demographic and Health Surveys (DHS); 2000, 2005 and 2011.

analysis of rural coverage for child survival interventions shows significant change between 2000 and 2011 for several high impact interventions including measles and DPT immunization, ORS coverage, access to an improved water source and care-seeking for suspected pneumonia. For several indicators the biggest coverage change occurred between 2000 and 2005 (tetanus toxoid, DPT3, improved water source and sanitation facilities and ORS) possibly reflecting early impact from the HEP, initiated two years prior to the 2005 DHS, particularly elements such as outreach services, greater access to curative care at health post level, the multi-sectoral approach and a focus on prevention and promotion through model families. Coverage of care-seeking for suspected pneumonia and coverage of ORS treatment for diarrhea was still low in 2011 (both around 25%) although this represents a significant increase from very low coverage levels (around 10%) for both indicators in 2000.

With respect to nutritional status of children, we report a significant decline in both stunting and underweight nationally and our LiST analysis has found that a total of 31% of deaths averted were estimated to be due to decreases in stunting and wasting rates. These shifts in nutritional status of children do not appear to be driven by improvements in breastfeeding practices as exclusive breastfeeding remained high across the period 2000–2011 at around 50% of infants 0–6 months. The changes could plausibly be due to major policy shifts in nutrition which occurred in the country between 2004 and 2008 with the scale up of community management of acute malnutrition at health post level and the development of a national nutrition strategy and program [5,19]. An impact evaluation of the community-based nutrition program in four regions, delivered by HEWs and community volunteers, found substantial changes in infant and young child feeding (increased exclusive breastfeeding) and reductions in stunting prevalence [20]. Furthermore, a recent ecological analysis of patterns in stunting and coverage of nutritional programmes concluded that between 2005 and 2011 the scale up of national nutritional programmes could plausibly have led to reductions in stunting [21].

It is difficult to disentangle the mechanisms whereby socio-economic change and improvements in health coverage interact to generate mortality reduction as these mechanisms can be either direct or indirect and take place concurrently [22]. There are a number of possible explanations for the discrepancy between the IGME-estimated under-five mortality rate and that estimated through our LiST analysis. First, some high impact interventions lack coverage data and so cannot be included in model. Second, it is likely that other contextual changes had influence, which are not captured in LiST. At an economic level, large chang-





**Figure 5.** Percentage of child lives saved in 2011 in Ethiopia, by intervention. ACTs – Artemisinin-based combination therapies, ITN – insecticide treated nets, ORS – oral rehydration solution, WASH – water, sanitation and hygiene.

es have occurred in the per capita GDP which tripled since 2000 to US\$ 355 in 2011; similarly per capita expenditure on health tripled to reach US\$ 17.5 in 2011. Furthermore, Ethiopia has received considerable official development assistance (ODA) for maternal, newborn and child health (MNCH) and has successfully guided partner support toward the health sector development program enabling joint financing to ensure implementation of government policies and plans [23]. The annual MNCH ODA has increased from \$105 million in 2003 to US\$ 215 million in 2010 [24]. Since 2003, Ethiopia has also received US\$ 1.4 billion from the Global Fund, 64% of which was spent on HIV/AIDS and between 2004 and 2011 Ethiopia received US\$ 1.78 billion from the United States President's Emergency Plan for AIDS Relief (PEPFAR) [25]. As a result, external resources for health, as a percentage of total health expenditure, increased from 16% in 2000 to 52% in 2011 [26]. This massive funding input could plausibly have had spillover effects on wider health system strengthening beyond the actual programmes it targeted [27,28].

In addition to meeting the MDG 4 target, Ethiopia has also met four other MDG targets including MDG 1 (poverty and hunger), MDG 6 (HIV, malaria and other diseases) and MDG 7 (environmental sustainability). Furthermore, at the end of 2015 the country was “on track” to meet MDGs 2 (universal primary education), 3 (gender equality and empowering women) and 5 (maternal health) and was only “off track” on one out of the eight goals (stabilizing debt) [29]. Evidence is emerging that progress made across these multiple sectors which address crucial health determinants has contributed to the

fast-track progress in reducing maternal and child mortality in Ethiopia [23,29,30]. This progress does come with some cautionary optimism given the increasing reliance on external resources for health. Other authors have noted this as a challenge facing Sub-Saharan African countries in the post-MDG era. English et al. [31] note that official development assistance (ODA) for health per capita/y in the WHO African Region increased from US\$ 2.7 in 2002 to US\$ 9.8 in 2010 and while governments' spending on health has increased, only 6/46 countries in sub-Saharan Africa have met their Abuja target of 15% of their expenditure on health [31].

Several indicators, particularly related to maternal and newborn intervention coverage, showed no improvement in rural areas over the period under analysis. Rural skilled attendance at birth and postnatal care coverage were 4% and 3% respectively in 2011. An analysis of neonatal mortality in Ethiopia found an annual rate of decline of 1.9% between 1995 and 2010, which was even lower (0.9%) for early neonatal mortality (death occurring before 7 completed days of life) the period in which 74% of neonatal deaths occurred [32]. A recently completed 2014 mini-DHS reveals some improvement in these indicators which have reached 9% and 7% respectively, in rural areas in 2014 [33]. Improvement is also seen in another important maternal indicator namely the total fertility rate which has declined from 5.5 in 2011 to 4.5 in 2014 in rural areas. These recent improvements in maternal indicators together with the 2013 launch of community-based newborn care [34] (including sepsis treatment) will hopefully enable the mortality reductions to continue with accelerated progress in reducing newborn deaths.

The endline data for this assessment, the 2011 Ethiopia DHS, occurred at the time of national scale up of the iCCM program and thus provides a picture of coverage and child survival in the absence of an established community-based treatment platform. It is recommended that a comparable analysis be undertaken following the next full DHS to establish the impact of the community delivery platform on child survival and health.

### Strengths and weaknesses of this study

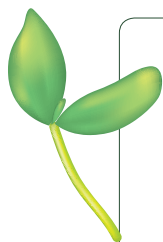
A strength of this study is the re-analysis of primary data to generate mortality and coverage estimates for 10 indicators and nutritional status measures over three time points together with lives saved modeling and a desk review of broader factors hypothesized to impact on child survival.

There are several weaknesses to this analysis. First, primary data were not available for the two MIS to enable us to determine significant changes in malaria interventions; however, for care-seeking and malaria treatment the changes in

point estimates are large (>20 percentage points) and the sample sizes for both surveys were over 5000 households, therefore it would be scientifically plausible that these changes are statistically significant. Second, with the LiST analysis, the household survey indicator definitions do not perfectly match LiST indicators in all cases, and some coverage indicators—particularly those related to delivery care—are imputed based on rates of home and facility births. Additionally, the DHS data used in this analysis does not capture some of the interventions included in LiST. These interventions are often high impact for children, eg, therapeutic feeding for severe wasting, and might have changed during the period under consideration.

## CONCLUSIONS

The collective effect of several positive changes in child nutritional status, and increased coverage of high impact interventions including WASH and ORS have contributed to the decline in under-5 mortality in Ethiopia. These proximal determinants however do not fully explain the mortality reduction which is plausibly also due to the synergistic effect of major child health and nutrition policies and decentralized delivery strategies. Ethiopia's progress confirms the importance of an integrated approach to child survival [29] and the post MDG era provides an opportunity, through the sustainable development goals, which are comprehensive in addressing specific health interventions as well as key social determinants, for Ethiopia to continue to close gaps related to the social determinants of health. Building on this success will require continued investments and support for universal health coverage with greater attention to maternal and newborn care.



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**Authorship contribution:** TD, KK, MK, DS, SR, DB, ML, IR and DN conceptualised the study. ML and TD developed the protocol, study design, and data collection materials. ML and DN participated in the country evaluation visit in October 2012. SM and DB conceptualised the mortality analysis and data quality assessments, which were done by them. SR and DB led the work on quality assessment and reanalysis of datasets on intervention coverage, with participation by SM. MK and KK did the LiST analysis. TD, SR, DB, KK, MK, SM, ML, DN, ED, WZ, NL and DS participated in a two-day workshop in Cape Town in February 2014, to review and interpret the preliminary results. TD and DB prepared the first draft of the paper. All authors reviewed and contributed to subsequent drafts and approved the final version for publication.

**Competing interests:** All authors have completed the ICMJE uniform disclosure form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available upon request from the corresponding author) and declare no conflict of interest. IR is an editor-in-chief of the Journal of Global Health. To ensure that any possible conflict of interest relevant to the journal has been addressed, this article was reviewed according to best practice guidelines of international editorial organizations. TD was employed by UNICEF in Ethiopia at the time of the study.

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# Self-reported diabetes education among Chinese middle-aged and older adults with diabetes

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**Background** To compare self-reported diabetes education among Chinese middle-aged and older adults with diabetes in three population groups: urban residents, migrants in urban settings, and rural residents.

**Methods** We used data from the 2011 China Health and Retirement Longitudinal Study. The sample included 993 participants age 45 and older who reported having diabetes diagnosed from a health professional. We performed multilevel regressions to examine the associations between characteristics and different aspects of diabetes education received.

**Findings** Our study shows that 20.24% of the participants received no diabetes education at all. Among those who received information, 46.82% of respondents with diabetes received weight control advice from a health care provider, 90.97% received advice on exercise, 60.37% received diet advice, 35.12% were spoken to smoking control, and only 17.89% of persons were informed of foot care. After controlling socioeconomic factors, life style, number of comorbidities and community factors, we found that compared with migrant population and rural residents, urban residents were more likely to receive diabetes education on diet. Urban residents were also more likely to obtain diabetes education and more aspects of diabetes education in comparison with migrants and rural residents.

**Conclusions** Our study suggests diabetes education is a serious concern in China, and a significant proportion of the participants did not receive advice on smoking control and foot care. Rural residents and migrants from rural areas received much less diabetes education compared with urban residents. Efforts to improve diabetes education are urgently needed in China.

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The prevalence of diabetes has dramatically increased globally, especially in China [1]. The prevalence of diabetes among the Chinese adult population has significantly increased from 5.5% to 11.6% during the past decade [2,3]; a total of 114 million adults have diabetes. Previous studies have shown that diabetes education, serving as the keystone of diabetes self-management, provides diabetics adequate knowledge and tools to facilitate them monitoring blood glucose value, preventing the complications of diabetes, and eventually improving their quality of life [4–6]. Literature on diabetes education in China focused on the diabetes education

receipt rate within people living in a certain region [7–13]. So far, only two previous studies reported the current status of diabetes education at national level [8,13]. These studies showed that over three quarters of the diabetics in China reported having received diabetes education and most of them obtained such education from a health profession. However, both of these studies were limited by a lack of explicit measures of the aspects of diabetes education and its associated factors that impact people receiving diabetes education.

In addition, disparities in health care systems between Chinese urban and rural areas may explain the variation in awareness of diabetes and access to health care, thus affecting people receiving diabetes education [14–16]. To our knowledge, no study has been done to examine diabetes education across place of residence, such as urban and rural settings. Also the urbanization process in China resulted in the dramatic growth of the internal migrants. This migrant population has grown to 221 million in 2010, the majority of which (72%) were from rural areas [17]. Migrants in China are likely to encounter hostility and discrimination from urban residents. For example, many jobs that migrants took are limited to certain types that urban residents are not willing to do. They are often denied access to many of the social and medical programs such as health insurance and unemployment benefits that their urban counterparts are entitled to have [18]. With low socioeconomic status and limited medical insurance, these migrants had limited access to health care, which would have negative impacts on the migrant workers' health status [18,19]. Previous research that targeted this population mainly focused on communicable diseases such as HIV/AIDS and occupational diseases [20,21]. No published literature has explicitly focused on chronic diseases education such as diabetes among migrant population in China. Considering the sheer size of the migrant population in China and the impact of urbanization on people's life style, it is pressing to examine the prevalence of non-communicated diseases especially diabetes among the migrant population.

The goal of this study is to investigate the variation of types of diabetes education received among Chinese middle aged and older adults with diabetes across three groups: urban residents, rural residents, and rural-to-urban migrants. We aim to address this knowledge gap by using a national sample with individual- and community-level data.

## METHODS

### Data source

Data were applied from the 2011 China Health and Retirement Longitudinal Study (CHARLS) data set for this study.

CHARLS is a biennial study that aims to collect data in three domains – health, financial, and family – from a nationally representative sample of Chinese residents age 45 and above [22]. The CHARLS National Baseline (2011 wave) was conducted in 28 out of 30 provinces in China and collected both individual- and community-level information from 17 708 individuals living in 10 287 households. The questionnaire included modules like family structure/transfer, health status and functioning, biomarkers, health care and insurance, work, retirement and pension, income and consumption, and assets (individual and household). The overall response rate for the 2011 CHARLS was over 80%: 94% in rural areas compared with 69% in urban areas [22]. In our study, we included 993 respondents who reported having diagnosed diabetes from a health care provider.

### Outcome measures

This study used seven diabetes education variables as the study outcomes: diabetes education received (Yes/No), five aspects of diabetes education: Weight control (Yes/No), Diet (Yes/No), Exercise (Yes/No), Smoking control (Yes/No), and Foot care (Yes/No), and a sum of diabetes education received. In the 2011 CHARLS questionnaires, the presence of received diabetes education was determined by the following question “Has your care providers ever given you diabetes education/advice on the following?” Possible answers included: weight control, diet, exercise, smoking control, foot care, and none of them above. Respondents were classified as having received diabetes education (Yes) if they chose at least one aspect of the five diabetes education. We also operationalized a variable regarding a sum of diabetes education received based on how many aspects of diabetes education each individual chose. Additionally, among those respondents who received at least one aspect of diabetes education, the researchers generated five dummy variables for each aspect.

### Condition specific measures

*Condition specific variables* included age, gender, smoking status (current smoker or not), drinking habit (Yes/No), defined as women have more than one drink per day while men have no more than two drinks per day [23], body mass index BMI (normal, overweight, and obese), categorized according to the BMI cutoff points for Asians, physical activities (Yes/No), years of being diagnosed of diabetes (1 = 0–1 year, 2 = 1–5 years, 3 = 5 years and above), and number of comorbidities (including hypertension, dyslipidemia, cancer or malignant tumor, chronic lung diseases, liver diseases, heart problems, stroke, kidney diseases, stomach or other digestive disease, emotional, nervous, or psychiatric problems, memory-related disease, arthritis or rheumatism, and asthma).

## Physical and social environment

*Physical and social environment* included both individual- and community-level variables. The individual level variable was the place of residence, which was coded into three categories: 1 = urban residents, 2 = migrant population, and 3 = rural residents. *Urban residents* included respondents living in urban areas with urban medical insurance. *Migrant population* was defined as respondents who live in an urban area with rural medical insurance, in most cases the New Cooperative Medical Insurance. *Rural residents* were respondents living in rural areas with rural medical insurance. Two community-level variables were 1) Physical accessibility of health facilities (Yes/No), which was defined by World Health Organization (WHO) that households that live within 15 minutes travel time to any public or private health facility, and 2) Use of community-level health facilities (Yes/No). These community-level characteristics were extracted from the CHARLS community survey.

## Individual and family factors

*Individual and family factors* included marital status (married vs other), education level, and household income. Because of the extremely low levels of education among Chinese older adults, education was categorized into four levels as illiterate (No formal education/illiterate), primary education only school (did not finish primary school but capable of reading and/or writing, Sishu/home school, elementary school), secondary education but no higher (middle school, high school, vocational school), and college level and above (two- to three-year college/associate degree, four-year college/Bachelor's degree, Master's degree and Doctoral degree/PhD). Household income included the following dimensions: wage income, self-employment income, agricultural income, pension income, and transfer income. In this analysis, the household income was aggregated into three levels: low = 0% to 33.3%, middle = 33.4% to 66.6%, high = 66.7% to 100%.

## Statistical analysis

Descriptive statistics of individual and community factors and were examined by using *t* and  $\chi^2$  test procedures to compare mean differences and frequency distributions. Then, two-step multilevel regression models were applied in the study. First, logistic regression models were used to examine the outcome of having diabetes education and regression models were used to examine the outcome of the sum of diabetes education received. Then, a series of logistic regression models were applied to test the each aspect of diabetes education. STATA 13 (College Park, TX, USA) was used to analyze data with a significance level of 0.05.

## RESULTS

### Bivariate analysis

**Table 1** shows the sample demographic and health related characteristics. The mean age of the sample was 62 years, and 54.55% were women; 19.77% of participants were migrants, 46.78% were urban residents, and 33.45% were rural residents. Overall 20.24% of the participants received no diabetes education at all. Among participants who received at least one aspect of diabetes education, 46.82% of respondents with diabetes received weight control advice from a health care provider, 60.37% received diet advice, 90.97% received advice on exercises, 35.12% were suggested about smoking control, and only 17.89% of persons were informed of foot care.

Respondents who reported being informed by a health care provider about diabetes education on diet, exercise, and foot care were more likely to be urban residents. A higher proportion of males, better educated, and with higher income received at least one aspect of diabetes education. Additionally, people who didn't receive any diabetes education were more likely to be those who had diabetes within a year. In addition, respondents who lived in a community with accessible health facilities were more likely to receive diabetes education.

### Multivariate analysis

**Table 2** presents the results of step 1 regression models. Results show that in comparison with urban residents, both migrant population (adjusted odds ratio (OR) = 0.44, 95% confidence interval (CI) 0.23–0.83) and rural residents (adjusted OR = 0.43, 95% CI 0.24–0.77) were less likely to obtain diabetes education. We also found older respondents were less likely to receive any diabetes education (adjusted OR = 0.96, 95% CI 0.93–0.98). Gender was another significant factor for receiving diabetes education: females tended to receive no diabetes education (adjusted OR = 0.40, 95% CI 0.23–0.67) compared with their male counterparts. Additionally, people with more comorbidities were more likely to receive diabetes education (adjusted OR = 1.15, 95% CI 1.01–0.31).

Similar results were found in the sum of diabetes education received: rural residents ( $\beta = -0.14$ ,  $P = 0.04$ ) along with migrants ( $\beta = -0.16$ ,  $P = 0.006$ ) from rural area were more likely to receive less diabetes education compared to urban residents. People who were female ( $\beta = 0.19$ ,  $P < 0.001$ ) and older ( $\beta = -0.17$ ,  $P = 0.002$ ) reported receiving fewer diabetes education contents. People with more comorbidities were more likely to receive more aspects of diabetes education ( $\beta = 0.15$ ,  $P = 0.002$ ). Additionally, people with longer period of diagnosis of diabetes: having diabetes for

**Table 1.** Sample characteristics, China Health and Retirement Longitudinal Study (CHARLS), 2011

	WEIGHT CONTROL	DIET	EXERCISE	SMOKING CONTROL	FOOT CARE	NONE	TOTAL (N = 993)
<b>Individual characteristics:</b>							
Age (mean)	60.76†	61.44	61.84	60.00‡	59.79*	63.82	62.16
Female	44.79*	47.04†	52.65	21.96‡	41.23†	65.41†	54.55
Married	83.7	85.6	85.18	85.4	92.29*	78.97	84.36
<b>Education:</b>							
Illiterate	16.27*	17.11‡	21.85	11.06†	13.54	29.32*	23.1
Primary only	32.52	31.33	35.55	35.56	40.47	41.68	36.43
Secondary but no higher	45.37	45.4	37.93	26.25	38.25	24.57	35.76
College and above	5.84	6.16	4.68	7.13	7.74	4.43	4.8
<b>Household income:</b>							
Low	33.94	39.12	36.71	31.31	35.54	40.24†	37.77
Middle	27.13	30.75	25.07	26.8	25.34	36.11	27.13
High	38.93	30.13	38.22	41.89	39.12	23.65	35.1
<b>Place of settings:</b>							
Migrants	20.1	17.67‡	19.55†	21.52	12.70*	20.46‡	19.77
Urban	52.78	59.27	50.67	47.69	60.35	31.76	46.78
Rural	27.11	23.06	29.78	30.8	26.95	47.79	33.45
<b>Health status:</b>							
Current smoker	23.71	20.67	17.74	42.47‡	31.66†	20.18	19.4
Drinking	4.78	4.73	3.87	8.7	2.84	5.11	4.34
Exercise	12.82	12.77	14.47	11.71	16.86	17.7	15.01
<b>Years of diabetes:</b>							
0–1	17.33†	37.13‡	24.52*	17.84†	17.28	35.95*	27
1–5	38.4	28.18	33.25	41.02	36.42	25.06	31.46
≥5	44.26	34.69	42.23	41.15	46.3	38.99	41.54
<b>Body mass index:</b>							
<24	32.91	41.02	37.74	38.75	32.77	41.03	39.07
24–27.9	40.53	40.77	40.36	37.09	42.25	39.98	39.94
≥28	26.56	18.21	21.89	24.16	24.97	18.99	20.99
Number of comorbidities (mean)	2.32	2.33	2.39	2.39	2.27‡	2.36	2.38
<b>Community characteristics</b>							
Access to health facilities	90.01	90.52*	88.92	88.95	88.38	82.85*	88.01
Use of community health facilities	74.13	74.87	73.64	75.5	69.96	74.78	73.6

\* $P < 0.05$ .† $P < 0.01$ .‡ $P < 0.001$ .

more than one year were more likely to obtain more aspects of diabetes education from a health professional.

**Table 3** summarizes the results of the step 2 logistic regressions. First, both rural residents (adjusted OR=0.41, 95% CI 0.20–0.82) and the migrant population (adjusted OR=0.41, 95% CI 0.18–0.90) were less likely to receive diet education. Also rural residents were more likely to receive diabetes education in terms of smoking control (adjusted OR=2.70, 95% CI 1.13–6.42). Second, for weight control, people who were overweight or obese, or having diabetes for more than five years were more likely to receive this education. For smoking control, higher level of education, male, current smokers, obesity, and having diabetes for more than one year were positively related to receiving diabetes education on smoking control. In addition, we found that respondents who received foot care education were more likely to be current smokers (adjusted OR=2.70, 95% CI 1.38–5.31) along with people having more comor-

bidities (adjusted OR=1.20, 95% CI 1.03–1.40). Although people living in communities with more accessible health facilities tended to have better diabetes education about diet and foot care, the results were not significant across all aspects of diabetes education in the full model.

## DISCUSSION

Our study is one of the first to examine the factors affecting people receiving diabetes education in China using a national representative sample. The results showed great variation in the receipt of diabetes education. Additionally, data from this study revealed that place of residence plays an important part in determining whether one will receive diabetes education and the aspects of diabetes education.

National standard guideline for diabetes education from the American Diabetes Association (ADA) and the China Diabetes Society (CDS) suggest that individualized diabetes



**Table 2.** Regression on receiving diabetes education and sum of diabetes education, China Health and Retirement Longitudinal Study (CHARLS), 2011

VARIABLES	RECEIVING DIABETES EDUCATION (AOR, 95% CI)	SUM OF DIABETES EDUCATION ( $\beta$ )
<b>Individual characteristics:</b>		
Age	0.96 (0.93–0.98)†	-0.17†
Female	0.40 (0.23–0.67)‡	-0.19†
Married	1.11 (0.60–2.04)	0.01
<b>Education (vs illiterate):</b>		
Primary only	0.91 (0.55–1.50)	-0.01
Secondary but no higher	1.22 (0.66–2.27)	0.09
College and above	0.55 (0.15–1.95)	0.02
<b>Household income (vs low):</b>		
Middle	1.05 (0.49–1.41)	0.03
High	1.11 (0.67–1.68)	-0.00
<b>Place of settings (vs urban):</b>		
Migrant	0.44 (0.23–0.83)*	-0.16†
Rural	0.43 (0.24–0.77)†	-0.14*
Current smoker	0.63 (0.36–1.11)	0.07
<b>Years of diabetes (vs 0–1):</b>		
1–5	1.41 (0.86–2.31)	0.19†
≥5	1.16 (0.72–1.88)	0.17†
<b>Body mass index (vs &lt;24):</b>		
24–27.9	0.84 (0.54–1.32)	0.06
28 and above	0.89 (0.52–1.52)	0.13*
Drinking	0.59 (0.24–1.46)	-0.09
Exercise	1.01 (0.61–1.65)	-0.06
Number of comorbidities	1.15 (1.01–1.31)*	0.15†
<b>Community characteristics:</b>		
Access to health facilities	1.42(0.81–2.49)	0.07

CI – confidence interval, AOR – adjusted odds ratio

\*P&lt;0.001.

†P&lt;0.05.

‡P&lt;0.01.

education may cover core topics such as nutritional management, physical activities, and preventing, detecting, treating complications [23,24]. Our study indicated that diet and exercise advices were the two most common diabetes education topics among all the five. However, smoking control and foot care education were the lowest two, which are more involving lowering the risk factors that damage blood vessels as well as preventing or delaying complications. Smoking is prevalent in China – the world largest tobacco consumer [25]. However, only 35.12% of the Chinese adults were aware of the health hazards related to smoking. Less than 50% of the current smokers in our study reported receiving quit smoking education, especially among urban residents. Thus, diabetes education regarding avoiding tobacco use is urgently needed. Apart from smoking, our results showed that diabetic patients in China received limited education on foot care, which is consistent with previous study [13]. People with diabetes could develop a series of foot problems including nerve damage, skin changes, and foot ulcer [26]. These complications could be easily prevented by performing regular foot care [26]. Guidelines for standard medical care for diabetes from the ADA and CDS [23,24], recommend that health professionals should provide foot care education to all diabetic patients. As a result, our findings call for future comprehensive diabetes education with a particularly focus on foot care.

Our study showed that residential settings are related to receipt of diabetes education. Migrant population and rural residents compared with urban residents were less likely

**Table 3.** Logistic regression models on types of diabetes education received, CHARLS, 2011

VARIABLES	WEIGHT CONTROL (AOR, 95% CI)	DIET (AOR, 95% CI)	EXERCISE (AOR, 95% CI)	SMOKING CONTROL (AOR, 95% CI)	FOOT CARE (AOR, 95% CI)
<b>Individual characteristics:</b>					
Age	0.98 (0.95–1.01)	0.97 (0.94–1.00)*	0.97 (0.93–1.01)	0.97 (0.93–1.01)	1.00 (0.96–1.03)
Female	0.92 (0.54–1.56)	0.96 (0.54–1.71)	0.98 (0.43–2.24)	0.16 (0.08–0.33)†	0.92 (0.49–1.71)
<b>Education (vs illiterate):</b>					
Primary only	0.76 (0.40–1.42)	1.18 (0.62–2.24)	2.21 (0.85–5.71)	1.01 (0.42–2.41)	0.85 (0.40–1.81)
Secondary but no higher	1.28 (0.64–2.58)	1.87 (0.90–3.88)	0.90 (0.35–2.33)	1.41 (0.54,3.70)	1.01 (0.44–2.31)
College and above	1.51 (0.38–6.06)	2.66 (0.48–14.84)	2.43 (0.25–23.36)	9.46 (1.50–59.69)*	1.31 (0.28–6.07)
<b>Place of settings (vs urban):</b>					
Migrant	0.93 (0.46–1.89)	0.41 (0.18–0.90)*	0.77 (0.31–1.92)	1.62 (0.59–4.45)	0.42 (0.17–1.04)
Rural	1.12 (0.60–2.08)	0.41 (0.20–0.82)*	1.32 (0.57–3.05)	2.70 (1.13–6.42)	0.80 (0.40–1.60)
Current smoker	1.76 (0.94–3.28)	1.25 (0.64–2.44)	0.53 (0.23–1.23)	17.85 (6.89–46.26)‡	2.70 (1.38–5.31)†
<b>Years of diabetes (vs 0–1):</b>					
1–5	2.91 (1.60–5.28)†	2.70 (1.48–4.95)†	1.39 (0.62–3.10)	2.21 (1.01–4.85)*	1.9 (0.94–3.82)
≥5	3.40 (1.89–6.11)‡	2.95 (1.63–5.36)‡	1.64 (0.73–3.69)	3.10 (1.39–6.88)†	1.73 (0.87–3.41)
<b>Body mass index (vs &lt;24):</b>					
24–27.9	2.10 (1.27–3.49)†	1.31 (0.77–2.23)	1.16 (0.57–2.37)	1.66 (0.83–3.33)	1.02 (0.56–1.84)
≥28	3.99 (2.13–7.49)‡	2.10 (1.09–4.04)*	1.17 (0.50–2.75)	2.33 (1.06–5.15)*	1.55 (0.79–3.04)

CI – confidence interval, AOR – adjusted odds ratio

\*P&lt;0.05.

†P&lt;0.01.

‡P&lt;0.001.

to receive any diabetes education and less aspects of diabetes education. Diabetic patients living in rural areas and migrant population were less likely to be educated about diet in comparison with their urban counterparts. These results were consistent with our exploratory analysis that identified the association between medical insurance type and receipt of diabetes education, which we found that people with urban employee or government medical insurance were more likely to receive diabetes education about diet, exercise, and foot care. It is possible that these disparities by place residence were partially due to medical insurance type. In comparison with New Rural Cooperative Health Insurance, urban employee and government medical insurance have higher outpatient coverage that help people to access to health services [27,28]. Previous studies have shown that individuals with urban employee and government health insurance were more likely to use outpatient services [27,29]. Diabetes education, as part of chronic disease management, would happen during outpatient visits. As a result, diabetic patients with health insurance that has a higher coverage of outpatient visit would have more outpatient care utilization, and subsequently would be more likely to receive diabetes education.

Besides the differences in health insurance, disparities of health resources may also relate to the receipt of diabetes education. Residents in urban area were more likely to see a doctor in tertiary or secondary hospitals, where diabetes education programs or certified diabetes educators were available. While rural residents and migrant population were more likely to use village clinics, township hospitals, or private clinics that lack of professional doctors and nurses, especially trained diabetes health care providers, which add another barrier of receiving diabetes education [27–29].

Aiming at providing universal health coverage, the Chinese government has launched different public health insurance programs for various populations, with a particular focus on the rural population [28]. Despite the rapid expansion of insurance coverage, with over 96% New Cooperative Health Insurance coverage among rural population, Chinese adults from rural areas still have a relatively high out-of-pocket payment during outpatient visits [28]. Regional disparities of health resources and health professional still existed [28]. Given the great epidemic of non-communicable diseases in China, such as diabetes, there is an urgent need to expand outpatient care coverage for rural population as well as improve quality of health services especially in rural community health centers. The government should focus on increasing reimbursement rates for outpatient care, especially for those from rural areas or migrant populations with chronic diseases. Community capacity building should also be prioritized to promote non-communicable disease prevention and control. In addition to the

policy and programs mentioned above, providing flexible reimbursement plans that would cover outpatient care both in rural and urban settings for migrant population may also encourage this segment of the population to use outpatient health promotion services, such as diabetes education classes when needed.

Twenty percent of the diabetics did not receive any diabetes education, which is similar to the rates reported in previous studies [8,13]. Participants with no diabetes education were more likely to be migrants or rural residents, older, or females. These findings were consistent with prior research that age and gender are significant factors associated with not receiving diabetes education. Older adult and females have a higher prevalence of diabetes [27], further diabetes education interventions should be more targeted to reach this group of people.

In our study, no significant association was found between community characteristics (access to health care facility, use of community health facility) and receipt of diabetes education. The lack of strong association could be partially contributed to the fact that most community health centers lack of qualified professional health care providers to provide health education related to prevention and control of non-communicable diseases, such as diabetes [28]. Previous studies provided evidence that the majority of health professionals who worked in primary health care facilities only received 2–3 years basic medical training [30,31]. The shortage of professional trained health care providers could limit the community health centers' capacity in providing adequate education to tackle the issue of non-communicable disease prevention. Further research is needed to assess whether access to different types of health care facilities is associated with the receipt and quality of diabetes education.

Findings in this study support that contextual factors (age, gender, comorbidities, year of diabetes) were associated with individuals receiving diabetes education, which is consistent with prior research [8,13]. We also found that other contextual factors, an individual's health behaviors, were associated with the aspects of diabetes education that health professionals provided them. Overweight and obese patients were more likely to receive weight control education. Smokers were more likely to be educated about smoking control. These results indicated that health professionals in China have the tendency to provide diabetes education based on a patient's health behaviors and health status. However, we still should notice that there was no difference in exercise education among patients with different BMIs. Given the fact that diabetes self-management involves various activities like maintaining a normal body weight, eating healthy diets, and being physical active, failure to provide adequate and comprehensive diabetes edu-

cation to diabetic patients may increase the risk of adverse health outcomes. With reference to diabetes education program development, our findings suggest that tailored diabetes education covering all aspects of diabetes knowledge are highly needed and would contribute to better diabetes self-management.

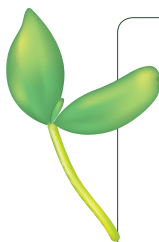
This study suffered from several limitations. First, the diagnosis of diabetes is a self-reported measure. It is possible that there is a huge undiagnosed diabetic population, especially in the rural areas. We may have different results if we recruit participants based on medical records or objective measure such as HbA1c. Second, the measure of diabetes education that the CHARLS included is crude so that we are not able to explore the specific education contents. In addition, the guideline from ADA and CDS suggests that diabetes education should include information about disease process, self-monitoring blood glucose, and individualized strategies to address psychological issues [23,24]. Due to limited information collected in the CHARLS data set, we are unable to explore whether these aspects of diabetes education is associated with place of setting. We also did not include health insurance as a contextual factor in our study because of the high colinearity with place of settings. Additionally, the CHARLS data set is cross-sectional. We could only assess the factors that are associated with disparities in receipt of diabetes education due to the nature of the data available. Longitudinal studies are essential to test the causal relationships. Finally, increasing evidence suggests that eye care and dental care are important for diabetes patients; however, the data does not list any of these as a response category. While very little attention has been paid to these care for the patients, practical guidelines and clinical practice needs to be improved to incorporate these as a part of their guideline and routine practice.

## CONCLUSION

Our study found that the receipt of diabetes education was strongly associated with people's residential locations. Aspects of diabetes education also varied by place of residence in China. Still a large amount of diabetic patients did not receive smoking control and foot care education. Gender, age, years of diabetes, and numbers of comorbidities were significant factors associated with to people receiving different aspects of diabetes education. Individuals health behaviors were also associated the aspects of diabetes education given by health professionals. However, we need to be aware that the results are based on self-reported information on the receipt of diabetes education; thus, the results may be subject to recall bias.

## IMPLICATIONS

Our study suggests that expanding outpatient care coverage and providing more tailored and comprehensive education are crucial for facilitating diabetes self-management and preventing diabetes complications for middle-aged and older adults in China. In addition, health policies should promote the strengthening of community-based non-communicable diseases health education and health promotion based on community health capacity building. In China, nurses serve as diabetes educators – a critical element in diabetes management. The shortage of nurses and uneven distribution of health care facilities require more adequate training for nurses to be able to educate diabetics self-managing their diseases. In addition, some innovative diabetes education interventions such as mobile health programs are urgently needed as a supplement of health professional diabetes education.



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# Factors influencing physicians' choice of workplace: systematic review of drivers of attrition and policy interventions to address them

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**Objectives:** The movement of skilled physicians from the public to the private sector is a key constraint to achieving universal health coverage and is currently affecting health systems worldwide. This systematic review aims to assess factors influencing physicians' choice of workplace, and policy interventions for retaining physicians in the public sector.

**Methods** Five literature databases were searched. Studies were included in the review if they focused on at least one of the following criteria: (i) incentives or motivators for retaining physicians in the public sector, (ii) pull factors that encouraged physicians to move to the private sector, (iii) push factors that forced physicians to leave the public sector, (iv) policy interventions or case studies that addressed physician retention in the public sector, and (v) qualitative reviews of policy interventions that were implemented in different health system settings.

**Results** Nineteen articles met the inclusion criteria. Six major themes that affected physicians' choice of workplace were identified including: financial incentives, career development, infrastructure and staffing, professional work environment, workload and autonomy. The majority of the studies suggested that the use of financial incentives was a motivator in retaining physicians in the public sector. The review also identified policy interventions including: regulatory controls, incentives and management reforms. Regulatory controls and incentives were the two most frequently reported policy interventions.

**Conclusion** While factors affecting physicians' choice of workplace are country specific, financial incentives and professional development are core factors. Other factors are highly influenced by context, and thus, it would be useful for future cross-country research to use standardized data collection tools, allowing comparison of contextual factors as well as the examination of how context affects physician retention in the public sector.

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The World Health Organization (WHO) estimates that in order to expand universal health coverage, the world needs an additional 12.9 million skilled health professionals by 2035—physicians, nurses and midwives [1]. Skilled health professionals are needed to achieve, maintain and accelerate progress on universal health coverage by ensuring effective coverage



for an expanding set of health care needs for all populations [1]. The human resource shortages are particularly acute in low and middle income countries in Africa, Asia and the Pacific and exacerbated by the movement of skilled physicians from the public to the private sector affecting health systems worldwide [2,3].

In both low- and high-income countries, physicians working in government hospitals and clinics also often practice privately in order to boost their earnings. This dual practice is common in many European countries including the United Kingdom and is particularly high in low- and middle-income countries such as Egypt, Vietnam and India [4]. The income gap between the public and private sector in these countries is a key factor motivating physicians to leave the public sector or work in both the public and private sector. Indeed, it is increasingly uncommon to find full-time health workers who are civil servants exclusively working in the public sector [4–7]. For instance, in Austria approximately 100% of senior health specialists work in both sectors, in the United Kingdom 60% of public physicians work in both sectors [8]. In Ireland, more than 90% of physicians employed in public hospitals also have privileges to practice in the private sector [8].

Other factors that have been identified as driving the movement of physicians from the public to the private sector include: lack of academic and career development opportunities in the public sector, poor infrastructure in public facilities, and greater autonomy in the private sector [2,9]. The pervasive practice of dual practice and the shift of doctors from the public sector to the private sector suggests a need to reassess the traditional models of physician education, placement and compensation, and the functioning of labor markets for highly skilled health workers [1]. There is limited evidence on the policies and regulatory mechanisms for promoting physician retention in the public sector [8,9].

The aim of this systematic review is to assess factors influencing physicians' choice of workplace and potential policy interventions for retaining physicians in the public sector. The review will identify the sources of dissatisfaction of physicians in the public sector (push factors), and sources of satisfaction of physicians in the private sector (pull factors), as well as the advantages and disadvantages of different policy interventions addressing physician retention in the public sector. The analysis will inform policymakers on the current evidence and identify policy options for retaining physicians in the public sector.

## METHODS

The analysis was undertaken by the first author and lead author. At each step of the process, the first author inde-

pendently assessed the eligibility of individual studies. Results were shared with the lead author, and differences were reconciled through discussions.

## Identification of studies

We conducted a systematic review of factors and policies related to attrition and retention of physicians in the public sector. Using key search terms, the following literature databases were searched: PubMed, EMBASE, World Bank database, WHO Global Health Observatory as well as Google Scholar. The search terms included: “physicians”, “doctors”, “specialists”, “retention”, “dual practice”, “recruitment”, “incentives”, “motivation”, “retaining”, “motivating”, “physician incentive plans”, “public sector”, “public health sector”, “private sector”, and “private health sector”. The references of the included studies were also scanned in order to find relevant literature that was not identified through the database search.

## Study selection criteria

Studies were included in the review if the original research was presented and if the study population included physicians. The studies also focused on at least one of the following criteria: (i) incentives or motivators for retaining physicians in the public sector, (ii) pull factors that encouraged physicians to move to the private sector, (iii) push factors that forced physicians to leave the public sector, (iv) policy interventions or case studies that addressed physician retention in the public sector, and (v) qualitative reviews of policy interventions that were implemented in different health system settings. Studies were excluded if they were: not in English, published before 1980, non-human studies, book chapters or book reviews, dissertations or theses, or published abstracts. Studies were also excluded if they were focusing on physician retention in rural vs urban areas since the review will be focusing only on public vs private retention, and if they were discussing retention of health workers other than physicians such as nurses or midwives.

## Data extraction and analysis

The studies were classified according to income level based on the World Bank classification. The study characteristics were extracted from all the studies and these include: first author, year, countries involved, study design and method (Table 1). The studies were then grouped into two categories: studies that were focusing on factors affecting physicians' choice of workplace (push-pull factors), and those that were discussing policy interventions for retaining physicians in the public sector.

Thematic synthesis was adopted in our review as codes were generated from illustrative quotes and then classified into themes [25]. During the data extraction process, the

**Table 1.** Studies included in the systematic review

INCOME LEVEL	FIRST AUTHOR	YEAR	COUNTRY	STUDY DESIGN	METHOD
Low and low-middle income	Abdul Rahim [2]	2012	Multiple countries	Descriptive study	Evaluation of five worldwide policy initiatives
	Luboga [10]	2011	Uganda	Mixed-method study	Focus groups and questionnaires
	Malik [11]	2010	Pakistan	Mixed-method study	Open ended questions, questionnaire and interviews
	Russo [12]	2014	Cape Verde, Guinea Bissau and Mozambique	Mixed-method study	Qualitative interviews and surveys
	McPake [13]	2014	Mozambique, Guinea Bissau and Cape Verde	Cross-sectional study	Survey
	Lonroth [14]	1998	Vietnam	Qualitative study	Individual interviews and group discussions
	Gruen [15]	2002	Bangladesh	Qualitative study	Open-ended questionnaire and in-depth interviews
Upper middle and high income	Jan [16]	2005	Multiple countries	Descriptive study	Critical analysis of dual practice policies
	Ashmore [3]	2013	South Africa	Qualitative study	Qualitative interviews
	Ashmore [17]	2015	South Africa	Qualitative study	In-depth interviews
	Ashton [18]	2013	New Zealand	Cross-sectional study	Postal survey
	Andreassen [19]	2013	Norway	Prospective cohort study	Modeling physicians labor supply choices
	Longmore [20]	2014	South Africa	Qualitative study	Open-ended questionnaire
	Gonzalez [21]	2004	Not listed	Modeling	Principal-agent modeling
	Heponiemi [22]	2013	Finland	Prospective cohort study	Four-year prospective questionnaire study
	Cohn [23]	2009	United States	Case-study	Case study on the journey of Banner Medical Group
	Kankaanranta [24]	2007	Finland	Retrospective cohort study	National postal survey completed at 5 y intervals
All income levels	Gonzalez [8]	2013	Not listed	Modeling	Two-stage theoretical modeling
	Eggleston [4]	2006	Not listed	Descriptive study	Comparative analysis of five models of dual practice

first author extracted illustrative quotes on push and pull factors from the studies focusing on physicians' choice of workplace. These quotes were coded according to trends in common answers, and sub-themes/factors were generated, 15 factors in total (Figure 1 and Table 2). The factors were then synthesized into six main themes, including: financial incentives, career development, infrastructure and staffing, professional work environment, workload, and autonomy. The results and discussion sections were organized according to those themes. Each study can include more than one push-pull factor and is counted more than once when calculating the proportions in the results section (Figure 1 and Table 2).

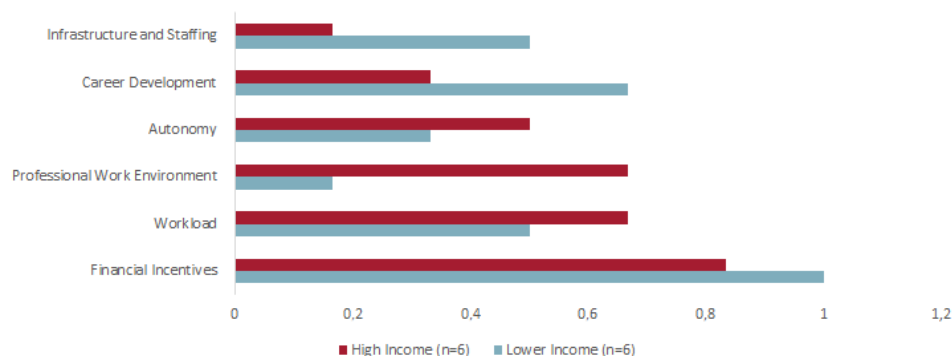
For the policy intervention studies, illustrative quotes were pulled for the advantages and disadvantages of each policy intervention. These policy interventions were then synthesized into three main themes. Each study could include

advantages and disadvantages for more than one policy intervention and was counted more than once when calculating the proportions in the results section (Figure 2 and Table 3).

## RESULTS

The database search identified 368 hits (208 PubMed, 144 EMBASE, 7 Google Scholar, 4 WHO Global Health Observatory, 1 World Bank, and 4 manual entries) (Figure 3). Using the study selection criteria, the titles and abstracts were screened and 45 articles remained. After the full-text examination of the articles, 19 articles were included in the review. Figure 3 uses the PRISMA framework to show the flow of the search during the different stages of analysis [26].

Decisions to include or exclude studies were made by the first author under the supervision of the lead author. The



**Figure 1.** Proportion of studies by income category discussing themes affecting physician's choice of workplace.

**Table 2.** Factors affecting physician's choice of workplace

THEME	SUB-THEME/FACTOR	FIRST AUTHOR'S LAST NAME	PUSH FACTORS (ILLUSTRATIVE QUOTES)	PULL FACTORS (ILLUSTRATIVE QUOTES)
Financial incentives	Adequacy of financial compensation	Ashmore [3], Luboga [10], Malik [11], Andreassen [19], Lonnroth [14], Gruen [15], Ashmore [17], Russo [12], McPake [13]	<p>“None of the physicians in our focus group discussions felt their <b>compensation</b> was acceptable” [10].</p> <p>“The <b>most frequently</b> mentioned conditions by those who would consider leaving government services were: <b>payment of a compensation for transition</b> (n = 18); a social pension scheme (n=13); tax relief (n=7); and credit offers (n=6)” [15].</p> <p>“<b>Median income</b> among physicians in the public sector was significantly <b>lower</b> than that of physicians in the private sector (<math>P&lt;0.001</math>) and dual practice (<math>P&lt;0.001</math>), but income differences between private-only and dual practice physicians were not statistically significant” [12].</p>	<p>“Some specialists interviewed appeared to value <b>high financial rewards</b> more than others, and thus felt more desire to work in the private sector” [3].</p> <p>“... physicians in private setups were motivated by the <b>availability of financial incentives</b> other than pay and good working conditions in their current jobs” [11].</p> <p>“Our study implies that <b>overall wage increases and tax reductions</b> give the medical doctors an <b>incentive</b> to move to full time jobs, in particular in the private sector, at the expense of working in other jobs in the health sector of the economy” [19].</p> <p>“In some districts, physicians are on the payroll, but may come to work only half the day, largely because they are attending to private practices as a means of <b>income supplementation</b>” [10].</p> <p>“When asked about the reasons for engaging with the private sector, answers from the survey were broadly consistent with the qualitative findings, with most physicians reporting “<b>increasing income</b>” as the main factor for practicing in the private sector (95.5% responding important or very important)...” [12].</p>
		Income relative to workload	Ashton [18]	“... the private sector is valued for the opportunity to work independently (4.45), the freedom to apply ideas in the workplace (4.28) and the <b>income earned relative to the workload</b> (4.06).”
		Sustainability of income	Lonnroth [14]	“All interviewees expressed <b>difficulties in living on the salary</b> in the public health care sector” [14].
Financial security		Longmore [20], Luboga [10]	<p>“There was much emotion surrounding remuneration inconsistencies and resulting <b>financial insecurity</b>, doctors feeling that it is simply not acceptable to <b>fail to pay salaries on time</b>...”[20]. [20]</p> <p>“The other problem is <b>job security</b>, in most cases you don't know where you will go, they can fire you at any time...” [10] [10].</p>	
		Professional development	Ashmore [3] [3], Luboga [10] [10], Malik [11] [11], Gruen [15] [15]	<p>“There was also <b>dissatisfaction</b> expressed in the public sector with the sense of <b>career progression</b>. It was repeatedly noted how once a senior specialist in the public sector, it is easy to become 'stuck', for example, since there are few chief or principal specialists jobs available” [3].</p> <p>“Only about <b>one fourth</b> of physicians (26%) said their employer offered <b>sufficient opportunities for promotion</b>” [10].</p>
Education and training opportunities		Luboga [10] [10], Gruen [15] [15]	“More than 66% of the doctors in primary and secondary care considered <b>training opportunities to be poor</b> , as opposed to 33% of the doctors in tertiary care facilities” [15].	“A sizeable number (66%) rated “ <b>access to higher education</b> ” as “very important”, and another large portion (60%) said this was an important enough issue for which to consider changing jobs” [10].
Physician reputation		Russo [12] [12], Kankaanranta [24] [24]		<p>“For dual practitioners, the main motivations were opportunities to increase income, to <b>consolidate professional reputation</b>, and to take advantage of the complementarities between the two job modalities” [12].</p> <p>“Also, <b>Generally held to be a prestigious position</b> seemed to have high t-test values each year, implying that it is also a good indicator of physician's job satisfaction, when the variable <i>Good income compared to workload</i> was modelled as a base variable” [24].</p>



Table 2. Continued

THEME	SUB-THEME/FACTOR	FIRST AUTHOR'S LAST NAME	PUSH FACTORS (ILLUSTRATIVE QUOTES)	PULL FACTORS (ILLUSTRATIVE QUOTES)
Infrastructure and staffing	Resource availability	Ashmore [3], Luboga [10], Malik [11], Gruen [15]	<p>“On the other hand, the public sector was noted to have <b>fewer resources and less equipment and drugs available</b>, factors which hindered the ability to do one's job as desired, often considered frustrating” [3].</p> <p>“There are significant problems with working conditions in all health facilities. <b>Access to equipment, supplies, drugs, electricity, and water are seriously compromised</b>” [10].</p> <p>“In contrast, demotivators in current jobs were mostly organizational factors including fewer opportunities for higher qualifications, <b>resource unavailability</b> and poor supervision” [11].</p>	<p>“So at least the other advantage of being in the private sector [is] you get to see <b>what's current and what's currently in use as well</b>, which we don't have on the other side.” [3]</p> <p>“Physicians (and other health workers) in the private (non-profit) sector were more likely to rate working conditions, more highly, with statistically significant differences measured for the <b>availability of supplies, equipment and drugs, utilities</b>, transportation, and time for workers to eat lunch.” [10]</p>
	Staffing shortages	Ashmore [3], Luboga [10], Gruen [15]	<p>“<b>Lack of public sector staff, relative to the private sector</b>, was another resource issue that caused public sector dissatisfaction” [3].</p> <p>“<b>Lack of doctors themselves</b> also caused dissatisfaction, implying there is a damaging cycle where retention is a problem, since lack of retention may encourage others to leave” [3].</p> <p>“Physicians discussed <b>staffing shortages</b>, unreasonable patient loads lack of available specialists, and <b>positions that have gone unfilled for months or even years</b>” [10].</p>	
Working conditions		Luboga [10], Malik [11], Gruen [15]	<p>“Physicians in five of eight focus group discussions complained of <b>infrastructure issues</b>, complaining about a lack of clean water or electricity, not enough beds for patients or space in the wards, and poor infection control” [10].</p> <p>“Conversely, physicians working in primary care health facilities more often reported <b>poor working conditions</b> as a demotivator” [11].</p> <p>“The most often agreed opinions referred to lack of drugs and equipment (22%), long waiting times (17%), lack of doctors and nurses (13%) and <b>lack of cleanliness</b> in government facilities (11%)” [15].</p>	<p>“Physicians (and other health workers) in the private (non-profit) sector were more likely to <b>rate working conditions, more highly</b>, with statistically significant differences measured for the availability of supplies, equipment and drugs, utilities, transportation, and time for workers to eat lunch” [10]. [10]</p> <p>“Conversely, physicians in private setups were motivated by the availability of financial incentives other than pay and good working conditions in their current job” [11]. [11]</p>
Professional work environment	Relationship with patients	Ashmore [3]	<p>“Patient relationships also seem to be <b>strained</b> in the public sector, due to relative unwillingness or inability of patients to follow directions, as well as, potentially, some classism and racism among doctors” [3].</p>	
	Relationship with supervisors and administration	Ashmore [3], Luboga [10], Longmore [20], Kankaanranta [24]	<p>“<b>Distrust of the public hospital 'administration' and DoH</b>, meanwhile, seemed universally high.”; “The above respondents were noticeably embittered towards state and hospital management, which seemed almost universal” [3].</p> <p>“In questionnaires, physicians were the <b>least likely</b> to say their immediate supervisor (presumably, upper management) “<b>cares about me as a person</b>”, and the <b>least likely</b> to say they received <b>recognition</b> for doing good work” [10].</p> <p>“Sixty-four per cent of doctors felt that they were <b>not respected and valued by HR staff</b>” [20].</p>	<p>“Whatever the reasons, in H1 at least, relations <b>between different health providers</b> (rather than between doctors) were generally perceived as <b>much better</b> in the private sector” [3].</p> <p>“In one focus group at a private facility, physicians spoke of <b>supervisors who respected staff, assisted in problem solving, and instilled a sense of ownership and responsibility in staff</b>” [10].</p>
	Managerial interference	Ashton [18]	<p>“Key sources of dissatisfaction were workload pressures, mentally demanding work and managerial inferences” [18].</p>	<p>“They also have a good income relative to their workload and little managerial interference” [18].</p>

Table 2. Continued

THEME	SUB-THEME/FACTOR	FIRST AUTHOR'S LAST NAME	PUSH FACTORS (ILLUSTRATIVE QUOTES)	PULL FACTORS (ILLUSTRATIVE QUOTES)
Workload	Work hours, amount of work and workload pressures	Ashton [18], Luboga [10], Malik [11], Russo [12], Kankaanranta [24]	<p>“While our survey did not include questions specifically related to levels of stress, dissatisfaction was higher in the public sector for all sources of dissatisfaction. These included factors related to stress such as poor employer/employee relations, <b>workload pressures and mentally demanding work</b>” [18].</p> <p>“Only about a third (36%) of physicians said they thought their workload was manageable. All focus group physicians <b>complained about work overload</b>” [10].</p> <p>“In public setups, tertiary physicians reported <b>long duty hours</b>, less personal safety and <b>heavy workloads</b> as important demotivators compared with those in private setups...” [11].</p> <p>“For factors affecting <i>job dissatisfaction</i>, variables such as <b>Tight, inflexible timetable</b>, <i>Poor employee/supervisor relations</i>, and <i>Tense atmosphere in workplace</i> had the highest t–test values, when the variable <b>Monotonous work</b> was modelled as baseline” [24].</p>	<p>“For those working exclusively in the private sector the motivations were higher earnings, autonomy, and <b>flexibility of working hours</b>” [12].</p>
Autonomy	Ability to apply their own ideas and flexibility in patient treatment	Ashton [18], Ashmore [3], Russo [12], Lonnroth [14], Kankaanranta [24]	<p>“The ability to work with more autonomy in the private sector, however, did appear to carry a distinct advantage for those who valued it. This seemed particularly true of those <b>frustrated with public ‘regulations and rules’</b>, who wanted to work on their own terms” [3].</p> <p>“Complicated procedures in the public sector mentioned by the interviewees include <b>‘bureaucratic’ procedures</b> to fulfill eligibility criteria for free or subsidized treatment as well as <b>rigid</b> diagnostic and treatment strategies that follow more or less <b>fixed guidelines</b>” [14].</p>	<p>“...<b>work autonomy and flexibility</b> are the key motivations at the base of their choice to dedicate exclusively to the private sector, since earnings are not significantly different from those of dual practice physicians” [12].</p> <p>“In contrast, when working in the private practice, specialists value the opportunity to work <b>independently</b> and to <b>apply their own ideas</b> in the workplace” [18].</p> <p>“Private physicians on the other hand can apply <b>more flexible</b> approaches to <b>diagnostic procedures and choice of treatment</b>, which are influenced by patients’ preferences and ability to pay” [14].</p> <p>“Both private and non-private physicians said that private practitioners provided more <b>flexible and individualized care</b>, which they described as appealing to patients” [14].</p> <p>“Each year, the variable <b>Chance to apply one’s own ideas in the work</b> emerged as one of the most important job satisfaction dimensions affecting intention to change work sector” [24].</p>

countries studied were from Sub-Saharan Africa (South Africa, Uganda, Cape Verde, Guinea, Mozambique and Bisau), Europe (Norway and Finland) Asia (Pakistan, Vietnam, Bangladesh, and Malaysia), North America (United States) and the Pacific (New Zealand) (Figure 4 and Table 1). The review included 12 studies on push-pull factors for physician retention and 7 studies on policy interventions for retaining physicians in the public sector.

### Factors affecting physicians’ decision to leave public sector/enter private sector

We identified six main themes that affected physicians’ choice of workplace including: financial incentives, career development, infrastructure and staffing, professional work environment, workload and autonomy (Table 2).

The majority of the studies (number n = 11; 92%) highlighted the importance of financial incentives in determin-

ing physicians’ choice of workplace [3,10–15,17–20]. Inadequacy of financial compensation and financial insecurity were found to be major factors that encouraged physicians to leave the public sector or practice in both the private and public sector (dual practice). Competitive salaries and higher income were the main reasons physicians were motivated to move to the private sector [3,10–15,17–20]. In one of the studies that focused on three lower income cities in sub-Saharan Africa, it was found that 95.5% of physicians reported increasing income as an important or very important factor in their decision to practice in the private sector [12].

Career development was also an important motivator and was discussed in around 50% (n = 6) of the studies [3,10–12,15,24]. One study in Uganda found that only one out of four physicians in the public sector reported that their employer offered them sufficient opportunities for promo-

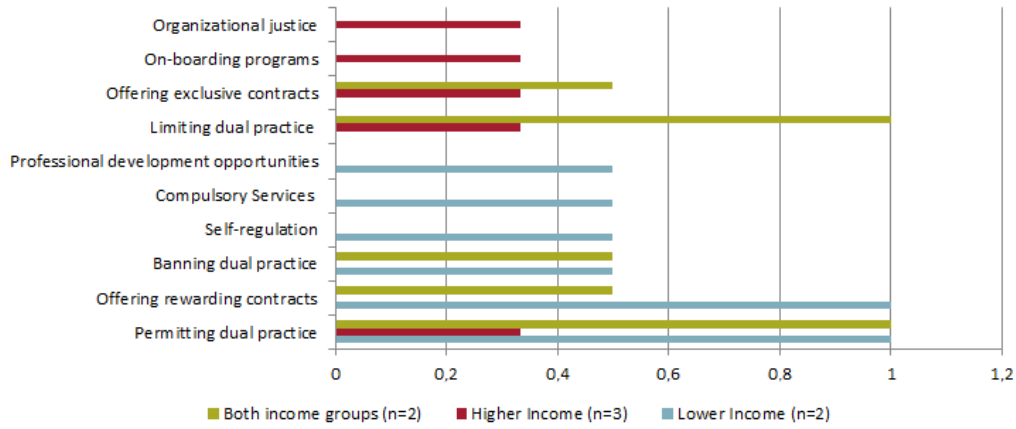


Figure 2. Proportion of studies by income category discussing policy interventions to address physician retention in the public sector.

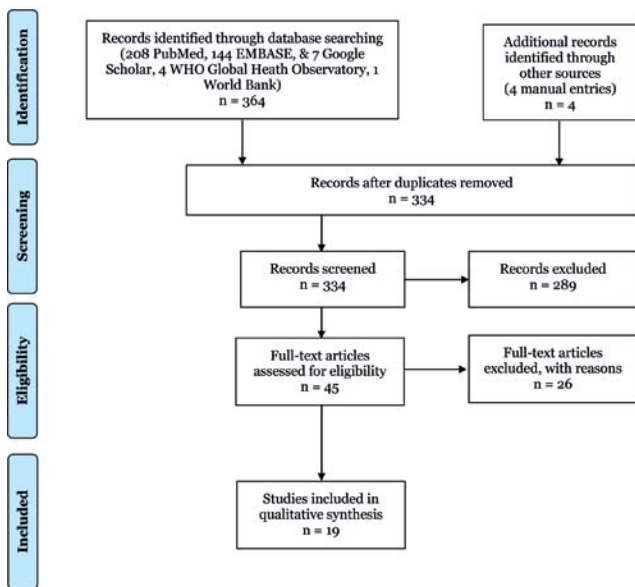


Figure 3. Flowchart on the database and the study selection.

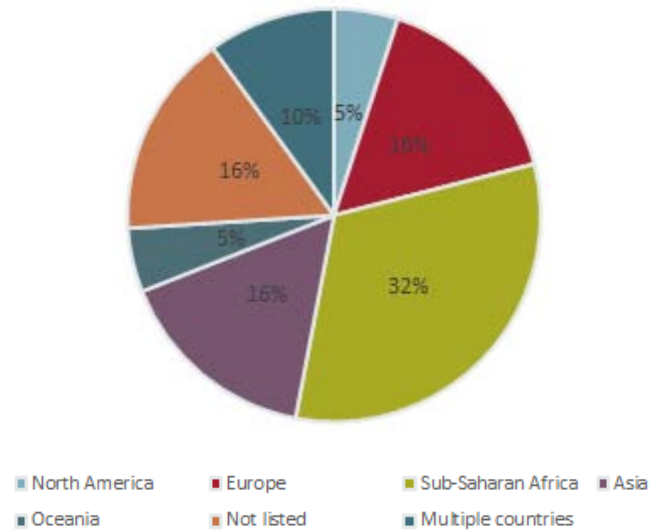


Figure 4. Geographic origin of included studies (n=19).

tion [10]. In the same study, a significant number of physicians (66%) ranked access to higher education as very important, and 60% of physicians reported that this was a significant issue that would lead them to consider changing jobs [10]. Physicians reported the lack of opportunities for professional and academic development, stagnant career progression and poor training opportunities as reasons that would push them to leave the public sector or practice in both the public and private sector. Opportunities for professional development, and being in a prestigious position were identified as main factors that were pulling physicians into the private sector in some of the countries [10–12,15,24]. On the other hand, in countries like South Africa and New Zealand where central hospitals are run by public academic institutions, physicians working in the public sector are presented with professional development

opportunities [3,18]. These include free use of research and other academic facilities, and greater opportunities for teaching and research [3,18].

Infrastructure and staffing were highlighted in 33% (n=4) of the studies as being important determinants of choice of work place [3,10,11,15]. Lack of resources, shortage of staff, unfilled physician positions, poor facility infrastructure and poor working environment were important push factors in the public sector. The availability of up-to-date resources and positive work environment were motivating factors that were pulling physicians to work in the private sector or both in the public and private sectors [3,10,11,15].

Approximately 42% of the studies (n=5) [3,10,18,20,24] indicated that professional work environment plays an important role in retaining physicians in the public sector.

**Table 3.** The advantages and disadvantages of policy interventions for addressing physician retention in the public sector

POLICY THEMES	POLICY INTERVENTIONS	FIRST AUTHOR	DISADVANTAGES (ILLUSTRATIVE QUOTES)	ADVANTAGES (ILLUSTRATIVE QUOTES)
Regulatory controls	Banning dual practice	Gonzalez [8], Jan [16]	<p>“The <b>more able</b> ones tend to be more involved in the <b>private sector</b> since their ability allows them to get a higher return. The <b>less able</b> tend to combine both public and private activities if dual practice is allowed, or work only in <b>public practice</b> when this is not the case. When dual practice is forbidden, the <b>population of physicians</b> working the public sector for a given salary <b>decreases</b>” [8].</p> <p>“In addition, when the public and private sectors do not share physicians, higher private sector earnings are expected to attract more highly skilled physicians, leaving those of <b>less ability in the public sector</b>” [8].</p> <p>“In practice, bans do not prevent these activities, but instead take them <b>outside the regulatory and policy jurisdiction</b> of government” [16].</p>	
	Permitting dual practice	Gonzalez [21], Eggleston [4], Jan [16], Abdul Rahim [2], Gonzalez [8]	<p>“We found that the physician’s dual practice has conflicting effects. On the one hand, his interest in curing patients and gaining prestige, generates an <b>over-provision of health services</b>” [21].</p> <p>“These theoretical predictions stand at odds with much of the policy discussion, which tends to assume that allowing public sector physicians to earn private revenue will harm the quality of services provided in the public sector, although it may <b>benefit private sector patients and physicians</b>” [4].</p> <p>“Since monitoring of provider time and effort is costly, often only minimal presence in a public practice is required to access the non-pecuniary benefits of public employment (eg, official salary and civil servant fringe benefits such as public housing)” [4].</p> <p>“A physician with both public and private practices may <b>use public resources to treat private patients</b>, whether by lifting supplies (eg, gauze, medications) or treating patients at the public facilities without paying any rent or charge for such use” [4].</p> <p>“Furthermore, dual practice providers may have incentives to induce demand for private practice services. The propensity of health care providers to <b>over-refer</b> to facilities in which they have financial interest is widely recognized” [4].</p> <p>“However, dual job holding by public sector health professionals is potentially a problem because it may create inappropriate incentives as the <b>boundaries</b> between a public health professional’s day-to-day job and his or her private practice <b>can become blurred</b>” [16].</p> <p>“Firstly, it can encourage the <b>misappropriation</b> of scarce <b>public sector resources</b> into the private sector” [16].</p> <p>“The second reason why private practice by public health workers has been posited as a problem is because it may lead to doctors <b>diverting patients from public facilities into private services</b>” [16].</p> <p>“Also, <b>no evidence</b> thus far supports dual practice as a method of <b>improving equitable delivery of healthcare</b>” [2].</p>	<p>“On the other hand, if the HA is able to control these incentives to over-provide services, then it can benefit from the physician’s increased interest in doing <b>more-accurate diagnosis</b>” [21].</p> <p>“Interestingly, some consistent results emerge from these diverse conceptualizations: (1) allowing dual practice may <b>improve social welfare</b>; and (2) allowing dual practice may improve the <b>quality of public services</b>, under specific circumstances” [4].</p> <p>“Allowing dual practice may enable the government to recruit <b>quality providers</b> at a <b>modest budgetary expense</b>” [4].</p> <p>“To the extent that physicians attempt to build a good reputation that will enhance future private practice revenue, allowing dual practice also gives a kind of <b>performance-based incentive</b> for physicians to exert effort” [4].</p> <p>“From the point of view of the public sector, allowing health professionals to engage in private practice can be a means of <b>minimizing the budgetary burden required to retain skilled staff</b>” [16].</p> <p>“In contrast to these measures, the potential value of recognizing and legitimizing dual practice is that, at one level, it enables some <b>degree of control</b> to be exercised over <b>quality and safety</b>” [16].</p> <p>“The importance, therefore, of providing official recognition is that it allows policy-makers to incorporate such activity within the bounds of its <b>regulatory and policy jurisdiction</b>” [16].</p> <p>“Practitioners would continue to enjoy the <b>prestige of public sector</b> positions and <b>ongoing career development</b> while mitigating <b>economic opportunity costs</b> otherwise incurred if solely servicing the government...” [2].</p> <p>“This implies that dual practice might be desirable because it allows the HA to <b>reduce the wage needed to retain</b> physicians working in the public sector” [8].</p>
	Limiting dual practice	Gonzalez [8], Gonzalez [21], Eggleston [4]	<p>“Overall, <b>profit limitations</b> have a <b>milder effect</b> on the amount of <b>dual practice</b> performed by physicians.” [8].</p> <p>“Secondly, focusing on limiting policies, we have shown that <b>limiting income</b> is always <b>less effective than limiting involvement</b>” [8].</p> <p>“Therefore, our conclusion is that this sort of regulatory policy may be beneficial from a social point of view, although it can generate as a non-desired effect a <b>reduction</b> on physicians’ <b>incentives</b> to perform <b>accurate diagnoses</b>” [21].</p> <p>“In either case, the limits on dual practice <b>only affect behavior</b> if physicians anticipate that the <b>contractual terms will be enforced</b>” [4].</p>	<p>“... as it only affects the <b>high skilled</b> physicians that are compelled to <b>reduce private involvement</b> in order to satisfy their earning constraint” [8].</p> <p>“In contrast, policies that limit involvement directly target the intensity of dual practice and are therefore <b>more effective in limiting its costs</b>” [8].</p> <p>“We have shown that if physicians’ payment contracts include <b>proper incentives</b>, then <b>limiting</b> physician’s <b>private income</b> can be <b>optimal</b>, whereas introducing exclusive contracts is always useless” [21].</p> <p>“Better ability to monitor and contract can <b>minimize shirking on public practice duties, appropriating supplies and using public equipment without paying rent</b>. Transparent contractual relationships between public and private practices, such as rental of facilities and subcontracting for specific services, can <b>offset many of the costs</b> associated with allowing the same physicians to practice in both” [4].</p>

Table 3. Continued

POLICY THEMES	POLICY INTERVENTIONS	FIRST AUTHOR	DISADVANTAGES (ILLUSTRATIVE QUOTES)	ADVANTAGES (ILLUSTRATIVE QUOTES)
	Self-regulation	Jan [16]	<p>“Indeed, in certain circumstances, this could lead to an <b>incentive to “overprovide” quality in the public sector</b>, particularly, in high-income settings, because the health facility rather than the individual doctor bears the cost of providing additional quality” [16].</p> <p>“Consequently, there is a certain trade-off between quality and access to health care because <b>higher-quality services</b> will tend to be <b>more costly</b>, and thus specific measures addressing <b>financial access</b> need to be <b>considered</b> when proposing such forms of self-regulation” [16].</p>	<p>“Self-regulation of this nature works because significant weight is given to an individual's <b>reputation</b> as a doctor in public practice, which influences his or her <b>income-generating</b> capacity in <b>private practice</b>” [16].</p> <p>“The role of such regulation could be viewed as <b>addressing the uncontrolled proliferation</b> of private providers and, in a sense, establishing <b>barriers to entry</b>” [16].</p> <p>“The rationale for professional self-regulation is that it <b>recognizes the collective interest</b> in instituting some form of cooperative behavior among individual agents” [16].</p>
	Compulsory services	Abdul Rahim [2]	“The <b>evidence</b> base on effectiveness of compulsory services to date remains <b>lacking</b> ” [2].	
Incentives	Offering exclusive contracts	Eggleston [4], Gonzalez [21], Gonzalez [8]	<p>“The problem with this measure is that in the context of the strict resources constraints that often exist within low- and middle-income countries, such payments can be prohibitively <b>costly</b>—particularly if incomes in the private sector are high and thus there is a <b>need for greater levels of compensation</b>” [4].</p> <p>“We have shown that if physicians' payment contracts include proper incentives, then limiting physician's private income can be optimal, whereas introducing <b>exclusive contracts is always useless</b>” [21].</p>	<p>“Exclusive contracts, however, are shown to be a <b>useful tool for cost-containment</b> when physicians are paid on a <b>salaried basis</b>” [21].</p> <p>“This illustrates how exclusive contracts offer <b>greater flexibility</b> for the HA to <b>mitigate loss of productivity</b> associated with dual practice, which makes the HA less interested in banning dual practice when rewarding policies are available” [8].</p>
	Offering rewarding contracts	Gonzalez [8], Abdul Rahim [2], Jan [14]	<p>“Rewarding policies, ie, those that pay an extra amount to physicians who give up their private practice, are <b>only desirable when limitations are difficult to enforce</b>” [8].</p> <p>“The Commission determines salaries for public sector workers and hence deems it <b>unfair to selectively raise wage of health employees and exclude other sectors</b>” [2].</p> <p>“The most immediate and overriding <b>constraint on the feasibility</b> of this option however is the <b>cost</b> to the <b>public sector</b>. In circumstances where there are tight resource constraints in the public sector, this option is unlikely to be feasible” [14].</p>	<p>“Remuneration should reflect the level of work responsibility and be deemed fair vis-à-vis other sector counterparts to ensure continued <b>attraction and retention</b> of staff” [2].</p> <p>“Furthermore, a <b>mix of payment mechanisms</b> such as time-based, service-based and population-based is linked with <b>enhanced provider performance</b>” [2].</p> <p>“On this basis, the incentive to <b>shift effort from public-sector to private-sector</b> work would be <b>offset by making remuneration for public practice</b>, like that of private practice, related to effort or output” [14].</p>
	Providing professional development opportunities	Abdul Rahim [2]		“Continued education, interactive training and professional development geared towards the priority health conditions and needs of the local population improves health worker <b>competency and motivation</b> ” [2].
Management reforms	On-boarding programs	Heponiemi [22]	<p>“Organizational justice was <b>not able to buffer</b> the association between being or becoming a new public GP and <b>turnover intentions</b>” [22].</p> <p>“Our results showed that new public GPs had 2.6 and those who stayed as public GPs both times had 1.6 times <b>higher likelihood of having turnover intentions</b> compared to those who stayed at other positions both times” [22].</p>	<p>“Our results suggest that by improving organizational justice primary care organizations could <b>improve GPs job satisfaction</b> and involvement and consequently maybe increase GP work's <b>attractiveness as a career option</b>. For example, organizations could <b>invest in supervisor training</b>, particularly because previous studies have shown that leaders can be trained to act in a more just manner and this in turn improves subordinates' attitudes and behavior” [22].</p>
	Organizational justice	Cohn [23]		<p>“One year after the on-boarding program was initiated, <b>not a single new physician left</b> BMG, which is a sharp turnaround from the 10 percent loss the group experienced previously” [23].</p> <p>“Since the onboarding program began, however, everyone who has worked with the new physicians (including allied health professionals) has noted an <b>improvement in physician morale and in the practice environment</b>” [23].</p>

Lack of trust with the hospital administration team, poor patient-physician relationships, high managerial interference, lack of respect and appreciation of physicians, and poor supervisor-employee relationships were the main push factors reported in the studies. The pull factors reported in the studies were: positive relationships between physicians, stronger patient-physician relationships, low

managerial interference, and strong supervisor-physician relationship [3,10,18,20,24].

Approximately 58% of studies (n = 7) mentioned workload and autonomy as important factors in physician retention [3,10-12,14,18,24]. Push factors that were mentioned include: workload pressures, mentally draining work, heavy workload, long hours, low autonomy, bureaucracy and ri-

gidity in patient treatment and inflexible schedule. The pull factors that attracted physicians to the private sector were: high autonomy, the ability to apply their own ideas and flexibility in diagnostic treatment and procedures [3,10–12,14,18,24].

## Policies for retaining physicians in the public sector

The review identified a range of policy interventions that focused on improving physician retention in the public sector along with their advantages and disadvantages. Of the seven studies included two discussed options for policy interventions in lower income countries, three focused on higher income countries and two compared policy interventions in both lower and higher income countries (**Figure 2**). We found three main categories of policies for retaining physicians in the public sector: (a) regulatory controls, (b) incentives and (c) management reforms (**Table 3**).

(a) Regulatory controls included banning dual practice, permitting dual practice, limiting dual practice, professional self-regulation and compulsory services. Around 72% of the studies ( $n=5$ ) highlighted regulatory controls as policy interventions to address physician retention in the public sector [2,4,8,16,21]. The studies did not identify advantages for banning dual practice, however, disadvantages included: the increased likelihood for highly skilled physicians to move to the private sector, and the risk of having physicians practicing in both sectors illegally [8,16].

In terms of permitting dual practice, the following advantages were reported: improvement of the quality of service in the public sector, increased interest of physicians to provide more accurate diagnosis, establishment of performance based incentives, enhanced ability to retain skilled physicians without a budgetary burden, and increased possibility of exercising a higher degree of control over quality and safety. As for the disadvantages these include: the possibility of over-provision of medical services, the potential harm to the quality of services in the public sector, utilization of public resources in private practice, over-referrals, lack of clear boundaries between the public and private sector, lack of evidence showing improvement of equitable health care delivery, and higher time allocation in private practice while taking advantage of employment benefits in the public sector [2,4,8,16,21].

The studies highlighted several advantages for limiting dual practice such as: effectiveness in reducing costs on the supply side, encouragement of highly skilled physicians to reduce private practice involvement, and high efficacy when physician contracts include incentives and offsets costs associated with dual practice. There are also disadvantages in limiting dual practice including: reduction in physicians' incentives to provide accurate diagnoses, and

limited efficiency of this intervention if contractual terms were not enforced [4,8,21].

Professional self-regulation, was identified as an important function that provided the opportunity to introduce higher standards among practicing physicians, which in turn helped to enhance the prestige among physicians who met established standards [16]. Self-regulation could also improve quality of physician services in the public sector, and establish de facto barriers to enter the private sector by controlling licensing or certification [16]. Compulsory public sector service was also noted as a potential policy intervention [2]. A disadvantage of this policy is the lack of studies that assess the effectiveness and success of compulsory services in retaining physicians in the public sector [2].

(b) Incentives for retention in the public sector included: exclusive contracts, offering rewarding contracts and/or financial incentives, and providing professional development opportunities. Around 72% of the studies ( $n=5$ ) highlighted incentives as policy interventions to address physician retention in the public sector [2,4,8,16,21]. Exclusive contracts were identified as being useful for salaried physicians, but noted to be expensive to implement and not be as useful when physicians had incentive contracts [4,21].

In terms of rewarding contracts and financial incentives, the advantages of this policy intervention were the attraction and retention of physicians in the public sector, the enhancement of physician performance, and the reduction in the loss of productivity in the public sector. As for the disadvantages, these included: costliness in some cases, limited feasibility and it is only considered when limitations are difficult to impose [2,8,16]. For example, Jan et al. stated that the cost to the public sector was the main obstacle that prevented the use of incentives as a policy option, particularly in situations where there are resource constraints in the public sector [16]. Gonzalez and Macho-Stadler also reported that policies that provided financial incentives for physicians who leave the private sector were only appealing when limitations on private practice could not be imposed [8].

Provision of professional development opportunities was also listed as an intervention that motivated, and improved the competency of physicians in the public sector. No disadvantages were identified, however [2].

(c) Management reforms identified in the studies included the establishment of on-boarding programs for newly hired physicians and organizational justice. Organizational justice refers to physicians' perceptions of fairness in the workplace. On-boarding programs for physicians generally focus on four key aspects: credentialing and employment, orientation, marketing, and staff integration [22]. Around 29% of the studies ( $n=2$ ) listed management reforms as a

policy intervention for addressing physician retention [22,23]. The advantages of these reforms included the potential retention of physicians in primary care and general practice, and improvement of physician morale and workplace environment. The disadvantage of this policy was the uncertainty in influencing intentions of new general practitioners [22,23].

## DISCUSSION

The studies included in this systematic review explored push and pull factors that affect physician movement from the public to the private sector. Six studies focused on low income and low middle income countries (lower income countries) and six studies focused on upper middle income and high-income countries (higher income countries) (**Table 1**). A country's economic context influenced the factors affecting physicians' choice of workplace. The influence of economic context was apparent in the variation in the number of studies that highlighted issues for each factor affecting physician's choice of workplace (**Figure 1**).

In terms of factors, it is interesting to note that managerial interference, relationship with patients and income relative to workload were only reported in higher income countries. Similarly, working conditions, sustainability of income and education and training opportunities were only mentioned in lower income countries.

The most frequently reported theme across all the studies was financial incentives. In lower income countries the most recurring themes in descending order were: financial incentives, career development, infrastructure and staffing, workload, autonomy and professional work environment (**Figure 1**). In higher income countries these were: financial incentives, professional work environment, workload, autonomy, career development and infrastructure and staffing (**Figure 1**).

In terms of infrastructure and staffing, lack of resources such as drugs and equipment, poor working conditions, poor facility infrastructure, lack of clean water and electricity, lack of cleanliness in government facilities and staffing shortages were reported as push factors in Bangladesh, Pakistan, and Uganda [10,11,15]. In addition, staffing, workload and autonomy were important driving factors for physician's choice of workplace in these lower income countries. In South Africa, a higher income country, the public sector was also found to have fewer resources and less equipment and drugs available, shortage in hospital staff, and poor working conditions compared to the private sector [3].

Career development was also one of the main key drivers for physicians to work in the private sector in higher income countries. Examples of the motivating factors that

were listed in the studies include: recognition and prestige, the opportunity to work independently, the ability to apply their ideas, and/or the ability to provide individualized care [3,12,14,24]. However, in higher income countries like South Africa and New Zealand that have strong public health systems, there are greater opportunities for further education, and professional development in the public sector compared to the private sector [3,18].

In terms of workload, in higher income countries, tight inflexible schedules and heavy workload were reported as factors pushing physician out of the public sector in higher income countries [18,24]. Lower income countries also reported similar factors such as long duty hours and heavy workloads [10,11]. The professional work environment also plays a role in driving physicians from the public to the private sector. Generally, lack of respect and appreciation of physicians by human resources staff, high managerial interference and lack of trust toward the government were reported in higher income countries as factors driving physicians away from the public sector [3,20]. However, these factors were also reported in Uganda [10].

The review identified a range of policy interventions that focused on improving physician retention in the public sector. The country's income category determined the type of policy interventions that was discussed. Regulatory controls and incentives were reported in both higher and lower income countries. Self-regulation and compulsory services were only reported in lower income countries. However, management reforms were only highlighted in higher income countries.

Regulatory interventions were among the most common policies used. Permitting dual practice was the most recurring policy intervention for both lower and higher income countries. Although there was no evidence to support compulsory services, self-regulation had some advantages such as establishing barriers for physicians to enter the private sector and addressing the uncontrolled proliferation of private physicians. There were no advantages reported for banning dual practice in both income settings.

The majority of the studies in lower and higher income countries reported using some type of incentive in addition to or instead of regulatory controls. Providing professional development opportunities was only reported in lower income countries and its advantages included improving physician competency and motivation [2]. Offering exclusive or rewarding contracts were highlighted as policy options in both lower and higher income countries. However, financial incentives were noted to be costly and posed a heavy burden on lower income countries.

Management reforms were specific to higher income countries; however, interventions such as supervisor trainings

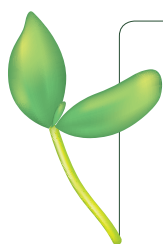
and on-boarding programs may increase physician retention in the public sector. As Heponiemi et al. reported that by enhancing organization justice, primary care facilities could improve general practitioners' (GP) job satisfaction and potentially increase the attractiveness of GP work as a career option [22]. Organizational justice and effective on-boarding programs may help increase physician retention in the public sector, and reduce turnover by decreasing recruitment costs.

An interesting finding from this review is the high degree of similarity that exists between the push-pull factors that we identified and the brain drain issues that drive physicians to migrate both within and across countries. In a systematic review that aimed to examine motivating factors that would reduce medical migration both within and across countries, the following themes were identified: financial incentives, career development, continuing education, hospital infrastructure, resource availability, hospital management and personal recognition or appreciation [27]. These themes were all highlighted in our review; however, workload and autonomy seem to be specific to physicians' choice of workplace between the public and private sector.

A major drawback in this review is the limited availability of published literature on physician retention in the public sector. Through the database search we only identified 19 studies that met our inclusion criteria, which might have impacted the interpretation of our findings as well as generalizability. Although we attempted to connect the variation in themes to different income levels, the sample size was too low to make any causal conclusions. Another factor affecting generalizability is the regional distribution of

the studies, 53% of the studies focused on Sub-Saharan African and Asian countries and only 26% of studies were on North America, Oceania and Europe. There were no studies on Latin America and the Caribbean, Middle East and North Africa. In addition, only studies in English were included and other databases such as those for humanities and social sciences were not considered. However, the majority of physician studies would be expected to be cross-listed in medical databases examined here. Another limitation, is the difficulty of drawing conclusions from studies that were conducted in different countries, at different times, with different methodologies, and in different health systems and regulatory environments.

To the best of our knowledge this may be the first systematic review that specifically focuses on examining factors influencing physician retention and different policy interventions for improving retention in the public sector. Given the limited literature on physician retention in the public sector additional research is required, particularly to test the effectiveness of policy options for retention of physicians. It would also be useful for future cross-country research to use standardized data collection tools, allowing comparison of contextual factors as well as the examination of how context affects physician retention in the public sector. Given that financial incentives were frequently reported in both lower and higher income countries, cost controlling mechanisms for the private sector should be implemented such as benchmarking physician salaries with the public sector. The lack of private sector regulation in lower income countries as well as higher income countries needs to be addressed, this could be implemented as part of the efforts for expanding universal health coverage.



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**Competing interests:** The authors completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author). None of the authors has any competing interests to declare.

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# Assessment of the impact of quality improvement interventions on the quality of sick child care provided by Health Extension Workers in Ethiopia

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**Background** Ethiopia has scaled up integrated community case management of childhood illness (iCCM), including several interventions to improve the performance of Health Extension Workers (HEWs). We assessed associations between interventions to improve iCCM quality of care and the observed quality of care among HEWs.

**Methods** We assessed iCCM implementation strength and quality of care provided by HEWs in Ethiopia. Multivariate logistic regression analyses were performed to assess associations between interventions to improve iCCM quality of care and correct management of iCCM illnesses.

**Findings** Children who were managed by an HEW who had attended a performance review and clinical mentoring meeting (PRCMM) had 8.3 (95% confidence interval (CI) 2.34–29.51) times the odds of being correctly managed, compared to children managed by an HEW who did not attend a PRCMM. Management by an HEW who received follow-up training also significantly increased the odds of correct management (odds ratio (OR) = 2.09, 95% CI 1.05–4.18). Supervision on iCCM (OR = 0.63, 95% CI 0.23–1.72) did not significantly affect the odds of receiving correct care.

**Conclusions** These results suggest PRCMM and follow-up training were effective interventions, while implementation of supportive supervision needs to be reviewed to improve impact.

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Approximately 6.9 million children younger than five years of age died in 2011, with the vast majority of these deaths occurring in low- and middle-income countries [1]. Pneumonia, diarrhea, and malaria are among the leading causes of under-five mortality, with malnutrition as an important underlying cause [2]. Most under-five deaths can be prevented with available and cost-effective interventions [3]. Antibiotic treatment for pneumonia [4–6], oral rehydration salts and zinc for diarrhea [6–8], and artemisinin-based combination therapy for malaria [9,10] are effective interventions for preventing death from these diseases among children under five. However, poor and inequitable access to primary health care [11–13] and low quality of care [14–17] are important barriers.

ers. Integrated community case management of childhood illness (iCCM, see **Box 1** for definitions of key terms as applied in this study) is increasingly promoted as a key strategy to increase access to appropriate treatments for childhood illnesses, to reduce child mortality, and to improve equity in access to health services [18–20]. Through iCCM, community health workers (CHWs) are trained and equipped to manage common childhood illnesses (usually pneumonia, diarrhea, and malaria) in the community.

Since 2011, Ethiopia has been implementing iCCM, including treatment of uncomplicated pneumonia, diarrhea, malaria, malnutrition, and measles through Health Extension Workers (HEWs) in most regions of the country. All HEWs are literate women with at least a tenth-grade education, who receive a one-year pre-service training. The pre-service training included management of childhood diarrhea, malaria, and malnutrition; pneumonia was not part of the package prior to the introduction of iCCM. Following the training, they are recruited as government employees and deployed to work out of health posts at the kebele (sub-district) level. There are typically two HEWs working at one health post, which serves approximately 5000 people, the average population of a kebele. Through the iCCM program, HEWs treat children 2–59 months of age; sick children under two months are referred to a health facility [21].

The iCCM program was designed to strengthen the capacity of HEWs to assess, classify, and treat childhood pneumonia, diarrhea, malaria, malnutrition, and measles

through training on iCCM, supportive supervision, provision of essential commodities, and enhanced monitoring and evaluation. Following the initial six-day clinical training on iCCM, a number of interventions were implemented within the iCCM program to ensure continued quality of care. These interventions were: follow-up training, performance review and clinical mentoring meetings (PRC-MM), and supportive supervision. A description of the iCCM quality improvement interventions is provided in **Table 1**.

Ensuring quality of services provided through an iCCM program is essential to achieving mortality reductions. Assessments of IMCI and iCCM suggest that quality of care is variable and depends on the strength of program implementation, which is defined here as the level of delivery of key components of a program, such as training, supervision, and provision of commodities [22–29]. Program processes such as training and supportive supervision are presumed to lead to improved health worker performance, but, in practice, this is not always the case [30–35]. Most of the evidence available on the impact of program activities on quality of care pertains to health facility-based workers and is limited to formal training and supervision. A wide range of approaches to training and supervision activities have been implemented for iCCM [36], but little is known about the extent to which iCCM quality improvement activities are associated with the quality of care provided by CHWs. As part of an independent evaluation of the iCCM program in the Oromia Region of Ethiopia, we conducted a survey of health posts to assess iCCM program implementation strength and the quality of iCCM services provided by HEWs. These data provide an opportunity to assess associations between iCCM quality improvement interventions and quality of care provided by HEWs at health posts.

## METHODS

Data on iCCM implementation strength and quality of care were obtained through a cross-sectional survey of rural health posts in Jimma and West Hararghe Zones of Oromia Region, Ethiopia in which HEWs work. Oromia is the largest region in Ethiopia, with a population of approximately 30 million [37]. The survey was conducted in May and June 2012, about one year after initiation of iCCM implementation and during the low malaria season. The survey instruments were adapted from a survey of Health Surveillance Assistants in Malawi [26] and the World Health Organization (WHO) Health Facility Survey Tool [38].

We randomly selected 104 health posts from the 490 health posts that were implementing iCCM. To determine the sample size we assumed that proportions of key indicators were 50%, confidence level was 95%, non-response was

### Box 1. Definitions of key terms

**Correct management:** This indicator of quality of care was used as the outcome variable in this analysis. Correct management is defined for this study as: The proportion of sick children for whom all HEW treatments matched gold standard treatments, including correct dose, duration, and frequency, and HEW referral matched the gold standard classification for referral for all major iCCM illnesses (pneumonia, diarrhea, malaria, malnutrition, and measles).

**Implementation strength:** This term refers to the quantity of effective program activities carried out to reduce child mortality. These activities include training, supportive supervision, and continued availability of essential iCCM commodities and supplies.

**Integrated community case management (iCCM):** In general, iCCM refers to the concurrent management of childhood pneumonia, diarrhea, and malaria in the community. iCCM in Ethiopia is integrated management by an HEW at the health post or community level of the following childhood illnesses: pneumonia, diarrhea, malaria, malnutrition, and measles.

**Quality of care:** For this study, quality of care refers to correct assessment, classification, treatment, and referral of patients according to iCCM clinical guidelines.

**Table 1.** Description of Ethiopia iCCM quality improvement activities

ACTIVITY	DESCRIPTION
Follow-up training	Refresher training in the health post within eight weeks of the iCCM training. This was a half-day to one-day visit by an iCCM trainer from the district or from an implementing partner agency. The purpose of the visit was to reinforce knowledge and skills learned during the initial iCCM training. They also carried out observation of sick child consultations, if possible, as well as reviewed sick child registers and administered case scenarios to assess HEW performance. Supervisors identified the HEW's skills gaps and then focused on improving these during the visit.
Performance review and clinical mentoring meetings (PRCMM)	Two-day meeting held every six months (originally planned to be quarterly) at the <i>woreda</i> (district) level, during which approximately 20 HEWs met with supervisors, <i>woreda</i> health officials, health center staff. Zonal and regional focal persons sometimes also participated. <i>Woreda</i> iCCM facilitators and staff from implementing partner NGOs facilitated the meetings. On the first day, facilitators abstracted data from iCCM patient registers, reviewed registers with HEWs, and discussed issues related to quality of care and utilization of services. The second day was dedicated to clinical practice for HEWs in a health facility with feedback from facilitators. PRCMM guidelines are presented in Appendix S1 in <a href="#">Online Supplementary Document</a> .
Supportive supervision	Standardized supportive supervision on iCCM in the health post was performed on a quarterly basis. Supervisors were usually implementing partner NGO staff, and sometimes health center staff or <i>woreda</i> health officials. Supervisors used a standardized supervision checklist (Appendix S2 in <a href="#">Online Supplementary Document</a> ), which included sections on case management, preventive services, supply of commodities, data collection, knowledge assessment, feedback, and next steps. Supervisors were instructed to either observe the HEWs conducting sick child consultations or review iCCM patient registers for completeness and consistency between recorded signs/symptoms, classification, and treatment.

HEW – health extension worker, iCCM – integrated community case management of childhood illness, PRCMM – performance review and clinical mentoring meeting

5% for health posts, 5% for HEWs, and 10% for patients, design effect to account for clustering of HEWs and patients within health posts was 1.3. Assuming an average of 1.5 HEWs and two children observed per health post, the sample sizes were expected to give estimates of health post- and HEW-level indicators with precision of  $\pm 10\%$  percentage points and  $\pm 9$  points for patient-level indicators.

Within health posts, all HEWs providing clinical services were included in the study. Children had to meet the following criteria to be included: 1) 2–59 months of age, 2) having at least one complaint consistent with an eligible iCCM illness, and 3) this was the initial consultation for the current illness episode. Eligible children were included in the study if they presented for care at the health post either spontaneously or because they were mobilized to seek care by the HEWs. If fewer than two children presented at the health post within one hour of the health post opening, the team supervisor, along with an HEW or community volunteer, recruited sick children from nearby households.

Data collectors were health professionals who had worked as iCCM trainers or supervisors. Survey personnel were trained for seven days, and all observers and re-examiners achieved at least 90% concordance with gold standard clinicians on three consecutive role play examinations.

During the survey, data collectors observed HEWs' consultations with sick children and recorded details of the HEW's assessment, classification, treatment, referral, and counseling. A separate data collector then carried out a re-examination of the same child to obtain the gold standard clas-

sification. Data collectors also conducted caretaker exit interviews, inspected commodities and patient registers, and interviewed HEWs. Data were entered directly into tablet computers using Open Data Kit (ODK) [39] as the data capture software and were stored in a Research Electronic Data Capture (REDCap) database [40]. Further details on the survey methods are available elsewhere [41].

Ethical approval was obtained from the Institutional Review Boards of the Oromia Regional Health Bureau and the Johns Hopkins University Bloomberg School of Public Health. Informed consent forms were read in local language to all participating HEW and caregivers of sick children and oral consent was obtained from all participants.

## Indicators

The primary indicators of implementation strength and quality of care were adapted from the WHO Health Facility Survey Tool [38] and the iCCM Global Indicators [42]. **Table 2** shows the list of indicators considered for use in this analysis. The outcome of interest was the proportion of children correctly managed for major iCCM illnesses (correct management), with a sick child as the unit of analysis. This is a summary indicator that includes management of pneumonia, diarrhea, malaria, malnutrition, and measles. A child was considered correctly managed if 1) the child received all recommended treatments and no unnecessary treatments; 2) the child was referred if and only if referral was indicated; and 3) the HEW prescribed the correct dose, duration, and frequency for all treatments.

**Table 2.** Selected indicators of iCCM quality of care and implementation strength and their proportions (or means (standard deviation), Jimma and West Hararghe Zones, Oromia Region, Ethiopia, 2012\*

VARIABLE	No.	% OR MEAN	95% CI OR SD
Outcome:			
Child correctly managed for iCCM illnesses	257	64.2	57.4, 70.5
Predictors:			
HEW received follow-up training within 8 weeks of iCCM training	134	46.3	36.7, 56.1
HEW attended performance review and clinical mentoring meeting	137	89.1	82.1, 93.5
Health post received at least one supervision on iCCM in the previous three months	100†	87.0	78.8, 92.9

CI – confidence interval, SD – standard deviation, HEW – health extension worker

\*Indicators of quality of care and implementation strength were previously published by Miller et al [41].

†Three health posts excluded because HEWs reported not being present for majority of previous three months.

The predictors of interest were the training- and supervision-related interventions presented in **Table 1** that were intended to improve health worker performance (1. HEW received follow-up training within eight weeks of iCCM training, 2. HEW attended PRCMM, 3. Health post received at least one supervision on iCCM in the previous three months).

Child characteristics, such as age or severity of illness, can be important predictors of quality of care. However, because the objective of this analysis was to assess the relationships between the interventions to improve HEW performance and correct management, rather than to assess all possible predictors of correct management, we did not include child characteristics as predictors of interest in the analysis. The role of child characteristics as potential confounders is discussed below.

### Model selection and data analysis

Analyses for this manuscript were limited to HEWs who had received the standardized clinical training on iCCM. We assessed whether each of the three predictors of interest was associated with the outcome of correct management of childhood illness. Separate multivariate logistic regression models were developed for each predictor. For each of the three models (one for each predictor), we assessed potential confounders of the relationship between each predictor and the outcome. The potential confounders assessed were: zone, distance from the health post to the nearest referral health facility, availability of iCCM commodities, malaria risk of the health post catchment area, the number of sick child consultations at the health post in the previous month (caseload), HEW age, years of experience as an HEW, whether the HEW was from the kebele in which she worked, whether the HEW currently lived in the kebele in which she worked, whether the HEW intended to continue working as an HEW through the coming year (as a proxy for motivation), child sex, child age, whether the child had a severe illness, recruitment method that brought the child to the health post (spontaneous consultation, mobilized by

the HEWs, or recruited by the survey team), and the other two predictors of interest.

We used purposeful selection of variables to assess potential confounders [43]. In the first step, we conducted bivariate logistic regressions of the outcome on potential confounding variables. Potential confounders with a  $P$ -value  $\leq 0.25$  from a Wald test were retained for further assessment. Starting with the variable with the weakest association, these variables were assessed as confounders for each of the models. We then compared a full model, with the predictor and all of the variables retained in step one above, to a null model with one of the potential confounders removed. If removing the variable changed the coefficient of the predictor of interest by  $\geq 15\%$ , the variable was included in the final model as a confounder. This was repeated for each of the potential confounders.

Finally, we performed multivariate logistic regression analyses using two-level random intercept models with child and health post levels to assess associations between each of the quality improvement interventions and the outcome, controlling for the retained confounders. An alpha level of 0.05 was used for tests of statistical significance. All analyses were carried out in Stata 13 [44].

### RESULTS

All but one of the selected 104 health posts implementing iCCM were successfully surveyed, giving a final sample of 103 health posts. All 137 HEWs encountered in health posts and 257 sick children were included in the survey. Sample characteristics and detailed results on iCCM implementation strength and quality of care are available elsewhere [41].

Bivariate analyses showed that PRCMM (OR=6.45, 95% CI 2.22–18.73) and follow-up training (OR=2.25, 95% CI 1.24–4.07) were significantly associated with the outcome. Supervision on iCCM (OR=1.15, 95% CI 0.44–2.99) was not significantly associated with correct management.

The final models for each predictor and the results of the multivariate logistic regressions are shown in **Table 3**. Attendance at PRCMM had the largest association with correct management, controlling for other covariates. Children who were managed by an HEW who had attended a PRCMM had about eight times the odds of being correctly managed (OR=8.3, 95% CI 2.34–29.51), compared to children managed by an HEW who had not attended a PRCMM. The HEW receiving follow-up training also significantly increased the odds of the child receiving correct management (OR=2.09, 95% CI 1.05–4.18). The HEW receiving supervision on iCCM (OR=0.63, 95% CI 0.23–1.72) was not significantly associated with a child receiving correct care.

## DISCUSSION

Previous studies that looked at associations between program inputs and health worker quality of care in low-income countries have typically focused on training and supervision of health workers in health facilities. These studies of health facility workers have had mixed results [30,45], with some showing significant or near-significant associations between indicators of quality of care and training [46–52] and others showing little or no association [32–34]. Similarly, supervision has been shown to improve health worker performance in some studies [53] and to have no or little effect in others [33,34,54,55]. Reviews of interventions to improve health worker performance found that quality improvement interventions with multifaceted interventions, such as training plus supervision, generally have a greater effect and that supervision with feedback is usually beneficial [30,45].

Only a few studies have assessed the effect of quality improvement interventions on quality of care provided by

CHWs. The evidence from this small number of studies is also mixed. Some found positive associations between quality of care and training [55,56] and supervision [56], while others showed no significant associations with training [57,58] or supervision [58]. Two recent studies in Ethiopia showed associations between supportive supervision [59] and PRCMM [60] and improved consistency in iCCM patient registers between HEWs' assessment, classification, and treatment of sick children.

We found that HEW attendance at a PRCMM and follow-up training were both significantly associated with the outcome. PRCMM, in particular, had a very strong association with correct management. These are important findings because these interventions are not always included in quality improvement programs.

These findings should be interpreted with caution, as there is the potential for unmeasured confounding. It is possible that the HEWs who provided lower quality care were less motivated and did not attend a PRCMM. This would spuriously inflate the observed association between PRCMM and the outcome. During the survey, a small number of HEWs (16) reported that they did not plan to continue working as an HEW through the coming year. Because this variable may be related to HEW motivation, we assessed whether there may be a negative association between attending a PRCMM and intention to continue as an HEW. In fact, all of the HEWs who reported an intention to leave their jobs as HEWs had attended a PRCMM. This is far from an ideal proxy for motivation and a very small sample size, but it does somewhat weaken the argument that HEW motivation confounded the relationship between correct management and PRCMM.

Routine supervision for iCCM was not associated with the outcome. PRCMM and follow-up training may have been

**Table 3.** Final models and results of multivariate analyses of associations between iCCM quality improvement interventions and correct management of major iCCM illnesses, controlling for selected covariates, in children 2–59 months, Jimma and West Hararghe Zones, Oromia Region, Ethiopia, 2012

PREDICTOR VARIABLE	COVARIATES	NUMBER OF CHILDREN (N = 257)	% CHILDREN CORRECTLY TREATED	OR (95% CI)	P-VALUE
Child managed by HEW who attended PRCMM:	–				
Yes		233	68.2	8.3 (2.34, 29.51)	<0.001
No		24	25.0	Ref.	
Child managed by HEW who received follow-up training within 8 weeks of iCCM training:	Child with severe illness				
Yes		116	74.1	2.09 (1.05, 4.18)	0.037
No		141	56.0	Ref.	
Child managed in health post that received at least one supervision on iCCM in the previous three months	PRCMM; follow-up training; child with severe illness				
Yes		225	65.3	0.63 (0.23, 1.72)	0.369
No		29	62.1	Ref.	

OR – odds ratio, CI – confidence interval, HEW – health extension worker, iCCM – integrated community case management of childhood illness. PRCMM – performance review and clinical mentoring meeting

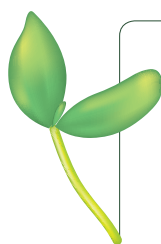
more effective than routine iCCM supervision because they were longer and more intensive, and were more specifically focused on reviewing case management guidelines and clinical practices. On the other hand, the observed lack of association between supervision and correct management may reflect a lack of focused improvement of clinical skills, with more emphasis on data collection and register review. The effect of supervision may also have been reduced in a context where a large majority of HEWs had received PRCMM. Supervision may have had a limited *additional* effect after the strong effect of PRCMM.

The discrepancy between these results and the previous study showing a significant association between supervision and quality of care among HEWs [59] is likely because of the use of different outcome variables. Ameha et al. used consistency between classification and treatment from patient registers as the outcome variable. We have previously shown that register review overestimates quality of care compared to estimates derived from observation of consultations and re-examination of sick children [61]. Because supervisions focus on register review, it is likely that they improve recording of cases, but this may neglect improvement of assessment skills, which can lead to incorrect classification.

Further research is needed on how to improve the quality and effectiveness of training and supervision interventions to achieve maximum impact. For example, supportive supervision may be more effective if it includes a component of case observation with feedback, rather than relying entirely on register review. However, the feasibility of doing this in a setting of small numbers of consultations needs to be assessed.

This study has several limitations. First, the observational design of the study limits the conclusions about causality that can be drawn. The absence of a comparison group makes it impossible to rule out unmeasured variables that may have confounded the observed associations between the interventions and correct management. Second, health workers may have performed better under observation than they would under normal circumstances [62,63]. Third, data on the predictors were based on HEW recall, which may be biased toward having received the interventions, although Hazel et al. found that HSAs in Malawi accurately reported implementation strength indicators [64]. Finally, because HEWs receive relatively more training and compensation than many CHW cadres in other countries, these results may not be generalizable to other contexts where iCCM is implemented.

The results of this study, as well as large variations in impact from quality improvement interventions studied in other contexts, suggest that it may be the quality of implementation of interventions, more than their inherent characteristics, which determines their effectiveness. Quality improvement interventions for health workers can lead to improvements in quality of care, but they do not necessarily do so. Therefore, efforts should be focused not only on achieving high coverage of quality improvement interventions, but also on the content and quality of these interventions to ensure that they have the expected impact. The positive associations between follow-up training and especially PRCMM suggest that these interventions should be considered as complements to standard trainings and supportive supervision to improve the quality of iCCM services.



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**Competing interests:** All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author). HL and TD were staff of UNICEF, which was an iCCM implementing partner, at the time of the study.

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# Population-level effectiveness of PMTCT Option A on early mother-to-child (MTCT) transmission of HIV in South Africa: implications for eliminating MTCT

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**Background** Eliminating mother-to-child transmission of HIV (EMTCT), defined as  $\leq 50$  infant HIV infections per 100 000 live births, is a global priority. Since 2011 policies to prevent mother-to-child transmission of HIV (PMTCT) shifted from maternal antiretroviral (ARV) treatment or prophylaxis contingent on CD4 cell count to lifelong maternal ARV treatment (cART). We sought to measure progress with early (4–8 weeks post-partum) MTCT prevention and elimination, 2011–2013, at national and sub-national levels in South Africa, a high antenatal HIV prevalence setting ( $\approx 29\%$ ), where early MTCT was 3.5% in 2010.

**Methods** Two surveys were conducted (August 2011–March 2012 and October 2012–May 2013), in 580 health facilities, randomly selected after two-stage probability proportional to size sampling of facilities (the primary sampling unit), to provide valid national and sub-national–(provincial)–level estimates. Data collectors interviewed caregivers of eligible infants, reviewed patient-held charts, and collected infant dried blood spots (iDBS). Confirmed positive HIV enzyme immunoassay (EIA) and positive total HIV nucleic acid polymerase chain reaction (PCR) indicated infant HIV exposure or infection, respectively. Weighted survey analysis was conducted for each survey and for the pooled data.

**Findings** National data from 10 106 and 9120 participants were analyzed (2011–12 and 2012–13 surveys respectively). Infant HIV exposure was 32.2% (95% confidence interval (CI) 30.7–33.6%), in 2011–12 and 33.1% (95% CI 31.8–34.4%), provincial range of 22.1–43.6% in 2012–13. MTCT was 2.7% (95% CI 2.1–3.2%) in 2011–12 and 2.6% (95% CI 2.0–3.2%), provincial range of 1.9–5.4% in 2012–13. HIV-infected ARV-exposed mothers had significantly lower unadjusted early MTCT (2.0% [2011–12: 1.6–2.5%; 2012–13: 1.5–2.6%]) compared to HIV-infected ARV-naïve mothers [10.2% in 2011–12 (6.5–13.8%); 9.2% in 2012–13 (5.6–12.7%)]. Pooled analyses demonstrated significantly lower early MTCT among exclusive breastfeeding (EBF) mothers receiving  $>10$  weeks ARV prophylaxis or cART compared with EBF and no ARVs: (2.2% [95% CI 1.25–3.09%] vs 12.2% [95% CI 4.7–19.6%], respectively); among HIV-infected ARV-exposed mothers, 24.9% (95% CI 23.5–26.3%) initiated cART during or before the first trimester, and their early MTCT was 1.2% (95% CI 0.6–1.7%). Extrapolating these data, assuming 32% EIA positivity and 2.6% or 1.2% MTCT, 832 and 384 infants per 100 000 live births were HIV infected, respectively.

**Conclusions:** Although we demonstrate sustained national-level PMTCT impact in a high HIV prevalence setting, results are far-removed from EMTCT targets. Reducing maternal HIV prevalence and treating all maternal HIV infection early are critical for further progress.

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Eliminating mother-to-child transmission of HIV (EMTCT) is pivotal to improving child survival in high HIV-burden, resource-limited settings [1]. South Africa, an archetypal high HIV prevalence, middle-income country, with social and political idiosyncrasies after an apartheid history, has prioritised EMTCT. Since 2014 this has been defined as <5% mother to child transmission of HIV (MTCT) at final endpoint in breastfeeding populations,  $\leq 50$  new infant HIV infections per 100 000 live births,  $\geq 95\%$  coverage of antenatal care among all women,  $\geq 95\%$  coverage of HIV testing and receipt of results and  $\geq 90\%$  coverage of antiretroviral drugs among HIV positive pregnant women [2,3]. Globally, strategies to prevent MTCT (PMTCT) are guided by a comprehensive four-prong approach, namely: (i) primary prevention of incident HIV infections; (ii) prevention of unplanned pregnancies; (iii) antiretroviral (ARV) drug interventions, and (iv) care, treatment and support, which aims to integrate PMTCT interventions into routine maternal, newborn and child health services [4].

Early, long-term triple combination antiretroviral therapy (cART) among HIV-positive women with higher CD4 cell counts (250–500 cells/mm<sup>3</sup>), or extended infant antiretroviral (ARV) prophylaxis have increased the impact of prong (iii) [5–7]. In 2010, the World Health Organization (WHO) PMTCT update recommended PMTCT Option “A” or “B” [8]: “A” provides antiretroviral prophylaxis (ARVP) from 14 weeks gestation for HIV-infected pregnant women with CD4 cell counts  $>350$  cells/mm<sup>3</sup> and infant nevirapine (NVP) prophylaxis throughout breastfeeding; or lifelong cART for HIV-infected pregnant women with CD4 cell counts  $\leq 350$  cells/mm<sup>3</sup> or WHO stage 3–4 disease with 6 weeks of infant NVP prophylaxis; “B” provides cART during breastfeeding for all HIV-positive pregnant and lactating women with six weeks infant NVP or continued maternal cART beyond breastfeeding cessation if maternal CD4 cell count  $\leq 350$  cells/mm<sup>3</sup> or WHO stage 3–4 disease. Since 2013 a rapid shift to PMTCT Option B+ has occurred, and 18 of the 22 Global Plan priority countries (countries that house  $>90\%$  of the world’s population of pregnant HIV positive women) have either endorsed, implemented or conducted national scale-up of PMTCT Option B+ [9]. “B+” has reduced final MTCT to  $<2\%$  in non-breastfeeding countries [10].

South Africa’s national PMTCT program began with maternal and infant single dose NVP (sdNVP) in 2002, and transitioned to dual ARV therapy in February 2008, to WHO PMTCT Option A in April 2010, PMTCT Option B in April 2013 and PMTCT Option B+ in January 2015 [11].

Between 2001 and 2010, in resource-limited, high HIV prevalence countries, such as South Africa, rigorous routine measurements of national PMTCT impact and trends were simply unavailable. In 2010, using cross-sectional non-routine surveillance methodology at immunisation service

delivery points we conducted the first national PMTCT effectiveness evaluation in South Africa, which documented a 3.5% (95% CI 2.9–4.1%) risk of MTCT, measured at 4–8 weeks postpartum (median 6 weeks), nationally under the 2008 PMTCT policy [12]. This paper presents the results of two subsequent national surveys, conducted to measure national and provincial-level PMTCT impact, measured 17–24 (August 2011–March 2012) and 31–38 (October 2012–May 2013) months after implementing PMTCT Option A, and during the first 2 months (April–May 2013) of transitioning to PMTCT Option B. During this time, the South African national PMTCT program aimed to reduce MTCT to less than 2% and less than 5% at six weeks and 18 months postpartum, respectively.

## METHODS

The methods have been explained in detail elsewhere [11,13]. In summary, two cross-sectional, facility-based, national epidemiological surveys were conducted between August 2011–March 2012 and October 2012–May 2013. Public health non-mobile facilities offering infant immunisation services in each of the nine provinces were stratified according to their six-week annual immunisation numbers and antenatal HIV prevalence [12,14]. Specifying relative precisions of 30% to 50% for the expected MTCT rate across provinces plus a design effect of 2 yielded a total desired sample size of 12 200 infant dried blood spot specimens (iDBS). Stratified two-stage sampling was used with facilities sampled with probability proportional size and with replacement [15]. At the second stage a fixed number of infants per facility, representing the median number of infants expected within the sampling window (three weeks in 8 provinces; four weeks in the sparsely populated, low HIV prevalence Northern Cape province), were sampled to ensure a self-weighting sample at provincial level. Data were gathered using a questionnaire adapted from several validated tools [13,16,17]. Trained study nurses recruited eligible consented infants (aged 4–8 completed weeks; receiving their six-week immunisation; not needing emergency care) and their caregivers [12]. Data on ARV exposure and infant feeding were self-reported [12]. Trained supervisors used standard operating procedures to monitor field work. Infants (not mothers) were tested for HIV antibodies to infant HIV exposure [11,13].

All infant dried blood spots (iDBS) were tested at the National Institute for Communicable Diseases, Johannesburg, using standardised accredited procedures, namely Enzyme immunoassay (EIA) (Genscreen HIV1/2 Ab EIA Version 2, Bio-Rad Laboratories, Schiltigheim, France) to detect HIV antibodies. All antibody-positive and 10% of negative specimens were re-tested using a second EIA (Vironostika HIV Uni-form II plus O, bioMérieux Clinical Diagnostics,

Marcy-L'Etoile, France). Discordant results were re-processed using Western blot (GS HIV-1, Bio-Rad, Schiltigheim, France). iDBS with concordant positive or discordant EIA results or from self-reporting HIV-positive mothers were tested using a qualitative total nucleic acid Polymerase Chain Reaction (PCR) to determine infant's HIV infection (COBAS AmpliPrep/COBAS TaqMan (CAP/CTM) Qualitative assay version 1.0, Roche Diagnostics, Branchburg NJ, USA).

For data analysis sample weights were calculated that consisted of two components: first realization weights were calculated depending on the realization within the strata of each province and second provincial weights. For the latter weight the number of live-births recorded across the nine provinces pertaining to the survey year was used. The sample weight was the product of realization weight and provincial weight and represents the number of live births the observed participant represents. The survey analysis took into account stratification, different sampling stages, the finite number of primary sampling units (PSU) and the design effect. Data were analyzed using SAS (SAS Institute N Carolina, Cary NC, USA) version 9.2 and 9.4.

During data analysis self-reported maternal antiretroviral uptake was classified into three main groups with nine sub-groups (Figure 1).

Early MTCT by ARV category was initially measured using ARV definitions from Figure 1. Thereafter to facilitate comparison with the 2010 survey antiretroviral exposure was re-categorised into three main groups with six main categories, namely (i) "advanced regimen" group including

mothers on cART or Azidothymidine (AZT) for >10 weeks and infant on sdNVP and/or AZT at birth (ARVP >10wks); (ii) "other ARV regimen" group including mothers on AZT for ≤10 weeks and infants on sdNVP and/or AZT at birth (ARVP ≤10 weeks) or mothers or infants (but not both) on any ARVs (incomplete ARVP) and (iii) "no known ARV group" including mothers and infants on no ARVs or with missing ARV information) [11].

Self-reported infant feeding was categorised using WHO definitions: exclusive breastfeeding (EBF), avoiding breastfeeding (FF) and mixed breastfeeding (MBF) [18].

Simple logistic regression followed by multivariable logistic regression was conducted to examine risk factors for early MTCT using pooled data from the 2011-12 and 2012-13 surveys. Clinically important predictors and risk factors with  $P < 0.25$  in univariate unweighted analysis were included in the preliminary main effects model. Variables with  $P < 0.05$  or those that changed the odds ratio of the key exposure variable by 10% or those that were thought to be important independent predictors of MTCT in theoretical models were included in the penultimate model. The final model was selected based on model fit statistics (the best fit) with the lowest likelihood ratio and a significant model chi-square test ( $P \leq 0.05$ ).

Ethical approval was obtained from the Medical Research Council and the United States Centers for Disease Control and Prevention. All caregivers included in analyses provided informed consent.

(1) Advanced regimen group, including those mothers on:	(2) Other ARV regimen group, including:	(3) No known ARV group, including:
<ul style="list-style-type: none"> <li>• (1a) triple antiretroviral therapy commenced in the first trimester or before, with postnatal infant nevirapine or infant AZT prophylaxis or</li> <li>• (1b) triple antiretroviral therapy commenced in the second trimester with infant nevirapine or infant AZT prophylaxis or</li> <li>• (1c) triple antiretroviral therapy commenced in the third trimester with infant nevirapine or infant AZT prophylaxis or</li> <li>• (1d) AZT prophylaxis commenced in the first trimester with infant nevirapine or infant AZT prophylaxis or</li> <li>• (1e) AZT prophylaxis commenced in the second trimester with infant nevirapine or infant AZT prophylaxis</li> </ul>	<ul style="list-style-type: none"> <li>• (2a) mother received AZT in the third trimester with infant nevirapine or infant AZT prophylaxis or</li> <li>• (2b) mothers or infants (but not both) received any ARVs (incomplete ARVP)</li> </ul>	<ul style="list-style-type: none"> <li>• (3a) mothers and infants reported receiving no ARV or</li> <li>• (3b) missing ARV information</li> </ul>

**Figure 1.** Classification of antiretroviral uptake 2011–2012 and 2012–13. Maternal self-reported antiretroviral uptake was classified into three overall groups with sub-categories in each group. AZT – azidothymidine, ARV – antiretroviral.

## RESULTS

In the 2011–12 and 2012–13 surveys, respectively, 11 377 and 10 533 participants were screened and 10 482 and 9679 were enrolled; of the enrolled participants, iDBS were available on 10 106 (96.5%) and 9120 (94.2%) infants respectively, yielding a sample realization of 83% and 75% (Table 1). Provincial sample realization ranged from 73%–89% in 2011–12 and 56%–91% in 2012–13. The lower sample realization in 2012–13 is explained by the late (year-end) start date, vaccine stock-outs, facility changes from daily immunisation to weekly immunisation days and increased use of mobile services.

### The weighted PMTCT cascade

Among all mothers self-reported weighted uptake of antenatal HIV testing was 98.3% (95% CI 98.0%–98.6%) in 2011–12 and 95.5% (95% CI 95.0%–96.0%) in 2012–13 (Figure 2). In both surveys 99.4–99.8% of tested mothers received their results. This demonstrated that in 2012–13 almost 95% of all mothers were tested and received their HIV test results.

Among self-reported HIV-positive mothers 86.4% (95% CI 84.2–88.7%) and 92.1% (95% CI 90.7%–93.5%) reported being tested for CD4 cell count in 2011–12 and 2012–13, respectively, and 77.4% (95% CI 74.9–80%) and 65.9% (95% CI 63.3–68.6) reported knowing their CD4 results. The median reported CD4 cell count was 359 cells/mm<sup>3</sup> (interquartile range IQR 240–499) in 2011–12 and 372 cells/mm<sup>3</sup> (IQR 264–500) in 2012–13.

The proportion of self-reported HIV positive women receiving maternal cART increased by 12.9%, from 41.9% (95% CI 39.7–44.2%) in 2011–12 to 54.8% (95% CI 52.6%–57.0%) in 2012–13, while receipt of any maternal

or infant prophylaxis dropped by 8.1%, from 52.0% (95% CI 49.7–54.2%) in 2011–12 to 43.9% (95% CI 41.8–46.1%) in 2012–13. Due to the increased cART uptake overall, ARV coverage among self-reported HIV positive women increased from 93.9% in 2011–12 to 98.7% in 2012–13.

Among EIA positive infants: 85.9% (95% CI 84.3–87.5) and 91.3% (95% CI 90.0–92.6%) were born to mothers who reported receiving any maternal antiretroviral therapy in 2011–12 and 2012–13 respectively; 93.4% (95% CI 92.4–94.5%) and 94.0% (95% CI 92.9–95.1%) reported initiating infant NVP prophylaxis in 2011–12 and 2012–13 respectively and 86.4% (95% CI 84.3–88.5%) and 91.4% (95% CI 95.1–96.2%) reported current infant NVP-use at the time of interview (six weeks postpartum); any breastfeeding increased from 53.0% (95% CI 50.4–55.5%) in 2011–12 to 72.2% (95% CI 70.1–74.2%) in 2012–13; EBF increased from 35.5% (95% CI 33.1–38.0%) in 2011–12 to 54.1% (95% CI 51.9%–56.2%) in 2012–13 and MBF increased from 14.0% (12.3–15.7%) in 2011–12 to 20.5% (18.8–22.1%) in 2012–13. Avoiding breastfeeding decreased from 47.1% (44.9–49.3%) in 2011–12 to 27.7% (95% CI 25.6–29.7%) in 2012–13.

### Weighted Infant HIV exposure and MTCT

In 2011–12 and 2012–13 self-reported maternal HIV positivity was 29.5% (95% CI 28.0–32.2%) and 32.1% (95% CI 30.8–33.4%) respectively while infant EIA positivity was 32.2% (95% CI 30.7–33.6%) and 33.1% (95% CI 31.8–34.4%) respectively (Table 1). The national population-level risk of early MTCT measured among EIA positive infants was 2.7% (95% CI 2.1–3.2%) in 2011–12 and 2.6% (95% CI 2.0–3.2%) in 2012–13. Early MTCT varied provincially from 2.0% (95% CI 0.6–3.3) to 6.1% (95% CI

**Table 1.** Sample realization, infant HIV exposure and early MTCT at 6 weeks (range 4–8 weeks) postpartum: 2011–12 and 2012–13

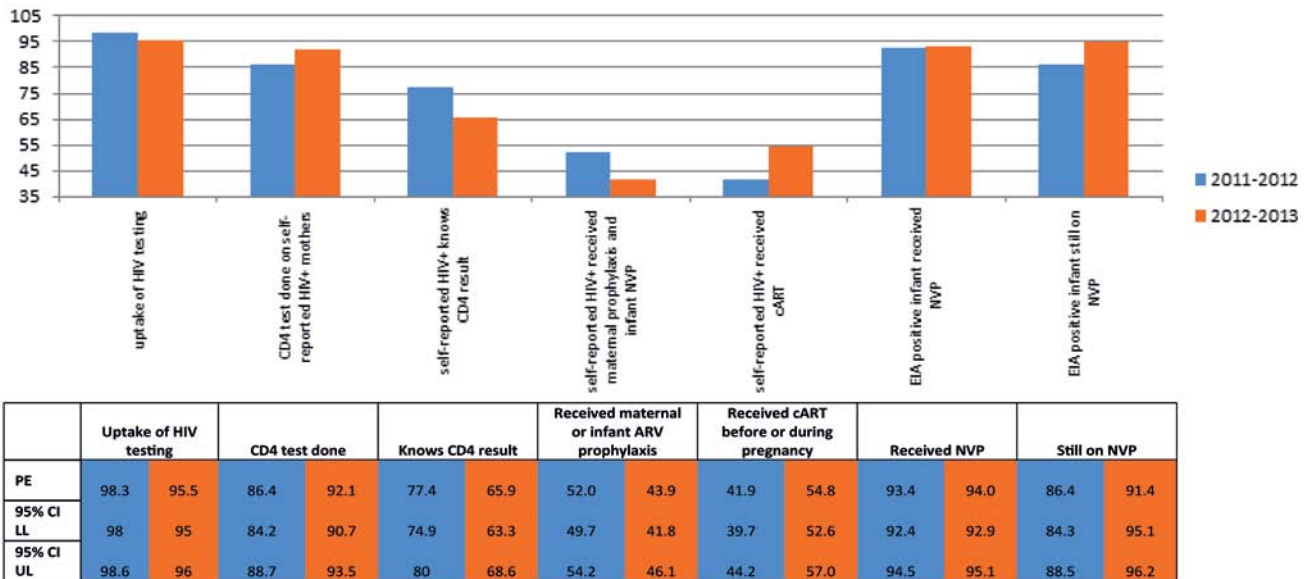
PROVINCE	AUGUST 2011 – MARCH 2012 SURVEY*			OCTOBER 2012 – MAY 2013 SURVEY†		
	Sample realization number (%)	Weighted % Infant HIV-exposure	Weighted % MTCT (95% CI)	Sample realization number (%)	Weighted % Infant HIV-Exposure	Weighted % MTCT (95% CI)
South Africa	10 106 (83%)	32.2 (30.7–33.6)	2.7 (2.1–3.2)	9120 (75%)	33.1 (31.8–34.4)	2.6 (2.0–3.2)
Eastern Cape	1194 (85%)	32.0 (29.6–35.5)	3.8 (2.1–5.5)	1035 (74%)	29.0 (25.1–32.9)	2.4 (1.1–3.8)
Free State	1056 (81%)	30.9 (28.6–33.3)	3.8 (2.3–5.3)	868 (67)	34.2 (30.6–37.7)	2.8 (1.5–4.1)‡
Gauteng	1607 (89%)	33.1 (29.8–36.4)	2.1 (0.9–3.4)	1637 (91%)	34.0 (30.6–37.4)	2.2 (1.3–3.1)
Kwa-Zulu Natal	1052 (75%)	44.4 (39.8–48.9)	2.1 (0.9–3.3)	1060 (76%)	43.6 (39.5–47.8)	2.9 (1.3–4.6)
Limpopo	1070 (76%)	23.0 (19.9–26.2)	3.1 (1.2–4.9)	1225 (88%)	25.2 (21.8–28.7)	2.1 (0.6–3.6)
Mpumalanga	1210 (76%)	35.6 (33.3–37.8)	3.3 (2.2–4.5)	898 (56%)	37.6 (33.6–41.7)	1.5 (0.6–2.3)‡
Northern Cape	506 (72%)	15.1 (12.7–17.5)	6.1 (2.5–9.6)‡	426 (61%)	20.9 (15.6–26.2)	2.2 (0.4–4.1)‡
North West	1037 (86%)	30.8 (28.5–33.1)	2.6 (1.1–4.0)	781 (65%)	31.4 (27.8–35.0)	5.4 (3.4–7.4)‡
Western Cape	1374 (98%)	17.8 (14.8–20.8)	2.0 (0.6–3.3)	1190 (85%)	22.1 (17.8–26.6)	1.9 (0.4–3.3)

MTCT – mother-to-child transmission, CI – confidence interval

\*Conducted during months 17 (August 2011) to 24 (March 2012) after PMTCT Option A became policy.

†Conducted during months 31–38 after PMTCT Option A was adopted and includes the first 2 months (April and May 2013) of PMTCT Option B policy implementation.

‡Sample realization <70%, thus these MTCT estimates may be subject to bias.



**Figure 2.** Weighted uptake along the PMTCT (prevent mother-to-child transmission) cascade among self-reported HIV positive women 2011–2012 and 2012–2013. PE – point estimate; LL – lower limit of 95% confidence interval (CI); UL – upper limit of 95% CI, cART – combination antiretroviral therapy, AZT – azidothymidine, ARV – antiretroviral, NVP – nevirapine.

2.5–9.6) in 2011–12 and from 1.5% (95% CI 0.6–2.3) to 5.4% (95% CI 3.4–7.4) in 2012–13 (**Table 1**). The unadjusted pooled early MTCT (2011–12 and 2012–13) was 2.6% (2.2–3.1%).

In 2011–2012 and 2012–13 among “mothers receiving any PMTCT intervention(s)”, early MTCT was 2.0%, (95% CI 1.6–2.5% and 1.5–2.6%, respectively); among mothers who did not know that their infants were EIA-positive, early MTCT was 10.2% in 2011–2012 (95% CI 6.5–13.8%) and 9.2% in 2012–2013 (95% CI 5.6–12.7%), respectively (**Figure 3**). Overall, the risk of unadjusted MTCT differed significantly by antiretroviral exposure (**Table 2**,  $P < 0.0001$  for Columns A–C). Columns B and C present early MTCT using the pooled 2011–13 data set analyzed according to the 2010 survey ARV categories [11], to facilitate comparison. Of note is that early MTCT decreased to 1.2% (0.6–1.7) among HIV positive mothers who commenced cART in the first trimester or before.

**Table 3** illustrates that controlling for maternal age, socio-economic status (SES), marital status, education, gestational age at first ANC visit, total number of lifetime pregnancies, whether or not the current pregnancy was planned, province, survey year and whether or not the infant weighed less than 2.5kg at birth, the adjusted odds of early MTCT increased significantly if mother started ARVP in the second trimester (after 12 weeks’ gestation) or if only mother or baby or neither received antiretroviral drugs, compared to mothers who received cART in the first trimester or before. There were no additional significant MTCT differences between any of the other ARVP groups, although this could

relate to small sample sizes. However the point estimates for early MTCT tended to increase as ARV exposure decreased.

**Table 4** demonstrates the protective effect of advanced antiretroviral regimens on early MTCT within exclusively breastfeeding populations (2.17% [1.23–3.09%]) in the EBF group with advanced regimens compared with 12.17% (4.7–19.6%) in the no ARV group. Among EBF women who initiated cART in the first trimester or before, early MTCT was 0.82% (0.06–1.58%), data not shown in the table.

## DISCUSSION

These PMTCT surveillance studies conducted at national and subnational (provincial) levels, in public health facilities that provide care for the majority of South Africa’s children, demonstrated that population-level early MTCT was sustained at 2.6%, 17–24 and 31–38 months after PMTCT Option A policy was adopted. HIV testing uptake was 95% and at least 99.7% of tested mothers received their HIV test results; thus almost 95% of all mothers receive their HIV test results. Therefore the  $\geq 95\%$  validation target for HIV testing uptake has just about been met in 2012–13. Maternal antiretroviral uptake among mothers with EIA positive infants was 91.3% (90.0–92.6%) in the 2012–13 survey, also meeting this EMTCT validation target at national level.

Although the 2.6% was a reduction from previous MTCT estimates in South Africa, these data show that the national target of  $< 2\%$  at 6 weeks postpartum was not achieved. Uptake of first trimester cART reduced early MTCT to

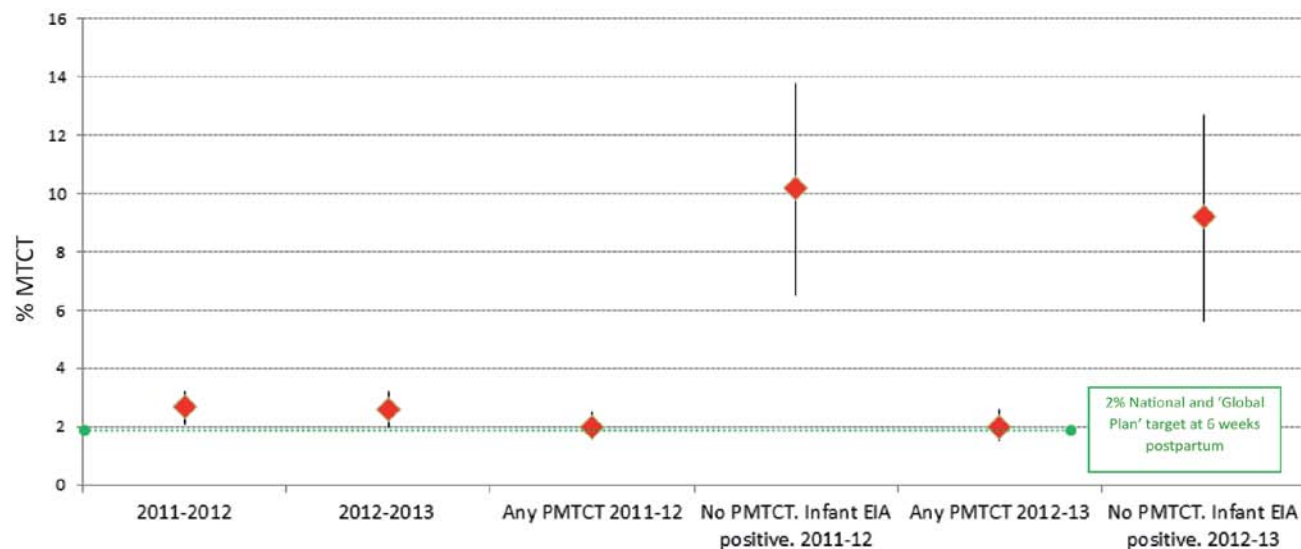
1.17% (0.61–1.72). Extrapolating these results to numbers, assuming 32% infant HIV exposure among 100 000 live births, 2.6% early MTCT means that by 6 weeks postpartum, 832 infants per 100 000 live births were HIV infected, and 1.17% early MTCT means that 384 infants per 100 000 live births were HIV infected. These extrapolations are far higher than the EMTCT target of  $\leq 50$  HIV infected

infants per 100 000 live births, and are driven by the high HIV prevalence in South Africa.; These stark findings illustrate the importance of a public health approach to PMTCT, which locates all PMTCT interventions within a comprehensive framework aiming to reduce new HIV infections among young women of reproductive age, thus reducing antenatal HIV prevalence. Although the paper confirms that early

**Table 2.** MTCT by various antiretroviral exposures: pooled 2011–12 and 2012–13 data

ANTIRETROVIRAL REGIMEN	UNWEIGHTED FREQUENCY OF OBSERVATIONS (WEIGHTED FREQUENCY)	UNWEIGHTED FREQUENCY OF HIV POSITIVE INFANTS (WEIGHTED HIV POSITIVE FREQUENCY)	WEIGHTED MTCT (%) (COLUMN A)	WEIGHTED MTCT (%) ACCORDING TO ARV GROUPS GENERATED IN THE 2010 PAPER [11] (COLUMN B)	WEIGHTED MTCT (%) ACCORDING TO ARV GROUPS GENERATED IN THE 2010 PAPER [11] (COLUMN C)
<b>Advanced regimen group:</b>					
(1a) cART commenced in 1st trimester or before with infant postnatal prophylaxis	1472 (187 986)	19 (2201)	1.17 (0.61–1.72)	<b>2010 1a</b> , 1.60 (1.15–2.05)	1.84 (1.44–2.25)
(1b) cART commenced in 2nd trimester with infant prophylaxis	727 (96 677)	14 (1638)	1.69 (0.76–2.62)		
(1c) cART commenced in 3rd trimester with infant prophylaxis	163 (35 699)	2 (330)	0.92 (0.00–2.22)		
(1d) AZT prophylaxis commenced in 1st trimester with infant prophylaxis (ARVP)	821 (102 640)	20 (2619)	2.54 (1.28–3.80)	<b>2010 1b</b> , 2.30 (1.42–3.2)	
(1e) AZT prophylaxis commenced in 2nd trimester with prophylaxis (ARVP)	1087 (151 221)	26 (3515)	2.31 (1.42–3.21)		
<b>Other ARV regimen group:</b>					
(2a) AZT prophylaxis commenced in 3rd trimester with prophylaxis (ARVP)	205 (27 856)	2 (368)	1.32 (0.00–3.16)	<b>2010 2a</b> , 1.32 (0.00–3.16)	2.49(1.36–3.61)
(2b) mothers or infants (but not both) received any ARVs (incomplete ARVP)	507 (62 419)	19 (2446)	3.90 (1.88–5.92)	<b>2010 2b</b> , 3.90 (1.88–5.92)	
<b>No known ARV group:</b>					
(3a) mothers and infants reported receiving no ARV	63 (8119)	8 (995)		<b>2010 3a</b> , 11.40 (3.75–19.05)	
(3b) missing ARV information	643 (76 929)	48 (5875)		<b>2010 3b</b> , 7.28 (5.03–9.53)	

MTCT – mother-to-child transmission, cART – combination antiretroviral therapy, AZT – azidothymidine, ARV – antiretroviral, ARVP – antiretroviral prophylaxis



**Figure 3.** MTCT (mother-to-child transmission) measured in 2011–12 and 2012–13, with and without any PMTCT (prevent mother-to-child transmission) intervention. EIA – enzyme immunoassay.



**Table 3.** Associations between key PMTCT interventions and weighted perinatal infant HIV positive status in HIV exposed infants, South Africa, pooled data 2011–2013

INDICATORS	FREQUENCY OF HIV EXPOSED INFANTS WITH PCR RESULTS*, N = 5889 (Nw = 762314)	FREQUENCY OF HIV INFECTED INFANT N = 160, (Nw = 20130)	UNADJUSTED OR, (95% CI)	ADJUSTED OR†, MODEL 1§	ADJUSTED OR†, MODEL 2	ADJUSTED OR†, MODEL 3¶	ADJUSTED OR‡, FINAL MODEL**
<b>CD4:††</b>							
≤350 cells/mm <sup>3</sup>	1682 (224217)	35 (3977)	0.87 (0.51–1.50)	0.98 (0.42–2.05)			0.96 (0.46–2.01)
>350 cells/mm <sup>3</sup>	1927 (258908)	35 (5258)	Ref	Ref			Ref
Missing	2230 (272433)	90 (10895)	2.01 (1.30–3.1)	0.79 (0.40–1.55)			0.78 (0.40–1.51)
<b>Advanced regimen group (as defined in Figure 1):</b>							
(1a)	1472 (187986)	19 (2201)	Ref	Ref			Ref
(1b)	727 (96677)	14 (1638)	1.45 (0.70–3.005)	1.84 (0.81–4.18)			1.82 (0.8–4.1)
(1c)	163 (35699)	2 (330)	0.79 (0.18–3.46)	0.43 (0.05–3.56)			0.44 (0.05–3.56)
(1d)	821 (102640)	20 (2619)	2.21 (1.08–4.52)	2.06 (0.78–5.44)			2.07 (0.79–5.43)
(1e)	1087 (151221)	26 (3515)	2.01 (1.09–3.7)	2.43 (1.13–5.23)			2.37 (1.1–5.15)‡‡
<b>Other ARV regimen group (as defined in Figure 1):</b>							
(2a)	205 (27856)	2 (368)	1.13 (0.25–5.06)	1.32 (0.25–6.83)			1.25 (0.24–6.39)
(2b)	507 (62419)	19 (2446)	3.44 (1.66–7.14)	4.12 (1.53–11.43)			4.16 (1.53–11.35)‡‡
<b>No known ARV group (as defined in Figure 1):</b>							
(3a)	63 (8119)	8 (995)	11.78 (4.83–28.75)	9.04 (2.14–38.19)			9.0 (2.17–37.38)‡‡P
(3b)	643 (76929)	48 (5875)	7.0 (3.85–12.65)	11.90 (4.64–30.49)			11.58 (4.46–30.05)‡‡
<b>Infant feeding practices:</b>							
FF	2212 (289615)	46 (6218)	Ref		Ref		Ref
EBF	1452 (192577)	41 (6044)	1.77 (1.09–2.87)		1.98 (1.08–3.66)		1.80 (0.95–3.42)
Mixed BF	365 (46619)	12 (1379)	1.67 (0.88–3.12)		1.48 (0.76–2.88)		1.04 (0.52–2.10)
<b>Delivery type:</b>							
Cesarean	1322 (178656)	31 (4385)	Ref			Ref	Ref
Vaginal	4404 (563637)	124 (15234)	0.91 (0.58–1.42)			0.46 (0.20–1.05)	0.82 (0.43–1.59)

PMTCT – prevent mother-to-child transmission, EBF – exclusive breastfeeding, FF – formula feeding (no breastmilk), MF – breastfeeding with other fluids or solids, ARV – antiretroviral, CI – confidence interval, OR – odds ratio, Nw – weighted population number, Ref – reference group

\*55 (unweighted) exposed infants with missing HIV DNA test results excluded from this analysis.

†Adjusted for maternal age, SES, marital status, education, gestational age at first ANC visit, total number of lifetime pregnancies, whether or not the current pregnancy was planned, province, survey year and whether or not the infant weighed less than 2.5kg at birth.

‡Adjusted for maternal age, SES, marital status, education, gestational age at first ANC visit, total number of lifetime pregnancies, whether or not the current pregnancy was planned, province, survey year and whether or not the infant weighed less than 2.5kg at birth.

§Observations used = 3571; –2LL = 107170; Wald  $P < 0.0001$ .

||Observations used = 3571; –2LL = 101093; Wald  $P < 0.0001$ .

¶Observations used = 3571; –2LL = 101775; Wald  $P < 0.0001$ .

\*\*Observations used = 3571; –2LL = 95350.75; Wald  $P < 0.0001$ .

††Self-reported databased on mother's last CD4 cell count.

‡‡Significant relationship between characteristic and MTCT.

**Table 4.** Stratified analysis of MTCT by infant feeding practice and PMTCT regimen

FEEDING PATTERN OVER PREVIOUS 8 D AT 6 WEEKS	CHARACTERISTIC	ADVANCED REGIMEN GROUP*, P = 0.27	OTHER ARV REGIMEN GROUP*, P = 0.44	NO KNOWN ARV GROUP*, P = 0.05
EFF	Unweighted number–UWNo. HEI (weighted number WNo HEI)	1770 (234655)	235 (30524)	210 (25226)
	UWNo HIV positive infants–HPI (WNo HPI)	29 (3383)	7 (739)	10 (1097)
	Weighted MTCT risk % (95% CI)	1.44 (0.92–1.97)	2.40 (0.53–4.31)	4.35 (1.39–7.30)
EBF	UWNo. HIV–exposed infants (HEI) (WNo HEI)	1166 (1554)	196 (25414)	97 (12775)
	UWNo HPI (WNo HPI)	25 (3374)	6 (1115)	10 (1555)
	Weighted MTCT risk % (95% CI)	2.17 (1.25–3.09)	4.39 (0.57–8.21)	12.17 (4.7–19.6)
MBF	UWNo. HEI (WNo HEI)	227 (29465)	53 (6171)	93 (11926)
	UWNo HPI (WNo HPI)	3 (329)	3 (326)	6 (726)
	Weighted MTCT risk % (95% CI)	1.12 (0.0–2.46)	5.27 (0–11.04)	6.08 (1.04–11.12)

MTCT – mother-to-child transmission, PMTCT – prevent mother-to-child transmission, EFF – formula feeding (no breastmilk), EBF – exclusive breastfeeding, MBF – breastfeeding with other fluids or solids, UWNo – unweighted number, WNo – weighted number; HEI – HIV–exposed infants, HPI – HIV positive infants, CI – confidence interval

\*As defined in Figure 1.

cART initiation is feasible and critical for further reducing MTCT in high HIV prevalence settings, it substantiates the view that prong 3 can reduce but not eliminate MTCT.

Advanced antiretroviral therapy (any cART or ARVP to mother before the third trimester, with infant prophylaxis) compared to no PMTCT drug interventions, reduced the MTCT associated with exclusive breastfeeding (EBF) from 12.17% to 2.17% (1.25–3.09%), and first trimester cART reduced EBF-associated MTCT to 0.82%.

The overall MTCT risk declined by 22% from the 3.5% (95% CI 2.9–4.2%) achieved under dual prophylaxis/2006 WHO PMTCT guidelines/2008 SA PMTCT guidelines [11]. Similarly any cART-use under PMTCT Option A policy demonstrated tendency toward lower early MTCT (Column B in **Table 2**, 1.6% [1.15–2.05%]) compared with cART-use reported in the 2010 survey [11], under 2008 SA PMTCT guidelines) (2.1% [95% CI 1.2–3.0%]), illustrating the population-level effect of cART initiation at higher CD4 cell counts. The results confirm that PMTCT impact can be sustained at national level, despite increasing breastfeeding uptake. The increased breastfeeding between 2011–12 and 2012–13 could be explained by the August 2011 national policy change (South African Tshwane Declaration of Support for Breastfeeding) to supporting breastfeeding among all women, regardless of HIV status. Formula feeding was only supported in special circumstances and for medical indications. The phasing out of free commercial infant formula for HIV positive women, as part of the PMTCT program began in January 2012 and free formula was fully withdrawn by September 2012.

This was the first national evaluation of PMTCT Option A in a breastfeeding setting. Interestingly, the two population-level surveys yield lower MTCT estimates compared with recent clinical trials conducted in breastfeeding settings [7]. Short-course maternal cART or long-course maternal ARVP with infant extended or short-term prophylaxis reduced early MTCT to 3.3%, 4.5% or 6.5%. The former result is from the Kesho Bora study which offered cART from 28–36 weeks gestation till 6 months postpartum to women with CD4 cell counts between 200 and 500 cells/mm<sup>3</sup> [19]. The latter two results are from the Breastfeeding Antiretroviral and Nutrition (BAN) study which provided daily infant NVP or maternal cART from 1 week till 6 months postpartum, respectively [20].

Also of note is that these population-based findings do not corroborate modeling estimates, which suggest that reducing MTCT to <2% at 6 weeks and <5% at the final endpoint can only be achieved with >90% coverage with ART, greater than 50% reduction in incident HIV infection and 0% unmet need for family planning [21]. In the pooled analysis MTCT under PMTCT Option A was <2% among wom-

en who received cART before or during the first trimester (1.17%, 0.6–1.7%). However our calculations demonstrate that number of HIV infected children remain unacceptably high, being driven by high maternal HIV prevalence.

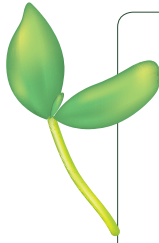
Among “middle-income” countries EMTCT has only been reported from Cuba, a non-priority country for MTCT elimination, where adult and antenatal HIV prevalence is very low (<0.1%) and a comprehensive national PMTCT program began in 1986, transitioning to PMTCT Option B+ in 2011 [22].

The results of our national surveys were limited by low provincial sample realization, which was addressed by weighting the data; exclusion of sick or dead infants, which may have over-estimated PMTCT effectiveness; lack of initial and current CD4 cell count and viral load data which precluded more in-depth analysis of MTCT by viral load or CD4 cell count, use of self-reported data on ARV use, and few events (outcomes) within antiretroviral regimen groups which reduced precision. Notwithstanding these, consistency between the PMTCT survey's self-reported HIV sero-prevalence (29.5%) and anonymous annual antenatal survey's HIV sero-prevalence (29.5%), despite the use of different sampling frames, confirms the robustness of the self-reported data.

## CONCLUSIONS

Three years after changing to PMTCT Option A, a sustained lower risk of early MTCT was measured at population level. Despite the existence of a mature PMTCT program with increasing cART coverage, there were still missed opportunities for PMTCT interventions particularly among undiagnosed HIV positive mothers. MTCT was reduced to less than 2% only among mothers who initiated cART during the first trimester or before. Despite a reduction in percentage MTCT, the number of infant HIV infections per 100 000 live births at six weeks postpartum, was above the global validation target. Eliminating unidentified maternal HIV infections [23,24], reducing maternal HIV prevalence and improving retention in HIV-related care (early cART initiation and adherence) [25] are critical to closing current gaps.

These periodic surveys, conducted nationally among all children attending public health facilities for immunization regardless of their mothers HIV status, have been pivotal in tracking national and subnational PMTCT impact in South Africa. While routine systems are being strengthened to monitor PMTCT impact, national surveys, such as these reported in this paper, conducted every two to three years are key for tracking PMTCT impact. Where routine systems are strong, periodic surveys conducted every four to five years may be important to validate routine data.



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# Predictors of diarrheal mortality and patterns of caregiver health seeking behavior in Karachi, Pakistan

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**Background** Pakistan is unfortunately among the five countries that contributed to the most deaths due to diarrhea and pneumonia in 2010. To explore factors associated with diarrheal deaths we assessed care-seeking behavior and other predictors of diarrhea-related mortality in children in selected low-income peri-urban communities of Karachi, Pakistan.

**Methods** A mixed methods study (qualitative and quantitative) using matched case-control design and focus group discussions with parents of children with moderate to severe diarrhea (MSD) was undertaken. Cases were children <5 years of age who died within 60 days of developing an episode of MSD. Controls were age-matched children who survived after 60 days of an episode of MSD. Demographic, clinical, and care-related behavioral predictors of mortality were assessed. Conditional logistic regression was performed, matched adjusted odds ratios (mOR) are reported.

**Results** Parents of 77 cases and 154 controls were interviewed. Cases were less likely to receive appropriate care compared to controls (mOR=0.2, 95% confidence interval (CI) 0.05–0.91). Refusal for hospital admission (OR=8.9, 95% CI 2.6–30.8), and delays in reaching the health facility (OR=3.6, 95% CI 1.0–12.9) were significant independent predictors of mortality. We found strong beliefs in traditional and spiritual healing in the population; use of both modern and traditional/spiritual treatments concurrently was common.

**Conclusion** Appropriate care seeking behavior predicts survival in children with diarrhea in Pakistan. There is a complex belief system relating to traditional and standard therapies. Health education for appropriate health care seeking should be implemented in order to achieve a substantial decline in diarrheal disease mortality in Pakistan.

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Mortality from diarrheal diseases can be reduced dramatically, and almost eliminated if appropriate preventive and case management services are available [1]. Despite this, almost 0.578 million children under 5 years die from diarrhea annually worldwide, with most deaths occurring in South Asia and sub-Saharan Africa [2,3]. A recent expert consultation identified several barriers and bottlenecks in reducing childhood diar-

rhea-related mortality in low-income countries [4]. These included: the absence of national coordination within ministries and other stakeholders to deliver interventions; insufficient financial resources; inadequate training and support for health workers; poor systems for monitoring and assessment of key programmatic indicators and sporadic availability of key commodities [4]. However, care-seeking behaviors by families, and their belief systems around diarrheal diseases were not identified as possible barriers, although these are well described in the literature [5].

Pakistan is a populous country of 185 million people with the fourth highest burden of child mortality globally, and insufficient progress in improving child survival [6]. Diarrhea and other infectious diseases remain major killers [7]. Low-income coastal areas of Karachi were one of seven participating sites in the, Global Enteric Multi-center Study (GEMS), a case-control study which aimed to determine the etiology, burden and adverse consequences of moderate-to-severe diarrhea (MSD), among children <5 years of age from 3 sites in Asia (Bangladesh, India, Pakistan) and 4 sites in Africa (Gambia, Kenya, Mali, Mozambique) [8,9]. One of the key findings in the GEMS was a combined odds ratio (OR) of death during the 60-day follow-up of 8.5 (95% CI 5.8–12.5) in children with MSD compared to controls without diarrhea. In Karachi the OR was the highest of all the South Asian sites at 13.1 (95% CI 0.99–172.4) [8].

To assess the high mortality at the Karachi site, we examined the potential quantitative and qualitative risk factors associated with diarrheal deaths among children under five years of age at our sites.

## METHODS

### Study population

This study was conducted at the four field sites of Karachi (Ibrahim Hyderi, Rehri Goth, Bhains Colony, and Ali Akbar Shah Goth) that participated in GEMS. The study setting has been described in detail elsewhere [9,10]. Families belong mostly to lower and middle income groups. The population at each field site had a baseline census, and maintained a demographic surveillance system (DSS). We estimated the under 5 population to be 25 094 (15.8% of total population) and the under 5 mortality to be 55 deaths per 1000 live births at the time of the study.

The data collection was done during the period of October 2009 till March 2010. Detailed methods and case definitions used in GEMS have been published elsewhere [10]. In brief, sentinel health centers were selected at each GEMS site where children from each DSS sought care when they had MSD. At the Pakistan site, we selected the Aga Khan University (AKU) Department of Pediatrics and Child

Health-run primary health centers (PHC), staffed with physicians and Lady Health Workers (LHWs), that served each of the four field sites. An age stratified sample of children from the DSS who presented to the PHC with MSD during the study period were enrolled as cases. Cases underwent a standardized assessment of the demographic, epidemiologic, and clinical features at enrollment in the PHC and at a 60-day follow-up visit in the home.

### Study subjects and data collection

Two methods of investigation were conducted: a matched case-control study and a qualitative study using in depth interviews.

1. *Quantitative analysis.* For the quantitative analysis, we conducted a case-control study of children with MSD who died (cases) or survived (controls) within the DSS. Two sources of case data were used. The first source included all 16 children enrolled in GEMS who died before the 60-day follow-up visit. The second source of cases was children not enrolled in GEMS who died from an episode of diarrhea, captured by the ongoing surveillance system via a verbal autopsy conducted 30 days after death, to allow a period of mourning [11]. Two controls for each case were identified. Controls were age-matched GEMS MSD cases who survived at 60 days after the episode of MSD. Data from the standardized questionnaires performed at enrollment and follow-up during GEMS are included in the analysis, and supplemented with additional questions that were asked during interviews conducted from 2 months to 2.5 years after the death of the child. For controls the time of interview was 3 months after the episode of diarrhea. Demographic and socioeconomic variables used in GEMS were analyzed as potential covariates [12]. Appropriate care seeking behavior was defined as care sought from licensed doctors within 24 hours from the recognition of the illness (defined as the first loose stool). Health seeking behavior characteristics questioned were use of public or private transport to reach health facility, decision maker within the family, time taken to reach the health facility, number of health facilities visited and number of visits made for the episode of MSD. Correct decision to hospital admission was a composite variable created for those who either got admitted after advice or were not advised for, compared to those who refused admission after a physician's advice.

2. *Qualitative analysis:* We conducted four focus group discussions, one at each of our study sites with the randomly selected mothers of the cases and the controls. There were total 29 participants in all the four discussions ranging from 6–9 participants in each. The duration of the sessions was from 40 minutes to one hour. Verbatim notes of focus group discussions were transcribed to provide a record of what was said. Transcription of data was done which pro-

vided a descriptive record and findings were aggregated and weighed against the quantitative results.

## Statistical methods

The sample size required used the following parameters: 80% power for detecting an estimated true effect of a magnitude of odds ratio 2.5, based on the probability of appropriate care (Po) of 30% in general population [13–15]. We estimated that 77 cases and two matched controls for each case (154 controls) were needed to fulfill the assumptions.

Conditional logistic regression was done using Statistical Analysis System (SAS) version 9.1 (SAS Institute Inc, Cary, USA). Coding was done of the descriptive data from the qualitative study and nodes and sub-nodes were formed and depending on the frequencies of responses of the participants specific themes and probes of focus group discussions were identified. Analysis was carried out by the principal investigator and the key findings were aggregated and weighed against the quantitative results.

The parent study as well as this study was approved by the Ethical Review Committee of the Aga Khan University.

## RESULTS

The majority (n = 59, 77%) of the deaths occurred in infants aged 0–11 months. The remainder were as follows: 12–23 months (n = 12, 16%) and 24–59 months (n = 7, 9%).

**Table 1** shows the social and demographic characteristics of the cases and controls. Significant differences in illness phenotype of cases and controls was observed, with 20 % of the cases having blood in stools compared to 7 % of the controls ( $P < 0.005$ ). 66% of cases had vomiting against 53% in the controls ( $P < 0.12$ ). The primary caretakers were mothers (n = 215; 93%), and the relationship of the caretaker was not significantly associated with the death of a child with severe diarrhea. Formal education was universally scanty in both groups though more so in the caregivers of the fatal cases (13% vs. 27%,  $P < 0.01$ ). Every ten year increase in caretaker's age (OR = 1.9, 95% CI 1.3–3.1) and no formal education (OR = 2.4, 95% CI 1.1–4.9) of the caretaker were independently associated with child diarrheal mortality.

Nearly all (92%) of the controls received appropriate care compared to 80% of the cases (**Table 2**).

On adjusted analysis (**Table 3**), children with bloody diarrhea, those whose parents refused admission to hospital or where the mother was not the decision maker were significantly more likely to die after the initial illness as were those who took longer to reach a health facility. The use of unboiled water or that from a public source additionally

predicted an adverse outcome. Formal education, parental age and education did not predict outcome.

## Qualitative findings

The caretaker's knowledge and perceptions regarding diarrheal illness, knowledge regarding prevention, treatment methods, and signs of dehydration and danger signs of diarrheal death was similar in both the groups. According to 84% of the caretaker of the cases and 80% of caretaker of the controls, the treatment methods are not known. Caretaker of 84% of the cases and 78% of the control children did not know any kind of prevention methods for diarrheal illness. The majority (93%) of the caretakers of controls followed health provider advice to either admit the child on advice or not to admit if not advised compared to only 61% of caretakers of cases. Seeking spiritual treatment (called "*dum*" in the local language) was found more commonly among caretakers of fatal cases.

The results of the qualitative part of our study also highlight self-treatment at home with medicines, oral rehydration salts (ORS) and food such as yogurt and "*khichri*" (a traditional food which is a mixture of rice and pulses) as the main reason for the delay in seeking health care, as was deferring to family matriarchs. Although all caretakers know about giving fluids and food but they said it is difficult to offer the child usual or more than usual amount of food due to vomiting. They were also of the opinion that "*there is a treatment but it all depends on fate*". There was almost no knowledge of prevention of AGE and little of the signs of dehydration other than that "*the eyes get smaller, the child gets weak and falls down*". The majority agreed that ORS helps in diarrhea but some did not and a couple of caretakers of children with both fatal and non-fatal severe diarrhea were of the point of view that it helps only sometimes. One of the caretakers of a child who had died due to severe diarrhea said that "*we try our best but still we think that we cannot keep cleanliness and take good care to help our children from diarrhea*". All the caretakers agreed that being educated can help them take better care of their children.

Additional findings from the qualitative study showed switching and simultaneous treatment from traditional, spiritual and modern healers by the caretakers of children 0–59 months with severe diarrhea was common, rather than following the advice of one provider. Limited decision making power of mothers, lack of belief in oneself for taking care of the child, inadequate knowledge of prevention of diarrheal illness, lack of awareness about water boiling, self-treating child at home resulting in delay in seeking formal care, and misconceptions regarding ORS as the factors associated more commonly with caretakers of children with severe fatal diarrhea than nonfatal diarrhea.

**Table 1.** Baseline characteristics and the crude matched odds ratio showing associations with child diarrhea mortality

	CASES (n = 77)		CONTROLS (n = 154)		CRUDE mOR	95% CI
	n	%	n	%		
<b>Characteristics of children and their illness:</b>						
Male	40	52	84	55		
Female	37	48	70	45	1.1	0.6–1.9
Birth order – median (IQR)	3 (2–5)		3 (2–5)		1.1	0.9–1.2
Blood in stools	15	20	11	7	3.0	1.3–7.0
Vomiting	51	66	82	53	1.7	0.9–2.9
<b>Caretaker's characteristics:</b>						
Caretaker's age – mean (SD)	30 (6.6)		27 (6.2)		1.9*	1.3*–3.1*
Caretaker's education – some formal schooling	10	13	41	27		
Caretaker's education – no formal schooling or only religious education	67	87	113	73	2.4	1.1–4.9
<b>Relationship of caretaker:</b>						
Mother	70	91	145	94		
Other than mother	7	9	9	6	1.7	0.6–4.9
<b>Socioeconomic and demographic characteristics:</b>						
Type of house material – cemented	70	91	139	90		
Type of house material – other than cement	7	9	15	10	1	0.3–2.7
Household density – median (IQR)	4 (3–6)		4 (3–6)		1.0	0.9–1.2
Number of children <5 years – median (IQR)	1 (1–2)		2 (1–2)		1.0	0.9–1.1
Number of children <5 years under care – median (IQR)	1 (1–2)		2 (1–2)		1.0	0.9–1.1
<b>Per capita annual income (US\$):</b>						
Lowest	19	25	26	17		
2 <sup>nd</sup> quintile	19	25	31	21	0.9	0.4–2.1
Middle	13	17	28	19	0.7	0.3–1.7
4 <sup>th</sup> quintile	14	18	34	23	0.6	0.3–1.5
Highest	11	15	30	20	0.5	0.2–1.4
Median (IQR)	103 (62–150)		125 (82–180)			
<b>Water source/facility:</b>						
Water source – bought from tank water	15	19	44	29	1	
Water source – piped into house	48	62	102	66	2.1	0.8–5.7
Water source – public sources	14	19	8	5	9.0	2.4–34.7
Waste facility – flush toilet	13	17	51	33		
Waste facility – no flush toilet	64	83	103	67	2.7	1.3–5.5
<b>Asset score:</b>						
0–63	9	12	31	20		
64–194	25	32.5	44	29	2.2	0.8 5.7
195–336	18	23	29	19	2.3	0.9 6.2
337–958	25	32.5	50	32	1.8	0.7 4.9
Median (IQR)	195 (64–337)		195 (64–337)			
<b>Home care behavior of caretakers:</b>						
Treatment of water – boiling	13	17	83	54		
Treatment of water – not boiling	64	83	70	46	7.4	3.3–16.6
Drink offered during illness – usual or more than usual	24	31	58	37		
Drink offered during illness – less than usual	44	57	92	60	1.2	0.6–2.3
Drink offered during illness – nothing	9	12	4	3	6.1	1.5–24.5
Offered to eat during illness – usual or more than usual	14	18	34	22		
Offered to eat during illness – less than usual	50	65	110	71	1.1	0.5–2.3
Offered to eat during illness – nothing	13	17	10	7	3.7	1.2–11.5

mOR – matched adjusted odds ratios, CI – confidence interval, SD – standard deviation, IQR – interquartile range

\*For every 10-year change in age.

## DISCUSSION

The mortality from diarrheal disease in children in Pakistan remains unacceptable. All the predictors of outcome are amenable to modification. The use of unboiled water, using public water sources, travel time and blood in the stools

all have potential for intervention. These findings highlight the fact that a small number of infrastructure and education interventions in the community have the potential to reduce child mortality to a great extent. Similar predictors of mortality have been reported earlier for other perinatal, neonatal and childhood illnesses [16,17].



**Table 2.** Healthcare seeking behavior of caretakers of children less than five years of age who died of severe diarrhea compared to those with non-fatal severe diarrhea and the crude odds ratio of the associations with diarrhea mortality

HEALTHCARE SEEKING BEHAVIOR CHARACTERISTICS	CASES (n = 77)		CONTROLS (n = 154)		CRUDE mOR	95% CI
	No.	%	No.	%		
<b>Appropriate care</b>	62	80	141	92	0.3	0.1–0.8
<b>Decision maker other than mother</b>	10	13	7	5	3.6	1.2–10.7
<b>Hospital admission:</b>						
Correct decision	47	61	143	93		
Refused to admission	30	39	11	7	12.9	4.5–36.9
Use of public or private transport to reach health facility	22	29	40	27	1.2	0.6–2.1
<b>Time taken to reach health facility:</b>						
Less than 60 min	63	84	143	95		
60 min or more	12	16	8	5	3.2	1.3–8.3
Median (IQR)	30	15–30	25	15–30		
<b>Number of health facilities used:</b>						
1–2	67	90	145	96		
3–4	8	10	6	4	3.3	0.9–11.4
Median (IQR)	1	1–2	1	1–2		
<b>Number of visits:</b>						
1	15	20	10	7		
2 or more	60	80	141	93	0.3	0.1–0.7
Median (IQR)	3	2–4	3	2–4		

mOR – matched adjusted odds ratio, CI – confidence interval, IQR – interquartile range

**Table 3.** Multivariable analysis of the healthcare seeking behavior for children less than five year of age who died of severe diarrhea compared to those with non-fatal severe diarrhea

	mOR	95% CI	P-VALUE
<b>Appropriate care</b>	0.2	0.05–0.91	0.03
<b>Time taken to reach the health facility:</b>			
Less than one hour	1		0.04
One hour or more	3.6	1.0–12.9	
Refusal to admission in hospital	8.9	2.6–30.8	0.0005
Blood in stools	6.9	1.7–28.6	0.003
Age of the caretaker (10 year change)	1.6	0.8–3.4	0.21
<b>Education of the caretaker:</b>			
Some formal schooling	1		0.12
No formal schooling	2.9	0.7–11.0	
<b>Source of drinking water:</b>			
Bought	1		
Piped into the house	3.0	0.7–13.4	0.14
Public place sources	11.9	1.6–88.2	0.01
No boiling of drinking water	12.6	3.5–45.0	<0001

mOR – matched adjusted odds ratio, CI – confidence interval

Community education and sensitization especially a focus on women's education will help in leveraging child health through not only better care and prevention but also through better understanding of the importance of seeking appropriate and early care for childhood illnesses. There are multiple pathways through which education of the primary care taker (who was the mother in most instances in this study), can influence child health like improved parenting, better income of the family ie, improved resources and enhanced decision making ability [17]. The other significant factor, blood in stools as a risk factor for diarrheal mortality

has long been known and WHO currently recommends antibiotics for the treatment of dysentery to reduce child mortality and morbidity. Mathematical modeling data shows that >99% of the deaths due to dysentery can be averted by use of appropriate antibiotics [18]. We however have no data to comment on whether the children with dysentery who died, received antibiotic treatment or not. Other significant factors, including delayed time to reach the health facility, blood in stools, age and education of the primary caretaker, are less amenable to public health interventions.

The role of seeking care from a qualified doctor in preventing child mortality due to diarrhea illness has was also reported to be a major factor associated with infant mortality in the poorest parts of Brazil [19] in which self-treatment at home was the main reason of delay in seeking care for children. Self-treatment at home proved the main cause of delay in seeking care for children and this is compatible with results in other settings across the spectrum of common childhood illnesses [20,21]. We defined care seeking from a licensed physician as "appropriate care", but for countries like Pakistan, with an extensive network of LHWs that are educated and entrusted to take care of relatively common illnesses such as childhood diarrhea, this criteria can be used as reference for future studies.

We found that a lack of education and women's autonomy were major risk factors which is compatible with other studies [22–26]. If women feel insecure about their social position, they lack confidence in seeking care for their child. Moreover lack of education keeps them back from having the confidence to seek care of their children.

A strength of our study lies in its mixed method design. The qualitative research methods helped interpret the complexity of the issues [27] of health seeking behaviors which are affected by multiple factors such as social norms, culture, community dynamics, household economics, health services related factors, individuals' experiences, context of the health facility (both geographic and social) and the inter-relation of these factors [28]. This approach allowed a rapport with mothers and families to develop, a critical element of in-depth interviewing and household visits in this particular social setting. This approach has previously been shown to enable the collection of sensitive data [29–31]. Finally, it sensitizes the community members on issues raised in the discussions (health problems, care seeking patterns and inappropriate practices) and facilitates entry of the study team into the community for quantitative surveys [32].

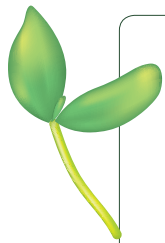
One potential limitation of the study is that of recall bias given that there was a delay in interviewing some parents after the child's deaths. Recall of events for the caregivers of children with fatal severe diarrhea could be different

from their comparison group in reporting child illness characteristics such as vomiting and blood in stools, health care seeking characteristics such as time to reach the health facility may have overstated facts which may bias the effect size away from the null.

However, bias is only likely to be an issue if the parents of index cases felt that hospital care would have averted the outcome which the interviews suggests was not the case. We are, therefore, confident that the direction of effect is valid.

## CONCLUSION

Appropriate care seeking behavior predicts survival in children with diarrhea in Pakistan. There is a complex belief system relating to traditional and standard therapies. Women's autonomy and education together with availability of basic health care facilities and health education for importance of appropriate health care seeking can help to achieve a substantial decline in diarrheal disease mortality in Pakistan.



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**Conflict of interest:** All authors have completed the Unified Competing Interest form at [www.icmje.org/doi\\_disclosure.pdf](http://www.icmje.org/doi_disclosure.pdf) (available on request from the corresponding author) and declare no conflict of interest.

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# Caregiver perceptions and utilization of oral rehydration solution and other treatments for diarrhea among young children in Burkina Faso

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**Background** More than 500 000 young children die from dehydration caused by severe diarrhea each year, globally. Although routine use of oral rehydration solution (ORS) could prevent almost all of these deaths, ORS utilization remains low in many low-income countries. Previous research has suggested that misperceptions among caregivers may be an obstacle to wider use of ORS.

**Methods** To better understand the extent of ORS utilization and the reasons for use or non-use in low-resource settings, the project team conducted a semi-structured, quantitative survey of 400 caregivers in Burkina Faso in 2014. All caregivers had a child below the age of five who had diarrhea lasting 2 days or more in the previous 2 months.

**Results** Although more than 80% of caregivers were aware of ORS, less than half reported using it to treat their child's diarrhea. Replacing fluids lost due to diarrhea was considered a low priority by most caregivers, and many said they considered antibiotics more effective for treating diarrhea. Users and non-users of ORS held substantially different perceptions of the product, though all caregivers tended to follow recommendations of health care workers. A significant proportion of users reported difficulty in getting a child to drink ORS. Costs and access to ORS were not found to be significant barriers to use.

**Conclusions** Misperceptions among caregivers and health workers contribute to low utilization of ORS. Better caregiver understanding of diarrheal disease and the importance of rehydration, as well as increased recommendation by health workers, will help to increase ORS utilization. Improving product presentation and taste will also help to increase use.

Among children under five years of age, diarrhea remains a significant cause of morbidity and mortality. It is estimated that more than 500 000 children in this age group die each year from dehydration caused by diarrhea, globally. In Burkina Faso alone, more than 6000 deaths of children under five years of age were due to diarrhea in 2013. [1] This is despite the availability of an inexpensive and highly efficacious treatment: oral rehydration solution (ORS). ORS was developed in the 1970s, and its use is credited with saving millions of lives. It is estimated that more

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than 90% of all diarrhea deaths could potentially be avoided with universal coverage of ORS [2]. Despite the benefits of ORS, and the widespread knowledge of ORS by mothers and caregivers, coverage has remained low in many developing countries and regions. In Burkina Faso in 2010, more than 75% of caregivers reported having heard of ORS, but only fewer than 25% reported using ORS [3].

The reasons behind this “know–do” gap have been the source of widespread speculation. One thought about why caregivers do not use ORS is that it fails to meet expectations for treating the symptoms and does not stop the diarrhea [4]. Other reasons for nonuse include the bad taste and the fact that it lacks the appearance of a “real” medicine [5]. Low coverage of ORS has also been attributed to the availability of alternative products such as herbal remedies and antibiotics.

Understanding the full extent of ORS utilization and the reasons for use or nonuse is important for governments, nongovernmental organizations (NGOs), and public health programs that are developing interventions to increase coverage. It is also important to understand the extent of use of alternative interventions, such as antibiotics, and the reasons for use.

From 2010 to 2014, PATH and colleagues at Ipsos Healthcare conducted extensive quantitative and qualitative surveys of caregivers and formal and informal health care providers in Burkina Faso, India, Kenya, Nigeria, and Zambia to probe the reasons for use or nonuse of ORS and other interventions to manage diarrhea [6]. This paper presents the findings from a quantitative survey of caregivers in Burkina Faso that examined the use of various interventions, the rationale for treatment decisions, treatment costs, and expectations associated with their experience in treating diarrhea in the past two months in a child under five.

## METHODS

The project team conducted a quantitative survey of 400 caregivers in Burkina Faso in June and July 2014. A complementary quantitative survey of 250 pharmacy staff and health care workers (“providers”) was simultaneously conducted but is not covered in this report. Development of the survey instruments was informed by a formative qualitative research process, which involved 60–minute, face-to-face, in-depth interviews with caregivers (predominantly mothers) who were aware of ORS.

### Selection and description of participants

All surveyed caregivers had a child between six months and five years of age who had an episode of diarrhea that occurred less than two months prior to the interview and that

lasted for more than two days. **Table 1** presents a demographic profile of caregivers. We used quota sampling methods to identify appropriate numbers of urban and rural respondents

The survey covered five regions – Centre (including Ouagadougou, the capital), Boucle du Mouhoun, Hauts–Bas-sins, Nord, and Est – representing the country’s major socio-cultural groups (Table S1 in **Online Supplementary Document** for demographics of each region). We also used quotas for regions, with the sample distributed according

**Table 1.** Demographics of surveyed caregivers (base: all caregivers, n=400)\*

VARIABLE	PERCENTAGE (%)
<b>Age of caregiver:</b>	
18–20	7
21–24	21
25–34	51
35–44	20
45–54	2
<b>Number of children aged between 6 months and 5 years per caregiver:</b>	
1	73
2	25
3+	2
<b>Age of child:</b>	
At least 6 months old but under 1 year	24
At least 1 year old but under 2 years	37
At least 2 years old but under 3 years	26
At least 3 years old but under 5 years	31
<b>Socioeconomic class:†</b>	
C1	1
C2	10
D/E	88
<b>Setting:</b>	
Rural	62
Urban	38
<b>Religion:</b>	
Christian	30
Muslim	66
Other	4
<b>Primary language:</b>	
French	22
Moore	36
Dioula	28
Other	14
<b>Location:</b>	
Centre	23
Boucle du Mouhoun	21
Hauts-Bassins	22
Nord	18
Est	17

\*Selection criteria: caregivers with a child under 5 who had diarrhea in the last 2 months lasting 2 days or more.

† Socioeconomic levels: A is highest and E lowest. Socioeconomic classification was based on the standard systems used for commercial market research in the respective countries; in Burkina Faso, as described in the Oracle General Consumer Survey – Brand Values Segmentation (GCS-S) data collection tool.

to the relative population of each region. Within regions, sampling points were purposively selected, and interviewers used systematic random sampling to identify respondents during recruitment (Table S2 in **Online Supplementary Document**). Unlike the qualitative research, the quantitative research did not set criteria related to ORS awareness or experience so we could establish a representative measure of population awareness and usage of ORS and other diarrhea treatments. More information about the selection of participants can be found in Appendix S2 in **Online Supplementary Document**.

### Survey focus and design

The survey focused on the child's most recent episode of diarrhea. In the 60-minute interview, topics probed included diarrhea duration, treatments used, sequence/time-frame of administration, and caregivers' expectations for each treatment (eg, "what did you think [the treatment] would do for your child?"). Caregivers were also asked about the treatment source, spending on treatment, care-seeking behaviors, and dosing of ORS and homemade sugar-salt solution (HSSS). The survey did not probe related costs such as transport or lost work time. Peak dosing estimates were calculated using conservative assumptions to err on the side of overestimating the amounts given. The survey questionnaire is available upon request from the corresponding author.

Other topics covered included awareness and previous use of treatments (ORS sachets, HSSS, other home remedies, herbal remedies, antibiotics, anti-motility drugs, and zinc syrups/tablets). After recording spontaneous recall of treatments used, interviewers used localized illustration cards to prompt or to assist in recall of treatment types. They also assessed perceptions of ORS by using positive-negative statement pairs and evaluated willingness to pay for a diarrhea treatment. Attribute association was carried out based on the four main treatments used (established previously in qualitative research): ORS, antibiotics, anti-motility drugs, and HSSS. This involved caregivers selecting which treatments they felt fulfilled each attribute (such as "easy for children to take," "stops the diarrhea," and "not expensive"). Interviewers also asked caregivers to rank the four treatments on effectiveness and value (HSSS was not included for the perception of value).

The survey was pretested with a small number of caregivers (n = 20) in Ouagadougou. This ensured that survey questions were appropriate and refined before widespread data collection.

### Analysis

Quantitative data were analyzed for all respondents as a whole as well as for key groups, such as ORS users vs ORS

non-users (based on usage at last episode of diarrhea) and urban vs rural respondents. We also evaluated data according to demographic and regional splits.

Data from open-ended questions were analyzed through a similar procedure. The process began with review of verbatim responses for each question. Key common themes were identified for each question, as well as factors associated with each theme. This represented a code frame. Each verbatim response was then analyzed and assigned to its appropriate code.

## RESULTS

### Duration of illness, treatments used and ORS dosing

Caregivers reported that the average diarrhea episode lasted 4 days (SD  $\pm$  1.96 days), with 15% of cases lasting 6 to 10 days. The vast majority of caregivers (84%) took some form of action when they realized their child had diarrhea. Notably, a greater number of caregivers in the Est region decided to "wait and see" before acting (42% vs 16% overall). Among caregivers who reported taking action after realizing their child had diarrhea (n = 385), 46% said they gave their child a special kind of food that would make him or her feel better or adjusted the child's diet in some way. Among these caregivers, 33% reported that they stopped or avoided certain food types, and 27% said they increased liquid given to the child.

When asked about treatments, 328 caregivers (82%) said they were aware of ORS as a treatment option, and 385 (96%) administered some form of treatment. Among those who administered treatment during the last episode, less than half reported using ORS, even when illustration cards were used to prompt responses (**Table 2**). However, this is twice the coverage reported in a meta-analysis by Wilson et al. in 2012 [7]. Antibiotics were the second most popular primary treatment, followed by zinc syrup or tablets. Among caregivers who used more than one treatment (n = 166; 43% of those using treatment), there were many secondary treatments: 33% used zinc remedies (19% syrup; 14% tablets), 20% used antibiotics, 15% used anti-motilities, 14% used herbal remedies, and 10% used ORS (**Table 3**).

Among ORS non-users, more than half used antibiotics, with especially high rates of use in the Nord and Centre regions (**Table 2**). Overall, most caregivers (57%) used only one treatment (ie, monotherapy), and only 10% used three or more treatments. Among caregivers who used only one treatment, 33% exclusively used ORS, and 30% exclusively used antibiotics. Among caregivers who did something to treat their child's diarrhea (n = 385), 8% exclusive-

**Table 2.** Usage at last episode\*

	SPONTANEOUS RESPONSE: WITHOUT ILLUSTRATION CARDS										PROMPTED USAGE: WITH ILLUSTRATION CARDS									
	ALL RESPONDENTS USING A TREATMENT AT LAST EPISODE (n = 385)					ALL RESPONDENTS USING A TREATMENT AT LAST EPISODE (n = 385)					ALL RESPONDENTS USING A TREATMENT AT LAST EPISODE (n = 385)					ALL RESPONDENTS USING A TREATMENT AT LAST EPISODE (n = 385)				
	Total (n = 385)	Centre (n = 87)	Boucle du Mouthoun (n = 81)	Hauts-Bassins (n = 80)	Nord (n = 70)	Est (n = 67)	Total (n = 385)	Centre (n = 66)	Boucle du Mouthoun (n = 34)	Hauts-Bassins (n = 35)	Nord (n = 38)	Est (n = 35)	Total (n = 385)	Centre (n = 66)	Boucle du Mouthoun (n = 34)	Hauts-Bassins (n = 35)	Nord (n = 38)	Est (n = 35)		
%	A	B	C	D	E	%	A	B	C	D	E	%	A	B	C	D	E			
<b>All treatments administered</b>																				
ORS	44	22 (B, C, D, E)	56	55	41	46	24 (B, C, D, E)	57	56	46	49	46	46	46	56	46	46	49		
Antibiotics	34	53 (B, C, E)	16	20	50	34	55 (B, C)	16	20	57 (B, C, E)	40 (B, C)	37	55 (B, C)	16	44 (A, B, D)	6	31 (A, B, D)	10		
Zinc syrup	19	5	15 (A, D)	45 (A, B, D, E)	4	25 (A, D)	6	16 (A)	28 (A, D, E)	16	11	20	6	28 (A, D, E)	16	11	14 (A, B)	15 (A, B)		
Herbal remedies	15	13	27	15	9	7	13	7	13	11	4	11	13	7	13	11	14 (A, B)	15 (A, B)		
Zinc tablets	8	1	4 (A, B)	18 (A)	9 (A)	12	1	4	22 (A, B)	10 (D)	1	11	1	4	22 (A, B)	10 (D)	14 (A, B)	15 (A, B)		
Anti-motilities	7	18 (B, C, D, E)	6 (D)	4	0	4	24 (B, C, D, E)	9 (D)	10 (D)	1	4	10	24 (B, C, D, E)	9 (D)	10 (D)	14 (A, B)	15 (A, B)			
Homemade sugar and salt solution (HSSS)	4	3	5	1	0	10 (C, D)	5	7 (D)	2	0	13 (A, C, D)	5	3	7 (D)	2	0	13 (A, C, D)	4		
Other home remedies (other than HSSS)	2	1	5	0	0	1	3	9 (D)	2	0	3	4	3	9 (D)	2	0	3	3		
Antibiotic injections	0	0	0	0	0	0	0	0	0	1	1	1	0	0	1	1	1	1		
Prompted usage: with illustration cards																				
	ORS USERS (n = 177)										ORS NON-USERS (n = 208)									
	Total (n = 177)	Centre (n = 87)	Boucle du Mouthoun (n = 81)	Hauts-Bassins (n = 80)	Nord (n = 70)	Est (n = 67)	Total (n = 208)	Centre (n = 66)	Boucle du Mouthoun (n = 34)	Hauts-Bassins (n = 35)	Nord (n = 38)	Est (n = 35)	Total (n = 208)	Centre (n = 66)	Boucle du Mouthoun (n = 34)	Hauts-Bassins (n = 35)	Nord (n = 38)	Est (n = 35)		
	%	A	B	B	D	E	%	A	B	C	D	E	%	A	B	C	D	E		
<b>All treatments administered</b>																				
ORS	100	100	100	100	100	100	0	0	0	0	0	0	0	0	0	0	0	0		
Antibiotics	18	19	15	4	31 (C)	27 (C)	54	67 (B, C)	18	40 (B)	79 (B, C, E)	51 (B)	54	67 (B, C)	18	40 (B)	79 (B, C, E)	51 (B)		
Zinc syrup	20	0	20 (D)	36 (D)	0	30 (D)	21	8	12	54 (A, B, D)	11	31 (A, D)	21	8	12	54 (A, B, D)	11	31 (A, D)		
Herbal remedies	10	5	13	7	16	6	21	15	47 (A, D, E)	29 (D)	8	14	21	15	47 (A, D, E)	29 (D)	8	14		
Zinc tablets	14	0	2	31 (A, B)	19 (A, B)	15 (A, B)	8	2	6	11	11	17	8	2	6	11	11	17		
Anti-motilities	3	14	4	0	3	0	16	27 (D, E)	14 (D)	23 (D)	0	9	16	27 (D, E)	14 (D)	23 (D)	0	9		
Homemade sugar and salt solution (HSSS)	8	10 (D)	13	4	0	15 (D)	2	2	0	0	0	3	2	2	0	0	0	11 (A, B, C, D)		
Other home remedies (other than HSSS)	5	10	9	4	0	3	2	2	9	0	0	3	2	2	9	0	0	3		
Antibiotic injections	2	0	0	2	3	3	0	0	0	0	0	0	0	0	0	0	0	0		

ORS – oral rehydration solutions

\*Letters (A, B, C, D, E) represent the respective regions noted in column headers. The presence of a letter in a cell indicates significant differences between the indicated regions. Significance is at the 95% confidence interval.

**Table 3.** Treatment sequencing (n = 385)\*

	USED FIRST (n = 385), %	USED SECOND (n = 166), %	USED THIRD† (n = 39), %
ORS	41	10	8
Antibiotics	28	20	8
Anti-motilities	4	15	0
Zinc syrup	8	19	33
Herbal remedies	9	14	8
Zinc tablets	3	14	13
Other home remedies	1	1	18
Antibiotic injections	0	1	5
Other	7	7	6

ORS – oral rehydration solution

\*Base: All respondents using treatment at last episode.

†Base too low for “used fourth” and for subgroup analysis.

ly used a combination of ORS and zinc remedies and 5% used a combination of ORS, zinc, and other treatments.

Of the 177 children treated with ORS, 101 (57%) were less than 2 years old (Table 4). On average, caregivers who used ORS started doing so 1.8 days after the onset of diarrhea, administering it for an average of 2.8 days and using an average of 2.5 sachets during the episode. The average volume of ORS given per day to children less than 2 years old was approximately 600 ml, and children aged 2 to 5 years received an average of 740 ml.

**Table 4.** Dosing at last episode of diarrhea\*

	TOTAL (n = 177)	CHILDREN UNDER 2 YEARS (n = 101)	CHILDREN 2-5 YEARS (n = 76)	URBAN (n = 50) A	RURAL (n = 127) B
Day started giving (mean)	1.8 (0.96)	1.8 (1.07)	1.8 (0.79)	1.8 (1.16)	1.7 (0.87)
For how many days (mean)	2.8 (1.39)	2.9 (1.24)	2.6 (1.56)	3.2 (1.81)	2.6 (1.13)
Number of sachets used during the episode (mean)	2.5 (1.06)	2.6 (1.01)	2.4 (1.12)	2.7 (1.16)	2.4 (1.01)
Amount given in one day (when the diarrhea episode was particularly bad; % children):					
250 ml	37	42	32	26, B	42
500 ml	12	13	11	14	11
750 ml	9	9	9	16, B	6
1000 ml	33	33	34	34	33
1250 ml	5	4	7	4	6
1500 ml	3	–	8	6	2

\*Letters (A,B) represent the urban/rural regions as noted in column headers. The presence of a letter in a cell indicates significant differences between the indicated region. Significance is at the 95% confidence interval. Base: All respondents using ORS at last episode (n = 177). Standard deviation for means shown in brackets.

**Table 5.** Caregiver ranking of key treatment goals (n = 400)\*

	MOST IMPORTANT (%)	SECOND MOST IMPORTANT (%)	THIRD MOST IMPORTANT (%)	LEAST IMPORTANT (%)
Prevent child's condition from getting worse	81	13	2	4
Restore child's energy and appetite	5	66	19	9
Reduce diarrhea motions	6	17	67	10
Replace fluid lost due to diarrhea	8	4	12	77

\*Base: All caregivers (n = 400).

## Treatment goals and reasons for using treatments

Caregivers were asked to rank four key diarrhea treatment goals. They ranked “prevent child's condition from getting worse” as the most important treatment goal, followed by “restore child's energy and appetite.” “Reduce diarrhea motions” was the third most important, and “replace fluid lost due to diarrhea” was the lowest priority (Table 5).

When caregivers who used ORS were asked why they decided to use this treatment, half said they were “instructed to do so by a nurse” (Table 6). Similarly, about half of those who used antibiotics reported that they had been given a prescription or a health care provider recommended it. Almost all those who used zinc products reported doing so because of a recommendation by a health care professional or community health worker.

## Caregiver perceptions of ORS

Overall, caregivers who were aware of ORS had positive perceptions of the product (Table 7). About two-thirds perceived ORS to be easy to prepare, and more than half said that clean water was easy to obtain and that instructions to prepare ORS were clear. About a third, however, reported that it was difficult to get the child to drink ORS, and many expressed uncertainty about whether use of ORS



**Table 6.** Reasons for using main treatments at last episode (% respondents)\*

REASON	%
<b>Base: All caregivers using ORS at last episode (n = 177)</b>	
Instructed to do so by nurse	50
Well known by caregivers and nurses	18
Recommended by someone	9
Rehydrate the child	7
Child to regain strength/energy	6
<b>Base: All caregivers using antibiotics at last episode (n = 144)</b>	
Medical prescription/ hospital or clinic recommendation	52
Treats diarrhea effectively	13
Treats diarrhea quickly	10
It kills the germ quickly at the start of diarrhea	8
<b>Base: All caregivers using zinc products (tablet and syrup) at last episode (n = 104)</b>	
Recommended by health care professionals/itinerant health agents	88
It is cheaper	12

requires a young child to drink too much liquid or whether the frequency of giving ORS is acceptable.

Most caregivers said they believed that ORS reduces the frequency of bowel movements, stops diarrhea, increases the child's energy and appetite, and replaces lost fluid/water and minerals (Table 7). Nearly two-thirds of caregivers indicated that ORS is not an expensive treatment.

Caregiver perceptions of ORS varied substantially across regions (Table S3 in **Online Supplementary Document**). For example, those in the Nord region especially perceived ORS as too much liquid for a young child to drink (56% agree).

Caregivers who did not use ORS at the last episode were prompted with a list of reasons for not using ORS and were asked to state whether the reason applied to them. The

main reasons why ORS was not used pertained to administration and palatability: 24% said it was too difficult to get their child to take ORS, 24% said their child did not like the taste of ORS; and 20% reported having ORS left over that was then wasted (Table 8). Fewer than 10% of caregivers said that ORS was too difficult to obtain or too expensive.

Asked to associate treatment types with a series of product attributes read aloud, ORS users associated ORS with positive attributes describing efficacy, availability, convenience, and trust (Table 9). Noticeably, ORS users, compared with non-users, more strongly associated ORS with being recommended by health care professionals, easily available, easy to prepare, good for restoring the child's energy and appetite, safe for children under 5 years old, and able to "significantly" reduce diarrhea motions. Additionally, ORS users were less likely to associate antibiotics with the same attributes, whereas non-users tended to associate both ORS and antibiotics with similar attributes.

Among all caregivers, ORS was ranked most effective at treating diarrhea (40% vs 24% for antibiotics) and the best value for money (53% vs 16% for antibiotics) (Table S4 in **Online Supplementary Document**). However, ORS non-users felt that antibiotics were more effective than ORS for treating diarrhea. Interestingly, ORS non-users said ORS and antibiotics had similar value for money. Also, there were substantial differences in rankings across regions.

When prompted to select a single preferred treatment (regardless of cost), caregivers generally preferred ORS. However, some regions showed a preference for antibiotics (Table S5 in **Online Supplementary Document**). In addition, herbal remedies were especially popular in the Boucle du

**Table 7.** Caregiver perceptions (% response) of ORS, on positive-negative paired statements\*

ORS-POSITIVE STATEMENT	AGREE (%)	ORS-NEGATIVE STATEMENT	AGREE (%)	DON'T KNOW (%)
Easy to prepare	66	Difficult to prepare	24	10
Reduces the child's stooling	61	Does not reduce the child's stooling	21	18
Not an expensive treatment	62	Expensive treatment	17	21
Increases child's energy and appetite	57	Does not increase child's energy & appetite	10	33
Is a medicine	70	Is not a medicine	14	16
Easy to obtain clean water to make it	58	Difficult to obtain clean water to make it	27	16
Stops the diarrhea	58	Does not stop the diarrhea	28	20
Easy to get the child to drink it	48	Difficult to get the child to drink it	32	20
Instructions on how to prepare it are clear	52	Instructions on how to prepare not clear	13	34
Not too much liquid for a young child to take	27	Too much liquid for a young child to take	30	43
Frequency of giving to the child is acceptable	27	Need to give to the child too often	27	46
Rarely have left over wasted liquid	20	Often have leftover waster liquid	50	30
Helps replace lost fluid/water & minerals	53	Does not help replace lost fluid/water & minerals	12	36
Stops vomiting	26	Does not stop vomiting	19	55
Necessary to treat diarrhea	12	Not necessary to treat diarrhea	63	24

ORS – oral rehydration solution

\*Positive – chose ORS-positive statement; Negative – chose ORS-negative statement. Base: All caregivers who are aware of ORS (n = 328).

**Table 8.** Caregiver reasons for not using ORS\*

CAREGIVER REASONS FOR NOT USING ORS	%
It is too difficult to get my child to take ORS	24
My child does not like the taste of ORS	24
It was not recommended to me when I asked for advice	21
I often have ORS left over, which is wasted	20
You need to give ORS to the child too often	13
ORS is not effective at stopping diarrhea	11
It takes too long/is too far to travel to obtain ORS	10
It takes a lot of time and effort to make up ORS	7
Diarrhea is not a serious enough illness to justify using ORS	5
ORS is too expensive; other treatment options are cheaper	5

ORS – oral rehydration solution

\*Base: All caregivers not using ORS at last episode (n=208).

Mouhoun region, and zinc syrup was preferred by many in Hauts–Bassins.

### Treatment sourcing

Community health workers were the primary source of treatment recommendations for users of ORS or antibiotics (Table S6 in **Online Supplementary Document**). Recommendations by doctors, nurses, or pharmacists were fairly infrequent. Most caregivers acquired ORS or antibiotics from pharmacists or public clinics/hospitals.

Additionally, 70% of caregivers said they had previously received information about ORS, and more than half of

those in the Nord region (53%) and Est region (62%) recalled hearing about ORS within the past 3 months. Among the 282 caregivers who recalled hearing about ORS, information was most commonly heard at a health center (38%), at a hospital (22%), from neighbors or relations (20%), or from television/radio advertisements (18%).

### Access to health services

Among all caregivers, the average travel time to a pharmacy, a community health center, and a general public hospital was reported to be 23.2 minutes, 29.3 minutes, and 35.9 minutes, respectively (Table S7 in **Online Supplementary Document**). The average travel time to a hospital varied across regions, from 25.5 minutes in Hauts–Bassins to 47.6 minutes in Nord.

Nearly half of all caregivers reported sometimes visiting a traditional healer when their child was ill (with any disease, not just with diarrhea) (Table S8 in **Online Supplementary Document**). The greatest use of traditional healers occurred in the Est (81%) and Boucle du Mouhoun regions (59%).

### Financial considerations and preferred product formats

Nearly all caregivers who reported using ORS or antibiotics paid for the product (97% and 96%, respectively), with a median product cost of US\$ 1.00 (CFA 1 = US\$ 0.0020181

**Table 9.** Comparative product associations\*

	ORS SACHET		ANTIBIOTICS		ANTI-MOTILITY DRUGS		HSSS	
	Users (%)	Non-users (%)	Users (%)	Non-users (%)	Users (%)	Non-users (%)	Users (%)	Non-users (%)
	A1	A2	B1	B2	C1	C2	D1	D2
<b>Efficacy:</b>								
Helps replace fluid	56, A2	30	11, B2	29	4	5	11, D2	4
Safe for giving to under 5 year–old	62, A2	26	16, B2	33	5	8	11	6
Restores the child's energy and appetite	66, A2	30	11, B2	31	3	6	7	6
Significantly reduced diarrhea motions	60, A2	21	19, B2	38	6	9	9	5
Stops the diarrhea	64, A2	29	21, B2	43	5, C2	11	10	6
Stops vomiting	35, A2	13	10, B2	22	2	4	7	4
<b>Availability:</b>								
Not expensive	72, A2	37	13, B2	40	3	6	13, D2	6
Easily available	73, A2	38	18, B2	43	4	8	11	8
<b>Convenience:</b>								
Easy to prepare	70, A2	33	18, B2	33	4, C2	10	10	7
Easy to take	55, A2	26	15, B2	31	3, C2	9	8	5
Nice tasting	44, A2	16	11, B2	24	2	6	9	6
Easy to use when traveling with a child	54, A2	27	17, B2	35	3, C2	11	4	3
<b>Trust:</b>								
Recommended by health care professionals	80, A2	44	23, B2	55	7	11	16	10

ORS – oral rehydration solutions, HSSS – homemade sugar and salt solution

\*Letters (A1, A2, B1, B2, C1, C2, D1, D2) represent the respective user groups noted in column headers. The presence of a letter in a cell indicates significant differences between the indicated user groups. Significance is at the 95% confidence interval. Base: Users of ORS (n=177); non-users of ORS (n=208).

as of September 2014) for antibiotics and US\$ 0.20 for a single ORS sachet (Table 10). In addition, nearly half (46%) of ORS users also purchased water to make the ORS.

On average, caregivers spent a total of US\$ 0.80 for both the ORS and the water. Rural caregivers tended to spend less (median = US\$ 0.40 for ORS sachets and US\$ 0.60 for water) than urban caregivers (median = US\$ 0.60 for ORS sachets and US\$ 1.00 for water). In addition to treatment costs, 51% of caregivers paid for other health-related expenses, such as consultation fees (92%; median = US\$ 0.30) or a medical card fee (12%; median = US\$ 0.30).

## CONCLUSIONS

Previous work has indicated that misperceptions among caregivers may be an obstacle to the adoption of ORS as the preferred treatment for diarrheal disease in children under five years of age in low-resource settings. We assessed caregiver knowledge and behaviors related to the treatment of affected children in Burkina Faso to inform strategic approaches for reducing morbidity and mortality. Specifically, we explored perceptions about ORS efficacy, alternative treatments, and obstacles to successful administration. Our conclusions do not address financing, policy, or manufacturing of ORS. These issues are well-discussed in previous research [7,8].

### Perception: ORS treats symptoms of diarrhea

Prior research has found that a primary contributor to non-use of ORS in some countries is the perception that ORS is ineffective for treating the symptoms of diarrhea. This perception, often held by providers as well as caregivers, influences both whether ORS is prescribed/recommended and whether it is requested by caregivers [9]. A number of studies have shown that a sense of unmet expectations underlies this perception. Caregivers expecting ORS to reduce or stop the diarrhea may be disappointed by the product [10].

Our findings, however, suggest that the perception that ORS is ineffective may not be the largest barrier to uptake. Among ORS non-users in this study, only 11% mentioned lack of efficacy in stopping diarrhea as a reason for not using ORS. Our data suggest that most caregivers, in fact, believe that ORS stops diarrhea, and only a small proportion of caregivers (12%) ranked rehydration as the most important or second most important treatment goal. This suggests a fundamental lack of understanding of the critical contribution of dehydration to diarrheal-related deaths and the role of ORS in rehydration. Among ORS users, only 7% chose ORS because of its role in treating dehydration, whereas 68% reported using it because it was recommended by a nurse or was well known by caregivers and nurses. However, 56% of ORS users perceived that ORS helps to replace fluid compared to only 30% of non-users. These findings suggest that ORS usage is mostly due to recommendations by providers and not to an understanding of the core function of ORS. However, it does appear that more ORS users than non-users associate ORS with treating dehydration, suggesting that personal experience improves perception and understanding.

To set appropriate expectations among caregivers, communication messaging should focus on the seriousness of dehydration due to diarrhea and the ability of ORS to prevent dehydration. Our findings highlight the potential to increase uptake of ORS through clear, consistent communication around dehydration and the role of ORS. As suggested by Coreil and Genece, caregivers who understand the importance of ORS in treating dehydration are significantly more likely to use it [11]. Additionally, marketing ORS as a medicine to increase strength, rather than as an antidiarrheal, may improve usage given the concerns around unmet expectations as noted by Green et al. [12]. Surveyed caregivers in Burkina Faso identified increasing strength and energy as an important treatment goal, and ORS users already associated ORS with this goal.

**Table 10.** Total cost of ORS\*

	TOTAL (n = 177)	CENTRE (n = 21)	BOUCLE DU MOUHOUN (n = 46)	HAUTS-BASSINS (n = 45)	NORD (n = 32)	EST (n = 33)
Paid for product, %	96	95	100	93	94	97
Paid per sachet, median, US\$	0.20 (0)	0.20 (0.18)	0.20 (0)	0.20 (0)	0.20 (0)	0.20 (0)
	<b>Total</b>	<b>Urban</b>	<b>Rural</b>			
All paying for ORS sachet	n = 170	n = 45	n = 125			
Median (total cost of sachets), US\$	0.60 (0.40)	0.60 (0.60)	0.40 (0.20)			
All paying for water	n = 82	n = 26	n = 56			
Median (total cost of water), US\$	0.60 (0.81)	1.00 (0.5)	0.60 (0.80)			
All paying for either sachet/water	n = 170	n = 45	n = 125			
Median (total cost of ORS + water), US\$	0.80 (0.83)	1.10 (1.00)	0.60 (0.80)			

ORS – oral rehydration solution

\*Base: All caregivers using ORS at last episode (n = 177). Interquartile range shown in brackets.

Implications of our findings for future program development in Burkina Faso include a shift in messaging from use of ORS as an antidiarrheal to use of ORS to address dehydration and increase energy. Awareness-raising around the central role of dehydration in child mortality would be beneficial. Additionally, given the importance of recommendations by health workers, some communication/education efforts should focus on providers to increase their desire to recommend ORS.

### **Perception: antibiotics and drugs offer a better alternative**

Prior research has documented widespread, inappropriate use of antibiotics and other drugs for treatment of diarrhea. This is likely due to a preference by caregivers for treatments they see as “powerful” [13], especially for treating the symptoms of diarrhea. Because of the self-limiting nature of most cases of diarrhea, the point at which caregivers begin ORS administration, and the role of ORS in rehydration and not treating the symptoms, it is not surprising that caregivers seek a treatment that they believe will give more immediate results in halting symptoms. In addition, there is a well-documented history of provider misinformation leading to recommendations of inappropriate treatments [14]. In a study in India, for example, 59% of prescriptions for children with diarrhea were for antibiotics [15].

Although we found ORS usage to be quite high in Burkina Faso (44% of caregivers used ORS at last episode), usage of antibiotics was also high (34%). Usage of both appears to be driven by professional recommendations, indicating a lack of consistent messaging among health care providers. ORS usage in Burkina Faso may be relatively high compared to antibiotic use, despite comparable views of efficacy, because ORS is perceived to be relatively inexpensive, easily available, and better value for money than antibiotics. Caregivers generally preferred ORS as their one preferred treatment, except in the Centre region, where antibiotics were preferred.

Zinc usage appears to be much higher in Burkina Faso than in India and Kenya [6]. Overall, 27% of caregivers used some form of zinc (either syrup or tablet) at the last episode of diarrhea. The relatively high use of zinc in Burkina Faso is likely due to the work of the Ministry of Health, supported by UNICEF and the Micronutrient Initiative. In a recent report, UNICEF noted that the proportion of community health centers using the combination of ORS and zinc to manage diarrhea went from 0% in 2010 to 42% by September 2012 [16]. Caregivers confirm this dramatic change, with 88% of those using zinc products noting a recommendation by a health care provider as the reason why they used the product.

The role of providers in decision-making and the fairly positive opinion of ORS efficacy among caregivers suggest that the elimination of inaccurate or mixed messaging regarding alternative treatments by providers will likely lead to improved use and outcomes. It is crucial for messaging to indicate that diarrhea will generally resolve without sophisticated or expensive medicines and that lost fluids must be replaced. Raising awareness about the rise of antibiotic resistance is a broader concern. Although pharmacist recommendation may be partly motivated by profit, providers are generally motivated to recommend the best available prescription despite caregiver requests for specific treatments. Well-informed providers and experienced mothers are the natural best advocates for successful dissemination of key messages.

### **Perception: ORS is not user friendly**

Prior research indicated that challenges with preparation and administration are the main reasons that ORS is perceived to not be user friendly. Measuring and mixing the proper amounts of ORS and water has been a challenge in household settings without proper measuring utensils [17]. In some settings, people describe duration and frequency of preparation and administration as a challenge [10]. Historically, adequate ORS dosing has been a hurdle, with most children consuming only minute quantities [18,19]. Palatability has also been investigated as an obstacle to administration of ORS. Findings from Burkina Faso echo findings from previous research studies in other countries in terms of the perception of ORS as not being user friendly.

Among caregivers aware of ORS, most do not have issues with administration aside from there being leftover liquid. However, 32% of caregivers in our study reported that it is difficult to get the child to drink ORS, and only 41% of children received a 1000 mL or more of ORS per day. Children under two and children in rural settings were at higher risk of receiving only a lower dose.

Our findings point to the potential for increasing ORS use through interventions to address ease of administration. The issue of leftover liquid may be addressed by offering a smaller ORS packet (200 mL, for example). Offering child-preferred flavors of ORS may be one way to improve upon the current difficulty of getting children to drink ORS. Unique product presentations such as a juice-box or pre-mix may provide one option to address administration and dosing challenges (though cost would need to be taken into consideration). In addition, a more sophisticated product presentation might simplify administration and enhance caregiver confidence that ORS is a “powerful” medicine. This is supported in the research by findings that the pre-mix was well received by caregivers. Flavor improvements might also improve uptake.

## Study limitations

Limitations of this study include:

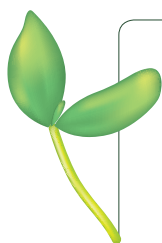
Caregivers' recall of reactions to a diarrhea event that happened up to 2 months before the interview may be inaccurate. Recall of measurements of treatments used may be particularly inaccurate. We tried to counter this by providing illustrations of bottles/cups and using the illustrations as an aid when asking respondents how much liquid was used.

There was some confusion among caregivers about which treatments fall into which categories. Caregivers often do not know what type of treatments providers advise/prescribe. Illustration cards with pictures of typical treatments

that fall into each category (eg, antibiotics, anti-motility drugs, etc.) were used to aid recall.

Caregivers may have been influenced by illustration cards and just chosen a treatment shown that they didn't actually use. However, we used spontaneous recall before using illustration cards, and the spontaneous and prompted recall of treatments was fairly consistent, indicating that prompted recall is reasonably reliable.

We did not probe into use of zinc (eg, doses used, timing, etc.). Higher-than-expected use indicates that motivations for use, sources of information, and usage practices, including use with ORS, should be explored further.



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**Ethics approval:** The study was reviewed by PATH's Research Determination Committee (RDC), who made a ruling that ethics approval for this type of study would not be required (Ref: PATH RDC-0581). Approval for the work was granted by officials in Burkina Faso through the Ethics Committee for Health Research within the Ministry of Health and Ministry of Research, Science, and Innovation.

**Competing interests:** All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare no conflict of interest.

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# Digital technology for health sector governance in low and middle income countries: a scoping review

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**Background** Poor governance impedes the provision of equitable and cost-effective health care in many low- and middle-income countries (LMICs). Although systemic problems such as corruption and inefficiency have been characterized as intractable, “good governance” interventions that promote transparency, accountability and public participation have yielded encouraging results. Mobile phones and other Information and Communication Technologies (ICTs) are beginning to play a role in these interventions, but little is known about their use and effects in the context of LMIC health care.

**Methods** Multi-stage scoping review: Research questions and scope were refined through a landscape scan of relevant implementation activities and by analyzing related concepts in the literature. Relevant studies were identified through iterative Internet searches (Google, Google Scholar), a systematic search of academic databases (PubMed, Web of Science), social media crowdsourcing (targeted LinkedIn and Twitter appeals) and reading reference lists and websites of relevant organizations. Parallel expert interviews helped to verify concepts and emerging findings and identified additional studies for inclusion. Results were charted, analyzed thematically and summarized.

**Results** We identified 34 articles from a wide range of disciplines and sectors, including 17 published research articles and 17 grey literature reports. Analysis of these articles revealed 15 distinct ways of using ICTs for good governance activities in LMIC health care. These use cases clustered into four conceptual categories: 1) gathering and verifying information on services to improve transparency and auditability 2) aggregating and visualizing data to aid communication and decision making 3) mobilizing citizens in reporting poor practices to improve accountability and quality and 4) automating and auditing processes to prevent fraud. Despite a considerable amount of implementation activity, we identified little formal evaluative research.

**Conclusion** Innovative digital approaches are increasingly being used to facilitate good governance in the health sectors of LMICs but evidence of their effectiveness is still limited. More empirical studies are needed to measure concrete impacts, document mechanisms of action, and elucidate the political and sociotechnical dynamics that make designing and implementing ICTs for good governance so complex. Many digital good governance interventions are driven by an assumption that transparency alone will effect change; however responsive feedback mechanisms are also likely to be necessary.



Worldwide, poor health sector governance results in inefficiency, waste, error and fraud, compromising the integrity of health services and the equitable delivery of patient care. The problem is particularly acute in low- and middle-income countries (LMICs), where corruption in medicine has been referred to as an “open secret” [1]. Observing that developing countries lose some US\$ 1.26 trillion per year to corruption, bribery, theft and tax evasion, the United Nations’ Sustainable Development Goal 16 calls for more transparent, accountable and participatory institutions at all levels of government [2]. The concept of “good governance” embeds these objectives within an overarching ethic of “responsible use of power at all levels of institutions” [3].

The complex organizational, political and socio-cultural dynamics associated with poor governance can seem intractable, but discrete and replicable interventions for tackling these problems have yielded encouraging results. For example, a randomized trial of Community Score Cards in Uganda was associated with substantial decreases in provider absenteeism and wait times, a 20% rise in outpatient service utilization, and a 33% reduction in child mortality in just one year, at a cost of only US\$ 3 per household [4].

With the spread of the Internet, mobile phones and social media, approaches toward encouraging good governance are taking new digital forms. Some are emerging organically through social movements aimed at effecting change through group pressure, while others have been intentionally designed to enable citizens or co-workers to report poor practices directly to health organizations or to an oversight body. Within the global health and development community such approaches are becoming well established if not yet widespread. For example, the anti-corruption platform *ipaidabribe.com*, developed by the not-for-profit organization *Janaagraha*, is now widely used across India [5] and UNICEF’s community empowerment platform *U-Report* boasts millions of users worldwide [6].

Reviewing such interventions is challenging because researchers use “governance” and related terms in various ways, as outlined in **Table 1**. This report focuses on uses of digital technology for “good governance”; promoting responsive, participatory, transparent, accountable, equitable and effective institutions [3]. Our review includes bottom-up (citizen-driven) transparency and accountability initiatives [16–19], top-down e-Governance (and e-democracy) projects [7], and public-private partnerships that build

**Table 1.** Differentiating “good-governance” from eGovernment and related terms\*

ICT for good governance	We use the term “ICTs for good governance” for interventions that involve ICTs, that are aligned with Sustainable Development Goal 16’s call for more transparent, accountable and participatory institutions [2], and that are concerned with “responsible use of power at all levels of institutions” [3]. This includes initiatives that are bottom-up, top-down, or include elements of both through public private partnerships. eGovernment is an overlapping term; all interventions in our review involved ICTs and many also involved non-digital elements.
eGovernment	The term eGovernment refers broadly to the digitization of government services, often with a technical orientation toward improving efficiency or quality of services rather than the responsible exercise of power [7]. While many sources use eGovernment and governance more or less interchangeably, our review focused exclusively on replicable governance interventions that targeted practical, concrete and measurable concerns with government performance by promoting responsible exercise of power.
Governance of eHealth / Health Information Governance	This literature has its origins in the large-scale implementation of information systems in health care, more recently including the use of mHealth and personal digital health devices. The storage, use and sharing of personal data in these new environments raises risks for information security and privacy, which have technological, legal/regulatory and ethical/societal implications. The word governance is often used to describe the policies and processes of oversight required to ensure the security and trustworthiness of such systems. It may also be used to refer to the management structures involved in collective oversight of eHealth initiatives.  Governance of health systems through information is another theme in this literature, concerning the best use of data for supporting health care planning, coordination, quality improvement and evaluation, in common with the “Learning Health Systems” concept [8].
Clinical governance	This term underscores continuous improvement of health care service quality [9], generally through organizational integration of financial, performance and clinical quality [10].
Participatory governance	This approach to governance emphasizes the strengthening of citizen voices, and particularly those of marginalized groups, in decision-making processes. Processes of deliberation, consultation and mobilization are particularly relevant [11].
Global governance	This literature takes a macro perspective in studying worldwide governance of contemporary health issues. For instance, it is concerned with the role of international organizations in assisting countries to manage cross-border risks to public health security and support improvement of health outcomes [12].  Recent work in this global governance vein has addressed the challenge of achieving the goal of “health for all by the year 2000” in a free market economy [13], the proliferation of global health NGOs and the potential of the World Health Organization as a coordinating and governing body [14], and structural governance challenges related to national sovereignty or the accountability of non-state actors [15].

ICT – Information and communication technologies, NGO – non-governmental organization

\*Includes terms most closely related to the review topic and not others such as corporate governance, which concerns companies.



or collaboratively implement governance-enabling technologies [20]. By “interventions” we mean potentially replicable projects, programs or social innovations that address dishonest or corrupt practices on the part of health care practitioners and leaders, or that foster citizen participation and make governance more responsive to health care consumers. These interventions address concerns as diverse as public participation, corruption, whistleblowing, bribery, fraud, theft, absenteeism, harassment, discrimination and unfair allocation of funding or government contracts. By “digital” we are referring to mobile ICT, social media and other digital innovations that may support these “good governance” objectives, rather than broader eHealth infrastructure such as electronic health record systems.

While relevant reviews exist in the contexts of sustainable development [21], and health information governance [22], to the best of our knowledge there has been no systematic overview of how ICTs are being used to increase the transparency, accountability or trustworthiness of health care providers, organizations and the public health sector as a whole in LMICs. The report summarized in this paper set out to map and describe the existing landscape of digital good-governance interventions for strengthening health systems in LMICs, and to highlight opportunities for future research and innovation [23].

## METHODS

### Study design

We undertook a phased scoping review including a landscape scan of implementation activities and a systematic keyword search of academic databases, guided by interviews with experts and practitioners in the field and an emergent theoretical framework. The scoping review methodology is increasingly used for mapping areas that are nascent or widely scattered [24], where conventional searches of academic databases are less likely to be fruitful. This approach can be used to understand key concepts, theories and sources of evidence as a means of guiding new innovations, empirical research or systematic reviews, and in-

forming policymakers. Scoping reviews typically do not involve critical appraisal of study methodology or detailed extraction of outcomes data, since they are chiefly concerned with mapping the landscape of evidence rather than establishing the effectiveness of particular interventions [24,25]. **Table 2** summarizes the differences between scoping reviews and comprehensive systematic reviews.

As outlined in **Box 1**, we performed all of the activities recommended in Arksey and O’Malley’s widely cited scoping review framework [25], as well as a landscape scan of implementation activities and consultation with experts, which are typically regarded as optional. We summarize each of these phases below and discuss our methodology more exhaustively in the complete version of the report on which this article is based [26].

### Mapping concepts and refining the research questions

The project began with a broad remit to review the evidence on innovative uses of mobile technology for strengthening “leadership, management and governance” in the health sectors of low- and middle-income countries in line

#### Box 1. Scoping stages used in this review

1. Refine research questions by reviewing the literature on relevant theoretical concepts
2. Undertake landscape scan of implementation activity: Identify key actors, project reports and gray literature relevant to digital technology and some aspect of good governance
3. Based on 1 and 2, define a strategy for systematically searching databases of peer-reviewed research
4. Apply agreed inclusion and exclusion criteria to select relevant studies
5. Converge results of database searches with products of snowball sampling from landscape scan
6. Chart and summarize the data
7. Consult with key experts to elaborate concepts and identify other research
8. Collate, summarize and report the results

**Table 2.** Differences between comprehensive systematic reviews and scoping reviews\*

COMPREHENSIVE SYSTEMATIC REVIEW	SCOPING REVIEW
Focused research question with narrow parameters	Research question(s) often broad
Inclusion/exclusion defined at outset	Inclusion/exclusion developed post hoc
Study quality filters applied	Study quality not an initial priority
Detailed data extraction	May or may not involve data extraction
Quantitative synthesis often performed	Synthesis more likely to be qualitative/thematic
Formally assess the quality of studies and generate a conclusion relating to focused research question	Used to map the landscape of peer-reviewed research and gray literature, identify gaps and opportunities

\*Based on a Cochrane update by Armstrong et al [24].

with the topic areas of the funding scheme. In order to better refine the scope and focus, and avoid duplication, we began by examining existing reviews and commentary in the field, to differentiate the above three sub-topics and determine where the important knowledge gaps lie. This revealed an important gap in the literature concerning uses of digital technology for health sector governance, in contrast to a more extensive literature related to health care management and leadership issues, specifically the “good governance” agenda described in our introduction and in **Table 1**.

### Landscape scan of implementation activity

Based on the above, and informal discussions with experts known to our team, we determined that ICT for health governance is an active area of applied activity, although somewhat under-researched. For this reason, we began by seeking case reports to better understand the nature of projects in this area, beginning with those we were familiar with and snowballing via web links, tracing the work of key organizations and funding streams, and undertaking targeted keyword searches in Google and Google Scholar. Case reports included “grey literature” such as project reports, compendia of mHealth/eHealth initiatives, and websites and blog posts describing active or completed projects. Searches at this early stage were conducted in English, Spanish and Portuguese; since members of the team are fluent in these languages. From an initially large and diffuse set of results we identified 22 case reports that reflected the review’s iteratively refined focus on good governance, rather than management or leadership. We also developed a list of key actors who surfaced repeatedly in relevant case reports, including funders (eg, US government, Swedish government), research organizations (eg, the Anti-Corruption Resource Centre, Transparency International) and technology organizations (eg, Ushahidi) [26]. In a spreadsheet we summarized each report’s “use case” and key themes. Based on this spreadsheet we continued to iteratively refine our search terms and initiate the search for peer-reviewed literature. Our approach reflects similar landscape scans undertaken as part of other scoping review exercises [27,28].

### Systematically searching academic databases and applying inclusion criteria

Based on the initial concept mapping exercise and landscape scan, we defined a strategy for systematically searching for articles published in English and indexed in PubMed (for medical literature) or Web of Science (for interdisciplinary literature). Searches included combinations of the following terms: “governance,” “transparency,” “accountability,” “participation,” “participatory,” “stakeholder engagement,” “corruption,” “absenteeism,” “mHealth,” “eHealth,” “mobile

phone”, “social media” and “digital.” Further articles were identified by examining reference lists and through key informant interviews.

To be eligible for inclusion articles had to describe *digital technology for good governance* purposes in the *health sector of a low or middle-income country*. Those that did not encompass all four features, or were purely concerned with information governance or project management in the context of an mHealth or eHealth project, were excluded. **Figure 1** shows a PRISMA diagram representing the formal literature review and sifting process.

### Charting and analyzing the data

Due to resource constraints, articles that could not be accessed through the University of Cambridge or University of Edinburgh e-libraries were excluded. The remaining articles were downloaded for full review. In keeping with standard scoping review frameworks, we charted these studies according to key themes rather than performing full data extraction. We also followed Levac et al.’s [29] recommendation to make charting an iterative process by continually updating the data-charting spreadsheet to fit the study data being extracted. The fields used for data compilation and analysis were as follows:

1. Author(s), year of publication, study location
2. Study type/methodology
3. Problem(s) the program aimed to address
4. Technology used
5. Intervention use cases (eg, data collection with mobile apps, interactive digital mapping) and categories (eg, information gathering, mobilization).

### Consultation with expert practitioners and researchers

To validate and develop our emerging insights, we posted questions to relevant ICT and global health-oriented email lists and online forums, including GHDonline, the mHealth Working Group listserv, and several LinkedIn groups. Through these posts we identified a number of additional gray literature reports and peer-reviewed articles. Key respondent interviews were also undertaken as a means of identifying additional unpublished work, testing emergent themes, informing iterative improvements to the analysis, and supporting interpretation with reference to “real world” challenges. Interview participants were 10 purposively sampled practitioners and researchers affiliated with key organizations or technology projects that emerged repeatedly in the searches, including men and women with work experience in Africa, Asia and Latin America. Interviews were informal and unstructured, lasting for approximately 45 minutes each.

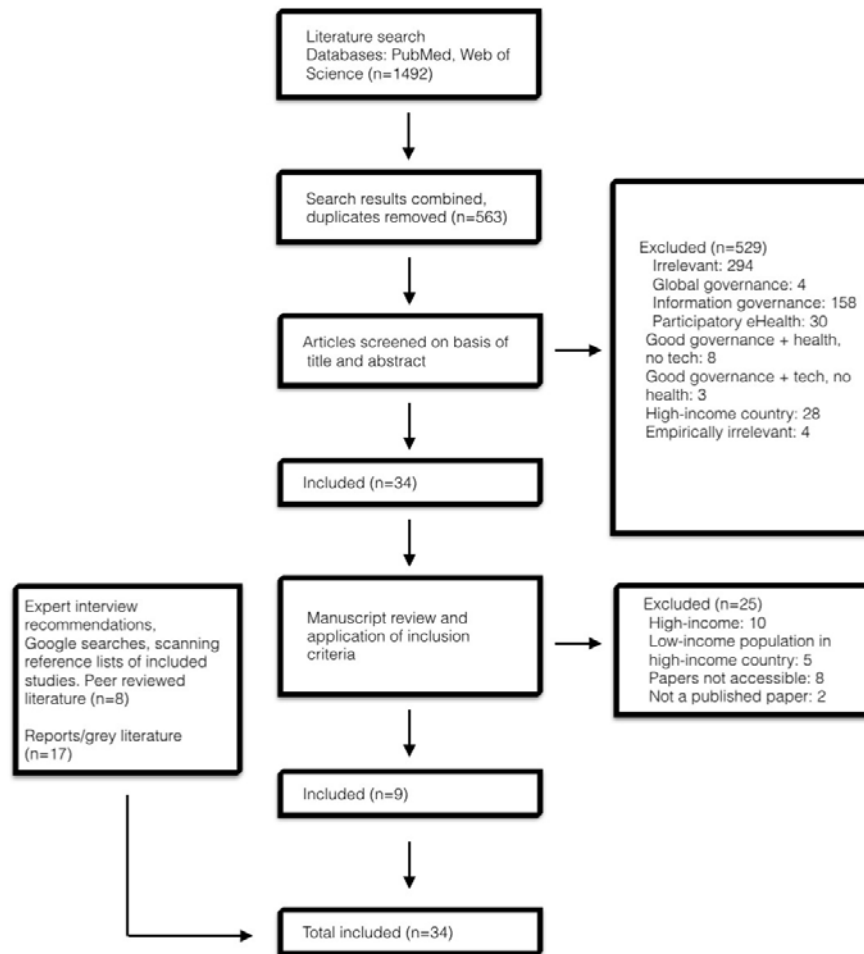


Figure 1. PRISMA flowchart illustrating the search process.

## RESULTS

PubMed and Web of Science searches yielded 1492 results, of which nine met all the inclusion criteria ( $n=9$ ). Expert interviews, social media recommendations, Google searches and analyses of websites and reference lists yielded 25 additional papers, including peer-reviewed articles ( $n=8$ ), and technical reports/gray literature ( $n=17$ ). In total thirty-four published research articles ( $n=17$ ) and reports ( $n=17$ ) were included (Appendices S1 and S2 in **Online Supplementary Document**).

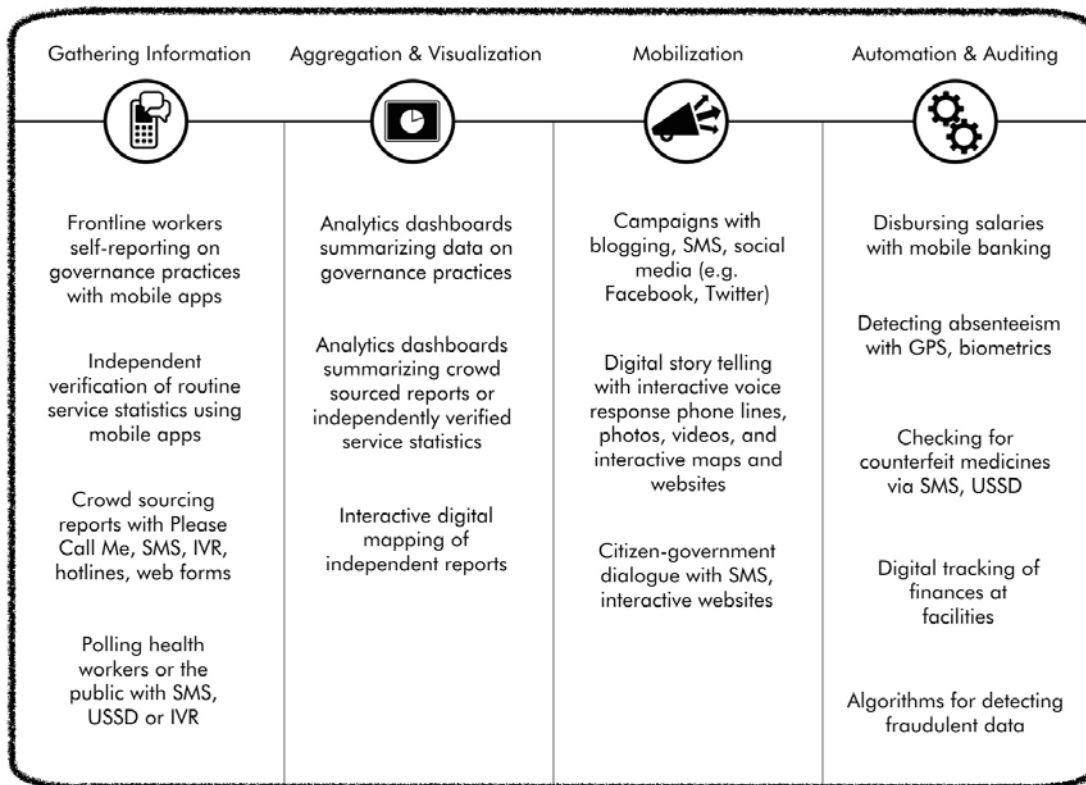
### Composition of the evidence-base

Peer-reviewed evaluative research was sparse relative to other article types. The majority of included articles were identified through iterative and adaptive online searches ( $n=25$ ) rather than using keywords to systematically search academic databases ( $n=9$ ). This reflects the fact that academic articles used different terminologies and came from disparate communities of practice, including political science, sociology and medicine, confirming the

appropriateness of our iterative scoping methodology. The technical reports came from WHO, the World Bank, or non-governmental organizations. Most of the peer-reviewed articles and technical reports included conceptual frameworks or descriptive case examples, rather than evaluative research.

### Common uses of ICT for Good Governance Interventions in the health sector

Our analysis revealed 15 distinct ways of using ICTs as components of health governance interventions, or use cases. We grouped these into four conceptual categories: 1) gathering and verifying information on health services to improve transparency and auditability, 2) aggregating and visualizing data to aid communication and decision making, 3) mobilizing citizens in reporting poor practices to improve accountability and quality, and 4) automating and auditing processes to address fraud or similar inappropriate practices. **Figure 2** illustrates how ICTs within these four broad categories have been used to support particular good-governance initiatives.



**Figure 2.** Information and communication technologies (ICTs) used for health governance interventions.

## Gathering and verifying information

Routine data collection is one of the more widely discussed use cases in the mHealth literature; it is well established that using mobile devices can improve data timeliness and quality [30]. Some governance initiatives have used the same or similar technologies to collect data for transparency or governance purposes. These initiatives include *organization-oriented* approaches, such as using mobile phones to collect data on governance practices or to independently verify routine government health statistics. For example, government health workers can use the USAID-funded GovScore app to report on institutional governance practices, such as in a project evaluating the formation of local health advisory committees [31]. The Performance Monitoring and Accountability 2020 project, sponsored by the Gates Foundation, uses the mobile app Open Data Kit to undertake public surveys about family planning and sanitation services in LMICs [32]. While this does not explicitly target governance challenges such as corruption, using data captured directly from civil society to verify routine health service statistics may enable external accountability in ways that are not possible for mHealth initiatives reliant on self-reporting by government health care providers.

Other information gathering approaches involve *engaging citizens* to crowdsource intelligence on health system per-

formance, such as stock-outs, absenteeism, bribery or corruption. Rather than providing equipment (eg, smartphones) to a relatively small group of data gatherers, projects that solicit the participation of large groups of people are more likely to rely on technologies that people can access via the Internet or, particularly in LMIC settings, via the least expensive and most widely available mobile phones. In this vein, the social enterprise “Open Health Networks” enlisted members of the public to submit SMS reports of drug stock-outs and health worker discrimination against indigenous patients in Guatemala [33]. According to a press release by the Canadian Government’s International Development Research Centre, this data and subsequent community meetings resulted in seven municipalities increasing the amount of funding allotted to keep medicines in stock or provide fuel for ambulances [34]. One of the larger crowdsourcing for global health initiatives is UNICEF’s social platform U-Report, which originated in Uganda and now operates in several countries, with over a million registered users in Nigeria alone [35]. The large database of registered users enables U-Report to conduct massive polls. For example, data from 16 117 U-Report respondents was used in conjunction with traditional survey methods in a project assessing client satisfaction with services in Uganda’s public health facilities [36].

## Data aggregation and visualization

While data gathered digitally may simply be summarized in written reports and discussed in face-to-face meetings, we identified a second category of use cases related to *data aggregation and visualization*. Digital analysis tools can become necessary as data sets grow extremely large or when information management teams are understaffed. While digital analytics and visualization tools, such as dashboards and maps, are increasingly common throughout the health sector, their use in good governance interventions involves distinctive data sets (eg, on absenteeism) or civil society verification of government statistics. Thus such tools might enable comparison of drug stock-outs across multiple catchment areas or draw attention to “hot spots” of corruption that would be less obvious when viewing massive spreadsheets. A number of digital technologies integrate data gathering, analysis and visualization tools, either for organization-oriented governance or for citizen-centered approaches such as crowdsourced maps that can be used to negotiate change [37].

## Mobilization

A number of the articles and interventions we identified involved a *mobilization* component. Projects of this kind use ICTs to raise public awareness of corruption in order to generate political pressure for change or otherwise spur collective action aimed at reforming unethical or negligent health care practices. Such efforts reflect an important tenet of the contemporary transparency and accountability movement; that transparency alone is insufficient to drive greater government performance or accountability [16].

Some digital mobilization efforts unfold primarily online; for example through social media and blogging, eg, [4]. Others blend digital and “offline” approaches, such as pairing community meetings and poster campaigns with the information gathering and analytics tools discussed previously eg, [33]. Another common approach involves digital diary methods, where people experiencing a health issue are invited to document their own perspective and share photographs, audio or video with others eg, [38]. In some cases dialogue and mobilization are proactively cultivated by governments or through public private partnerships aiming to improve responsiveness or “feedback loops” among citizens and government actors [39,40]. In other cases, however, mobilization efforts are prioritized because government actors were initially unresponsive to citizen concerns. For example, in the 1990s over 300 000 indigenous Peruvian women and 20 000 indigenous men underwent forced sterilization through a state government “poverty reduction” campaign that was funded by international donors and initially supported by women’s rights organizations. With the aim of pressuring the government to acknowledge

that the health policy was harmful, the Quipu Project uses mobile phones, radio, and an interactive documentary to communicate testimonies of those affected [41].

## Automation and auditing

Finally, *automation and auditing* may help to address inappropriate practices by taking processes or decisions out of the hands of individual health care personnel and intermediaries. For example, new algorithms can automatically detect “outlier” data sets that show signs of having been faked by an absentee worker rather than having emerged from a genuine patient encounter [42]. Electronic billing and e-cash registers may address informal payments or bribes [43] and disbursing money via mobile phones can address a major source of corruption, enabling ministries to ensure that full salaries go to the intended workers in a timely manner [32,44].

Digitizing processes can also increase auditability. For example, doubts regarding whether community health workers actually visit the homes of remote patients in their care may be addressed using biometric fingerprint technology to verify each patient visit [45]. Auditable databases of dispensed drugs are also being used to tackle the widespread problem of counterfeit medicines. This typically involves labeling all medicines with serial numbers so that purchasers who text message a unique code to an SMS hotline can verify that their product is registered eg, [46,47].

## Discussion

While a growing number of anecdotal reports suggest that digital interventions for good health sector governance hold promise, the relevant evidence is undeniably mixed. For every success, there have been outright failures, as is the case with conventional good governance interventions (for which there are more randomized trials) [16]. Numerous reports and expert interviews stressed that ICT for health governance interventions hinge on nuanced contextual factors and the challenge of linking transparency and action.

Our analysis revealed fifteen unique use cases of ICT for good governance, clustering into four conceptual categories associated with better information for transparency, usable data for decision making, citizen mobilization for accountability and process automation for fraud prevention. While most of these use cases targeted government-sponsored services, some extended to the private sector, such as those aimed at combatting drug counterfeiting. Since the private health care sector is dominant in many low- and middle-income countries we anticipate seeing more ICT for good-governance focused on these settings in the future, mindful of the role of government in ensuring that these are effectively regulated.

It should be noted that, while we organized our findings around a collection of generic digital tools, in practice there is a tendency to mix and match two or more of these as components of integrated interventions that enable governance processes. Such integrated governance interventions aim to strengthen citizen–government “feedback loops” [42,48], or complete an “action cycle” [16], using data to drive performance improvement or responsiveness in government services through particular mechanisms. For example, the My Voice project in Nigeria enabled citizens visiting health facilities to send feedback via SMS; the feedback was visualized for government leaders through an online dashboard, and these leaders then completed a feedback loop by using citizen–generated data in their routine review meetings regarding the performance of specific health facilities [42]. This reflects a growing acknowledgment that transparency alone (eg, having an Open Government data portal) is insufficient to influence governance [16,49]. To put this in other terms, it should not be assumed that digital technologies or eGovernment platforms will deliver good governance–related benefits unless they explicitly address specific and measurable concerns with performance or facilitate concrete mechanisms of responsive governance.

Factors limiting the effectiveness of digital good governance inventions in developing countries include lower rates of Internet access and mobile phone ownership among women and vulnerable groups [42,50,51]. Poor local network access or smartphone penetration could further marginalize people who already have less influence in governance. Understanding local patterns of technology use is therefore vital when determining which components of good governance interventions should be digitized and which are better left offline. The extent to which governments are responsive to public concerns also has implications for which approaches are likely to succeed [16]; indeed complaining about the government can be dangerous for citizens in some countries.

Finally, the preponderance of reports and expert interviews indicated that digital good governance interventions in health care are deeply complex. Their outcomes hinge on distinctive political factors in addition to the myriad organizational and sociotechnical dynamics that shape digital health innovation generally [52]. The value of human–centered design (HCD) in addressing such complexities is increasingly recognized in reports on ICT for health governance [31,33,42] as well as broader consensus statements, such as the widely ratified Principles for Digital Development [53]. HCD principles and practices include grounding the project in insights from fieldwork undertaken in the context of use, involving end–users in the design process, and iteratively adapting to feedback and experiential

insights. Such approaches share important conceptual and philosophical links with transparency and accountability interventions, the former influenced by Scandinavia’s participatory design movement [54], and the latter by the broader participatory global development community [16]. In both communities, participatory approaches reflect practical priorities as well as the democratic view that ordinary people should have a say in matters that affect them. While participatory co–design will not guarantee the effectiveness of digital good–governance interventions, it offers practical resources for dealing with complex design situations and merits further attention, given its links with participatory approaches to governance.

### Limitations

In keeping with our research aims and with methodological guidance for scoping reviews [24,25], our search and study inclusion process was broader than would be typical for a fully systematic review but also more limited, in terms of databases, keywords and the absence of critical appraisal. As already noted, scoping reviews are best understood as *hypothesis generating* activities rather than *hypothesis testing* endeavors, and are useful for mapping emerging areas with scattered literatures. In this case, the scoping process proved extremely valuable in helping us to refine our research focus, align with appropriate theoretical literature and converge different types of evidence to better understand this evolving interdisciplinary area. In addition to undertaking all of the research stages recommended for scoping reviews, we conducted two stages that are typically considered optional: a landscape scan of implementation activities and consultation with experts and practitioners. We recommend that future systematic reviewers wishing to build on this work use a wider range of databases, including those specializing in research from LMIC, as well as more exhaustive search methods.

### CONCLUSIONS AND RECOMMENDATIONS

Recent years have seen a rapid growth in the number and scale of ICT for health governance projects in LMICs. This trend seems likely to continue, with advances in digital infrastructure and Sustainable Development Goal 16 drawing further attention to strong institutions, public participation and combatting corruption [2].

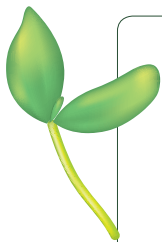
Among the numerous reports discussing ICTs and good governance that we examined, we observed a tendency to emphasize data or transparency alone, with the implicit assumption that improvements in the quality or equity of health services would inevitably follow. However, the evidence suggests that the link between ICTs, transparency

and improved performance should not be taken for granted, echoing observations from our recent scoping review on the use of social media for e-government [55]. In order to be effective ICT enabled good governance interventions should address practical, specific and measurable concerns with health sector performance, with the long-term aim of improving the lives of citizens. We recommend that policymakers, sponsors and implementers of these initiatives prioritize the proactive use of data to drive reform, establishing citizen-government feedback loops and mechanisms of accountability, with a view to completing “action cycles” rather than settling for transparency or better information alone [16].

Further research is required to strengthen the theoretical models underpinning these approaches and articulate their pathways to impact, while empirical studies are needed to evaluate their outcomes and understand factors mediating

their adoption or effectiveness. Human-centered and participatory approaches to intervention design also merit greater attention, not only as a practical means of dealing with local complexities, but also for their links with participatory approaches to governance.

To our knowledge, this is the first formal scoping review to have examined the literature on ICT for good governance interventions in the context of LMIC health care systems. These interventions show great promise for improving transparency, accountability and public participation, thereby facilitating ethical, responsible and equitable health care. However, existing evidence of their use and effectiveness is mixed and successes appear highly context-dependent. As well as adding to the wider multi-sector literature on this topic, we hope our observations provide useful insights for policymakers, practitioners, developers and sponsors considering new projects in this area.



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**Competing interests:** All authors have completed the ICMJE uniform disclosure form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available upon request from the corresponding author) and declare no conflicts of interest. IH is a board member at Medic Mobile, a non-profit social enterprise developing mHealth solutions for LMIC.

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# Burden of *Neisseria meningitidis* infections in China: a systematic review and meta-analysis

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**Background** *Neisseria meningitidis* is a leading cause of bacterial meningitis and septicemia in children and young adults worldwide. The disease burden associated with *N. meningitidis* infections has not been systematically assessed in China. Therefore, we undertook this study to determine the burden of meningococcal disease in China.

**Method** We performed a systematic review and meta-analysis of articles on *N. meningitidis* incidence, carriage, seroprevalence and mortality rates in China by searching the Chinese BioMedical Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang database and PubMed for publications from January 2005 to Aug 2015.

**Results** In total, 50 articles were included in our analysis. The overall incidence of meningococcal disease and associated mortality were estimated to be 1.84 (95% confidence interval (CI) 0.91–3.37) per 100 000 persons per year and 0.33 (95% CI 0.12–0.86) per 100 000 persons per year, respectively. *N. meningitidis* carriage rate among the healthy population was estimated to be 2.7% (95% CI 2.0–3.5%). Prevalence of antibodies against *N. meningitidis* serogroup A and C were estimated to be 77.3% (95% CI 72.4%–81.6%) and 33.5% (95% CI 27.0%–40.8%), respectively. No studies were found for serogroup specific disease burden.

**Conclusions** The overall incidence of meningococcal disease in China is low. The lower seroprevalence of serogroup C within the population suggests that it may pose a greater risk for meningococcal disease outbreak than serogroup A. The lack of data on serogroup disease burden by age groups suggests the implementation of laboratory based meningococcal surveillance systems are urgently needed in China.

*Neisseria meningitidis*, a Gram-negative diplococcus, asymptotically colonizes the upper respiratory tract of approximately 10% of healthy humans, and is a leading cause of bacterial meningitis and septicemia in children and young adults worldwide [1,2]. It is transmitted through direct contact with respiratory secretions or aerosol droplets released by coughing/sneezing from patients with meningococcal disease or asymptomatic carriers. Humans are the only host [3]. Most cases of meningococcal disease are caused by serogroups A, B, C, Y and W [4]. Meningitis caused by *N. meningitidis* continues to be a serious threat to global health, account-

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ing for 1.2 million cases and 135 000 deaths worldwide each year [5], despite the existence of effective vaccines [6].

Serogroup A has historically been the dominant serogroup in China accounting for over 95% of meningococcal disease cases from the 1960s to 1980s, with annual disease incidence rates up to 400 cases per 100 000 population in some regions [7,8]. Following the introduction of a serogroup A polysaccharide meningococcal vaccine into the national immunization program in 1982, the incidence rates in the subsequent two decades were reduced and remained low and relatively stable ranging 0.2–1 cases per 100 000 [9,10]. However, during 2003–2004, serogroup C (type ST–4821) meningococcal disease outbreaks emerged in the Anhui province [11]. This new strain appeared more invasive, causing serious complications more frequently and was associated with a higher case–fatality rate than serogroup A [12]. Serogroup C meningococcal disease quickly became endemic in the Anhui Province, with ST–4821 the dominant lineage. This lineage rapidly spread nationwide causing several meningococcal disease outbreaks in 2004–2005 [12,13]. In response to these outbreaks, meningococcal group A and C polysaccharide vaccines were subsequently used for routine immunization. Nonetheless, serogroup C continues to be isolated every year throughout China with ST–4821 dominant [14].

Understanding changes in epidemiology of meningococcal disease after use of meningococcal A/C polysaccharide vaccines and *N. meningitidis* carriage rates and seroprevalence can help predict the potential public health impact of routine vaccination. To date, the disease burden associated with *N. meningitidis* infections has not been systematically assessed in China. We therefore conducted this systematic review and meta-analysis to evaluate the incidence of meningococcal disease and associated mortality, as well as carriage rates and prevalence of antibodies against *N. meningitidis* in China.

## METHODS

### Search strategy

We undertook a systematic search across the following electronic databases: Chinese BioMedical Database (CBM), China National Knowledge Infrastructure (CNKI), Wanfang database and PubMed. The specific details of the search strategies undertaken across these databases are presented in Appendix S1 in **Online Supplementary Document**. In brief, the following search terms were used to search the databases: “meningococcus”, “meningococcal”, “meningococcic” and “*meningitidis*”. The search in PubMed included ‘China’ as a search term. We restricted our search to articles published in Chinese “core journals”, as listed by

the Peking University (2014 edition) and evaluated according to predefined criteria; journals considered to be of low quality are excluded from the list [15]. We focused our search on recent data, published from January 2005 to August 2015.

### Inclusion and exclusion criteria

Studies were selected for inclusion based upon the following criteria: 1) included humans; 2) reported at least one outcome relevant to our study objectives; 3) published in Chinese or English language. We excluded case reports and other systematic reviews or meta-analyses. Where multiple studies on the same cohort were identified, the latest publication or that with the most complete data was included in our meta-analysis.

### Literature screening and data extraction

Two groups of reviewers screened the titles, keywords and abstracts of the citations identified (DW and XG independently reviewed records 1–1850; MH and LY independently reviewed records 1851–3703) and excluded those that clearly did not meet the inclusion criteria. YZ screened the citations identified in a similar manner. The full texts of all selected publications were assessed for relevance. Any disagreement or uncertainty between the reviewers about the eligibility of a study was resolved by YZ, and in the case of persistent disagreement, the full text of the article was examined. The reference lists of articles identified for inclusion were inspected for other appropriate articles not identified by the electronic search.

The reviewers independently extracted and entered data from each included study into a database. The following data were extracted from the studies where available: authors; year of publication; study design; study period; location of the study; number of meningococcal disease cases or reported incidence (crude and age-specific); number of deaths or reported death rates; *N. meningitidis* carriage rates; and prevalence of antibodies against *N. meningitidis* and corresponding serogroup. The data extracted were checked for inconsistencies between the reviewers and resolved by a fifth author. We did not attempt to contact the authors of the studies identified for missing information or resolve ambiguities.

### Quality assessment

The analysis included studies with different outcomes. Therefore, no pre-existing scale is directly suitable for the quality assessment. The quality of each included study was assessed by YZ and DW using predefined criteria as previously described [16]. In brief, the quality of the studies was based on the clarity of information provided on the following 5 items scored on a three-point scale (from 0 – poorest

to 2 – best quality): population and representativeness; diagnostic criteria; specimen collection methods; pathogen or antibody detection methods; and statistical methods. The scoring is defined as 2 points for detailed reporting, 1 point for non-detailed reporting and zero point for no reporting of the selected criteria for the assessment. The score for each item was then added to give a composite score for the study, with a highest total score of 10. Studies with total scores  $\geq 8$  were regarded as “good” quality.

## Statistical analysis

All meta-analyses were performed using the MetaAnalyst (Beta 3.13; [http://tuftscaes.org/meta\\_analyst](http://tuftscaes.org/meta_analyst)) software package. Since we were expecting considerable heterogeneity across the included studies, we used the random-effects model of the Der-Simonian Laird method. Publication bias was investigated via Stata 12.0 (StataCorp LP, Texas, USA) using Egger’s test.

## RESULTS

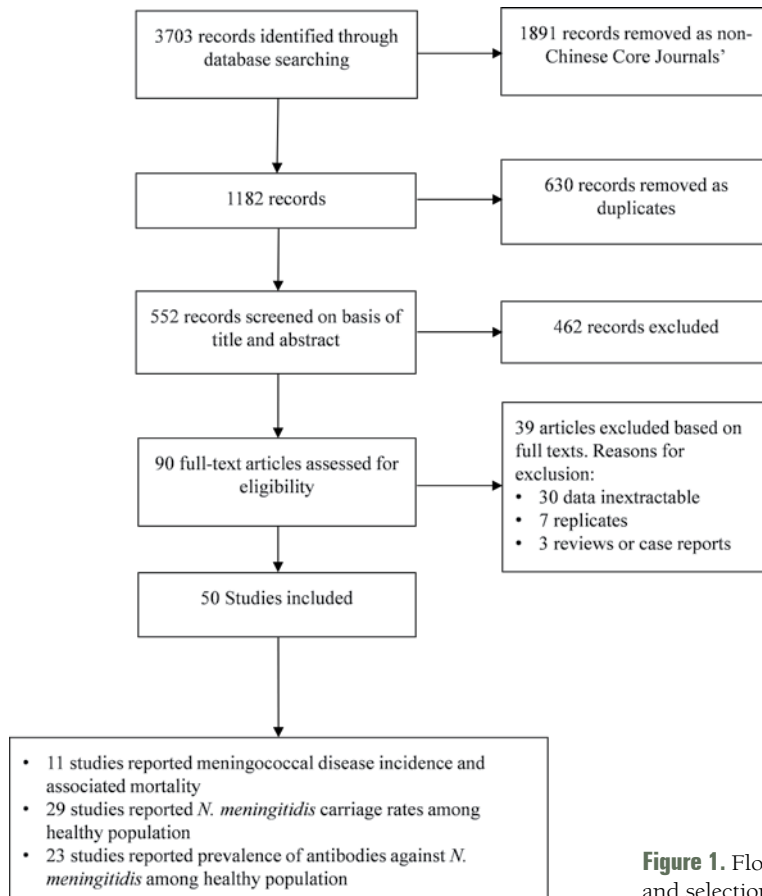
### Studies included

The electronic search identified 3703 citations (**Figure 1**). After removal of non-Chinese core journals and duplicates,

and screening titles and abstracts, 90 studies were judged as potentially relevant with the full text retrieved to assess their eligibility for inclusion. Overall, 50 studies [17–66] met the eligibility criteria and were thus included in our analysis. These studies reported data collected from 1991 to 2013. The quality evaluation score for these studies ranged from 5 to 10 points, with a mean  $\pm$  standard deviation of  $8.1 \pm 1.2$ . There were 36 (72%) studies with a score of  $\geq 8$ . A summary of the characteristics of included studies associated with their respective quality assessment is presented in Appendix S2 in **Online Supplementary Document**. Studies included the analysis are listed in Appendix S3 in **Online Supplementary Document**.

### Meningococcal disease incidence and associated mortality rate

Eleven studies [21,24,25,29,44,46,48,57–60] conducted in 7 provinces provided data on the meningococcal disease incidence and associated mortality rate. The annual meningococcal disease incidence and mortality rate for a representative period between 2000 and 2010 is summarized in **Table 1**. The highest incidence rates occurred in the years 2006, 2007 and 2010; the incidence rates reported in these years were  $>2.0$  per 100 000 persons per year. The corresponding highest mortality rates occurred in the years



**Figure 1.** Flow diagram of literature search and selection.

**Table 1.** Meta-analysis of annual meningococcal disease incidence and associated mortality rate from 2000 to 2010 (per 100 000 persons per year)

YEAR	INCIDENCE		MORTALITY	
	Number of studies	Rate	Number of studies	Rate
2000	5	0.71 (0.18–2.44)	3	0.37 (0.02–3.79)
2001	5	0.66 (0.17–2.28)	3	0.01 (0.00–9.96)
2002	5	0.91 (0.23–3.00)	3	0.44 (0.06–2.52)
2003	6	1.23 (0.31–3.85)	3	0.44 (0.66–2.52)
2004	7	1.09 (0.19–4.33)	3	0.02 (0.00–9.18)
2005	10	1.07 (0.26–3.53)	4	0.02 (0.00–7.82)
2006	8	2.18 (0.69–5.13)	4	0.02 (0.00–7.68)
2007	8	2.30 (0.76–5.21)	4	0.01 (0.00–8.91)
2008	5	1.41 (0.17–6.14)	3	0.01 (0.00–9.97)
2009	5	1.88 (0.53–4.89)	3	0.40 (0.03–4.01)
2010	3	2.17 (0.06–5.42)	2	0.44 (0.03–4.35)
Total	11	1.84 (0.91–3.37)	5	0.33 (0.12–0.86)

2002, 2003 and 2010; the mortality rate reported in these years was 0.44 per 100 000 persons per year. The average incidence of meningococcal disease and associated mortality during the study period assessed were estimated to be 1.84 (95% confidence interval (CI) 0.91–3.37) per 100 000 and 0.33 (95% CI 0.12–0.86) per 100 000, respectively.

### *N. meningitidis* carriage rate among the healthy population

Twenty-nine studies [17–19, 22, 24, 26–28, 30–32, 34, 35, 37, 39–44, 47, 49, 51, 52, 56, 57, 62, 64, 65] conducted in 14 provinces reported *N. meningitidis* carriage rates among the healthy population. The analysis for *N. meningitidis* carriage rate included 1248 positive cases identified from 45 462 throat swabs from healthy people between 2000 and 2013, representing an overall carriage rate of 2.7% (95% CI 2.0%–3.5%).

### Prevalence of antibodies against *N. meningitidis* among the healthy population

Twenty-three studies [20, 22, 23, 28, 30, 33, 34, 36, 38, 39, 42, 43, 45, 50, 52–55, 57, 61, 63, 65, 66] conducted in 11 provinces reported the prevalence of antibodies against *N. meningitidis* among the healthy population. The age-specific prevalence of antibodies against *N. meningitidis* is summarized in **Table 2**. Serogroup A specific *N. meningitidis* were generally highest in those aged 5–24 years and for serogroup C it was highest in those aged 25 years or older. The overall prevalence of antibodies against *N. meningitidis* serogroup A and C was 77.3% (95% CI 72.4%–81.6%) and 33.5% (95% CI 27.0%–40.8%), respectively, for the period 2001–2012.

### Sensitivity analysis and publication bias

Sensitivity analyses undertaken to include only 'good' quality studies did not significantly alter the outcomes. Overall

**Table 2.** Meta-analysis of age-specific prevalence of antibodies against *N. meningitidis* among the healthy population

AGE-GROUP (YEARS)	NUMBER OF STUDIES	ANTIBODY-POSITIVE	TOTAL NUMBER OF PARTICIPANTS	POSITIVE RATE (%) (95% CI)
<b>Meningococcal serogroup A:</b>				
0–4	22	3101	4701	70.9 (63.4–77.4)
5–9	15	1367	1722	81.4 (75.5–86.2)
10–14	15	1515	1912	78.2 (72.4–83.1)
15–24	15	1623	2071	78.2 (71.7–83.6)
25–34	14	1101	1488	75.0 (66.1–82.2)
35–44	14	1058	1357	76.3 (65.3–84.7)
45–	14	1038	1424	72.5 (61.6–91.2)
Total	22	10803	14676	77.3 (72.4–81.6)
<b>Meningococcal serogroup C:</b>				
0–4	22	1658	4395	23.6 (16.0–33.5)
5–9	14	610	1367	34.9 (23.5–48.4)
10–14	14	533	1347	24.1 (14.7–36.9)
15–24	14	606	1539	32.0 (24.4–40.7)
25–34	13	616	1347	39.9 (31.9–48.5)
35–44	13	656	1210	42.6 (32.2–53.7)
45–	13	703	1283	46.7 (37.0–56.6)
Total	22	5382	12 488	33.5 (27.0–40.8)

CI – confidence interval

*N. meningitidis* carriage rate among the healthy population reported in 22 good quality studies was 3.2% (95% CI, 2.4%–4.2%) and the prevalence of antibodies against *N. meningitidis* serogroup A and C among the healthy population reported in 20 good quality studies were 75.9% (95% CI 70.5%–80.6%) and 34.3% (27.5%–42.0%), respectively. The Egger's test did not reveal any significant publication bias (–0.51, 95% CI –4.72 to 2.87,  $P=0.616$ ) for *N. meningitidis* carriage rate among the healthy population. As the majority of studies were captured in the analysis of carriage data, we did not consider further sensitivity analysis of the other data to be necessary.

### Discussion

Our study is the first to systematically review, collate and analyze available published studies on the disease burden of *N. meningitidis* infections in China using robust meta-analytical methods. We found that the incidence of meningococcal disease and associated mortality are low ranging 0.66–2.30 per 100 000 persons per year and 0.01–0.44 per 100 000, respectively. The incidence of meningococcal disease from our study is consistent with that reported in developed countries, typically <2 per 100 000, but lower than that reported in developing countries (typically >10 per 100 000), particularly in Africa [67].

In China, meningococcal disease historically occurred in a cyclical pattern at intervals of 8–10 years, with nationwide epidemics in 1959, 1967, 1977, and 1984 [7,68]. The spring of 1967 had the highest incidence of meningococcal disease with reported rates of 403 per 100 000, corresponding to more than 3.04 million cases. The associated

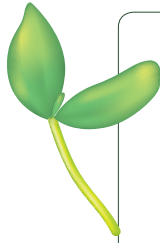
mortality rate in that year was 5.5% corresponding to more than 160 000 deaths [69]. The epidemic in 1977 had an incidence of 59.7 per 100 000 and a 4.0% fatality rate. These deadly cyclic epidemics and seasonal patterns clearly highlight the unpredictability of outbreaks of meningococcal disease despite our observed low incidence rates in the study period.

In our analysis, the prevalence of antibodies against *N. meningitidis* serogroup C was 33.5% and tended to increase with age, whereas the prevalence of serogroup A antibodies was highest in the 5–9 year age group and decreased with age. The lower seroprevalence of serogroup C within the population suggests that it may pose a greater risk for meningococcal disease outbreak than serogroup A, particularly in the youngest age group (less than 5 years) who have the lowest seroprevalence. Despite over 90% uptake for meningococcal serogroup A/C polysaccharide vaccines, the observation of low seroprevalence against serogroup A and C in children less than 5 years old suggests that the implementation of conjugate meningococcal vaccine is necessary particularly for those less than 2 years old to whom the polysaccharide meningococcal vaccines have limited benefits and protection.

We estimated the nasopharyngeal *N. meningitidis* carriage to be 2.7%, which appear lower than the generally quoted overall rate of 10% [70], and the average 3.5–35% reported in studies conducted in Africa [71], but at least consistent with that reported in Mexico (1.6%) [72]. The low carriage rates found in our study and those reported in Mexico are consistent with the low disease incidence rate reported in these two countries. Currently the burden of meningococcal disease in Mexico is low, with total national cases as low as two per year [73,74]. The prevalence of *N. meningitidis* carriage in healthy children and adolescents aged 10–19 years in Chile was reported to be 6.5% [75], and slightly lower in university students ages 18–24 years (4%) [76]. The corresponding incidence of meningococcal disease in Chile was also low, varying from 0.33–0.59 per 100 000 in the six years up to 2012 [77]. A European meta-analysis including 143 114 individuals found that the carriage rate increased from 4.5% in infants to 24% in 19-year olds and decreased to 8% in 50-year old adults [78]. Data on age-specific carriage rates in China are currently lacking. Since information on carriage rates is important for understanding the epidemiology and transmission of meningococcus and developing vaccination strategies, studies on age-specific carriage rates are recommended in China.

Our study has a number of limitations that should be considered. The meta-analysis was based on observational studies and as such is constrained by the inherent heterogeneity in such studies (for example, differences in sampling techniques, laboratory methods, age groups assessed, period of study/seasonality effects) and underlying confounding factors. In addition, we combined data from different regions and time periods. To account for this, we adopted a random-effects model to pool all results, leading to a wider 95% CI that provided a more conservative estimate of the overall results. There were few studies found for certain geographic regions of west China, such as Gansu, Xinjiang and Tibet, which may also contribute to low precision estimates in those areas and overall. We did not search the gray literature; therefore, data that were not published in the 4 selected search databases may have been missed. Nevertheless, our study is likely to capture all important Chinese data on meningococcal disease since we included all available core journals in our study. Other shortcoming are, we only considered studies published in English and Chinese and did not contacted to authors for missing information or resolve ambiguities. However, it is unlikely there would be any significant literature in other languages. Since most important study data were available to obtain during data extraction, we feel that clarifications with the authors are not necessary and do not expect to have any impact on the study results. In addition, there were no studies identified that reported disease burden by serogroup, which limits our understanding of seroepidemiology of meningococcal disease and for developing recommendations for the selection of meningococcal vaccines in different age groups. Nevertheless, almost all meningococcal disease was caused by serogroup A and C based on the limited available data [11,79]. Therefore, the use of meningococcal conjugate vaccines including serogroups A/C/W/Y can further reduce the burden of meningococcal disease and prevent the occurrence of large outbreaks in China.

In conclusion, although the overall incidence of meningococcal disease in China is low, the lower seroprevalence of serogroup C within the population suggest that it may pose a greater risk for meningococcal disease outbreak than serogroup A, especially for children aged less than 5 years. The lack of data on serogroup-specific disease burden by age group suggests that the implementation of laboratory-based meningococcal surveillance systems is urgently needed in China.



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**Authors' contributions:** Study design (MHK, YZ); data collection (DW, XG, MH, LY); data analysis and interpretation (YZ, DW, XG, MH, MHK); development of initial draft of manuscript (YZ, MHK), critical revisions for intellectual content of manuscript (YZ, DW, XG, MH, LY, MHK); study supervision (YZ, MHK). All authors approved the final manuscript for submission, and are responsible for the veracity and completeness of the data reported.

**Competing interests:** All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare no conflict of interest. MHK is an employee of Sanofi Pasteur.

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# Infection prevention and control of *Clostridium difficile*: a global review of guidelines, strategies, and recommendations

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**Background** *Clostridium difficile* is the leading cause of health care-associated infections. Given the high incidence of *C. difficile* infection (CDI) and the lack of primary prevention through immunization, health care professionals should be aware of the most current guidance, as well as strengths and limitations of the evidence base underpinning this guidance.

**Methods** We identified publicly available national or organizational guidelines related to CDI infection and prevention control (IPC) published between 2000 and 2015 and for any health care setting through an internet search using the Google search engine. We reviewed CDI-targeted IPC recommendations and describe the assessment of evidence in available guidelines.

**Results** We identified documents from 28 countries/territories, mainly from acute care hospitals in North America, the Western Pacific, and Europe (18 countries). We identified only a few specific recommendations for long-term care facilities (LTCFs) and from countries in South America (Uruguay and Chile), South East Asia (Thailand), and none for Africa or Eastern Mediterranean. Of 10 IPC areas, antimicrobial stewardship was universally recognized as essential and supported by high quality evidence. Five other widely reported “strong” recommendations were: effective environment cleaning (including medical equipment), case isolation, use of personal protective equipment, surveillance, and education. Several unresolved and emerging issues were documented and currently available evidence was classified mainly as of mixed quality.

**Conclusion** Our review underlines the need for targeted CDI IPC guidelines in several countries and for LTCFs. International harmonisation on the assessment of the evidence for best practices is needed as well as more robust evidence to support targeted recommendations.

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*C. difficile* is the leading cause of health care-associated infections (HAI) worldwide affecting especially the elderly and hospitalised patients [1–5]. The burden of CDI remains under-recognized and challenges associated with case detection hinder prevention. It was estimated that in 2011, over 450 000 CDI cases occurred in the United States and 172 000 in Europe [6,7]. Mounting evidence of the rising importance of CDI in other regions, such as Asia [8,9] and Latin America [10,11] contributes to concerns



about the wide-ranging reach of CDI morbidity [6,12,13]. Given the high incidence of CDI and the lack of primary prevention through immunization, health care professionals should be aware of the most current guidance, as well as strengths and limitations of the evidence base underpinning this guidance.

There are wide variations in the availability or levels of implementation of effective Infection Prevention and Control (IPC) measures for CDI. A national survey in Canada identified an extensive lack of antimicrobial stewardship programmes, less than 25% of the 33 participating hospitals [14] in 2005. More recently, attention was drawn to the lack of clinical awareness and testing [15], disparities in the strength of recommendations across different IPC guidelines [16], and the lack of knowledge on the independent effects of common IPC strategies [17–19]. As guidelines are useful tools to promote coordinated IPC efforts, a detailed documentation of current published strategies has the potential to highlight commonalities and discrepancies in recommended practices. A comprehensive overview of published guidelines also has the potential to inform the decision-making of infection control stakeholders at the national, provincial, and institutional level and help researchers in targeting current gaps in the literature.

In this review, we describe the availability of documents that outline recommendations and actions for the prevention and control of CDI. We present a structured assessment of key elements of CDI–IPC strategies together with their strengths of recommendation and levels of evidence across 10 IPC areas followed by a discussion of current issues. A summary of unresolved issues to inform future research is also provided.

### Search strategy and selection process

Two reviewers (EB, TF) conducted an internet search (with the Google search engine) in July 2015 of publicly available national or organizational guidelines, related to CDI control (published between 2000 and 2015 and for any health care setting). Keywords used included “*difficile*”, “*clostridium difficile*”, “policy”, “strategies”, “control”, “prevention”, “recommendation”, “guideline”, and “protocol.” Guidelines were defined as documents with systematically developed statements to assist practitioners and patients to make decisions about appropriate health care for specific clinical circumstances [20] or documents guidance from professional entities, which described IPC guidance and strategies for CDI. We retrieved the most updated and/or comprehensive documents principally from national departments/ministries of health and the websites of professional societies including those members of the International Federation of Infection Control. No language restrictions were applied. GoogleTranslate was used as the

main translation tool for documents in languages other than English, Spanish, and Romanian (which were read directly by reviewers). Manuals containing generic HAI guidelines and documents with guidelines for treatment or policies of individual hospitals were not included. Structured abstraction of the recommendations from guidelines was conducted independently by the two reviewers and compared for 10 areas relevant to CDI–IPC, drawing from previous work [16,21,22].

### Presentation of results

For each area, we first present a brief description of the guidance identified, followed by a summary of the quality of evidence assessment and strength of recommendations identified in the guidelines (see below). We then present a discussion of current literature supporting recommendations or an overview of relevant issues.

### Quality of evidence and strength of recommendations

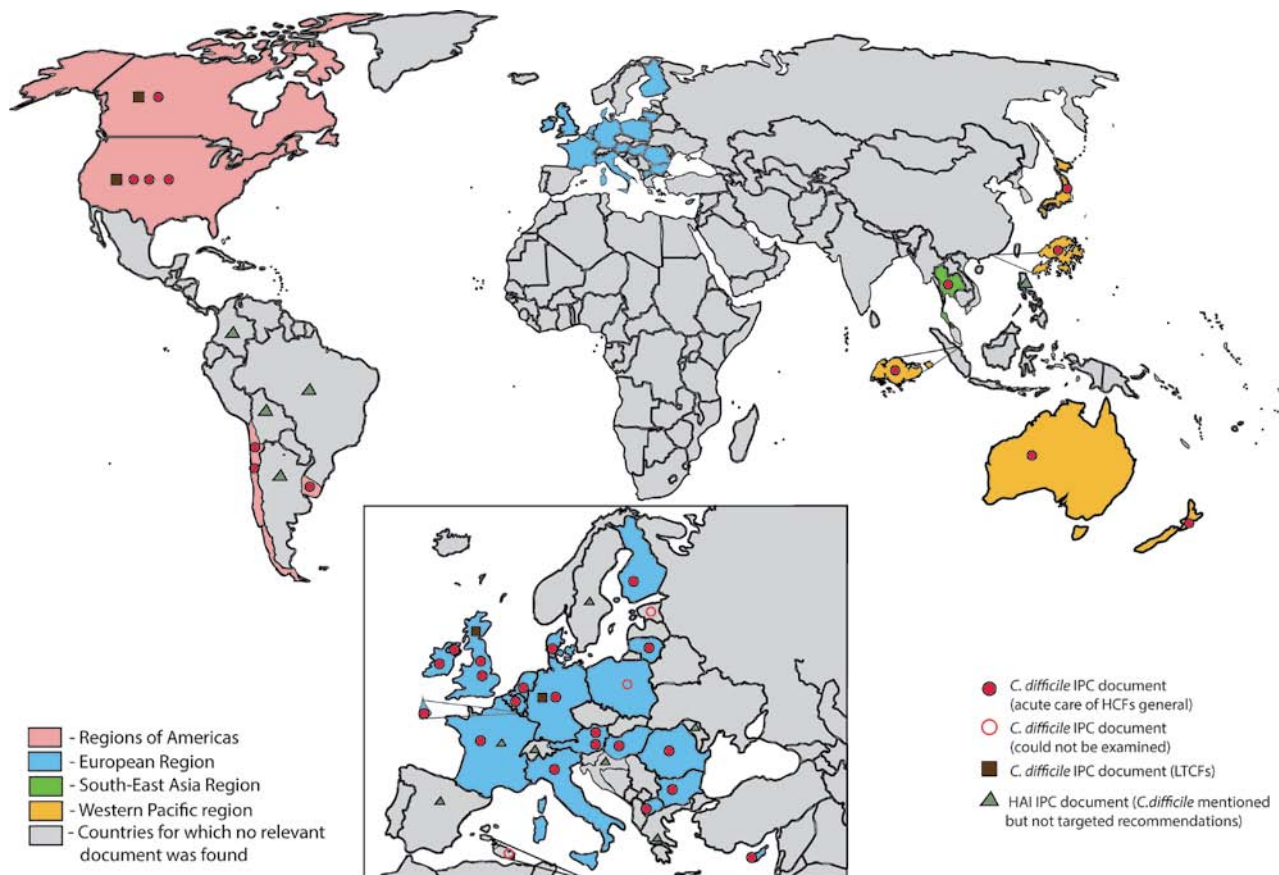
Seven documents graded the quality of evidence [23–29] (four ranking systems used) and nine provided strength of recommendations [23,24,27–33] (five ranking systems). The data quality categories of the ranking systems were broadly similar, and were grouped in three descriptive categories (high, medium, and low). The strength of recommendations for implementation were grouped into the following categories: *strong recommendation* (two levels differentiated by quality of supporting evidence); *recommended*, *consideration*, and *legal requirement*. Strategies were also classified as *Basic*, *Special* (ie, likely to reduce risk but concerns exist about undesirable outcomes), or *Unresolved Issue/Area of Research/Inconclusive* in one guideline [26]. (See Appendix S2 in [Online Supplementary Document](#)).

## RESULTS

### Availability of guidance for CDI–IPC

Globally, 42 documents with targeted IPC recommendations for CDI were identified (**Figure 1**). These documents described guidance from 28 different countries/territories in 4 WHO regions. A summary of the main characteristics of these documents is available in Appendix S1 in [Online Supplementary Document](#).

In North America, 2 Canadian government advisory documents [34,35] and 4 documents from US-based professional bodies (3 guidelines [23,26,27], and an implementation guide [36]) were identified. In Europe, documents from government and professional organizations from 18 countries [24,25,28,30–33,37–54] and by the European Centre for Disease Control (ECDC) [29] were reviewed.



**Figure 1.** Geographic distribution of CDI-targeted IPC guidance reviewed. Countries with documents included in the review are colored by WHO regions (see legend left). Regional guidance by professional organizations (ECDC and ASID) are not depicted. Other results from the web-based search are also shown with different symbols (see legend right). Documents from countries with empty red circles were not examined as could not be translated (Poland) or full text could not be obtained (Malta, Latvia) but have previously been assessed [16].

Eleven guidelines reported grading for either the quality of evidence or strength of recommendation for implementation in their statements [23–33]. In the Western Pacific region, descriptive advisory reviews of guidelines by governmental agencies [55–58] and two professional groups (Australasian Society for Infectious Disease (ASID)/Australian Infection Control Association (AICA)) were included [59,60]. In South America, government guidelines from Chile [61,62] and Uruguay (draft) [63] were identified. In South East Asia, a document by a Thai professional organization which combines a review of the literature with a short section (6 items) on the prevention of CDI [64] was identified. No documents were identified from the Eastern Mediterranean or Africa regions.

### CDI-IPC strategies in non-acute care facilities

No specific recommendations were identified for CDI patients in skilled-nursing facilities, such as residential care

and nursing homes, outpatient care, rehabilitation, and long-term care facilities (LTCFs). *C. difficile*-targeted IPC strategies mainly drew from evidence from acute care settings. Four guidance documents were specific to LTCFs and in other nine, recommended strategies were combined with guidance for acute hospitals. Relevant issues and challenges for the prevention of CDI in LTCFs were highlighted including: the vulnerable health status of residents which may pose difficulties in maintaining precautions (eg, cognitively impaired patients [58], frequent stool incontinence [36]); the placement of CDI cases in LTCFs in shared rooms due the limited number of single rooms [36]; and the lack of convenient hand-washing facilities [27,35]. The importance of surveillance, monitoring of outbreaks, and communication between ambulance services and staff in acute care facilities (when residents with CDI needed to be transported) was discussed [58], especially in the light of the under-recognized burden of CDI and imperfect adherence to IPC guidelines in LTCFs (including private and voluntary nursing homes) [25,31].

## Recommended strategies within IPC areas

Approaches to reduce transmission and to minimise host susceptibility by prudent antibiotic use were widely reported, but differences in other areas existed, as shown in **Table 1**, **Table 2** and **Table 3**.

### IPC Area 1: Pharmacological methods

**Antibiotics:** The strong risk posed by antibiotics for CDI was mentioned in the majority of documents (**Table 1** and **Table 2**). Recommendations included: to minimise use among patients already at increased risk, stop any CDI-inciting antimicrobials such as broad-spectrum cephalosporins (3rd generation), penicillins, fluoroquinolones, and clindamycin in suspected cases [23,24,29], or promoting the implementation of antibiotic stewardship programmes (ASP). Few documents detailed the specific roles and responsibilities of different stakeholders (eg, infection control teams, administration, pharmacists, microbiologists, clinicians, and senior management). Detailed overviews of procedures recommended for establishing, implementing, and monitoring ASP in different settings were also reported [25,31,32,34–36].

**Evidence assessment:** Concordance between the evidence grades given in different guidelines was high. Guidelines strongly recommended the cautious use of antibiotics to prevent CDI and the evidence grade was awarded the highest levels.

**Discussion:** Although one guideline established that available evidence on the effect of ASP did not fully meet all criteria for the highest level of quality (research has mainly relied on before-and-after studies) [26], judicious use of antibiotics was widely recognized as essential for CDI prevention. Despite the limitations in the evidence, the beneficial effect of prudent antibiotic use on CDI is noteworthy. A recent systematic review and meta-analysis quantified the effect of both persuasive (education and guidance) and restrictive (approval required, removal) ASP for CDI [65]. A significant protective role (overall risk ratio 0.48, 95% confidence interval CI 0.38–0.62) was found, with the strongest evidence for restrictive programmes and those with the longest duration. Similarly, another review found that ASP and environmental disinfection were the two most important IPC for CDI in hospitals [18].

ASP require adequate resourcing (human and financial), thus they need to be well designed, integrated, audited, and monitored as parts of larger HAI IPC strategies [66]. Furthermore, the potential effects of utilizing antibiotics considered to be non-CDI-inciting, such as gentamicin, have been raised as important considerations to monitor [67]. Globally, an assessment of ASP showed that although strategies within programmes in 67 countries vary significantly,

commonalities do exist and important challenges demand concerted worldwide action, such as the continuous prospective measurement of well-defined outcomes and appropriate resourcing [68].

**Probiotics:** Several guidelines recognized the suggested use of probiotics for the prevention of CDI. Nine documents labeled it as an *area of research* or declared *no recommendation can be made*. Others mentioned probiotics within descriptions related to CDI treatment and their potential role in preventing recurrences of CDI, but offered no formal recommendation (**Table 1** and **Table 2**).

**Evidence assessment:** One guideline [23] stated that moderate evidence existed supporting the use of two probiotics to decrease the incidence of antibiotic-associated diarrhea, but quality of evidence was low for CDI.

**Discussion:** Recently, a group of experts proposed a statement recommending utilization of two specific probiotics (*L. acidophilus* CL1285 and *L. casei* LBC80R) for CDI [69]. Although systematic reviews and meta-analyses report a protective effect of probiotics [70–72] and some publications reviewed here mention their potential use, studies exploring the contribution of probiotics to CDI prevention are largely limited by high heterogeneity between studies, high risk of bias, inadequate study power or significant levels of missing outcome data [26]. In light of these limitations in the evidence base, guidelines that systematically graded evidence stated that current scientific evidence on probiotics' effect on CDI is insufficient to recommend their use for IPC.

**Gastric acid suppressants:** Guidance indicates that proton pump inhibitors (PPI) and histamine receptor antagonists (H<sub>2</sub>RA) should be considered as important risk factors for CDI but conclude that the issue remains *unresolved* with no official recommendation for CDI (**Table 1**).

### IPC Areas 2–4: Transmission based control measures – patient-care related strategies

#### Isolation of cases

Isolation of CDI cases, confirmed and suspected, was widely recommended together with the use of en-suite bathrooms or individual bedpans. Guidelines also recommended cohorting CDI patients (**Table 1** and **Table 2**), if necessary. The benefits and considerations stated, beyond preventing the spread of *C. difficile* spores, included effective allocation of human and economic resources and the development of specific expertise among dedicated staff managing the isolated patient/cohort. Maintaining contact precautions until at least after diarrheal episodes have stopped (most commonly for 48 hours or longer) was generally recommended. However, extended contact precautions until the discharge

of the CDI case [26,60,63] were also advised. Administrative support and communication were underscored as key factors given that isolation of cases can incur managerial difficulties and costs.

### Personal protective equipment (PPE)

Adequate use of PPE by health care workers caring for CDI cases, particularly gloves and gowns, was consistently and strongly recommended as an important precautionary measure in all documents. Use of PPE by visitors was recommended, but knowledge on the beneficial effect was labeled as an *unresolved issue* [26].

### Hand hygiene

The importance and challenges associated with effective hand hygiene in the context of *C. difficile* IPC were discussed in all documents. Special attention was drawn to limitations of disinfection hand with alcohol-based hand rubs (ABHR) as they are non-sporicidal and do not remove *C. difficile* spores from contaminated hands. Guidance on best practices varied and included the preferential use of soap and water when caring for patients with CDI, especially during outbreaks, raising awareness and warning health care providers about the limitations of ABHRs [38,48,49], or stressing the WHO hand hygiene recommendations and the primary use of ABHR to prevent confusing messages [60].

*Evidence assessment:* The reported quality of the evidence on the protective effect of isolation/cohorting and on the optimum duration of contact precautions for CDI ranged from low to high. Evidence was graded of high quality for outbreak situations, in one guideline [23].

The use of gloves and gowns was strongly recommended, but the quality of available evidence was deemed mixed.

The evidence on the effect of different hand hygiene practices was reported to be of moderate quality and the efficacy and usefulness of disinfection over hand-washing for hand hygiene purposes was reported as an *area of controversy* [26]. These differences in reporting the value of hand hygiene practices stem from research showing that hand-washing with soap and water is the most efficacious way to remove *C. difficile* spores. However, while the use of ABHR alone is not effective, its use does not appear to be detrimental in terms of impacting directly on CDI rates [73].

*Discussion:* It is noteworthy that there is a reliance on evidence from studies of multidrug-resistant organisms to prevent CDI through patient-care strategies [29] and a paucity in studies that have evaluated their efficacy during endemic periods [17,22]. Additional studies are necessary to further clarify the effects of the use of ABHR on CDI and make a more robust conclusion.

Challenges to elucidate the effect of isolation procedures as a means to prevent transmission of CDI will be influenced by each facility's ability to detect CDI cases promptly, availability of isolation rooms, and duration of measures. Nonetheless, recent attempts have been made to provide an estimate of the effect of isolating CDI cases. For instance, a retrospective cohort study reported a 43% (95% CI 7–65%) drop in *C. difficile* acquisition rate in a facility with single-rooms in its ICU wards compared to multi-bed rooms [74]. An increased risk of recurrence (odds ratio OR: 3.77 95% CI 1.37–10.35) among previously cohorted patients has also been reported [75]. Although shedding of *C. difficile* spores and evidence of contamination after resolution of diarrhea has been found [76,77], the effect of longer isolation periods and isolation on the incidence of CDI or risk of transmission remains poorly understood.

Hand hygiene and adequate use of PPE is vital for HAI prevention. Although the use of ABHRs is inadequate to eliminate *C. difficile* spores and hand washing is preferred (a message conveyed in most guidelines), concerns exist about compliance and detrimental effects of mixed instructions for hand hygiene [73]. Recently, a study found that compliance with WHO-recommended practices by health care workers caring for patients with CDI was observed to be approximately 60–70%, with no hand hygiene conducted inside isolation rooms. A higher compliance was observed for the use of gloves (~85–90%) and gowns (~88–97%) [78]. Clearly more research is needed, especially for the effect of different hand hygiene practices on CDI incidence during endemic periods [22], but a stronger emphasis on the use of gloves has been underscored as an important, economical, and potentially more effective measure to prevent *C. difficile* transmission [79].

### IPC Area 5–6: transmission control – environmental contamination

All documents addressed the importance of environmental cleaning to prevent *C. difficile* transmission. Chlorine-based and sporicidal agents were the most commonly recommended solutions. The use of other technologies, including UV light or hydrogen peroxide vapor, was discussed and highlighted as an *unresolved issue* [80,81]. The vast majority of guidelines advised that medical equipment used for CDI cases should be patient-dedicated or disposable, where possible. Commonly reported potential sources of contamination included items that come into direct contact with patients (blood pressure cuffs, stethoscopes, thermometers) or are at risk of contamination due to soiling (beds, furniture, sinks, floor, curtains, etc.). Thorough cleaning of all equipment used after caring for CDI cases or that entered the isolation/cohort room (including dishes and laundry) was also advised. Recommendations explicitly addressing

the role of electronic or rectal thermometers were identified in 17 documents (**Table 1**, **Table 2** and **Table 3**).

*Evidence assessment:* Despite the high level of agreement across guidelines on the use of sporicidal chlorine-based solutions, the optimum type of solution used for environmental cleaning of *C. difficile* was considered to remain as an *area of controversy* [26]. The strongly recommended use of patient-dedicated or of single-use devices was common and guidelines concurred that currently available evidence is of moderate quality (individual randomly-controlled trials and non-randomized studies). The quality of evidence in support of replacement of electronic for single-use disposable thermometers was graded as high/moderate quality.

*Discussion:* Published data on the effect of environmental decontamination with solutions currently recommended to prevent CDI transmission “*have not been consistent*” and the effect of bleach has only been demonstrated in outbreak situations [82] and in combination with other IPC measures. Additionally, concerns about their corrosive properties and potentially harmful effect on the health and safety of staff need to be weighed carefully against the benefits of their use [83]. Beyond the physical environment, attention has been drawn to other potential sources of contamination. For instance, whole genome sequence-based studies have the potential to clarify issues about patient-to-patient transmission including the role of asymptomatic *C. difficile* colonised patients, but more research is needed [77].

### IPC Area 7: education of staff and patients/visitors

Education was defined as instructions, information, training, educational campaigns or workshops for health care facility workers, patients, or visitors on any aspect of CDI-IPC. Over half of the guidelines recommended an education component for education of staff (health care, cleaning, or auxiliary personnel), patients and/or visitors (**Table 1**, **Table 2** and **Table 3**).

*Evidence assessment:* Education was strongly recommended across guidelines, with the quality of evidence for its effect being graded high to low.

*Discussion:* The effect of educational programmes as CDI-IPC interventions has not been fully assessed. However, studies have reported a worrying gap in the knowledge about CDI among health care workers [84–86] and the suboptimal quality of educational materials for patients [87]. Lack of clinical suspicion was identified as a key factor leading to under- and misdiagnosis of CDI cases in Europe [15], which can hinder adequate and timely implementation of IPC measures.

### IPC Area 8–9: case detection and surveillance

Surveillance was recommended at various levels in guidelines: from national, including LTCF/NH [25,31,32] to at least facility-based level with a minimum of hospital-onset health care-associated cases [26,62]. Documents providing information on surveillance recommended the use of standardised case definitions. Most guidelines included a statement or clarifications that discouraged conducting *test of cure*. Over half of the guidelines explicitly recommended against testing or treating asymptomatic patients (**Table 3**).

Regarding testing policies and laboratory assays, the use of standardised criteria (eg, Bristol stool chart [25,31,38]) or definitions ( $\geq 3$  unformed stools in  $\leq 24$  consecutive hours [26]) was reported to identify adequate samples to be tested. However, other documents described, generally, the importance of testing “unformed/diarrheal stools”. Additional strategies included no testing of infants (mainly in Europe), no (or limited) repeat testing. General descriptions were also identified for the use of molecular typing methods for severe cases or during outbreaks. **Table 1** includes information on case detections methods in documents reviewed. Notably, guidelines reported toxin enzyme immunoassays as not suitable as stand-alone, molecular tests were strongly recommended as standard test in the US [23], and multi-step algorithms were generally described in other documents.

*Evidence assessment:* The quality of evidence to not conduct a test of cure after CDI's symptoms resolution was awarded the highest score in Europe, but moderate and low scores in recent guidelines by US-based organizations [23, 26]. Guidelines agree that, currently, there is no evidence to support the detection or routine screening of *C. difficile* among asymptomatic patients, with published studies being of moderate and low quality. The strength of recommendation for CDI-targeted surveillance systems ranged from strong to conditional, and of legal character. Mandatory or legal components regarding reporting of cases were described for the UK, Ireland, and Hungary, compared to recommended laboratory-based sentinel and facility-based voluntary systems in other countries.

*Discussion:* Prompt case detection is vital for the implementation of IPC strategies for CDI. Concerted efforts to better understand and address the burden of CDI, such as for the development of case definitions for surveillance [88] and improved understanding of laboratory tests' limitations [89] and diagnosis procedures have been promoted since the mid-2000s.

The use and implications of differential CDI case detection methods have been described in recent studies [6,15,90,91]. In Europe, it was shown that testing policies varied widely,



**Table 1.** Overview of selected IPC strategies in health care facilities in guidelines and documents reviewed, by IPC area\*

	CANADA	USA	ECDC	AUSTRIA	BELGIUM	BULGARIA	CYPRUS	DENMARK	FINLAND	FRANCE	GERMANY	HUNGARY	IRELAND	ITALY	LITHUANIA	LUXEMBOURG	MACEDONIA	NETHERLANDS	ROMANIA	UK-ENGLAND	UK-N. IRELAND	UK-SCOTLAND	ASIA (AICA)	HONG KONG	JAPAN	NEW ZEALAND	SINGAPORE	THAILAND	CHILE	URUGUAY	USA	CANADA	GERMANY																		
<b>Pharmacological methods:</b>																																																			
Antibiotic stewardship	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓																	
Probiotics		Inc <sup>a</sup> , UI <sup>b</sup> RNM <sup>c</sup>	RNM	† <sup>d</sup>	✓	✓	RNM	†	✓	✓	✓	†	†	RNM	✓	✓	†	✓	†	RNM <sup>f</sup>	†	†	RNM <sup>h</sup> , AR	†	✓	†	†	✓	✓	✓	✓	✓	✓	✓																	
Decrease use of PPI, H2RA		† <sup>d</sup> , UI <sup>b</sup>	†																	✓ <sup>e,f</sup>	†	†																													
Vaccines or immunotherapy		† <sup>c</sup>																		†																															
<b>Contact precautions:</b>																																																			
Isolation room	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓																
Cohorting	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓															
Duration precautions	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓															
Decrease in case movement (transfers)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓															
<b>Personal protective equipment:</b>																																																			
Gloves	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓														
Gowns	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓													
Hand hygiene:	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓													
Wipes (W) Aseptic soap (AS)	✓	W	† <sup>a</sup>	AS; UI										†						AS; AR																															
<b>Environmental cleaning:</b>																																																			
Cleaning solution	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓												
Terminal cleaning	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓												
<b>Contamination sources:</b>																																																			
Individual devices	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓											
Thermometers (no re-use)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓											
Laundry (L)/Dishes (D)	SP	SP <sup>a</sup>	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†	L:AR	D <sup>†</sup>	†	L <sup>†</sup>	L <sup>†</sup>	L <sup>†</sup>	L <sup>†</sup>	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†	†									
<b>Education:</b>																																																			
Staff	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓						
Patients/visitor	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓					
<b>Case detection:</b>																																																			
Test of cure	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
No test if asymptomatic	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓			
No testing infants	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		
Diagnosis algorithm	†	PCR <sup>c</sup> †2-3 <sup>b,b,c</sup>	†	†	†	†	†	†	†	†	†	†	2-s	†	2-s	†	2-s	†	2-3s	2-s <sup>g</sup>	†	2-s	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s	†	2-s		
Surveillance <sup>†</sup>	✓ <sup>v</sup>	✓	§§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§	§		
Molecular methods	§	✓	§§	§	§	†	§§	§	§§	§§	§§	§§	§	§§	§§	§§	§§	§§	†	§§	§§	§§	§§	§§	†	§§	§§	†	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§	§§		
<b>Outbreak management</b>																																																			
	✓	✓ <sup>a,b,c</sup>	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

LTCF – long-term care facilities, AR – area of research, RNM – recommendation cannot be made, UI – unresolved issue, Inc – inconclusive, AICA: Australian Infection Control Association  
 \*Documents (if multiple, per country): a: APIC Association for Professionals in Infection Control and Epidemiology (2013), b: SHEA/IDSA Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (2014), c: AJG American Journal of Gastroenterology (2013), d: Position Statement (2014) e: England (2008), f: England (2013), g: England (2012), h: ASID: Australasian Society for Infectious Diseases (2011). A tick (✓) means that a recommendation is available.  
 †Information available/No detailed recommendations.  
 ‡Some information obtained from other sources (eg, Department of Health websites) v: voluntary, m: mandatory components Diagnosis algorithm: 1–, 2–, 3–step (1–s, 2–s, 3–s): 2 or 3–s: combination of sensitive (eg, Glutamate dehydrogenase) followed by specific test (to confirm toxin: Enzyme immunoassay toxin A or AB, polymerase chain reaction or toxigenic culture).  
 §, §§Molecular methods: § – outbreak, §§ – severe cases.

**Table 2.** CDI–IPC: pharmacological agents and transmission control (patient–care related)\*

	IPC AREA							
	Pharmacological methods		Contact precautions			Personal protection		Hand hygiene
	Antibiotic stewardship	Probiotics	Single room	Cohort-ing	Duration (based on cases' diarrhea)†	Gloves	Gowns	
<b>Acute care – North America:</b>								
Canada (2013)	✓		✓	✓	R or NI	✓	✓	S/W (preferably at point-of-care or as soon as sink is available or ‡) ABHR
APIC (2013)	✓	Inconclusive	✓	✓	R>48h	✓	✓	S/W and ABHR, or ABHR (endemic)
SHEA/IDSA (2014)	(II, Basic)	UI	(III, Basic)	(Basic)	R or R>48h (Basic), if ‡: D (III Special)	(II Basic), UI	(III Basic), UI	WHO 5 moments, if ‡, S/W, ABHR
AJG (2013)	<b>Strong (H)</b>	RNM <b>Strong (L)</b>	<b>Strong (H)</b>	<b>Strong (H)</b>	R; <b>Strong (H)</b>	<b>Strong (M)</b>	<b>Strong (M)</b>	S/W <b>Strong (M)</b>
<b>Acute care – Europe:</b>								
ECDC (2008)	<b>IA (1a)</b>	RNM	<b>IB (1b, 2b)</b>	<b>IB (1b, 4)</b>	R>48h; <b>II (4)</b>	<b>IB (1b, 2b)</b>	<b>IB (1a, 1b, 4)</b>	S/W (not ABHR alone), <b>IB (2a, 2b, 2c)</b>
Austria (2007)	<b>IA (1a)</b>	Tx, R–CDI, PS	<b>IB (1b, 2b)</b>	<b>IB (1b, 4)</b>	R>48h; <b>II (4)</b>	<b>IB (1b, 2b)</b>	<b>IB (1a, 1b, 4)</b>	S/W and ABHR (limitations), <b>IB (2a, 2b, 2c)</b>
Belgium (2008)	✓		✓	✓	R>48 or 72h; <b>(Level 2)</b>	(Level 1)	(Level 1)	S/W and ABHR
Bulgaria (2009)	✓		✓	✓	R>48h	✓	✓	S/W
Cyprus (2014)	✓	RNM	✓	✓	R>48h	✓	✓	S/W, ABHR after S/W (limitations)
Denmark (2011)			✓	✓	R>48h	✓	✓	S/W, ABHR (limitations)
Finland (2007)			✓	✓	R>48h	✓	✓	S/W then ABHR (limitations)
France (2010)	✓		✓	✓	R	✓	✓	S/W then ABHR (limitations)
Germany (2009)	✓		✓	✓	R>48h	✓	✓	S/W (preferred and if soiling), ABHR
Hungary (2011)	IA, IB, IC	Tx, R–CDI	IB	IB	R>72h <b>II</b>	IB	IB	S/W and ABHR; <b>IB</b>
Ireland (2014)	✓	Tx, R–CDI	(C–D)	(D)	R/R>48h (D)	(A)	(D)	S/W (A)
Italy (2009)	<b>IA (1a)</b>	RNM	<b>IB (1b, 2b)</b>	<b>IB (1b, 4)</b>	R>48h <b>II (4)</b>	<b>IB (1b, 2b)</b>	<b>IB (1a, 1b, 4)</b>	S/W; not ABHR alone; <b>IB, (2a, 2b, 2c)</b>
Lithuania (2011)	✓		✓	✓	R>48h	✓	✓	S/W
Luxembourg (2007)	✓		✓	✓	R	✓	✓	S/W then ABHR
Macedonia (2014)	✓	Tx, R–CDI	✓	✓		✓	✓	S/W, ABHR (limitations)
Netherlands (2011)	✓		✓	✓	R>48h	✓	✓	S/W, (ABHR not added value)
Romania	✓	Tx, R–CDI	✓	✓	R>48 or 72h	✓	✓	S/W, no AB–solutions
England (2008)	B	RNM <sup>2013</sup>	B	B	R>48h C	A	A–B	S/W then ABHR A
N. Ireland (2008)	✓		✓	✓	R>72h§	✓	✓	S/W (ABHR limitations)
Scotland (2014)	IA, IB, II	Tx, R–CDI: insufficient evidence	IB	IB	R>48h <b>II</b>	IB	IB	S/W (not ABHR alone), <b>IB (staff); II (visitors)</b>
<b>Acute care – Western Pacific:</b>								
ASID/AICA (2011)	✓	RNM <sup>PS</sup>	✓	✓	R>48h, if ‡:D	✓	✓	WHO 5 moments, Primary use ABHR, If soiled: S/W
Hong Kong (2014)	✓	AR	✓	✓	R or NI	✓	✓	WHO recommendations, S/W
Japan (2008)	✓	✓	✓	✓		✓	✓	S/W
New Zealand (2013)	¶		✓	✓	R>48 h§	✓	✓	WHO 5 moments, S/W or ABHR, if ‡: S/W and ABHR
Singapore (2013)	¶		✓	✓		✓	✓	S (antiseptic)/W or ABHR
<b>Acute care – South East Asia:</b>								
Thailand (2009)	✓	Tx, R–CDI				✓		S/W
<b>Acute care – Latin America:</b>								
Chile (2012–13)	✓		✓	✓	R or D	✓	✓	S/W
Uruguay (2015)	✓		✓	✓	D	✓	✓	S/W
<b>Long term care:</b>								
SHEA (2002)	A–B (I, II, III)	RNM	<b>B (III)</b>	✓	R	<b>A (I)</b>	RNM	S/W or antimicrobial agent ; <b>B (III)</b>
Canada (2013)	✓		✓	✓	R or NI	✓	✓	S/W (preferably at point-of-care or where sink is available, or if ‡), ABHR
Germany (2012)			✓	✓	R>72h	✓	✓	S/W and ABHR

APIC – Association for Professionals in Infection Control and Epidemiology, SHEA – The Society for Healthcare Epidemiology of America, IDSA – Infectious Diseases Society of America, AJG – American Journal of Gastroenterology, ECDC – European Centre for Disease Prevention and Control, ASID – Australasian Society for Infectious Diseases, AICA – Australian Infection Control Association, S/W – soap/water, ABHR – alcohol–based hand rub, AR – area of research, PS – position statement, UI – Unresolved issue, R–CDI – prevention of recurrent CDI, Tx – treatment, RNM – recommendations cannot be made

\* If grading of evidence available: **Strength of recommendations bold font**; (Quality of evidence). Type of documents and scope of included documents vary: eg, Denmark, Finland, and the Netherlands focus on hygiene. Table adapted from Martin et al [16]. Strong recommendations: **IA–IB, A–B, Level 1, I–II**; To be considered: **II, C, Level 3, III**. Quality of evidence grading: High: (1a–1c), (H), (I), (A); Medium–Low: (2a–4), (M–L), (B), (II–III), (B–C); Expert opinion: 5; D.; Legal: IC. A tick (✓) indicates recommendation available.

† Lifting of contact precaution measures: case diarrheal status: resolved (R) or non–infectious (NI) or period (hours) after symptoms resolved, (D) Discharge.

‡ Outbreak.

§ Bristol Stool chart.

¶ Information available/No detailed recommendation.

**Table 3.** CDI–IPC strategies for transmission control (environment), education, and case detection\*

	Environmental cleaning†	IPC AREA							Out-break
		Medical equipment		Education		Case detection		Surveillance‡	
		Patient–dedicated or single–use	No electronic (E) or rectal (R) thermometers	Staff	Visitors/patients	No test of cure	No testing/treating asymptomatic patients		
<b>Acute care – North America:</b>									
Canada (2013)	S, C [1]	✓	E	✓	✓	✓	✓	✓	✓
APIC (2013)	C§	✓	E, R	✓	✓	✓	✓	✓	✓
SHEA/IDSA (2014)	S§, C (III) UI	✓	E	(III, Basic) UI	(III, Basic)	(III, Basic)	(II)	(III Basic)	✓
AJG (2013)	S§, C; <b>Strong (H)</b>	<b>Strong (M)</b>	E; <b>Strong (M)</b>	<b>Strong (M)</b>		<b>Strong (M)</b>	<b>Strong; Test: (High); Tx: (Low)</b>	<b>Conditional (M)</b>	✓
<b>Acute care – Europe:</b>									
ECDC (2008)	S, C [1]; <b>IB (2b, 2c)</b>	<b>IB (1b)</b>	E; <b>IA (1b, 2b)</b>	<b>IA (1a, 2b, 4, 5)</b>		<b>IA (1a)</b>	<b>IB (2b, 3b, 4)</b>	<b>IB (2b, 3b, 4, 5)</b>	✓
Austria (2007)	S; <b>IA [1]</b> <sup>¶S</sup>	<b>IB (1b, 2c, 4)</b>	R; <b>IA (1b, 2b)</b>	<b>IA; (1a, 2b, 4, 5)</b>	¶¶	<b>IA (1a)</b>	<b>IB (2b, 3b, 4)</b>	<b>IB (2b, 3b, 4, 5)</b>	✓
Belgium (2008)	C [1,2]	(Level 1–2)		✓	✓		✓	✓	✓
Bulgaria (2009)	S, C, not alcohol	✓				✓			
Cyprus (2014)	C [1]	✓	R			✓	✓		
Denmark (2011)	C [1]	✓	R		✓				
Finland (2007)	C [1,2]	✓		✓	✓	✓	✓	✓	
France (2010)	S, C	✓	**		✓	✓	✓	✓	✓
Germany 2009)	S, C, peracetic acid	✓		✓	✓	✓	✓	✓	✓
Hungary 2011)	S, C; <b>IB–IC</b>	✓	E; <b>IA</b>	<b>IA</b>		<b>IA</b>	<b>IB</b>	<b>IB–IC</b>	✓
Ireland (2014)	C [1] (D)	✓		(D)	(C–D)	(D)	(D)	(B)	✓
Italy (2009)	C [1]; <b>IB (2b, 2c)</b>	<b>IB (1b)</b>	E,R; <b>IA (1b, 2b)</b>	<b>IA (1a, 2b, 4, 5)</b>		<b>IA (1a)</b>	<b>IB (2b, 3b, 4)</b>	<b>IB (2b, 3b, 4, 5)</b>	✓
Lithuania (2011)	C	✓		✓	✓		✓		
Luxembourg (2007)	S, C	✓					✓		
Macedonia (2014)	S, C	✓					✓		
Netherlands (2011)	C	✓						✓	✓
Romania	D, S,C [1], other ††	✓	E		✓	✓	✓		
England (2008)	C [1]; <b>B</b>	<b>B</b>	E	A–C			<b>B</b>	Mandatory <b>B</b>	✓
N. Ireland (2008)	C or D/C [1]	✓		✓	✓	✓	✓	Mandatory	✓
Scotland (2014)	C [1]; <b>IB</b>	<b>IB</b>	E; <b>IA</b>	<b>IA</b>		<b>IA</b>	<b>IB</b>	Mandatory	✓
<b>Acute care – Western Pacific:</b>									
ASID/AICA (2011)	S, C [1], if ¶: FM, 1–step: D/S	✓	R	✓	✓	✓	✓	Min: Facility	✓
Hong Kong (2014)	✓	✓	**	✓	✓		✓	Facility	✓
Japan (2008)	✓	✓							
N. Zealand (2013)	S, D/C [1]	✓			✓	✓			
Singapore (2013)	S, C [1]	✓	E, R						
<b>Acute care – South East Asia:</b>									
Thailand (2009)	S, C, other ††	✓		✓					
<b>Acute care – Latin America:</b>									
Chile (2012–13)	S, C [1,2]	✓		✓	✓		✓	Facility based	✓
Uruguay (2015)	C [1,2]	✓		✓	✓	✓	✓	✓	✓
<b>Long term care:</b>									
SHEA (2002)	S, C; <b>B (II)</b>	<b>B (III)</b>	E; <b>A (II)</b>	<b>B (III)</b>		<b>B (II)</b>	Tx: <b>A (I)</b>	<b>B (III)</b>	
Canada (2013)	S, C [1]	✓	E	✓	✓	✓	✓	✓	✓
Germany (2012)	S: no alcohol; ammonium	✓			✓	✓		✓	

APIC – Association for Professionals in Infection Control and Epidemiology, SHEA – The Society for Healthcare Epidemiology of America, IDSA – Infectious Diseases Society of America, AJG – American Journal of Gastroenterology, ECDC – European Centre for Disease Prevention and Control, ASID – Australasian Society for Infectious Diseases, AICA – Australian Infection Control Association, UI – Unresolved issue

\*Type of documents and scope of included documents vary: eg, guidelines from the Netherlands and Denmark focus on hygiene. Table adapted from Martin et al [16]. If grading of evidence available: **Strength of recommendations bold font**; (Quality of evidence). A tick (✓) indicates recommendation available. Strong recommendations: **IA–IB, A–B, Level 1, I–II**; to be considered: **II, C, Level 3, III**. Quality of evidence: High: (1a–1c), (H), (I), (A); Medium–Low: (2a–4), (M–L), (B), (II–III), (B–C); Expert opinion: (5); (D); Legal: (IC).

†Cleaning solutions/methods: C: Chlorine–based; S: Sporicidal; D: Detergent; FM: Fluorescent markers. [Chlorine–based concentration] 1: at least 1000 ppm; 2: 5000 ppm

‡Some information obtained from other sources (eg, Department of Health website).

§EPA–approved.

¶Outbreak.

\*\*Information available/No detailed recommendation.

††Alkaline glutaraldehyde, ethylene.

a factor that contributed to a large number of CDI cases being missed on a daily basis. A notable exception was the UK, where both under- and misdiagnosis is uncommon, as national guidelines have been introduced to standardise laboratory diagnosis including confirmatory procedures [15,43]. In the US, 43% of 120 laboratories surveyed used molecular assays as first- or second-line for diagnosis of CDI, similarly to the percentage using enzyme immunoassay tests alone (42%) [91]. In this survey, use of molecular tests was more likely to be accompanied by higher rejection rates for unnecessary testing (ie, formed stools, test for cure, or duplicates within 7 days). Although faster molecular methods have the potential to reduce isolation costs and treatment delays as compared to multi-step algorithms, the unknown proportion of cases diagnosed by high-sensitive molecular tools who may not be CDI cases needs careful consideration as inconsistent results have been found on the impact confirmatory procedures can have on clinical practice [89,92]. False positives can lead to unnecessary implementation of IPC measures and treatment (which in itself increases the risk of developing CDI due antibiotic use) and distort the epidemiological picture of burden of disease.

### IPC Area 10: outbreak management

Over half of documents included a labeled and separate section for recommendations during outbreaks or periods of increased incidence [23-25, 28-30, 32-37, 44, 45, 49, 54, 60, 62, 63]. Case definitions of outbreaks were not clearly reported in most guidelines. Surveillance systems were recognized as an essential tool to identify and monitor outbreaks [26]. Two formats for case definition of CDI outbreaks were identified:

- Definitions based on exceeding triggers based on local CDI epidemiology (hospital or ward's, as available) [25,34,35] with the addition of a specified period of time criteria [29] (eg, expected incidence of CDI exceeded for 1 [62] or 2 [32,63] weeks in a specific area).
- Defined thresholds and criteria (eg, 3 or more cases of hospital-acquired CDI for 2 weeks in a specific area [44]; 2 or more cases caused by the same strain over a defined period and related in time and place [31]).

IPC recommendations in different guidelines for outbreaks ranged in detail and depth but most convey a common message: during CDI outbreaks, all IPC measures should be enhanced. Additional key recommendations during outbreaks included:

- Promoting timely communication between healthcare workers and other infection prevention and control efforts.
- Assessing antibiotic prescribing and environmental cleaning practices to prevent further use of high-risk

CDI antibiotics and ensure high quality control of decontamination.

- Collecting samples for molecular typing of CDI cases to determine if outbreak is associated with hyper-virulent strains (eg, 027, 176, or 078) (Table 1).
- As resources and logistics allow, setting up dedicated administrative systems to manage admissions and staff to CDI-affected wards.

Documents lacking a clear section for IPC of outbreaks, drew attention to specific strategies by differentiating best practices during outbreaks as compared to endemic periods (eg, environmental cleaning – increase frequency [52] or hand washing practices [58] – consider restricting hand hygiene to handwashing with soap and water) (Table 1, Table 2 and Table 3).

### Prevention of CDI and the need for coordinated strategies

Implementation of general HAI IPC strategies is crucial to minimise risk of CDI and, as this review shows, several targeted efforts for *C. difficile* exist. Furthermore, clear and consistent guidance is needed to integrate CDI prevention efforts into larger HAI-control programmes effectively. We reviewed documents with CDI-IPC recommendations in 28 countries and found a general consensus on a selected number of strongly recommended strategies: prudent use of antimicrobials, adequate environmental cleaning with agents with sporicidal effects, time-sensitive isolation, and barrier methods for staff including gowns and gloves. However, we also some noted important variations.

Differences in availability of strategies in documents were found, which can be explained by differences in the scope and type of documents, the recognized CDI burden, health care systems infrastructures, and national legislation requirements. However, varying or imprecise guidance suggests that there is still room for further primary studies but also greater harmonisation of CDI-IPC guidelines, namely in the assessment of the quality of the evidence. For instance, clear recommendations on most accurate laboratory algorithms can be provided rather than descriptions of available methods. Such guidance has the potential to promote best and standardised practices but also raise awareness of the limitations of the alternatives and inform allocation resource for IPC. Optimum CDI case detection methods are changing and updated guidelines will soon become available [93]. Due to the systematic methods used to develop guidelines by professional bodies, such as ECDC and SHEA/IDSA, these are important resources from which to draw information for establishing or updating national guidance and achieve a greater international alignment, yet allowing for national matters to be taken into consideration.

In light of previous widespread of *C. difficile* hyper-virulent strains, a clear section with detailed measures for endemic and epidemic periods should be available in guidelines, to address the burden of CDI effectively. We found a general absence of such distinction in half of the documents, as well as differential appraisal of the quality of evidence for key strategies (eg, the effect of isolation during epidemics was graded mixed to high). Our review underlines previous findings of a lack of uniformity in the assessment of evidence in guidelines [16] and suggests a need for stronger international alignment of CDI-IPC guidance guided by an objective assessment of the literature.

Agreement about best practices across guidelines has been indispensable for advancing efforts in an integrated manner on the role of antibiotics, which could also enable coordinated efforts in other areas. The CDC's recent recommendations for both acute health facilities [66] and LTCFs [94] are significant resources informed by CDI-IPC efforts. Future studies on the effect of the introduction of ASP and close monitoring of the effect of previously considered "low risk" antibiotics are required to continue informing our understanding of antibiotics and CDI. It is imperative that coordinated efforts are undertaken to elucidate strengths and weaknesses of the evidence base and update guidance and convey clear CDI-IPC statements for other areas. For instance, beneficial effects of probiotics for CDI are not supported by high quality studies, as described previously. We identified consensus on the recommendation from guidelines with systematic assessment of the literature, but also ambiguous guidance in descriptive documents. *C. difficile*'s epidemiology continues to evolve and review of guidelines by qualified local professional bodies is necessary to recommend best practices, based on the strongest quality of research. Such exercises have the potential to support the development of context-appropriate tools for different stakeholders, such as checklists, cleaning regimes, or education packages for health care workers (an example [95]), cleaning staff, and patients.

The paucity of guidelines pertinent to different types of health care settings is concerning due to the increased incidence of CDI in the last 20 years. It is also of concern that the overall effect of interventions in high risk settings such as LTCFs is under-recognized, where suboptimal compliance to recommendations has previously been identified [37], where *C. difficile* is a common pathogen causing diarrhea [96], and where over-prescription of antibiotics is prevalent. In the USA, over 4 million Americans reside in LTCFs and a substantial majority (70%) are at increased risk of CDI due to high use of antibiotics in this setting (40–75% prescribed incorrectly) [94]. It is important to adapt guidance based on acute care settings experiences with evidence from interventions in LTCF and nursing homes [96,97]. We recommend high quality studies on the

effect of IPC strategies in nursing homes and LTCFs are synthesized, appraised, and as possible, incorporated into guidelines to inform targeted IPC of CDI efforts.

Beyond single and targeted strategies, organizational accountability, mentioned in few of the guidelines, demands particular attention as it is essential for development of country-specific implementation of strategies. Stakeholders' roles and responsibilities, including that of governments and senior management staff, need to be clear and informed by evidence relevant to national structures. For instance, in the UK, investigations on significant recent outbreaks have resulted in reports with recommendations which inform the roles of responsibilities of care and management staff [98,99]. Recognition of gaps in the system enabled development of new guidance, such as procedures to capture *C. difficile*-associated deaths, and detailed methods to strengthen coordination of IPC teams.

### Bundles for prevention and control of CDI

Available evidence indicates that multi-faceted programmes of CDI prevention have the potential to be substantially effective and cost-saving. In the UK, CDI-IPC strategies include legislative support (ie, mandatory national surveillance systems and wider organizational accountability, including defined roles and responsibilities for all groups of health care staff and senior management), hand and environmental hygiene campaigns, and optimised testing/diagnosis techniques [7]. In addition to cost savings, quality improvement in health care and patient safety are also major priorities. Based on this comprehensive IPC approach, the estimated cost reduction associated with a decrease in the number of CDI cases (5–15%) ranged from GBP 4.65–13.94 million [100]. In the United States, a recent study estimated that if basic recommendations by the SHEA/IDSA were introduced nationally, over 5 million CDI cases among patients 65 years of age or older would be averted during a 5-year period. This reduction in number of cases would result in US\$ 2.5 billion of savings [19]. Of note, this study adopted a conservative economic model which estimated the cost of isolation until discharge, rather than until symptom resolution.

### Emerging topics and the need for more research

**Box 1** presents a summary of research questions as identified in the documents reviewed. The need for innovative prevention technologies and more effective cleaning solutions were discussed. High quality studies on the effect of interventions such as the use of case notification systems, on the potential roles of different health care workers in detection of cases and implementation of IPC, and on unresolved issues were recognized as important areas of research.

**Box 1** CDI prevention and infection control emerging topics and future steps**Area of controversy**

- Ability of diluted sodium hypochlorite or other sporicidal agents used for environmental decontamination [26].
- Reliance on alcohol-based hand hygiene products [26].
- Management, including detection or isolation, of patients colonized (asymptomatic) with *C. difficile* without CDI history [26,45].

**Unresolved issues (UI) or other (O) strategies identified in guidelines**

Case detection, including roles of different health care workers in CDI-IPC

Notification systems or laboratory-based alert systems

O: Role of community pharmacists [25], medical equipment and health care staff in ambulances [31,58].

UI: Alert for changes in the rate, complications, or severity of CDI that may indicate the introduction of new strains [29] or for cases readmitted or transferred) [26,45].

UI: Role of nurses (standing orders or nurse-driven protocols) [26].

**Transmission control**

O: Use of bleach or cleaning wipes for disinfection or Fluorescent markers or adenosine triphosphate to measure organic material [25,34–36].

O: Development of protocols for disinfection of equipment and environment and monitoring [34,35].

O: Visitor and staff management: visitors/staff with diarrhea should not visit patients in the hospital [45].

O: Facility design (eg, selection of materials for surfaces, adequate number of hand washing facilities) [34,35].

UI: Use of gown and gloves by visitors [26].

UI: Use of soap that contains antiseptic substances [45].

UI: No-touch disinfection technologies as component of IPC strategies (UV, hydrogen peroxide vapor) [26].

**Pharmacological agents**

UI: Use of Vaccines and immunotherapies [32].

UI: Role of probiotics as primary prophylaxis [26].

UI: Restriction of gastric acid suppressants [25,26].

**Education**

UI: On-going assessment of CDI knowledge and intensified CDI education among health care and cleaning personnel [26].

**LTCF Research questions and relevant issues**

Notification of CDI among LTCF residents to relevant staff in the acute care setting if transfer is necessary [25,58].

Attention to CDI cases' activities and placement (shared rooms) [35].

Monitoring compliance with infection prevention and control guidance and adequate implementation of strategies (including diarrheal, outbreaks, and waste management and access to laboratory services) [37].

**The following research questions [27]**

- Are older patients truly at increased risk of acquiring *C. difficile* or CDI? If so, what determinants are responsible?
- Are therapeutic strategies equally effective in older population and in younger adults?
- Are differences between risks for CDI outbreaks explained by variations in antibiotic exposure or are there other factors?
- What are the variables that influence transmission of *C. difficile* between residents in long-term care settings?; What is the role of environment, and patient care practices?
- What level of environmental cleaning, hand hygiene, or glove use is optimal to limit transmission of the organism?
- Are infection control recommendations different for patients with diarrhoea compared with those without?

Notably, there is a need for higher quality and comparable evidence on the attributable effects of existing CDI prevention measures, especially during endemic periods [17,18,22]. Adequate surveillance and improved detection of cases require critical attention, as our review found that differences in approaches exist. Although best practices are still a matter of debate, well-established, resourced, and audited surveillance systems for CDI are essential. Surveillance supported by consistent, clear, and cost-effective laboratory testing practices (including rejection policies) has the potential to inform the effect of CDI-targeted IPC and novel interventions, such as “bundles” or vaccines. Costs associated with implementation of effective surveillance and case detection methods should be assessed in light of the benefits for patients' safety and care. Further, adequate reporting of aspects of infectious control measures is needed in future studies to identify optimum CDI control programmes (eg, dedicated personnel time, laboratory supplies, and outbreak investigations) [18]. We echo previous recommendations that future studies should adhere to the

ORION statement to be able to synthesize evidence in a more transparent and consistent manner [15,18,19], thus support greater harmonisations of CDI-targeted IPC efforts.

Understanding the prophylactic effects of pharmacological methods is an area of great interest for CDI-IPC. Passive immunization to toxins TcdA and TcdB has been tested for the prevention of recurrences. Given its high cost and transient protection, active immunization is currently viewed as a potentially more cost-effective strategy. Both toxoid-based and peptide vaccines are currently under development [101,102]. Another developing area of research is the prevention of recurrent episodes and severe disease outcomes with more effective antibiotics. Recently, a 3–4 fold decrease in CDI recurrence and 28-day mortality was observed in hospitals with routine use of fidaxomicin as first-line treatment, and at a greater rate than in hospitals with selective use of this antibiotic [103]. As burden of disease associated with CDI remains high, cost-effective pharma-

cological methods to prevent incident, recurrent, or severe outcomes represent a key area for targeted IPC.

## Limitations

The present review has limitations. We relied on electronic search methods of publicly available documents. We also relied on translation to examine the full text of several guidelines and one document could not be translated [51]. However, we identified and reviewed a large number of documents obtained through comprehensive searches undertaken by two reviewers. While the interpretation of some of the guidelines' through our review may be influenced by language restrictions, the majority of documents included in analysis are in languages that reviewers manage fluently. Finally, we did not review compliance with national guidelines, treatment of CDI, or strategies not within the 10 selected IPC areas as it was beyond the scope of this review.

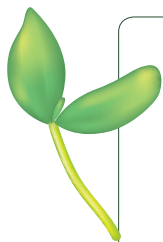
## CONCLUSIONS

Our review findings indicate a widespread awareness of the importance of CDI–IPC guidelines but there are significant gaps which still exist. The review identified published guidelines from regions which have experienced an increase in the incidence of CDI in recent years (such as the USA, Canada, Europe and the Western Pacific) and also countries where epidemiology of *C. difficile* has not been extensively examined (such as Thailand, Chile, and Uruguay). However, we did not retrieve IPC guidelines for CDI from several countries in South America, South East Asia, and Europe and none from Africa and Eastern Mediterranean. We reviewed documents for Bulgaria, Hungary, Macedonia, Poland, and Romania, which were not included in a previous assessment of European guidelines. Our review also found only a few clear and specific recommendations for LTCFs and nursing homes, mainly from North America, Europe and Western Pacific. This represents a

large gap in an important global infection control area. Thus, this review adds to the existing collection of IPC guidance availability for *C. difficile* [16,104] and provides a global overview of approaches and challenges for those interested in developing or revising protocols for CDI prevention and control.

This review of guidelines also highlights the need for greater international harmonisation in the assessment of the evidence underpinning IPC recommendations for CDI and for more research. Key strategies strongly and consistently recommended in published guidelines included: ASP, environmental and medical devices cleaning, use of protective equipment (gloves and gowns), and prompt isolation of CDI cases. Surveillance and education were also strongly recommended. High quality research, other than for high-risk antibiotics, is still needed. Our review shows that much of the evidence underpinning the guidance was graded of medium to low level, by the use of 4 different ranking schemes (assessed only in guidelines from the USA and Europe) and different primary studies were considered in different guidelines. The recommended establishment of surveillance and standardised monitoring systems will help develop comparable studies and better evaluate the effect of interventions on CDI incidence in the future.

Our review of unresolved issues and inconsistently identified strategies indicates that implementation of CDI–IPC measures variations between world regions exist, mainly for hand hygiene and case detection approaches (including laboratory testing policies). Country-specific organizational accountability roles require key attention for successful IPC efforts and control outbreaks associated with *C. difficile*. Strategies on the use of probiotics, gastric acid suppressants, and on the potential roles of IPC stakeholders could benefit from clear recommendations statements. Studies that provide more robust estimates of interventions' effects in high-risk settings such as LTCF and of emerging IPC technologies, such as vaccines, have the potential to inform coordinated efforts and advise priority setting exercises.



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# Linking household and facility data for better coverage measures in reproductive, maternal, newborn, and child health care: systematic review

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**Background** Currently many measures of intervention coverage obtained from household surveys do not measure actual health intervention/service delivery, resulting in a need for linking reports of care-seeking with assessments of the service environment in order to improve measurements. This systematic review aims to identify evidence of different methods used to link household surveys and service provision assessments, with a focus on reproductive, maternal, newborn and child health care, in low- and middle-income countries.

**Methods** Using pre-defined search terms, articles published in peer-reviewed journals and the grey literature after 1990 were identified, their reference lists scanned and linking methods synthesized.

**Findings** A total of 59 articles and conference presentations were carefully reviewed and categorized into two groups based on the linking method used: 1) indirect/ecological linking that included studies in which health care-seeking behavior was linked to all or the nearest facilities or providers of certain types within a geographical area, and 2) direct linking/exact matching where individuals were linked with the exact provider or facility where they sought care. The former approach was employed in 51 of 59 included studies, and was particularly common among studies that were based on independent sources of household and facility data that were nationally representative. Only eight of the 59 reviewed studies employed direct linking methods, which were typically done at the sub-national level (eg, district level) and often in rural areas, where the number of providers was more limited compared to urban areas.

**Conclusions** Different linking methods have been reported in the literature, each category has its own set of advantages and limitations, in terms of both methodology and practicality for scale-up. Future studies that link household and provider/facility data should also take into account factors such as sources of data, the timing of surveys, the temporality of data points, the type of services and interventions, and the scale of the study in order to produce valid and reliable results.

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Access to quality health care is critical in order to ensure better population health outcomes in areas like maternal and child health. Throughout the MDG era, increases in access to services have been observed, but improvement in population health outcomes has not been consistently documented [1–4]. Consequently, much effort has been put towards improving population access to health care; yet adequately measuring the quality of care received remains challenging [5]. Many measures of coverage obtained from household surveys only estimate service contact (eg, coverage of antenatal care) instead of actual service delivery. Even when surveys do attempt to measure content of care (for example, for sick children), this measurement can be inaccurate [6,7]. In many cases, care-seekers are not able to reliably recall or report on different aspects of the quality of care in household surveys [8]; yet this information is important for several reasons. First, in order to improve population health outcomes a minimum level of quality of care must be guaranteed at the point of care. Second, it gives a more comprehensive assessment of the provider–client interaction and allows gaps in the quality of care to be assessed and improved upon. Third, for health planning and program evaluation purposes, it is necessary to measure the proportion of the population that actually receive an intervention with adequate quality.

In response, methods linking household data on care-seeking or service contact to health provider assessment data on service readiness or quality have emerged as a potentially effective strategy for improving coverage measurement. A growing number of studies have employed different linking approaches to either examine associations between the service environment and care-seeking behav-

ior, or seek to improve coverage measures of health interventions. We conducted a systematic review of the literature to document different methods used to link household surveys and service provision assessments in low- and middle-income countries. We also investigated the feasibility, as well as methodological and practical advantages and limitations of the linking methods employed. The primary focus of the review was on reproductive, maternal, neonatal, and child health interventions.

## METHODS

### Search strategy and inclusion criteria

We conducted the literature search using a combination of search terms (**Table 1**), and scanning of reference lists of identified papers. The search was based on the following published databases: PubMed, Medline, JSTOR, Google Scholar, LILACS, and Population Health Metrics, which is a specialist online journal on this topic. Within each database, we used a combination of search terms (eg, “maternal health, service use, link, access to care”), changing one search term at a time. We also did a hand search of the grey literature on websites of the WHO, MEASURE Evaluation project, the Demographic and Health Survey (DHS) program, the World Bank, Carolina Population Center at UNC (UNC/CPC), and Google. Only reports and articles produced in 2004 or later were available on the UNC/CPC website. The search was conducted in English, Spanish, and French. Although the focus of the review was reproductive, maternal, neonatal and child health, we included a few relevant studies examining primary and curative care as they were identified during the search.

**Table 1.** Search terms that were used in the systematic search

TOPIC AREA	HOUSEHOLD/POPULATION-BASED DATA	CONNECTION	FACILITY-BASED ASSESSMENT
[null]	[null]	Link	Access to care
Maternal health	Service use	Linkage	Service quality
Antenatal care	Service utilization	Match	Quality of care
Postnatal care	Help seeking	Combine(d)	Service readiness
Delivery	Care seeking	Merge	Service provision
Childbirth	Doctor visit	Attach	Service delivery
Reproductive health	Clinic visit	Join	Where care was sought
Obstetric care	Facility visit	Pair	Facility survey/data/assessment
Women's health service	Household survey/data/assessment	Connect	
Pregnancy complications			
Postpartum care			
Neonatal care			
Newborn care			
Child health care			
Child immunization			
Sick child visits			
Well child visits			
Family planning			
Contraception			

In order to be included in this review, a study had to meet the following criteria: 1) it was conducted from 1990 to March 2015, because of rapid development of maternal health care since the 1990s; 2) the study was in a low- or middle-income country; 3) household care-seeking information was linked with facility or provider characteristics; and 4) the study addressed coverage of interventions in the above mentioned areas.

## Definitions

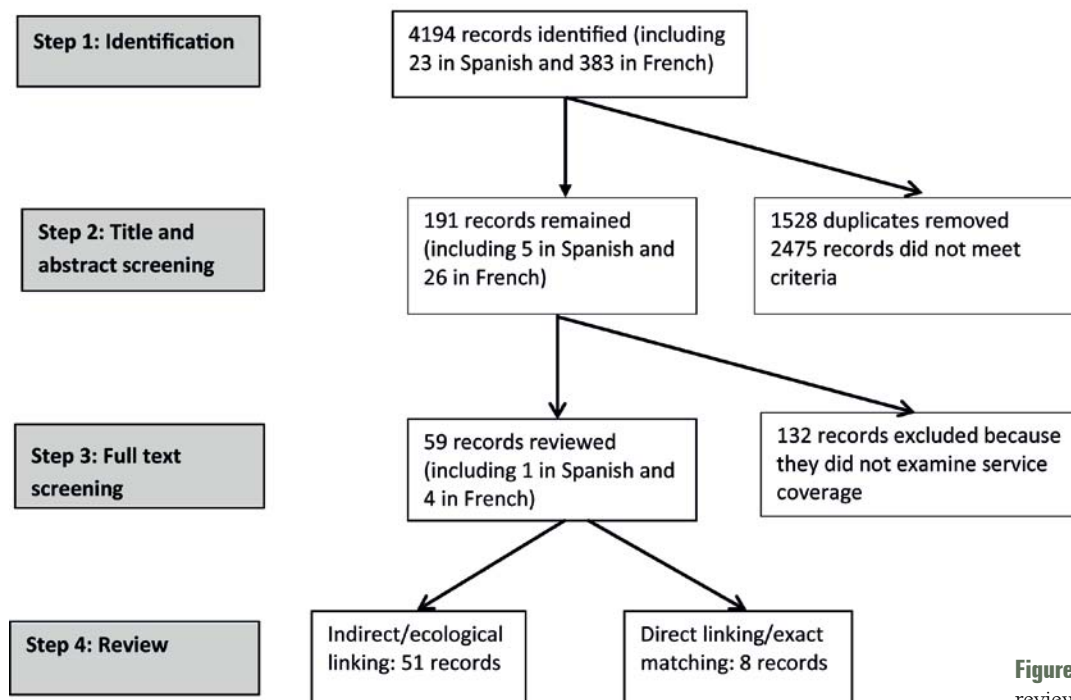
We employed the WHO's definition of coverage which is "coverage of health services can be measured by the percentage of people receiving the services they need" [9]. An intervention coverage indicator would be calculated based on the number of individuals in need of a particular service or intervention (ie, the denominator) and the number of individuals in need who are using or receiving the services (ie, the numerator). It is also important to note that in this review we used "service/intervention coverage" interchangeably with "health care-seeking behavior" since the latter seemed more common in the literature and we were primarily interested in methodologies used to link service and provider's characteristics with individual care-seeking rather than the actual content of health care service or intervention.

## RESULTS

**Figure 1** shows the number of articles identified after each step of the literature search. The initial number ( $n=4194$ ) included a number of articles that turned up in more than

one database. After removing 1528 duplicates, screenings of the title and abstract removed the majority of the articles ( $n=2475$ ), because the studies presented either employed only one source of data (either household or facility). Further full-text screening of the remaining 191 articles resulted in the exclusion of about two-thirds of them because the articles did not examine coverage or service characteristics at the provider or facility level. The remaining articles and conference presentations ( $n=59$ ) were carefully reviewed and categorized into two groups based on the linking method used: 1) indirect/ecological linking that included studies in which health care-seeking behavior was linked to all or the nearest facilities or providers of certain types within a geographical area, and 2) direct linking/exact matching where individuals were linked with the exact provider or facility where they sought care. These articles were summarized in Table S1 in the **Online Supplementary Document**.

Among the studies reviewed, 13 were published in the 1990s; the rest after 2000. The studies were mostly from Asia and Africa, seven were from Latin America and the Caribbean [10–16]. Many ( $n=35$ ) studies were conducted in rural areas of a country or limited to an administrative sub-national region (state or province). Care-seeking behaviors also varied: from curative care for sick adults to family planning, maternal and child care, malaria and HIV related services; they also varied from care-seeking that does not always require visits to a health facility, such as FP knowledge, intention, and use, to interventions that are by default facility based, such as institutional delivery.



**Figure 1.** Flowchart of the review process.

## Linking approach – indirect (ecological) linking

This approach was employed in 51 of 59 included studies, and was particularly common among studies that were based on independent sources of household and facility data like the DHS and Service Provision Assessment (SPA) [17]. With this approach, surveyed households and individuals were often linked to all or the nearest providers of certain types within a geographical area, eg, cluster, local government areas (LGA), local council areas, region or zone. In other words, health seeking behaviors reported in the household survey in a region were linked to provider data that had been aggregated to the same region level [18–20]. The higher level of geographical areas (LGA, region, or zone) was often used if there were a small number of providers within a cluster, or if there were concerns of the representativeness of providers at the lower level [21]. For example, the SPA is not designed to provide representative results on facilities at the cluster level; as a result, in studies that used nationally representative data like the DHS and SPA, provider data for linking were often aggregated to the region or zone level rather than the cluster level. Consequently, surveyed households were not necessarily attached to measures of intervention at the providers from which household member might have realistically sought care.

Linking from households to providers or facilities within a geographical area could also be done using the cluster/area identification where one or many providers within the area were linked to each household in the same area. In some cases, linking was done administratively between households and providers designated to serve each village or cluster [5,22–28] or to the one most frequently used [29]. In other cases, boundaries of the geographical area were established and each household was linked to providers/facilities within their cluster/geographical area and possibly with providers within the neighboring clusters [30]. In the latter, GPS coordinates were often used to establish geographical distances from each household to each of the connected providers [16,31–35]. In general, distances could be calculated as a straight–line distance or travel distance and travel time using the most convenient road(s) as reported by the households or key community members [1,33,36–41]. One study provided a detailed review of four geographical techniques often used to link household clusters with facilities [42]: 1) administrative boundary link, 2) Euclidean buffer link, 3) road network link, and 4) Kernel density estimation link (**Box 1**).

In a small set ( $n=11$ ) of studies in the indirect linking group, physical accessibility was the only characteristic of the service environment measured and linked with household data on care–seeking; no provider assessment was conducted. Each surveyed household was connected with

**Box 1.** Geographical methods used to link household surveys and assessments of service (Skiles, 2013) [41]

Administrative boundary link: health facilities are linked to DHS clusters within the same administrative limit (eg, district).

Euclidean buffer link: each DHS cluster is the center of a 5 km Euclidean buffer (the 5km Euclidean buffer is an approximation for a 1–hour walking maximum distance between the DHS cluster and the health facility). Each cluster is then linked to each facility within this buffer and administrative boundaries are not considered.

Road network link: uses the road network to calculate the distance between each cluster and a facility (only a total distance of less than 15 km between a cluster and a facility is considered a link). The distance from each cluster or each facility to the road should be less than 5 km.

Kernel density estimation (KDE) link: this is a fairly sophisticated GIS–based spatial analysis technique used to distribute a value associated with a discrete point across a plane or continuous surface. This technique assumes that each facility serves a specific catchment area and that the draw on the population to those services decreases with increasing distance from the facility. This “draw” of each facility varies according to the type, size, and availability of services. Therefore, with this technique, it is possible to incorporate facility characteristics and distance decay when estimating the potential draw a facility may have on a population cluster.

one or more nearest health facilities using measures of physical accessibility, regardless of whether they sought care at these facilities [23,24,33,35,43–48]. Physical accessibility was often measured by straight–line distance, driving distance, and walking or driving time.

**Data sources.** In most studies, two independent sources of household and facility data were used. For example, 16 out of 46 studies employed DHS household data, combined with a SPA (or its predecessor Service Availability Module SAM) or a situation analysis [49–54]. In these cases, the scope of the study was usually at the national level or limited to rural areas. Few studies employed data from a population census and a facility census—either at the national level (Zambia) [55] or the district level (Burkina Faso) [22]. The other studies often employed data from household and facility surveys that were conducted as part of a larger project, such as COMPASS (Community Participation for Action in the Social Sectors) in Nigeria [21] or DISH (Delivery of Improved Services for Health) in Uganda [30].

With this type of linking, the proportion of individual reporting care–seeking can be obtained from the household survey, and it may be possible to calculate the percentage of providers who provide a specific intervention. The measure of coverage, however, may be more useful at the pop-



ulation level than at the individual level as each individual is linked to an aggregate measure of service environment. Additionally, if the health intervention of interest was often utilized by the population in a facility's catchment area, it would be reasonable to assume that measures of readiness and quality of care, when aggregated to the facility level, represent the level of care that surveyed individuals received.

The time interval between the household survey and the linked provider/facility assessment varied between studies and by the type of intervention: it ranged from current use of FP to child vaccination of children up to 10 years of age [33]. In the majority of the studies, they were conducted within two years. If they were part of a larger project, like in COMPASS or DISH, they were likely conducted within the same year. In some cases, particularly for studies that relied on secondary data like the DHS and SPA, the gap could be longer: four to five years [19,55–57]; yet because of the 3–5 year recall period often used in the DHS, the actual gap between care-seeking and provider assessment could be shorter if the DHS was linked to an earlier SPA. It is important to note that even when the surveys were conducted in the same year, recall periods in the household survey (eg, antenatal care sought for live births in the five years prior to the survey) meant that the actual gap between measured care-seeking behavior and service characteristics was often wider.

**Limitations.** Limitations of the indirect linking approach were not discussed in all of the studies reviewed but we have identified the following limitations from the different approaches used. A major limitation was that the linked facilities/providers may not be ones that surveyed individuals sought care from as bypassing of facilities is a common phenomenon [32]. Although also applied to direct linking, the time interval between surveys was mentioned as a limitation in linking in several studies as many characteristics of the service environment, eg, supply and medicine stock-outs may change rapidly over time [15,16,42,56,57]. Another limitation was that the surveyed facilities may not represent the entire market of services that individuals can choose from [21,22,57–59]; this was particularly important for interventions like FP, ANC, child immunization, etc. as individuals can obtain the intervention from providers outside of the formal health sector and therefore not included in most service assessment. In addition, administrative linking using cluster identification may also be susceptible to errors due to mis-identification and displacement of cluster and cluster boundaries [12,60]. Finally, several limitations related to the use of geographical distances were mentioned, including that straight-line distances did not take into account differences in terrains and transports [15,38,55,56].

## Linking approach – direct linking (exact matching)

Only eight of the 59 studies included in this review employed direct linking methods. In this case, individuals were linked with the exact provider or facility where they sought care from. This type of matching was typically done at the sub-national level (eg, district level) and often in rural areas, where the number of providers is more limited compared to urban areas. The type of health services/interventions varied, from sick care for adults or children to child vaccination, and delivery care. On the service provision side, a number of measures of service availability, access (including physical access, hours of operation), and readiness (availability of drugs, equipment, trained providers) were used. Studies did not always assess the actual quality of care that individuals interviewed received in the past. Instead, provider-client interactions were observed on a separate sample of clients, independent of those interviewed in the household survey. A necessary assumption is that the quality of care does not substantially change during the period between the household and the facility surveys.

Although two sources of data were typically used, the sequencing of data collection varied between studies. In the first approach, data were first collected on readiness and/or service quality from clinics, then facility records were used to identify patients (adults or children) who would then be followed up at home. This approach was employed in four studies [61–64]. A limitation of this approach was the possibility of self-selection bias amongst care-seekers, which means that those who sought care at these providers were different from those who did not seek care or sought care elsewhere in many characteristics. Another limitation is the potential underestimation of some indicators; for example, one study [63] reported that even if facility records showed that some children missed immunization shots, they might have received the shots elsewhere as families could move around. Consequently, this data cannot be used to produce estimates of coverage at the population level.

In three studies [13,65,66], the opposite approach was adopted: individuals who sought care were first asked for the names of specific facilities from which they sought care and these facilities were subsequently surveyed. For instance, in the Ghana study, women of childbearing age in a demographic surveillance district were matched with health facilities where they reported having received delivery and post-partum care for all live births during a one year period; the data were then linked with a census of all health facilities within the district [65]. Similarly, in the Kenya study, women were linked to the facility that they reported having received services from last [66]. Another study [67] employed a similar approach but using existing data: all children under five at a demographic surveillance site were

linked to clinic visits using a unique identification number. An apparent strength of the Ghana study relative to the others was that data were collected from all live births and all health facilities in the district [65,67]. On the other hand, the use of a demographic surveillance site in these two studies has implications for the replicability of the approach.

## DISCUSSION

There is a growing body of research in which household survey data are linked with provider assessments: 59 articles have been published in peer-reviewed journals or in the grey literature since 1990. It is noteworthy that most of the reviewed studies aimed to examine the associations between service environment characteristics and care-seeking behavior at the individual or household level rather than trying to better understand intervention coverage, ie, the proportion of individuals in need of an intervention who actually receive it with adequate quality. These linked study designs present a number of complex methodological issues, which we discuss below with particular attention to how these issues might affect the use of linking designs to estimate intervention coverage.

This review highlights two major linking methodologies: indirect/ecological linking and direct linking/exact matching. Most studies that sought to link household survey and service provision data used indirect or ecological linking, generally using two independently collected and sampled data sources linked at national level. We found eight studies that employed direct linking or exact matching. Unlike for indirect linking, these studies were generally conducted at sub-national level, often in rural settings where the provider mix was less complex. In addition, the data sources used for direct linking were not independent.

These two linking approaches have trade-offs in terms of ease of implementation and usability of the data. Indirect linking appears less expensive and simpler to use than direct linking. In most cases, the indirect linking studies used two independent samples of households and facilities, such that both samples could be designed to be representative of a geographic area. Cautions need to be exercised, however, if one is to use nationally representative data like the DHS and SPA, as these surveys are often not designed to be representative at a level lower than region. Independent sampling also simplifies implementation, as the sampling for one survey does not depend on the other. However, one drawback of this approach is that, since the surveys are sampled independently, it is possible that households may be linked to providers that are not representative of the providers used by the household. A second limitation is related to bypassing of facilities, meaning that individuals do not always seek care from the nearest provider or one

that is designated to serve the area, and in fact may travel quite a distance to a provider that is perceived to provide better quality of care. If geographical linking of individuals to the nearest providers is used in a setting where bypassing is prevalent, the results may be invalid. For studies that use DHS data, in which there is geographical displacement of clusters, linking of individuals to the nearest providers may also produce invalid results; instead linking by administrative boundary methods may be less affected by the displacement [42]. In general, there is a need for further validation of indirect linking methods as compared to direct linking, particularly as relates to coverage measurement. While we assume here that ecological linking is less likely to produce valid results than direct linking, there have been no head-to-head comparisons of the two methods in the same population.

Unlike indirect linking, the objective of direct linking is explicitly to link an individual to his/her actual source of care. Thus, many of the limitations of indirect linking do not apply to direct linking. However, this approach has a number of limitations related to sampling. In this review we saw two approaches to linked sampling: either households were sampled from registers at health facilities, or else health providers were sampled based on sources of care reported by households. The first case would yield a sample of households that is not representative of the general population, meaning that this approach cannot be used for estimating population-based intervention coverage. The second case would yield a sample of providers that is not representative of the universe of providers, but would allow for population-based measures, as households are sampled to be representative of the population. In either case, the requirement to link the sampling for the two surveys is likely to complicate data collection.

Although linking is potentially a promising approach for estimating intervention coverage, it cannot be used for all interventions. In order for linking to be useful, it must be possible to measure care-seeking for the intervention through a household survey, and the intervention must be delivered through a recognized provider that can be sampled. If the intervention does not always require a visit to an identifiable provider, this method may not be useful. For example, family planning users do not have to go to a clinic or even a pharmacy to obtain condoms or oral pills. In many settings, self-treatment for a sick child or adult may be common, and treatments may be obtained from shops and informal vendors in addition to pharmacies. In other words, researchers need to ensure that sampled health providers are representative and inclusive of different types of possible providers of the intervention.

An important component of measuring care-seeking in household surveys is correctly identifying the denomina-

tor, ie, the individuals in need of the service or intervention. Depending on the intervention, need may be defined based on age, sex, or pregnancy status, or may require the respondent to accurately report on symptoms of disease, such as fever or diarrhea. In the included studies, service needs were not explicitly defined; rather it was implicit using criteria like age groups (eg, children under five, women of reproductive age) or life stage (eg, pregnant women). In included studies examining care-seeking for sick adults or children, service needs were self-perceived, based on household members' report of fever and other symptoms. Measurement of care-seeking for treatment of disease may be biased due to differences in respondents' perceptions of illness and their ability to recognize, recall, and report symptoms.

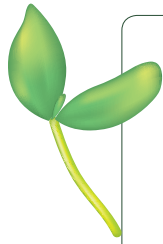
It is unclear whether the respondents in household surveys are able to accurately report on whether care was sought, and if so, from which type of facility or cadre of provider. A recent study noted challenges in identifying the type of providers using DHS-type questionnaires due to respondents' knowledge of source of care and the five year reference period used by DHS for these questions [8]. For example, if delivery care takes place at home, it may be difficult for the respondents to identify if the caregiver is from the public or private sector. Similarly, providers from the non-profit sector may not be easily identified by respondents if they are not well branded or if they work through the public or private sector. Valid measurement of care-seeking, including the type of provider or facility visited, is essential if we want to estimate intervention coverage using a linking approach, and therefore more data are needed on the validity of respondents' categorization of sources of care.

This review highlights a few issues to consider when using a linking method to estimate intervention coverage. In most cases, it is not possible to measure service quality, readiness or what actually happens during service delivery to those who sought care. It is therefore assumed that measures of the service environment at the time of facility data collection are comparable to the (unmeasured) service characteristics at the time that care was sought. Meanwhile the service environment (availability, readiness and quality) may change rapidly because of changes in policy, funding, and development or quality improvement programs. In addition, factors like drug stock-outs are time-variable and can substantially impede the ability of a facility to provide quality care. It is therefore important that the time

gap is minimized to reduce measurement errors. This time restriction may be a barrier especially for linked coverage measures of maternal and newborn interventions, since the reference period typically used in household surveys for collecting data on maternal and newborn care seeking behavior can be as much as five years prior to the survey. It is unlikely that the service provider data collected at a single point in time would be relevant to an entire 5-year period. It might therefore be desirable to conduct the service assessment within a short interval (eg, 12 months) of the household survey. Since recall of care-seeking in household surveys is retrospective, it will likely also be important to ensure that the service assessment is conducted before the household survey, in order to minimize the interval between when an intervention was received (and care-seeking was reported in the household survey) and when the quality of service at a provider was actually measured.

Finally, it is important to note that compared to surveys like MICS and DHS, which include urban and rural areas, linking studies that include only or primarily rural areas may be simpler and produce more valid results with regard to the service environment because the universe of health providers/facilities and their catchment population are easier to define. For this reason, some linking methods may be more appropriate to rural than urban and vice versa. For example, administrative boundary linking may work well in rural, but GPS-based physical distances may be more valid in urban settings. Further research is needed to understand the validity of various linking methods in different contexts.

In conclusion, several different methods linking care-seeking data from household surveys to readiness or service quality data from provider assessments have been employed in a growing body of research on health intervention coverage and can be classified into two broad categories: indirect linking and direct linking/exact matching. Each has their own advantages and limitations, in terms of both methodology and practicality. Future studies that aim to link household and provider data should also take into account important factors such as the timing of surveys and temporality of data points, the type of service and intervention, and the scale of the study in order to produce valid and reliable results. There is also a need for additional data on the validity of different linking approaches and the validity of care-seeking as reported in household surveys in order to inform development of these methods.



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# Can surveys of women accurately track indicators of maternal and newborn care? A validity and reliability study in Kenya

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**Background** Tracking progress on maternal and newborn survival requires accurate information on the coverage of essential interventions. Despite widespread use, most indicators measuring maternal and newborn intervention coverage have not been validated. This study assessed the ability of women delivering in two Kenyan hospitals to recall critical elements of care received during the intrapartum and immediate postnatal period at two time points: hospital discharge and 13–15 months following delivery.

**Methods** Women's reports of received care were compared against observations by trained third party observers. Indicators selected for validation were either currently in use or have the potential to be included in population-based surveys. We used a mixed-methods approach to validate women's reporting ability. We calculated individual-reporting accuracy using the area under the receiver operating curve (AUC), population-level accuracy using the inflation factor (IF), and compared the accuracy of women's reporting at baseline and follow-up. We also assessed the consistency of women's reporting over time. We used in-depth interviews with a sub-set of women (n=20) to assess their understanding of key survey terms.

**Results** Of 606 women who participated at baseline and agreed to follow-up, 515 were re-interviewed. Thirty-eight indicators had sufficient sample size for validation analysis; ten met criteria for high or moderate reporting accuracy ( $0.60 < \text{AUC}$ ) alone and ten met criteria for low population-level bias alone ( $0.75 < \text{IF} < 1.25$ ). There was a significant decline in the individual level reporting accuracy between baseline and follow-up for ten indicators. Seven indicators had moderate or higher ( $0.4 \leq r_{\text{phi}}$ ) consistency between self-reports at baseline and follow-up. Four indicators met all criteria at follow-up: support person was present during the birth, episiotomy, caesarean section, and low birthweight infant ( $< 2500$  g).

**Conclusion** The few indicators that women reported accurately at baseline were consistently recalled with accuracy at 13–15 months follow-up. Although there is deterioration in women's recall in some indicators over time, the extent of deterioration does not appreciably compromise reporting accuracy for indicators with high baseline validity. Indicators related to initial client assessment and the immediate postnatal period have generally low accuracy and poor reporting consistency over time.

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Continued regional, national, and sub-national disparities in maternal and newborn deaths, 99% of which occur in low and middle-income countries (LMIC), underscore the need to accurately track progress in the coverage of proven lifesaving interventions [1]. Given that weak health systems infrastructures often characterize high mortality areas, measuring access to and the quality of maternal and newborn intrapartum and immediate postnatal care often relies on women's responses to household survey questions, such as those included in the Multiple Indicator Cluster Surveys (MICS) and the Demographic and Health Surveys (DHS). Indicators of intrapartum care tracked in MICS and the DHS include facility-based delivery, skilled attendance at birth, the initiation of breastfeeding in the first hour of birth, and caesarean section. Such indicators are routinely used to track progress in maternal and newborn health. Nevertheless, the accuracy of intervention coverage data as measured through household surveys of female respondents has yet to be empirically established [2].

In response to the need for reliable data to guide maternal and newborn health efforts, several studies have sought to validate women's reporting on indicators of the content of maternal and newborn health care in LMIC [3–6]. In general, these validation studies have found that a few concrete and particularly salient aspects of care, such as cesarean section [3,5,6], a support person present during the birth [3,6], a nurse-midwife provider during delivery [6], experience of hemorrhage [6], and low infant birthweight [6], can be accurately reported. The accuracy of reporting on other indicators, however, such as the initiation of breastfeeding, the practice of newborn skin-to-skin contact, and the administration of a uterotonic for the prevention of postnatal hemorrhage, has been shown to be high in some settings but not others, highlighting the need for further and context-specific research.

One limitation of extant validation research is that existing studies have not replicated completely the conditions of household survey programs such as the DHS and MICS that collect data on maternal and newborn intervention coverage. Women interviewed in these programs are asked to recall events related to a birth that took place within the two (or five) years prior to the survey; existing studies are not able to assess the extent to which women's reporting accuracy and reliability may change as the time since the birth increases.

The present study addresses this gap in the evidence base by informing how women's recall of maternal and immediate postnatal interventions changes over time. We conducted household interviews with women who had delivered in a Kenya hospital 13–15 months prior. To assess the validity and reliability of her recall, we compared women's self-report at follow-up to: 1) observations by a third par-

ty at the time of labor and delivery, and 2) her previous exit interview at the time of hospital discharge. To elucidate factors that influence women's reporting ability, in-depth interviews were conducted with a subset ( $n=20$ ) of respondents. Findings on the accuracy of women's reporting at the time of hospital discharge has been previously published [6].

The main objectives of the study are: (1) to assess how accurately women report on the coverage of maternal and newborn health interventions received during the intrapartum and immediate postnatal period 13–15 months prior to the survey, (2) to examine the extent to which deterioration in recall compromises the validity of women's reporting, and (3) to provide insight into factors that influence women's ability to recall events surrounding the birth and understand survey questions.

## METHODS

### Participants

The sample population was comprised of women whose births were documented by research staff in study facilities at the time of delivery (July to September, 2013) and who provided consent and contact details to be visited for re-interview in their home approximately 13–15 months later ( $n=609$ ). Baseline data collection took place in two health facilities in Kisumu County and Kiambu County. Both study facilities are large public hospitals serving women who are either self-referred for care or who are referred from other health facilities due to high-risk pregnancies.

At baseline, women aged 15–49 years, who were admitted to the labor ward at the two study facilities were eligible for inclusion ( $n=662$ ;  $n=388$  in Kiambu,  $n=274$  in Kisumu) [6]. Participants were consecutively enrolled until the requisite sample size was reached. Women who provided written informed consent for participation completed an exit interview following delivery and prior to facility discharge. Further details on the study setting and methods for data collection for the reference standard are reported in our baseline paper [6].

At follow-up women who participated at baseline and who agreed to participate at follow-up were re-interviewed in their home or other mutually agreed upon location in the community (July to November, 2014).

### Test methods

Our reference standard for the study was direct observation by trained observers who used a structured checklist to document the care received and interactions between women and health providers in the maternal admission room and labor and delivery rooms. Study observers were



registered nurse/midwives with at least three years of experience in maternal, newborn and child health. Direct observation reflected all aspects of caregiving and data collectors supplemented observations by asking providers or checking medical records if clarification was needed [6].

Interviews with women were administered by data collectors who were degree holders in social sciences. Study interviewers were women from the local area, fluent in the local dialects (Kiswahili, Dholuo and Kikuyu) and not the same individuals as the study observers. All data collectors received a four-day training on administering the interview protocol and the appropriate procedures for ethical research with human subjects.

### Questionnaire instruments

To assess changes in reporting accuracy over time, women were asked the same set of questions at follow-up as at the baseline hospital exit interview. Survey questions reflected key maternal and newborn interventions in the intrapartum and immediate postnatal period (upon admission to the labor ward until 1 hour following delivery). While the full process for indicator selection has been described previously [6], in brief, indicators to be assessed were identified by conducting a landscaping scan of published and grey literature in 2012. A total of 80 out of an initial list of 285 indicators were selected by a group of public health experts specializing in validity assessment. Where possible, question wording identical to that used in the DHS and MICS was used.

Several assessed indicators are included in global health initiatives such as the Global and National Targets 2020–2035 of the Every Newborn Action Plan and the WHO 100 Core Global Health Indicators [7,8]. Additionally, tracking of skilled birth attendance is proposed for inclusion in the Sustainable Development Goals [9], while the WHO Strategies towards Ending Preventable Maternal Mortality (EPMM) emphasizes documenting major causes that lead to maternal deaths [10]. Table S1 in **Online Supplementary Document** indicates survey questions that correspond with elements of such global health initiatives. For example, given that the type of provider who is legislated to perform lifesaving functions varies by setting [11], it is essential to know how accurately women can identify the type of provider who assisted them. As such, this study assesses the accuracy of women's reporting on the type of the main provider who assisted them during labor and delivery. Similarly, intravenous oxytocin is the standard of care recommended for the prevention of postpartum hemorrhage [12]. As a proxy to asking women the names of medications received during delivery (which women are less likely to be informed of), women were asked about all potential administration routes that medication might have been received within a few minutes following delivery.

A randomly selected subset of women who agreed to participate in the in-depth interview were asked open-ended questions related to their understanding of key terms and concepts included in the questionnaire. A sample size of 20 women was considered sufficient to gain insight into the most common factors that influence women's understanding of the survey questions.

### Ethical review

Prior to re-interview, all women were provided with a description of the study, including the right to refuse participation with no consequence, or to stop the interview at any time. Participants were informed that they may be randomly selected to answer additional open-ended questions regarding their understanding of terms used in the interview questionnaire and that participation in both activities was voluntary. Only women who participated in the survey interview were asked to complete the in-depth interview. Written informed consent for both activities was obtained in the woman's native language (Kiswahili, Dholuo, or Kikuyu) prior to participation. In Kenya, adolescents under the age of 18 who are pregnant or a parent are considered "emancipated minors" and are able to provide written informed consent [13–15].

The study and consenting procedures were approved by the Population Council [Protocol No. 594] and the Kenya Medical Research Institute (KEMRI) [Protocol No. 395], prior to participant enrollment.

### Analysis

Briefly, as described in the baseline study, a target sample of 600 women was sought. Sample size was calculated for a type one error level of 5%, sensitivity of  $60 \pm 6\%$  precision, 70% specificity  $\pm 6\%$  precision, assuming 50% indicator prevalence and 20% attrition between baseline and follow-up [6,16].

Statistical analysis was performed using Stata Version 13 (StataCorp, College Station, TX, USA). We assessed validity and reliability of women's responses at the individual-level as well as validity at the population-level. In order to assess changes in women's reporting accuracy over time, all baseline analyses are restricted to women who participated at follow-up. To assess for the potential for systematic bias in the types of women lost to follow-up, we conducted chi-square tests and used the Holm–Bonferroni correction to adjust for multiple comparisons.

For individual-level validity, the sensitivity and specificity of women's recall was computed for each indicator by first constructing two-by-two tables of women's responses (Yes, No) vs the reference standard (Yes, No). "Don't Know" responses were treated as "No" responses (ie, women were

not positive that the intervention had occurred). Pairwise missing data were excluded from the analysis.

Next, we quantified the area under the receiver operating curve (AUC) for all indicators with sufficient sample size (at least 5 counts per cell) to summarize validity in a global statistic [3,6]. The AUC plots each indicator's true positive rate (sensitivity) against its false positive rate ( $1 - \text{specificity}$ ) to produce a summary estimate of validity [17]. Perfect indicator classification would have an AUC value of 1.0, while a random response would produce an AUC value of 0.5. AUC estimates were calculated to assess women's reporting at follow-up compared to the observer classification (reference standard).

The change in the validity of women's reporting over time was assessed by comparing follow-up and baseline AUC estimates using an equation which allows for tests of equality of two or more AUC estimates obtained from correlated samples [18,19]. For sensitivity, specificity and AUC values, corresponding 95% CI estimates are provided, assuming a normal approximation to the binomial distribution. We considered  $0.70 < \text{AUC}$  to reflect high accuracy;  $0.60 < \text{AUC} < 0.70$  as moderate accuracy, and  $\text{AUC} < 0.60$  as low accuracy [3,6].

We assessed indicator reliability at the individual-level by comparing women's responses to survey questions administered at follow-up to their responses at baseline. The agreement between two binary responses is measured by the phi coefficient ( $r_{\text{phi}}$ ). The  $r_{\text{phi}}$  can range from  $-1$  to  $1$ , where  $0$  represents no correlation and  $1$  represents perfect agreement. The Dancy and Reid classification of correlation was used with  $r_{\text{phi}} < 0.40$  indicative of poor agreement,  $0.4 \leq r_{\text{phi}} < 0.6$  moderate agreement,  $0.6 \leq r_{\text{phi}} < 0.8$  high agreement;  $0.8 \leq r_{\text{phi}}$  for almost perfect agreement [20].

To assess population-level accuracy, we calculated the inflation factor (IF) (also known as the Test to Actual Positives ratio) [21]. The IF reflects the prevalence of the indicator that would be obtained by women in a survey (Pr) divided by its true prevalence (ie, observer report) (P). The prevalence based on women's report in a survey (Pr) is calculated by applying each indicator's estimated sensitivity (SE) and specificity (SP) to its true prevalence (P), using the following equation:  $\text{Pr} = P \times (\text{SE} + \text{SP} - 1) + (1 - \text{SP})$  [22]. The ratio of the indicator survey-based prevalence to its true prevalence estimates the extent each indicator would be over or under-estimated if obtained by survey self-report in the study setting ( $\text{IF} = \text{Pr}/P$ ) [21,22]. We categorized the degree of bias reflected by the IF as low ( $0.75 < \text{IF} < 1.25$ ), moderate ( $0.50 < \text{IF} < 1.5$ ) and large ( $\text{IF} < 0.50$  or  $\text{IF} > 1.5$ ) [4,6]. Changes in population-level accuracy over time were assessed by comparing changes in IF classification between baseline and follow-up.

We summarize indicator performance in terms of both in-

dividual (AUC and  $r_{\text{phi}}$ ) and population-level (IF) reporting. Indicators which had moderate or higher individual-level accuracy and reliability, and low population bias are considered to have overall acceptable validity ( $0.60 < \text{AUC}$ ,  $0.4 \leq r_{\text{phi}}$  and  $0.75 < \text{IF} < 1.25$ ). We caution readers that indicator usability depends on the purpose of measurement. An indicator with poor individual-level reporting may produce an acceptable estimate of population-level coverage if the ratio of false positive to false negative reports is approximately 1. We refer readers to the full-presented validation results.

For the analysis of qualitative interview data, individual in-depth interviews were audio recorded and transcribed verbatim. Transcripts were translated into English and imported into NVIVO 10 software for coding (QSR International Limited, London, UK). A codebook was developed a priori by the research team to assess main themes of interest. These themes related to women's understanding of terms and concepts in survey questions that were reported with difficulty at baseline, including: how women ascertained the skill level of their provider, women's understanding of 'skin-to-skin' practice for newborn thermal care, and understanding of the timing and sequencing of events, such as the term "immediately". Two independent researchers familiar with the local context coded the transcripts. As a check for internal consistency, a subset of transcripts ( $n = 5$ ) were compared and reconciled.

## RESULTS

### Sample description

Of the 662 women whose births were documented at baseline, 606 agreed to a follow-up interview (91%). Data collectors were able to locate 568 women and re-interview 515 women in their home community (85% follow-up of those who provided baseline consent) and complete matched data was obtained for 514 women (**Figure 1**). The majority of women re-interviewed resided in the two counties where the baseline hospital facilities were located.

**Table 1** presents the background characteristics of women who participated in the baseline and follow-up interviews, respectively. Participants who were lost to follow-up were more likely to have delivered in the Kisumu County facility than those who remained in the study (53% vs 38%) and were less likely to have delivered in the Kiambu County facility than those who remained in the study (47% vs 62%) (Pearson chi-square: 11.4,  $P = 0.001$ ). Women lost to follow-up were also less likely to have three or more prior births than those who remained (15% vs 26%) (Pearson chi-square: 6.8,  $P = 0.009$ ).

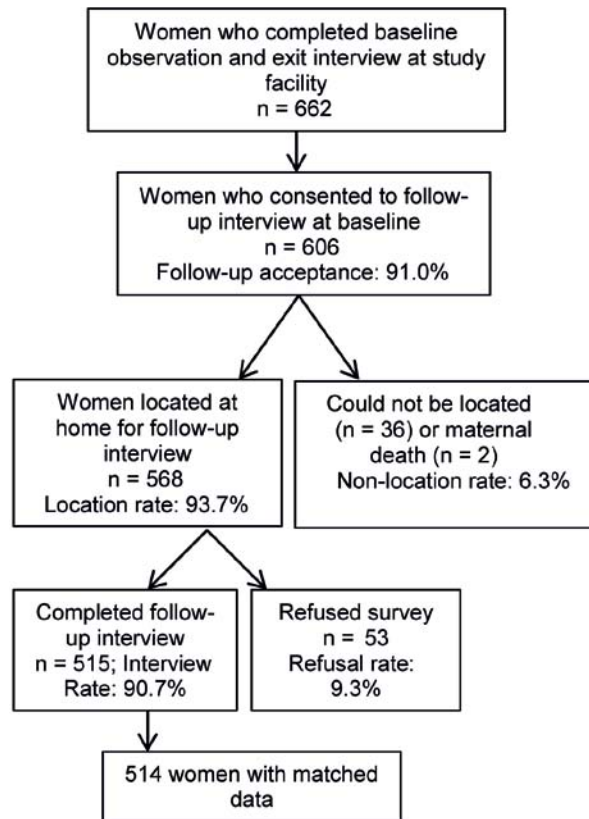


Figure 1. Participant enrollment.

## Validation results

The percentage of women who responded to survey questions is an important reflection of recall ability. More than 5% of women responded “I Don’t Know” to 11 indicators at follow-up, compared to four indicators at baseline (Table 2). In general, there was a high degree of overlap between indicators with high levels of ‘Don’t Know’ responses at both time points. Women were least likely to recall events related to provider hygiene and the immediate postnatal period.

**Reporting accuracy.** Of the 57 indicators measured, 38 had sufficient variation for robust analysis (Table 3). Of these, four indicators met our criteria for both moderate or higher individual validity, reliability and low population-level bias at follow-up: (1) a support person was present during the birth, (2) episiotomy, (3) cesarean section, and (4) low birthweight infant (Table 3). All but the episiotomy indicator also met the AUC and IF criteria at baseline.

In total, seven of 38 indicators are classified as having high validity, eight as moderate and 23 as low. There was a statistically significant deterioration in reporting accuracy for 10 indicators between baseline and follow-up (Table S2 in **Online Supplementary Document**). There was an additional significant increase in AUC for one indicator (mem-

Table 1. Respondent background characteristics by attrition status

CHARACTERISTICS	IN BASELINE ONLY (%, N = 150)	IN BASELINE AND FOLLOW-UP (%, N = 514)	P-VALUE
<b>Facility:</b>			
Kisumu	53.3†	37.9†	0.001*
Kiambu	46.7†	62.1†	
<b>Age (in years):</b>			
			0.134
15–19	19.3	13.3	
20–24	40.0	41.0	
25–29	28.0	30.5	
30–34	8.7	8.6	
35–39	3.3	6.3	
40+	0.7	0.4	
<b>Parity:</b>			
			0.020*
1	59.3	48.2	
2	25.3	26.2	
3 or more	15.3 <sup>1</sup>	25.6†	
<b>Education level:</b>			
			0.049*
None	13.3	9.4	
Primary	42.7	44.3	
Secondary	22.7	31.5	
Higher	21.3	14.8	
<b>Marital status:</b>			
			0.088
Single, never married	20.7	13.0	
Married / living together	78.0	85.0	
Separated/ divorced / widowed	1.3	2.2	
<b>Cesarean section</b>			
	14.0	13.3	0.820

\*Based on chi-square test, statistically significant at  $P < 0.05$ .

†Statistically significant pairwise comparisons using the Holm–Bonferroni correction to adjust for multiple comparisons.

brane rupture) that is likely attributable to random fluctuation due to its low validity at both time points. Five indicators with high validity at baseline significantly declined at follow-up; however, only two declined enough to lose the high validity classification at follow-up. These were: (1) injection received at some time before the birth (proxy for uterotonic to induce or augment labor), and (2) injection received to strengthen labor (proxy for uterotonic to augment labor). These indicators fell to moderate validity at follow-up.

Three indicators that had a moderate baseline AUC level significantly declined to low validity AUC level at follow-up: (1) allowed to have a support companion present, (2) blood pressure taken at first postnatal physical exam, and (3) temperature taken at first postnatal physical examination. There were significant differences between baseline and follow-up AUC levels for three indicators with low baseline reporting accuracy; all of these indicators retained low validity at follow-up. These were: (1) artificial rupture of the membranes performed, (2) provider encourages or assists woman to ambulate during labor, and (3) the provider checked for bleeding in the first postnatal physical examination.

**Table 2.** Indicators with “Don’t Know” responses >5%

SURVEY QUESTION	FOLLOW-UP “DON’T KNOW” %	BASELINE* “DON’T KNOW” %
Did the health provider(s) wash his/her hands with soap and water or use antiseptic before delivering your baby?	43.3 (n=437)	36.2 (n=445)
Did the health provider(s) wash his/her hands with soap and water or use antiseptic before examining you?	41.2 (n=515)	32.4 (n=512)
Was your baby dried off with a towel or cloth immediately after his/her birth?	13.3 (n=513)	8.4 (n=511)
Why did you decide to delivery in this facility?	8.7 (n=515)	0.0 (n=512)
After the delivery of your baby, in the first few minutes after the delivery of the placenta, did anyone give you an injection in your thigh?	8.5 (n=437)	4.5 (n=445)
Were you allowed to drink liquids or eat any foods while you were in labor?	7.2 (n=515)	4.7 (n=512)
Just after the delivery of your baby, in the first few minutes after the delivery of your baby, did anyone give you an injection in your thigh or buttock?	6.2 (n=437)	1.1 (n=445)
In the first physical examination/ check after delivery, did a health provider do a perineal exam?	5.8 (n=514)	10.6 (n=512)
Did you or anyone else give anything to the baby other than breastmilk to eat or drink within the first hour after delivery?	5.7 (n=513)	3.5 (n=512)
Did someone place the baby on your chest, against your skin, immediately after delivery of the baby?	5.3 (n=513)	2.9 (n=512)

\*Women who participated in both baseline and follow-up only.

**Reliability.** Across all indicators, women’s reporting consistency was generally poor (31 of 38 indicators had  $r_{\text{phi}} < 0.40$ ). Only seven indicators met the criteria for moderate to high reliability (Table S3 in **Online Supplementary Document**). The consistency of reporting of caesarean sections was nearly perfect ( $r_{\text{phi}} = 0.90$ ), while low birthweight infant and episiotomy had substantial agreement ( $0.6 \leq r_{\text{phi}} < 0.8$ ). There was moderate agreement ( $0.4 \leq r_{\text{phi}} < 0.6$ ) for four indicators: (1) skin-to-skin contact of mother and newborn following birth, (2) injection received some time before birth (ie, proxy for uterotonic to induce or augment labor), (3) a support person present during birth, and (4) injection received to strengthen labor (ie, uterotonic to augment labor). Results show poor reliability for indicators related to the type of provider, immediate postnatal care for the mother, and complications.

**Population-level bias.** Table S2 in **Online Supplementary Document** presents the prevalence of intervention coverage that would be obtained from women’s reports in a household survey given the specificity and sensitivity observed in the follow-up survey. In total, 14 indicators met the criteria for low bias in population-level coverage estimates at follow-up, three indicators had moderate population-level bias and 21 indicators had large bias.

The top five indicators with the largest predicted overestimation of self-reported prevalence from a household survey of women ( $\text{IF} > 1.5$ ) at follow-up related to the immediate postnatal period, including receiving an injection following the delivery of the placenta (proxy for uterotonic for the preventing of postnatal hemorrhage), immediate newborn care, and complications. Indicators with the largest predicted underestimation related to some aspects of care in which the provider may not have been explained the purpose to women, such as “*In the first physical examination after delivery, did a health provider do a perineal exam?*” and “*Did a health provider check your belly to see if your womb*

*was becoming firm after the birth of your baby?*” and “HIV status checked”, which may have been done by checking records rather than by asking women.

For the majority of indicators (29 of 38) IF levels at follow-up did not change appreciably from baseline. Specifically, five of the 12 indicators with low bias at baseline, five of the nine with moderate bias and 17 of the 18 with large bias remained in the same classification category at follow-up. Of the eight indicators that changed classification categories: four indicators changed to a higher bias category and four indicators changed to a lower bias category at follow-up. Ten indicators had large magnitude changes, an IF difference of greater than 0.5. All large magnitude changes occurred among high baseline IF indicators.

**Qualitative results.** Qualitative data provide insight into what women recall about the labor and delivery process at 13–15 months postnatal, as well as their understanding of terms and concepts used in survey questions. When describing their hospital delivery experience during the in-depth interviews, women often mentioned emotions and physical experiences. These included fears about having a healthy delivery and the pain of labor.

*“I just wanted to give birth normally and successfully.”*

*“The labor was so intense you cannot even tell the aspects of care you received. . . I was feeling bad, when in labor pains you just feel bad. . . The only thing on my mind is what I would give birth and rest.”*

Many respondents also reported experiencing fatigue, relief and joy following delivery. In some instances, these experiences may have outweighed recall of an intervention received during this period.

*“I felt so blessed to be alive though I had not seen my baby. When I was given the baby I didn’t have the strength to look at the baby because I was still in much pain.”*

**Table 3.** Summary of validation and reliability results\*

INDICATOR	INDIVIDUAL-LEVEL ACCURACY (0.60 < AUC: ✓)		POPULATION-LEVEL ACCURACY (0.75 < IF < 1.25: ✓)		TEST-RETEST RELIABILITY (0.4 ≤ R <sub>PM</sub> : ✓)
	Baseline	Follow-up	Baseline	Follow-up	
<b>Initial client assessment:</b>					
Takes blood pressure	- -		✓ ✓		-
HIV status checked	- NA†		- -		-
Receives HIV test	- NA		- ✓		-
Provider washes hands with soap and water or uses antiseptic before any initial examination	- -		- -		-
<b>Provider respectful care:</b>					
Encourages/assists woman to ambulate during labor	- -		✓ ✓		-
Allowed to drink liquids/eat	- -		✓ -		-
Encourages/assists woman to assume different positions in labor	- -		- -		-
Allowed to have a support person present	- -		- -		-
A support person is present during birth	✓ ✓		✓ ✓		✓
<b>First stage of labor:</b>					
Induces labor with a uterotonic (IV line, injection or tablet)	✓ ✓		- -		-
Augments labor with a uterotonic (IV line, injection or tablet)	✓ ✓		- -		✓
Uterotonic received some time before birth (to induce or augment labor)	✓ ✓		- -		✓
Performs artificial rupture of the membranes	- -		- -		-
<b>Skilled birth attendance:</b>					
Main provider delivery—skilled (doctor, medical resident or nurse/midwife)	- -		✓ ✓		-
Main provider delivery—doctor or medical resident	✓ ✓		- -		-
Main provider delivery—nurse/midwife	✓ ✓		✓ ✓		-
<b>Second &amp; third stage labor:</b>					
Uterotonic administered in 1–3 min following delivery (injection, IV line or tablets) (women who had vaginal delivery)	- NA		✓ NA		-
Uterotonic administered after delivery of placenta (women who had vaginal delivery)	- -		- -		-
Method of uterotonic post-birth by injection (women who had vaginal delivery)	✓ NA		✓ NA		-
Episiotomy	✓ ✓		- ✓		✓
Cesarean section	✓ ✓		✓ ✓		✓
<b>Immediate postnatal care—newborn:</b>					
Newborn placed with mother immediately following birth (all women)	- -		✓ ✓		-
Breastfed infant in first hour after birth	- ✓		✓ ✓		-
Skin to skin	- -		- -		✓
3 essential elements of newborn care (immed. dried + newborn placed immediately skin to skin with mother + breastfed within 1 hour of birth)	- -		- -		-
<b>Immediate postnatal care—mother:</b>					
Uterine massage after delivery of placenta (denominator: vaginal delivery)	- -		✓ ✓		-
In first examination post-delivery, did provider ask or check for bleeding?	- -		✓ ✓		-
In first examination post-delivery, did provider examine perineum?	- -		- ✓		-
In first examination post-delivery, did provider take temperature?	- ✓		✓ ✓		-
In first examination post-delivery, did provider take blood pressure?	- ✓		✓ -		-
In first examination post-delivery, did provider check for involution?	- -		✓ ✓		-
<b>Maternal and newborn morbidity:</b>					
Low birthweight infant (<2500 g)	✓ ✓		✓ ✓		✓
Complications – hemorrhage	✓ ✓		- -		-
Complications – prolonged labor	✓ ✓		- -		-
Complications – none	✓ -		✓ ✓		-
Complications – yes (to any)	✓ -		- -		-
Asked for pain relief medication	- -		- -		-
Received pain relief medication	✓ ✓		- -		✓

\*Note: See Table S1 in **Online Supplementary Document** for full description of survey questions that comprise each indicator.

†NA results had insufficient data (n<5 in cell of two by two table) for robust analysis in respective survey round; indicators with insufficient sample size at both baseline and follow-up are omitted from table. Horizontal dash (–) indicates that the acceptability threshold was not met.

*“You know that time [after the birth] I was over excited so after the caesarean section I was happy to see my child like this and I gave God my thanks, so I cannot know because once I saw the baby I was tired so whatever happened after that I don’t know”.*

*“...When you asked me if the baby was placed on my chest against my skin, that was hard for me to remember because at that time I was tired because I had gone without sleep for two days.”*

*“Like when you asked if I was injected after delivery, yes I can remember I was injected only once, but not sure if it was after delivery of baby or placenta... And you know [I] am always so afraid of injections but the joy [of giving birth] made me forget about the pain and the fear of injection.”*

Despite the influence of a woman’s physical state on her recall, interventions considered of immediate importance to her health, either by facilitating a healthy delivery (eg, inducing/augmenting labor or having a cesarean operation) or treating a complication, remained memorable. One aspect of care viewed as critical to ensuring a healthy delivery was who assisted with the delivery. For example, when asked to recall a particularly memorable aspect of care, one respondent reported, *“The doctor who assisted me to deliver because she gave me glucose to get more energy to push the baby”.* Another woman noted, *“The one who performed the surgery is the one who helped me the most.”*

In some instances support companions were also found to deliver needed care. As one respondent reported, *“If your relatives have not yet arrived to visit you suffer a lot because they do not give anything to eat or drink.”*

Aspects of care deemed by women to be less critical to their health were less readily recalled.

*“Issues of the nurses washing their hands, I could not remember what I remember is just them wearing the gloves... Because I was not keen to check if they were doing that, to me gloves are just enough.”*

A defining characteristic used by women to differentiate higher vs lower skill level providers was the ability of the provider to ensure that she received the needed elements of care. As illustrated below, there was generally agreement on the interventions higher cadre providers were able to administer relative to lower level providers (ie, prescribe drugs, perform surgeries, and manage complications).

*“During my delivery a doctor came and said I should be given tablets... I was given five of them. He said that the tablet is not working on her so they were told to put IV on me. To me I thought that is the senior doctor.”*

Distinctions between qualified providers and medical students were more apparent as women reported relying on a variety of clues such as uniform, seniority and the types of services provided. However, many participants noted dif-

ficulty in discerning between types of providers considered ‘qualified’, such as doctors or nurses, if both were able to provide the needed care.

*“I knew it was a doctor because she is the one who tested me ruptured my membrane to assist the baby to come out, took my blood pressure and then tested my urine... I knew this is a doctor it is not a TBA or a student. [Interviewer: Okay, how do you differentiate a doctor and a nurse?] A doctor and a nurse, that one is hard.”*

*“That is the only one I can say the rest ask me the difference of the student but the rest is it is hard to tell who is a doctor and a nurse.”*

*“Sometimes he makes noise to the other telling them that is not what should be done. So I knew that is a doctor but I am not able to differentiate a doctor and a nurse.”*

Women’s understanding of the terms used in survey questions also influenced reporting. The concept of timing, for example, was invoked in several questions. Timing is critical to measuring access to lifesaving interventions such as postnatal interventions for the newborn, such as newborn thermal care. For example, women were asked, *“Did someone place the baby on your chest, against your skin, immediately after delivery of the baby?”* When asked to define the number of minutes that would have passed in an ‘immediate’ time frame, responses varied widely. One participant states, *“... let us say immediately because it didn’t pass twenty minutes or so”.* Others report, *“...immediate means just now, just a few minutes, one or two minutes”* and *“when you talk about immediately it should be five to seven.”* These results suggest indicators in which accurate reporting on timing is a necessary element may not be able to be reported with accuracy.

## DISCUSSION

Findings from this study show that the relatively few indicators that women are able to report with high accuracy at baseline are recalled with moderate or high accuracy after 13–15 months. Although the findings demonstrate that recall accuracy for some indicators declines with time, high validity indicators are more likely to be reliably reported by women and retain moderate-to-high accuracy at follow-up. Specifically, 6 of the 7 moderate-to-high reliability indicators ( $0.4 \leq r_{phi}$ ) also had moderate-to-high diagnostic accuracy ( $0.60 < AUC$ ). These results suggest that the more salient the intervention or event, the more accurately and reliably the indicator can be recalled over time.

Indicators with overall validity ( $0.60 < AUC$  and  $0.75 < IF < 1.25$ ) were mostly related to aspects of care received between the first stage of labor and the birth. It is notable that no indicators related to the initial client assessment phase or immediate postnatal care for the mother or newborn met our

criteria for moderate or high diagnostic accuracy, and all but one indicator (skin-to-skin contact of the mother and newborn) had low reliability. Furthermore, nearly all indicators with greater than 5% “Don’t Know” responses were related to these two phases. For example, the indicator of provider hand-washing or antiseptic use, had a >30% “Don’t Know” response and is not recommended in the current setting. The highest validity indicators related to particularly memorable aspects of birth either due to pain (eg, caesarean section, episiotomy), because they were considered significant to having a health delivery (eg, an intervention received in order to bring on (induce) or strengthen (augment) labor, a nurse/midwife or doctor/medical resident was the main provider present), or brought emotional support and comfort (eg, a support person was present).

For most indicators, however, we found women’s reports had low diagnostic accuracy (22 of 38 indicators have  $AUC < 0.60$ ), large population-level bias (23 indicators have  $IF < 0.5$  or  $1.5 < IF$ ), and poor reliability (31 of 38 indicators have  $r_{phi} < 0.40$ ). The low validity of indicators not immediately pertinent to the event of birth or health status of the mother or newborn may be due to the high background ‘noise’ of experiences preceding the first stage of labor and immediately following birth. As suggested from the qualitative findings, women’s recall of practices in the initial client assessment period may be clouded by the anxiety of labor and delivery, while the fatigue, pain, and joy associated with birth may interfere with recall of the care received immediately postnatal. For example, questions about receiving an injection *before* labor (to induce or augment labor) were recalled with moderate or high accuracy, while questions related to an injection immediately *following* birth (ie, uterotonic for prevention of postnatal hemorrhage) had mixed results and high “Don’t Know” responses. Taken together, we advise caution when assessing the coverage of interventions received immediately postnatal, especially when recall of timing is key. When self-reported data are used, we recommend the use of multiple questions regarding when and how the intervention was received in order to triangulate findings to enhance internal validity.

Despite generally poor reporting consistency by women, particularly in the early and late phases of birth, reporting discrepancies did not result in statistically significant changes in AUC levels or IF classification from those at exit interview for the majority of indicators. Where significant changes in individual level accuracy did occur (11 of 38 indicators), women were less accurate (10 of 11 indicators) over time. In contrast, we found that where changes in population-level bias occurred, IF estimates were equally likely to become larger or smaller with time. The discrepancy in the direction of change for these measures is due

to the fact that while the AUC reflects individual-level accuracy, the IF reflects the balance of true positives and false negatives at the aggregate level. An indicator that meets criteria for the IF but not the AUC, such as ‘skilled birth attendance’ may generate an acceptable estimate of intervention coverage at the population level. Results from this study should be interpreted with respect to whether the goal is individual or population level measurement.

Findings from this study confirm the findings of prior literature; many indicators of intrapartum care and associated morbidities have generally low validity and reliability when assessed by women’s reports [3,23,24] but some salient indicators are reported with accuracy. Of the four indicators that met both validation criteria in this study, a support person present during birth [3], and cesarean section [4,5] have also been found to be reported accurately by women in prior studies.

The low reliability of women’s reports of complications corresponds with the conclusion of a 2012 review of several validation studies conducted in LMIC which found that the reliability of self-reported complications based on women’s recall is poor, even if the woman suffered from a life-threatening complication [25]. A study of similar design in Benin that compared clinic exit interviews (within 1 week of discharge) and interview responses of women at six months postnatal also found self-reported data to be neither reliable nor valid for measuring obstetric complications [24]. That all complication related indicators in the present study had large IF bias may be in part due to their low observed prevalence. A limitation of the IF is that when the coverage of a given quality of care indicator is low, even a small false positive rate will result in a biased IF estimate. Therefore, estimates of population-level survey results from this study suggest that self-reported data on rare labor and delivery events, such as the prevalence of complications, will be overestimated, as documented in prior studies [26]. To assess population-level bias in other contexts where intervention coverage may vary, one can model the estimated survey prevalence by applying the sensitivity and specificity calculated in this study to the estimated ‘true’ prevalence of the intervention for the given context, as detailed in the Analysis section. We refer readers to our previous article, which illustrates the implications of IF estimates for other contexts [6].

This study provides insight into the potential of self-reported data to assess accurately maternal and newborn health intervention coverage. The strengths of the study are the use of direct observation as the reference standard and the longitudinal study design, in which the re-interview of women 13–15 months postnatal more closely reflects conditions of household survey programs, such as the DHS and MICS.

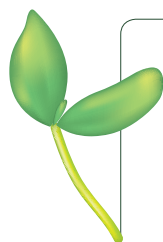
We also note several limitations. For example, women participating in standard household surveys are typically not interviewed twice, and the recall of participants may have been influenced by repeated measurement. Furthermore, the 13–15-month recall period does not reflect the range of plausible recall periods of the MICS and DHS, which ask women to report on a birth that occurred within the preceding two or five years. Results from this study are reflective of women who delivered in the two study facilities, and may not be generalizable to other contexts. The majority of births take place in a facility and are delivered by a skilled provider in both study counties [27]. However, women who reside in rural areas, have lower education and less wealth are less likely to deliver in a facility and our results are less likely to reflect the reporting patterns of this population. As noted in the baseline study [6], the fact that the standard of care for both facilities was consistently high, also limited the ability to validate all indicators due to lack of variation in received care. Additional validation research that takes place across facility settings and time points is warranted.

Despite the limitation of this study in terms of facility setting, 61% of births in Kenya took place in a health facility in 2014 [27]. With the announcement of the Kenya Gov-

ernment to provide free maternity services in all public facilities in 2013 [28], this percentage is likely to continue to increase in the coming years and may extend the utility of the study results.

## CONCLUSION

Women are able to report on some aspects of maternal and newborn intervention coverage with accuracy. Results from this study do not suggest that there is significant deterioration in women's recall ability over time for indicators that are reported with accuracy at baseline. Results confirm that the population-level coverage of low prevalence indicators is challenging to measure accurately. We found generally poor accuracy and reliability for indicators related to interventions received during the initial client assessment and immediate postnatal care for both the mother and newborn, which may result from high background 'noise' of physical and emotional experiences relative to the intervention. If self-reported data are used to measure intervention coverage in these periods, particularly if time is an essential element of the received care, we recommend caution and triangulation with other data sources.



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# Burden of severe maternal morbidity and association with adverse birth outcomes in sub-Saharan Africa and south Asia: protocol for a prospective cohort study

AMANHI Maternal Morbidity study group

AMANHI – Alliance for Maternal and Newborn Health Improvement

**Objectives** The AMANHI morbidity study aims to quantify and describe severe maternal morbidities and assess their associations with adverse maternal, fetal and newborn outcomes in predominantly rural areas of nine sites in eight South Asian and sub-Saharan African countries.

**Methods** AMANHI takes advantage of on-going population-based cohort studies covering approximately 2 million women of reproductive age with 1- to 3-monthly pregnancy surveillance to enrol pregnant women. Morbidity information is collected at five follow-up home visits – three during the antenatal period at 24–28 weeks, 32–36 weeks and 37+ weeks of pregnancy and two during the postpartum period at 1–6 days and after 42–60 days after birth. Structured-questionnaires are used to collect self-reported maternal morbidities including hemorrhage, hypertensive disorders, infections, difficulty in labor and obstetric fistula, as well as care-seeking for these morbidities and outcomes for mothers and babies. Additionally, structured questionnaires are used to interview birth attendants who attended women's deliveries. All protocols were harmonised across the sites including training, implementation and operationalising definitions for maternal morbidities.

**Importance of the AMANHI morbidity study** Availability of reliable data to synthesize evidence for policy direction, interventions and programmes, remains a crucial step for prioritization and ensuring equitable delivery of maternal health interventions especially in high burden areas. AMANHI is one of the first large harmonized population-based cohort studies being conducted in several rural centres in South Asia and sub-Saharan Africa, and is expected to make substantial contributions to global knowledge on maternal morbidity burden and its implications.

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Pregnancy, childbirth and their related complications present a high level of risk to the survival, health and well-being of women and their babies in low and middle income country settings. Maternal mortality is the most commonly cited maternal health statistic: approximately 289 000 women die annually from pregnancy-related causes, 85% of these deaths occur in sub-Saharan Africa and South Asia alone [1]. The

major direct causes of maternal deaths include hemorrhage, infection, unsafe abortion, eclampsia and obstructed labor [1–3]. With each maternal death, however, an additional 20 to 30 women are estimated to suffer acute morbidity and disabilities with substantial impact on their physical, psychological, social and economic functioning [4–7]. An estimated 15% of all pregnant women, approximately 20 million women globally, suffer a spectrum of maternal illnesses ranging in severity from mild disease to acute severe, life-threatening complications or near death events [3,8–10]. The challenge is that maternal ill-health and its effects are not well defined and seldom measured [11]; estimates are imprecise and likely underestimate the true burden [2,6,11,12], thereby undermining efforts to harness resources to address them.

Most studies on maternal morbidity are facility-based and are conducted in developed countries. There are marked disparities between developing and developed countries with respect to the prevalence of maternal morbidities. This could be a function of the higher frequency of childbirth, poorer general health of women, lack of care seeking and low quality of care available in developing countries. There is also a suggestion that women from some geographic regions might carry relatively high risk of maternal morbidity even if their environment is improved. For instance, a multi-country study among migrant populations in Australia, Canada and Denmark, found that, compared to non-migrants, migrants from sub-Saharan Africa appeared to have higher maternal morbidity risks and these findings were consistent with findings from studies conducted in Italy, Belgium the Netherlands and the UK [13–18]. In low- and middle-income countries (LMICs, especially those in sub-Saharan Africa and South Asia where the burden of morbidity is largest), there is a dearth of data on morbidity because maternal access to facilities is poor and vital registration systems are lacking or incomplete. Facility-based data are not enough to describe the true burden of morbidities but data from the community level, where many births and pregnancy-associated complications occur, are also particularly lacking and the quality of reporting is often poor. Prevalence estimates for morbidities are based on statistical models with substantial uncertainties around them. There is a clear need to generate high quality and reliable population-based estimates of severe maternal morbidity using robust epidemiological methods especially in sub-Saharan Africa and Asia.

The Alliance for Maternal and Newborn Health Improvement (AMANHI) maternal morbidity study directly responds to this need. The study aims to describe and quantify severe maternal morbidities and assess their associations with adverse maternal, fetal and newborn outcomes. It is being implemented at nine sites in eight countries of sub-Saharan Africa and South Asia. The study uses harmonized

methods to collect prospective population-level maternal morbidity data. AMANHI morbidity study, coordinated by the Maternal, Newborn, Child and Adolescent Health department of the World Health Organization (WHO/MCA) will contribute to improving estimates of severe maternal morbidity; provide a better understanding of the contributory factors that require consideration when designing interventions; and inform the focus of future interventions in order to optimize impact. This manuscript describes the protocol for the harmonized implementation of the study.

## OBJECTIVES

The objectives are to determine the burden of severe acute maternal morbidity, describe the care received by pregnant and delivered women, and examine the association of severe maternal morbidity and care received with adverse maternal, fetal and neonatal outcomes.

## METHODS

### Study design and setting

The AMANHI morbidity study is a population-based, prospective cohort study. Trained AMANHI morbidity study fieldworkers conduct routine surveillance home visits to identify pregnant women, enrol them for follow-up through the pregnancy till after 42 days postpartum to collect data on morbidity, care seeking and outcomes for mothers and babies including preterm birth, intrauterine growth restriction (IUGR), stillbirths and neonatal mortality. It is built on an existing platform of neonatal health studies being implemented in Bangladesh (Sylhet), India (Uttar Pradesh), Pakistan (Karachi and Matiari) in south Asia; and Democratic Republic of Congo (Equator), Ghana (Kintampo), Kenya (Western province), Tanzania (Pemba) and Zambia (Southern Province Zambia) in sub-Saharan Africa. The study spans a period of 24–36 months, with staggered implementation across sites, starting in 2013 and expected to end in 2016.

### Study population and setting

The AMANHI morbidity study is being implemented in predominantly rural populations where women's educational levels are low. A summary of the characteristics of the study sites is as shown in **Table 1**. Families mainly engage in subsistence agriculture, petty trading and fishing. A variety of health facilities ranging from community clinics (providing only first aid and referral services) to district hospitals serve the population. In AMANHI, these health facilities were mapped according to their type (health post/community clinic, health center, district or provincial hospital) and range of services provided (out-patients only; basic delivery services; basic or comprehensive emergency

**Table 1.** Summary description of the parent studies, surveillance system, surveillance population and annual number of births at AMANHI sites

SITE	PARENT STUDY TITLE AND OBJECTIVE	EXISTING PREGNANCY SURVEILLANCE SYSTEM	TOTAL SURVEILLANCE POPULATION	REPRODUCTIVE-AGED WOMEN IN SURVEILLANCE	APPROXIMATE ANNUAL BIRTHS
Bangladesh	Etiology of Neonatal Infection in South Asia (ANISA): To estimate community level etiology-specific incidence predictive risk factors and clinical features, treatment and prevention strategies for serious infections among young infants (0–59 days).	2-monthly by trained community health workers (CHWs)	600 000	88 000	13 000
Democratic Republic of Congo (DRC)	African Neonatal Sepsis Trial (AFRINEST): to test the safety and efficacy of simplified antibiotic regimens for treating possible serious bacterial infection in 0–59 day-old infants	3-monthly by CHWs	699 288	65 000	12 000
Ghana	Neonatal vitamin A supplementation (Neovita) study: to determine if vitamin A supplementation to neonates once, orally, <48 hours of birth will reduce neonatal, early and late infant mortality	Monthly by fieldworkers	700 000	147 000	21 000
India–Shivgarh	Topical emollient application to babies to prevent infection especially in preterms & ANISA studies	3-monthly by fieldworkers	1 350 000	184 430	44 000
Kenya	AFRINEST study: same as DRC	3-monthly by CHWs	400 000	30 000	10 000
Pakistan–Karachi	ANISA study: same as Bangladesh	3-monthly by fieldworkers	270 000	63 000	9 500
Pakistan–Matiari	ANISA study: same as Bangladesh	3-monthly by fieldworkers	215 200	64 000	8 000
Tanzania–Pemba	Chlorhexidine (CHX) study: to evaluate the efficacy of chlorhexidine cord cleansing on neonatal mortality	6 weekly by trained CHWs	390 000	72 000	14 000
Zambia	Chlorhexidine (CHX) study: to evaluate the efficacy of chlorhexidine cord cleansing on neonatal mortality	No pregnancy surveillance; facility ANC enrolment	25 000*	25 000	9 000

\*Zambia to recruit only from antenatal clinics.

obstetric care). This mapping was done as part of on-going community-based pregnancy and birth surveillance that involves 1– to 3-monthly household visits by trained fieldworkers to all women of reproductive age (15 to 49 years). The exception to the community surveillance is Zambia where recruitment is facility-based as explained below. With each woman visited at least once every three months, pregnancies are identified early and any complications or adverse outcomes are documented close to when they occur. Any woman of reproductive age who resides in the study area is eligible for enrolment into the study once they fall pregnant and consent to participate. In order to generate comparable data that will be amenable to pooled analyses, the implementation of the study is harmonised across sites as described in the following sections.

### Harmonization of protocols and implementation strategies

When the study was planned in 2012, investigators from all participating sites agreed on common protocols, standard operating procedures, methods and strategies for implementation.

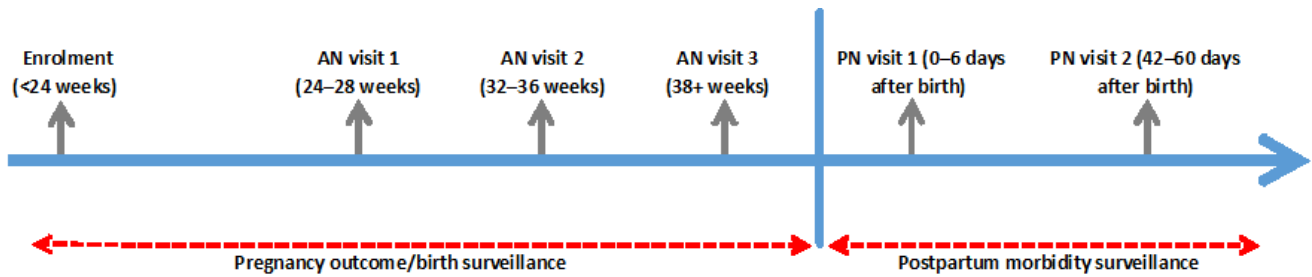
### Protocols

The principal investigators put together an agreed common protocol for the study. They developed an initial generic protocol from which all the sites developed specific adaptations for their sites. These protocols were submitted to and approved by ethical review committees of the WHO and at the respective sites.

### Standard operating procedures & implementing strategies

**Core variable tables.** The AMANHI investigators discussed common data to collect and collated these into a core variable table (CVT) to be used across sites (tables in the **Online Supplementary Document**). The table specifies and defines signs and symptoms that are elicited during interviews with women, measurements, outcomes and important baseline variables such as maternal age, education, household assets and the format in which these data should be collected and stored across the sites (ie, as text, numeric or time/date formats). The variables on this table are included in questionnaires that were used across all sites.

**Timing and frequency of visits.** A uniform schedule for household visits by fieldworkers was used across AMANHI sites, as shown in **Figure 1**. Timing and frequency of the visits have been chosen to enable detailed information on women's morbidity experiences, within each trimester of pregnancy, to be collected close to their occurrence. The first visit to the pregnant woman and her household is immediately after enrolment where fieldworkers conduct basic assets inventory and collect socio-demographic data. The first antenatal visit to collect morbidity information during pre-pregnancy and in early pregnancy prior to the visit is made at 24–28 weeks of pregnancy. Two more household visits are made during the antenatal period at 32–36 weeks and after 37 weeks of gestation to collect data on morbidities during the interval between the index and the previous visits and any care seeking around the preg-



**Figure 1.** Antenatal (AN) and postnatal (PN) follow-up visit schedule—AMANHI morbidity study

nancy. Sites estimate gestational ages of pregnancies using women's reported date of last normal menstrual period (LMP) to plan the antenatal visits. Two additional visits are made after delivery; within the first week (days 0–6) and after 42 days of birth to collect data on pregnancy outcomes, morbidities and their outcomes as well as care sought for the mother and baby. Measurements of blood pressure and urine proteins is made at each of the visits.

**Training of trainers for implementation.** The WHO/MCA trained and standardized AMANHI investigators from all the sites on the strategy for uniform implementation of the study across sites. The training involved the approach to consenting, collecting self-reported morbidity, measurement of blood pressure and testing urine for proteins for all participants in the study during household visits. Issues around confidentiality and sensitivity around eliciting unpleasant experiences from families were discussed. The complexity of measuring blood pressure within the home setting, collecting non-contaminated urine samples and ensuring accuracy of the measurements was particularly emphasized. Participants were trained to repeat all blood pressure (BP) measurements after 30 minutes of the initial recording. They discussed protocols for referral of women with abnormal findings (such as elevated BP and/or proteinuria) for appropriate care within health facilities. They were trained to conduct interviews with birth attendants and to review facility records in order to validate women's reported morbidities. During practice sessions, participants followed the step-by-step process to practiced BP measurement on each other. Key areas of emphasis during training of fieldworkers in the sites were discussed.

**Training of data collectors at sites and quality assurance around data collection.** The investigators who participated in the harmonized training in turn trained study fieldworkers at their respective sites for the data collection. The study fieldworkers should have secondary/high school education (at least 10 years of formal education). The team also agreed on a common process for monitoring implementation and data quality across sites by the WHO/MCA. As part of the quality assurance protocol, ranges were specified for all variables and this was used to check the data.

Data checks were done both on the field and in the data management centres within the respective sites. Inconsistent data are identified and rectified on the field, at the data centres or both. In addition, sites send cumulative study data to the WHO/MCA on a quarterly basis. Similar range and consistency checks are conducted on these data and outliers identified. The WHO data manager sends feedback to the sites for response and, where indicated, the WHO data set is updated accordingly. Trends in outliers and inconsistent data are analyzed according to the fieldworker who collected them and feedback sent to the sites to inform re-training of staff.

### Study supplies/equipment

Fieldworkers are provided equipment and training to directly assess pregnant women for hypertensive disorders during home visits. Each fieldworker uses urinalysis kits (Uristix<sup>®</sup> by Siemens, Gujarat, India) to assess proteinuria and a digital sphygmomanometer (Microlife<sup>®</sup> WatchBP<sup>®</sup> Home A BP3MX1–3, Widnau, Switzerland) [19,20] to measure women's blood pressure. All these study materials were procured from a common source.

### Surveillance for pregnancy identification

During home visits, fieldworkers use a variety of methods to identify pregnant women. These include direct disclosure by women or eliciting information on missed menstrual periods from women's LMPs. When unsure, women in Bangladesh, Pakistan (Karachi and Matiari), India (UP) and Tanzania (Pemba) had the option to request a urine pregnancy test to confirm pregnancies. Zambia is the exception where, because over 96% of women in the study area attend antenatal care (ANC) clinics during pregnancy [21], recruitment into AMANHI is done at these ANC clinics. Once a woman is found to be pregnant, an information sheet containing a comprehensive summary of the study objectives, risks and benefits is read to potential participants in their local or their preferred language to help them make an informed decision to participate in the study. Consented mothers receive a unique study identification number (study ID).

## Follow-up on enrolled women

The AMANHI morbidity study employs both active and passive surveillance for collecting maternal morbidity data. In each site, fieldworkers use structured questionnaires (generated from the core variable table) to actively collect data on women's self-reported morbidity and directly assess for hypertensive disorders during pregnancy and postpartum visits. As detailed in the next sub-section, questions on self-reported morbidity explored programmatically relevant morbidity causes such as antepartum hemorrhage, infections, miscarriage and abortions, signs and symptoms of hypertensive disorders of pregnancy such as severe headaches, blurred vision among others. For all births, fieldworkers also interview birth attendants (in the attendant's home or place of work) to obtain additional details on complications each AMANHI study woman (whose delivery they assisted/attended) encounter during labor and delivery. Birth attendant account on morbidity will be used as validation for the women's self-reported morbidity. The unique study ID provided to each enrolled woman links data from the two types of forms.

**Baseline home visit.** At baseline/enrolment fieldworkers collect household characteristics and baseline socio-demographic data on participants. They conduct an assets inventory which is used to classify households into socio-economic quintiles. This will be used to evaluate inequities in the distribution of severe maternal morbidity in the AMANHI cohort. The fieldworkers also collect data on previous medical and obstetric history, history of cigarette smoking or alcohol ingestion and morbidity experiences since the onset of the pregnancy.

**Listings for antenatal visits.** Women's gestational age information is collected from either self-reported LMP or from any record of ultrasound scan conducted by the time of the visit. This information is used to estimate the gestational age of women. Each week, the study team generates a listing of women who are due for any of the antenatal visits and grouped into clusters that allow for fieldworkers to visit them for morbidity data collection. Whenever a woman is found to be temporarily away at the time of a scheduled visit, she is moved to the top of the listings for the next week and her visit is given priority and completed first.

**Antenatal home visits.** During the first antenatal home visit (conducted between 24–28 weeks), fieldworkers first ascertain the status of the pregnancy (whether woman is still pregnant or the pregnancy has terminated) and collect data on morbidity experiences. If the woman has commenced routine antenatal care (ANC) clinic attendance within the routine health system, fieldworkers abstract data on morbidity, results of any laboratory investigations (eg, hemoglobin level and presence of malaria parasites), ultrasound scans and maternal anthropometric measures (height, weight, mid upper arm circumference) taken by health professionals. At the end of the visit, they measure women's BP and check their urine for proteins.

At subsequent antenatal home visits at 32–36 weeks and after 37 completed weeks, the same questionnaire is used to collect morbidity data covering the interval between the previous and the index visit.

The visit covers collection of reported morbidity and screening for hypertensive disorders in pregnancy. **Table 2** shows a summary of data collected at various visits in the

**Table 2.** Summary of data collected at various visits in the AMANHI maternal morbidity study

MAIN CATEGORY	THEMATIC AREAS OF DATA COLLECTION	SOURCE OF DATA	VISIT AND TIME OF DATA COLLECTION
Maternal morbidity	1. Antepartum hemorrhage	1. Maternal self-report	Antenatal home visits (24–28 weeks, 32–36 weeks, 37–40 weeks), postnatal home visits (day 1–6 and day 42–60 after birth), birth attendant interviews 0–6 days after birth, health facility records
	2. Postpartum hemorrhage	2. Maternal self-report and birth attendant interview	
	3. Hypertensive disorders of pregnancy	3. Measurements of blood pressure and urine protein at all home visits, maternal self-report	
	4. Difficulty in labor	4. Maternal self-report and birth attendant interview	
	5. Infection	5. Maternal self-report	
	6. Obstetric fistula	6. Maternal self-report	
Background characteristics	Socio-economic, baseline characteristics of the woman and her household, including an asset inventory	Maternal self-report	Baseline home visit at enrolment
Medical history	Previous obstetric and gynecological history, birth defects, prematurity, stillbirths and IUGR among previous babies, previous medical and surgical history	Maternal self-reports and health facility records	Baseline home visit at enrolment
Risk factors and exposures	Cigarette smoking, alcohol ingestion, smoke from biomass cooking fuels	Maternal self-reports	Baseline home visit at enrolment
Anthropometry	Paternal and maternal weights and heights, maternal mid-upper arm circumference	Health facility records	All antenatal and postnatal home visits
Screening for hypertensive disorders of pregnancy	Measurement of blood pressure and testing urine for proteins	Direct measurement during home visits	All visits except delivery visits

AMANHI maternal morbidity study. Details on the process of data collection on each of the visit components are as follows:

i. **Reported morbidity.** Study fieldworkers ask questions around morbidities during the pregnancy using the study antenatal questionnaire derived from the core variable tables. These questions are to elicit any occurrence of severe maternal morbidity notably haemorrhage (antepartum and postpartum), infections, prolonged/obstructed labour, fistula, signs of pre-eclampsia or eclampsia. Since there are no current global standards for asking valid and reliable questions at the population level on maternal morbidity, AMANHI investigators agreed, pre-tested and validated questions to elicit maternal morbidities using scientific and pragmatic considerations of what data can be elicited from women at the community level. For example, for obstetric haemorrhage, the study used an adaptation of criteria suggested by Ronsmans [22] based on evidence of possible organ failure or life-saving surgical intervention. The limited evidence suggests that prolonged labour and postpartum haemorrhage (PPH) are particularly poorly reported. The standard definition of severity requires a quantification of the amount of blood lost (at least 500 ml for spontaneous vaginal delivery and 1000 ml for caesarean) to define PPH. In the home settings especially for deliveries that take place at home, it is difficult to quantify the amount of blood lost. AMANHI therefore used pragmatic definitions for these outcomes and prescribed these within the core variable table. In enquiring about severe PPH, AMANHI fieldworkers are trained to ask about any bleeding from the vagina after the birth of the baby, whether the bleeding was so much that it not only wet her clothes and the floor but also that the woman had to have an “operation” to stop it, she collapsed or lost consciousness as a result of or during the bleed. Similarly, for each morbidity included in the study, fieldworkers elicit information on the timing of onset, severity and any interventions received and from who this care was received.

ii. **Screening for hypertensive disorders of pregnancy.** Trained fieldworkers directly measure women's BP and test their urine for proteins as part of active assessment for hypertensive disorders of pregnancy using a step-by-step protocol agreed across sites. The fieldworker first explains the rationale and procedure for the BP measurement and the urine sample testing. They make sure the woman sits and is made comfortable on a chair and the fieldworker places the digital sphygmomanometer on a surface at the level of her heart. Her blood pressure is then measured. If the pressure is found to be high, a repeat measurement is taken after 30 minutes of wait during which period the woman rests and is re-assured of the safety of the procedure. The blood pressure measurement is again repeated. To collect the urine sample, women are taught how to wipe

her urethra with clean tissue and provided with a urine collection tube to obtain a sample of their urine for testing. Colorimetric methods are used to assess the degree of proteinuria coded from none through to 4 plus. At all visits, women with high blood pressure (systolic blood pressure >140 mm Hg or diastolic pressure >90 mm Hg) are referred to participating health facilities for appropriate care.

If the pregnancy has been aborted/miscarried, they terminate the AMANHI pregnancy follow-up and complete postnatal forms for the woman. At the first postnatal visit, data are collected on women's reported morbidity during labor, delivery and immediately after birth including care seeking and outcomes for mother and baby. Fieldworkers also abstract morbidity data and the birthweight of babies from available health facility records (hospital folders, postnatal clinic record cards, etc.) during the postnatal visits.

Also following the realization of the difficulty in obtaining reliable data on complications such as hemorrhage through women's self-reports, AMANHI uses an alternative source of data to corroborate women's reported morbidity experiences during home visits – birth attendant accounts of morbidities during childbirth. These data are collected for all deliveries conducted by “professional” birth attendants (including traditional birth attendants, midwives, nurses and doctors).

**Birth attendant interviews.** Within the first week after every birth, fieldworkers identify and interview all delivery attendants in health facilities or who assisted five or more AMANHI deliveries (whether trained health professional or untrained traditional birth attendant – TBA). These interviews are done using structured questionnaires to provide more detail on women's morbidity experiences (including complications) during labor, delivery and the immediate postpartum while under the care of the attendant. These interviews are held at the attendants' home or place of work.

**Health facility records review.** In a few of the sites, data are collected, using a structured questionnaire, on the subset of women who attend health facilities for care during pregnancy, childbirth or in the postpartum period and used to validate morbidities from women's and birth attendants' reports. During home visits, data on premature births, intra-uterine growth retardation (IUGR) and mortality outcomes are also collected from this cohort.

**Verbal Autopsies for deaths.** Protocols for the conducting VAs in AMANHI are being published concurrently [23]. In summary, fieldworkers conduct verbal autopsies (VAs) whenever a woman of reproductive age, her fetus or a neonate dies using standardized tools and procedures. Trained field supervisors administer a verbal autopsy tool that has been developed using the WHO verbal autopsy tool as template. Additional questions were added on from tools used

in other computer-based VA software available at the time. The supervisors obtain a narrative on the circumstances leading to the death, administer a semi-structured questionnaire to probe for specific signs and symptoms according to physiological systems and abstract data from any existing records including death certificates to help ascertain the type of death (eg, pregnancy-related or not, neonatal death or stillbirth), timing and the cause. Harmonised protocols are used by physicians who are selected from the respective countries and trained to confirm timing, type and to assign causes of these deaths based on principles of the International Classification of Diseases.

## Outcomes

The main outcome of the study is the prevalence of severe acute maternal morbidity (operationally defined to include acute problems suffered during pregnancy, through childbirth to the end of 42 days postpartum). Severe acute maternal morbidity will include, but is not limited to, pre-(eclampsia), antepartum and postpartum hemorrhage, abortion complications, maternal infections, obstructed labor and other complications arising out of these. Denominators for rate estimates will be total pregnancies or the number of women who become pregnant among the cohort while those who suffer any severe acute morbidity will contribute data to the numerators. In estimating prevalence of hypertensive disorders for which AMANHI is directly assessing women's blood pressure and urine proteins at baseline (pre-pregnancy levels) and after 42 days postpartum (when those who developed pregnancy-induced hypertension will have returned to baseline states), it will be possible to describe a wide spectrum of hypertensive disorders including the classical pregnancy induced hypertension where women are normotensive pre-pregnancy, develop pregnancy-induced hypertension and return to normotensive state after delivery. Care seeking and care given for each morbidity will be described.

## Sample size considerations

The sample size contributions from each of the sites are as shown in **Table 3**. The 160 000 total participants in the study are sufficient for assessing association of severe maternal morbidity with adverse maternal, fetal and neonatal outcomes based on an assumption that all individual sites should have adequate power to detect association between preterm birth and any morbidity with a prevalence of 7.5% or more. Data will be pooled across sites for evaluating morbidities with lower prevalence, especially in assessing associations with stillbirths and early neonatal deaths.

## Data management

**Data processing.** The study uses paper forms or tablet-based software for data collection. Forms are independently double entered by two clerks into study databases with stringent range and consistency (R&C) checks with the exception of Zambia where field monitors collect data using forms designed in the TeleForms® system (HP, Cambridge, UK). After Zambian supervisors review the forms for completeness, they are scanned, entered, and exported into an Access database. Similar R&C checks are built into the software used for data capture at sites using tablets. Data managers within the sites conduct inter-database checks to reconcile and synchronize data from various forms using the woman's unique study ID as the link. Cleaned data are saved on special study servers with password-protected access to only principal investigators in the sites. They generate data back-ups on external drives at regular intervals. Every three months, sites transfer back-up data to a dedicated server at the WHO/MCA for external quality control and storage.

**Data analyses.** Analyses will be done using Stata® statistical software package [24]. Incidence of severe maternal morbidities will be estimated. The burden of adverse birth outcomes will also be estimated. Associations will be inde-

**Table 3.** Expected number of participants to be enrolled from the AMANHI sites (by region) and precision that can be obtained around estimates

REGION	STUDY COUNTRY	SAMPLE SIZE	EXPECTED WIDTH OF 95% CI IF PREVALENCE OF MORBIDITY = 2%	RELATIVE PRECISION
Sub-Saharan Africa	DRC	20 000	1.8% to 2.2%	±10%
	Ghana	10 000	1.7% to 2.3%	±14%
	Kenya	20 000	1.8% to 2.2%	±10%
	Tanzania (2 sites)	15 000	1.8% to 2.2%	±11%
	Zambia	25 000	1.8% to 2.2%	±9%
	<b>Pooled</b>	<b>90 000</b>	<b>1.9% to 2.1%</b>	<b>±5%</b>
South Asia	Bangladesh	19 000	1.8% to 2.2%	±10%
	India	35 000	1.9% to 2.1%	±7%
	Pakistan (2 sites)	16 000	1.8% to 2.2%	±11%
	<b>Pooled</b>	<b>70 000</b>	<b>1.9% to 2.1%</b>	<b>±5%</b>

CI – confidence interval, DRC – Democratic Republic of the Congo



pendently explored between various maternal characteristics (confounders) such as socio-economic status, educational attainment, age, parity, etc. and severe maternal morbidity as well as the adverse birth outcomes. The effect of exposure to severe acute maternal morbidity on adverse birth outcomes will be estimated using appropriate regression models. Test of interaction will be done to assess effect modification of treatment received by study women on association between severe maternal morbidities and adverse pregnancy, birth and neonatal outcomes.

### Quality monitoring

The WHO/MCA centrally coordinates and monitors the harmonized implementation, quality of fieldwork and data in the AMANHI morbidity study. Individual sites send monthly fieldwork progress reports to WHO/MCA, highlighting their key challenges. At quarterly intervals, the WHO/MCA team run quality control checks on all transferred data to identify outliers and provide feedback to the sites. Data are also reconciled with the monthly fieldwork progress reports to check consistency. WHO/MCA sends experts to the sites once or twice each year to assess progress and quality of implementation, provide technical input and to enhance the harmonized implementation. They also discuss challenges with the sites and provide a detailed report to the WHO/MCA highlighting key issues of benefit to and for follow-up with the other sites.

### Ethical considerations

All women are individually consented to participate in the AMANHI morbidity study. Local and institutional ethics committees from all nine sites approved the AMANHI study protocols. The Ethics Review Committee of the WHO has also approved a combined master protocol with components on the role of the WHO/MCA.

### Dissemination plan

The results of the study will be disseminated among the public health, maternal and newborn health community of researchers, policy-makers and program managers. Channels for dissemination will include peer-reviewed journals, print and electronic media and academic presentations (oral and poster) at appropriate fora. In each participating country, there will be extensive briefing on their country-specific and overall study results, and the team of researchers and stakeholders will discuss implications of the study for interventions and programmes in those settings.

### Importance of the AMANHI morbidity study

Inadequate attention to reducing the burden of maternal morbidity may be contributing to the slow progress in re-

ducing preventable maternal mortality [25]. Beyond survival, another significant statistic is the number of women who develop severe acute morbidities and/or severe chronic disabilities that are incompatible with normal physical, psychological or economic viability and who are abandoned by loved ones, families, friends and society [4,5,7]. One of the biggest hurdles to planning and delivery of effective interventions is the dearth of data on maternal morbidities.<sup>11</sup> Good quality data are essential for strategic planning and targeting of interventions. In LMICs of sub-Saharan Africa and South Asia where resources are limited and a disproportionate burden of severe acute maternal morbidities exists, evidence-based data-driven strategic prioritization of investments and resource allocation to address these is paramount [4,6,26,27].

The AMANHI maternal morbidity study will generate reliable estimates of severe maternal morbidity from one of the largest population-based, multi-country studies in sub-Saharan Africa and South Asia. AMANHI has many advantages; implementation is being harmonized across sites and common definitions of severe maternal morbidity are being used. This will ensure comparability of data and facilitate pooled analyses across sites. The methodological contributions and implications of the AMANHI study design for routine data collection platforms such as demographic and health surveillance sites is obvious: the need for validation of definitions of morbidities and harmonization of protocols for data collection across sites is urgent. The absence of these limits data utility in routine surveillance systems especially where regional or global estimates are to be derived from these data. If AMANHI tools can be validated within other routine surveillance systems, it is a major contribution to harmonization of data collection tools or if not directly, provides the template for developing such valid, reliable and globally useful tool for population-based data collection systems.

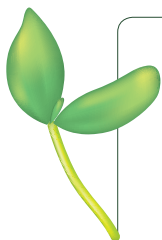
The AMANHI sample size is large and with the active pregnancy and birth surveillance allowing for accurate denominators, estimates generated will be precise and reliable. The combined comparative advantages of large sample size and homogeneity in the data across sites will additionally allow for analyses on very rare maternal health outcomes and with the linked data on household wealth, inequities in the distribution of maternal morbidities could be explored.

AMANHI will provide the dual benefit of a unique opportunity to assess associations between various exposures, severe maternal morbidity and adverse pregnancy outcomes and also address the gap in the availability of quality data for validation of model-based estimates. The data will also form the baseline for generation of more accurate estimates of the real impact of severe acute morbidities on health and well-being of women after pregnancy and

childbirth. Moreover, the implementation strategy informs global researchers, academics, funders and institutions on how to maximise the utility of data from on-going studies that could contribute to answering related questions.

While this contribution of reliable and good quality data on maternal morbidity from the AMANHI study to global

public health is significant in that it will inform policy direction, interventions and programmes, we do recognize that it remains the first step needed to create a sustainable platform for prioritization and ensuring equitable coverage of maternal health interventions for the benefit of both mothers and their newborns.



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# Burden, timing and causes of maternal and neonatal deaths and stillbirths in sub-Saharan Africa and South Asia: protocol for a prospective cohort study

AMANHI study group. Maternal, neonatal deaths and stillbirths mortality cohort study

AMANHI—Alliance for Maternal and Newborn Health Improvement

**Objectives** The AMANHI mortality study aims to use harmonized methods, across eleven sites in eight countries in South Asia and sub-Saharan Africa, to estimate the burden, timing and causes of maternal, fetal and neonatal deaths. It will generate data to help advance the science of cause of death (COD) assignment in developing country settings.

**Methods** This population-based, cohort study is being conducted in the eleven sites where approximately 2 million women of reproductive age are under surveillance to identify and follow-up pregnancies through to six weeks postpartum. All sites are implementing uniform protocols. Verbal autopsies (VAs) are conducted for deaths of pregnant women, newborns or stillbirths to confirm deaths, ascertain timing and collect data on the circumstances around the death to help assign causes. Physicians from the sites are selected and trained to use International Classification of Diseases (ICD) principles to assign CODs from a limited list of programmatically-relevant causes. Where the cause cannot be determined from the VA, physicians assign that option. Every physician who is trained to assign causes of deaths from any of the study countries is tested and accredited before they start COD assignment in AMANHI.

**Importance of the AMANHI mortality study** It is one of the first to generate improved estimates of burden, timing and causes of maternal, fetal and neonatal deaths from empirical data systematically collected in a large prospective cohort of women of reproductive age. AMANHI makes a substantial contribution to global knowledge to inform policies, interventions and investment decisions to reduce these deaths.

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The past two decades have seen significant global declines in both maternal and child mortalities. These declines may be attributable, in part, to the attention they received due to the millennium development goals (MDGs) [1]. However, gains have not always been realized in areas with the highest burden. Three million neonatal deaths, 2.6 million stillbirths and over 280 000 maternal deaths still occur annually [2]. The vast majority (99%) of these deaths continue to occur in low- and middle-in-

come country settings (LMICs); a disproportionate 85% occur in South Asia and sub-Saharan Africa alone [3,4].

An incomplete understanding of the burden, timing and causes of maternal, fetal (stillbirths) and neonatal deaths remains a major challenge in addressing mortality in mothers and their newborns. In many LMICs, routine vital registration systems are lacking or incomplete. Facility and community data are often not systematically collected and medical death certification systems are non-functional. For example, in sub-Saharan Africa and South Asia, less than 12% of countries meet criteria for reasonably complete cause of death reporting [5].

Given these limitations, methods to directly estimate mortality have been developed [6]. These estimates rely on national surveys, demographic surveillance systems or samples of populations to determine causes of deaths [6–10]. While they provide a basis for action, these estimates are subject to biases and limitations of the data sources and may over- or under-estimate the true burden of these deaths [11,12]. Sadly, these are the only sources of evidence to inform planning, prioritization and distribution of resources in many LMICs [12].

## OBJECTIVES

The Alliance for Maternal and Newborn Health Improvement (AMANHI) mortality study aims to determine the burden, timing and causes of maternal deaths, stillbirths and neonatal deaths using harmonized methods across eleven sites in sub-Saharan Africa and South Asia. This prospective study, centrally coordinated by the department of Maternal, Newborn Child and Adolescent Health of the World Health Organization (WHO/MCA), uses harmonized tools, training and implementation strategies across participating sites to collect data from a large cohort of women of reproductive age, their pregnancies and the outcome of these pregnancies for both mothers (up to 42 days postpartum) and their newborns (till end of the neonatal period). The study will also assess the comparability of the estimates generated from these prospectively collected data with existing model-based estimates of maternal mortality, stillbirths and neonatal mortality. The data will also be used to test other innovative approaches (including computer-based “machine learning” methods) to estimate the causes of these deaths. This manuscript describes the protocol for the AMANHI mortality study highlighting key steps that have been implemented to ensure reliability and external validity of the findings.

## METHODS

AMANHI is a multi-centre, multi-country, population-based, cohort study in which women of reproductive age

are followed through pregnancy, childbirth and the postnatal period. The AMANHI mortality study includes sites from Bangladesh (Sylhet), India (Haryana and Uttar Pradesh), Pakistan (Karachi and Matiari) in South Asia; and Democratic Republic of Congo (Equator), Ghana (Kintampo), Kenya (Western province), Tanzania (Ifakara and Pemba) and Zambia (South Zambia) in sub-Saharan Africa. A summary description of the sites' characteristics is provided in **Table 1**. All the sites involved in the AMANHI mortality study were those that had planned or on-going studies on neonatal health funded by the Bill and Melinda Gates Foundation. All these studies planned to enrol greater than 5000 pregnant women, and had established a surveillance system for identifying all pregnant women in a geographically defined area. They also planned to follow up pregnant women through pregnancy and up to 72 hours after birth.

## Training for harmonized implementation

The AMANHI mortality study teams undertook two main training sessions, facilitated by experts from the WHO, in Geneva Switzerland to harmonize the implementation of study procedures. The first session in June 2012 involved principal investigators from sites. At this training workshop, sites developed common data collection tools (core variable tables) and implementation strategy. Sites adapted the generic protocol to suit their context and submitted to the Ethics review committees of the WHO/MCA and other relevant institutions.

In August 2014, AMANHI brought together two site coordinators per site for a week-long training to harmonize physician assignment of causes of deaths (CODs). Participants used principles of the International Statistical Classification of Diseases (ICD) to assign CODs and complete death certificates. Participants used these principles contained in an AMANHI VA manual to practice until they assigned the same CODs for five consecutive forms. These participants, in turn, trained physicians in their respective sites.

## Mortality surveillance

The AMANHI mortality surveillance utilizes an existing 1–6 monthly routine household surveillance visits by trained fieldworkers to over 2 million women of reproductive age across sites to identify and follow-up pregnant women through pregnancy, childbirth to 42 days postpartum. The surveillance comprises active and passive components. In the former, fieldworkers identify pregnant women, obtain their consent and enrol them for follow-up, providing them with unique study identification numbers (study ID). The study will therefore obtain data on all women who become pregnant, every pregnancy and their outcomes (including abortions/miscarriages, stillbirths and livebirths). These will serve as denominators for estimating rates of maternal, fetal and neonatal mortality. Fieldwork-

**Table 1.** Summary description of the parent studies, surveillance system, surveillance population and annual number of births at AMANHI sites

SITE	PARENT STUDY TITLE AND OBJECTIVE	EXISTING PREGNANCY SURVEILLANCE SYSTEM	TOTAL SURVEILLANCE POPULATION	REPRODUCTIVE-AGED WOMEN IN SURVEILLANCE	APPROXIMATE ANNUAL BIRTHS
Bangladesh	Aetiology of Neonatal Infection in South Asia (ANISA): to estimate community level aetiology-specific incidence predictive risk factors and clinical features, treatment and prevention strategies for serious infections among young infants (0–59 d).	2-monthly by trained community health workers (CHWs)	600 000	88 000	13 000
Democratic Republic of Congo (DRC)	African Neonatal Sepsis Trial (AFRINEST): to test the safety and efficacy of simplified antibiotic regimens for treating possible serious bacterial infection in 0–59 day-old infants.	3-monthly by CHWs	699 288	65 000	12 000
Ghana	Neonatal vitamin A supplementation (NeovitA) study: to determine if vitamin A supplementation to neonates once, orally, <48 hours of birth will reduce neonatal, early and late infant mortality.	Monthly by fieldworkers	700 000	147 000	21 000
India – Haryana	NeovitA study: same as Ghana.	Monthly by trained CHWs	1 400 000	313 399	34 600
India – Shivgarh	Topical emollient application to babies to prevent infection especially in pre-terms & ANISA studies.	3-monthly by fieldworkers	1 350 000	184 430	44 000
Kenya	AFRINEST study: same as DRC.	3-monthly by CHWs	400 000	30 000	10 000
Pakistan – Karachi	ANISA study: same as Bangladesh.	3-monthly by fieldworkers	270 000	63 000	9 500
Pakistan – Matiari	ANISA study: same as Bangladesh.	3-monthly by fieldworkers	215 200	64 000	8 000
Tanzania – Ifakara	NeovitA Study: same as Ghana.	3-monthly by fieldworkers	300 000	72 000	6 000
Tanzania – Pemba	Chlorhexidine (CHX) study: to evaluate the efficacy of chlorhexidine cord cleansing on neonatal mortality.	6 weekly by trained CHWs	390 000	72 000	14 000
Zambia*	Chlorhexidine (CHX) study: to evaluate the efficacy of chlorhexidine cord cleansing on neonatal mortality.	No pregnancy surveillance; facility ANC enrolment	25 000	25 000	9 000

\*Zambia to recruit only from antenatal clinics.

ers record all maternal, fetal/stillbirth or neonatal deaths that occur among enrolled participants during surveillance visits. A listing of these deaths is used by specially trained supervisors for the VA interviews. This list will be used to generate numerators for the mortality rate estimates after the type (maternal, pregnancy-related, fetal or neonatal) and timing (details below) are confirmed from the VA interviews. Fieldworkers also collect baseline socio-demographic data and assets inventory for classifying households into wealth quintiles. This will allow for evaluation of inequities in the distribution of mortality burden within the population.

The primary study outcomes include all-cause maternal mortality ratio (MMR) defined as number of women who die whilst pregnant or within 42 days of a pregnancy's end, irrespective of the duration or site of the pregnancy per 100 000 livebirths. Stillbirth rate (SBR) will also be calculated either as the number of stillbirths per 1000 births (true rate) or per 1000 livebirths (ratio). Neonatal mortality rate (NMR) will be defined as the number of deaths among live born infants within the first 28 days after birth per 1000 live births. Timing of maternal deaths will be classified as deaths in early pregnancy, late pregnancy, intrapartum, immediate postpartum and late postpartum; stillbirths will be classified as antenatal or intrapartum and

neonatal deaths by day of death for each day in the first week after birth and then weekly till day 28. Cause-specific mortality rates/fractions will also be determined. The data will also be disaggregated and rates estimated separately for sub-Saharan Africa and South Asia.

In nine of the eleven sites where a maternal morbidity surveillance runs concurrently, women receive five scheduled visits—three in pregnancy and two postpartum. Mortality surveillance is incorporated into these visits. The fieldworkers review health facility records to identify mortality events for VA interviews. In the interval between visits, families report deaths or pregnancy losses to AMANHI for follow-up (passive surveillance). The Zambia site is the only exception because pregnancy identification is only done at antenatal clinics. This approach was used because of high antenatal care coverage (over 96%) within the study district [13].

### The AMANHI Verbal Autopsies: confirming type, timing and obtaining causes of deaths

In all sites, when a stillbirth occurs, a baby or woman of reproductive age dies, trained VA supervisors visit the household, after the mourning period, and conduct VA interviews to obtain detailed information on the circumstances leading to the death. The VA supervisors identify a reliable infor-

mant, defined as any person who lived closely with the deceased in the period immediately preceding the death and who is capable of providing reliable and coherent account of the circumstances leading to the death, for the interview. The objectives for administering the AMANHI VAs are three-fold: first, to confirm deaths and the type of death especially the critical discrimination between maternal or pregnancy-related deaths (for women) and between stillbirths and early neonatal deaths. Second, the VAs will also confirm the timing of the deaths as described in the previous section. The third objective is to assign causes to the deaths. AMANHI uses a uniform tool and harmonised methods for the collection and interpretation of the VA data.

### The AMANHI VA tool

Principal investigators from each site, together with the WHO/MCA coordinating team, developed a table of core variables to be collected across sites for all deaths. These variables were derived from three existing tools: the WHO VA [14], InterVA [15] and SMARTVA (Tariff method) [16] tools. The WHO tool was used as the template and questions from the other tools were added if they were not already in this template. When questions were found to be similar but response options differed between tools, both questions were maintained in the AMANHI tool. This will allow for data generated in AMANHI to be analysable using these top two available software platforms (InterVA and SMARTVA). The AMANHI core variable table therefore includes questions to be asked, the response options and how variables should be captured in the final common study database. This harmonised data collection tool will also facilitate pooling of data across sites and hence increase statistical power for analysis on rarer outcomes.

### AMANHI VA interviews—form completion

Questions in core variable tables were translated into site-specific questionnaires in three sections: a narrative, close-ended questions and records review and data abstraction sections.

**Semi-structured narratives.** Interviewers ask respondents to provide detailed, chronological narratives on the circumstances leading to the death. Where needed, they further probe for specific details about current or any pregnancies that had ended around the time of death; the onset of any illness, signs and symptoms exhibited, any pre-existing medical conditions and care-seeking during the pregnancy and/or fatal illness. Irrespective of pregnancy outcomes, interviewers probe into pregnancy and labour history, whether a baby was stillborn or died after birth. Where technical or local words are used for signs they probed and write down what the respondent meant rather than their own interpretations.

**Close-ended questions.** Interviewers collect basic demographic and socio-economic characteristics of the deceased and systemically elicit responses for all signs and symptoms that the deceased exhibited before death. These close-ended questions as well as providing details on some of the signs and symptoms also elicit important signs and symptoms that respondents may not mention in the narratives. For instance, for haemorrhage, they probe for the onset, severity, duration and any care sought and the outcomes of the care-seeking. In case the narrative conflicts with the close-ended responses, interviewers probe further to ensure data are internally consistent.

**Records review and abstraction.** Interviewers abstract relevant data from hospital, antenatal, childbirth, postpartum clinic attendance records or death certificates onto the VA questionnaire.

### Interpreting AMANHI VAs through harmonised assignment of causes of deaths

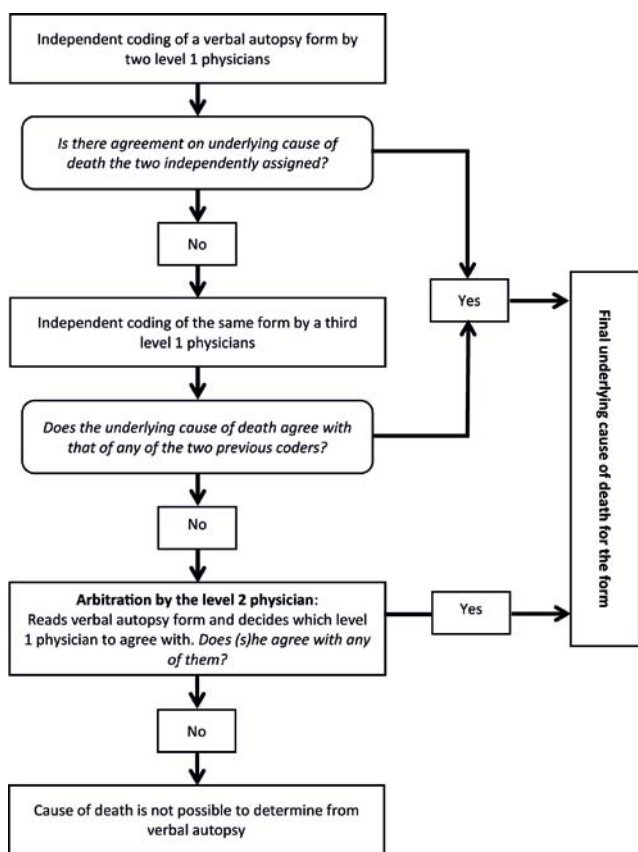
The AMANHI mortality study uses harmonized protocols (in an AMANHI VA manual) to assign CODs. This is to improve objectivity and transparency of the COD assignment and increase validity and reliability of physician-assigned causes. The manual provides uniform criteria and processes for selection and training of physicians; common definitions and procedures for assigning causes [17]; centralised accreditation and certification of trained physicians and streamlining the entire process on a specially-designed software platform.

**Training and accreditation of physicians.** PIs and study coordinators recruited and trained selected local physicians on the principles of AMANHI VA using the VA manual. A list of all trained physicians is then submitted to the WHO/MCA for accreditation. The trained physicians were provided online access to 20 standardised VA forms (stillbirths/neonatal – 12 and women of reproductive age – 8) that had CODs assigned by global VA experts. The numbers were so selected to reflect the relative frequency of occurrence of these deaths as well as provide enough numbers to test a variety of cases. Upon completion, the physicians submit the forms online to the WHO/MCA who compare the physician assigned CODs with the standard CODs for agreement. Physicians are only accredited when 80% or more of their assigned CODs agree with the standard. The 80% mark was selected because we considered that one in every five forms may be difficult to code due to poor quality of data. Physicians are given three attempts at accreditation and when they fail, they are not allowed to assign CODs in AMANHI. After each unsuccessful attempt, coordinators and an expert from WHO retrained physicians. AMANHI certificates were given to all accredited physicians.

**Assigning CODs.** The study employed ICD principles adapted from the revised WHO Verbal Autopsy Coding Standards (2012) [14,17]. A list of programmatically-relevant causes of maternal, fetal and neonatal deaths (Table 2, Table 3 and Table 4) were selected and their operational definitions for AMANHI were specified. When the cause is known but not included in the AMANHI list, an option is given to code as such or as indeterminate if no COD can be assigned.

**Procedure for consensus building.** The AMANHI algorithm for the process of consensus building around CODs is shown in Figure 1. The underlying cause of death (UCOD) assigned by physicians is used for consensus building. In AMANHI, at least two out of four physicians must agree on a cause to be assigned as final UCOD. Physicians are classified at two levels based on clinical and previous VA coding experience. Two level 1 physicians (practitioners who routinely manage pregnant women and newborns) first code each VA form independently followed by a third level 1 physician if their assigned UCODs differ. When all three level 1 physicians do not agree, the form is elevated to a level 2 physician (specialists in obstetrics, neonatal or child health and/or very experienced in VA coding) for arbitration. If the level 2 physician agrees with the

UCOD assigned by any of the level 1 physicians, that cause is assigned to the death. However, when they do not agree with all three, the form is coded as indeterminate. The level 2 physicians also determine whether it was a neonatal or



**Figure 1.** Algorithm for consensus building around cause of death in AMANHI.

**Table 2.** AMANHI list of underlying causes of pregnancy-related deaths

Underlying cause of pregnancy-related deaths:
Ectopic pregnancy
Abortion-related death
Pregnancy-induced hypertension (pre-eclampsia)
Pregnancy-induced hypertension (eclampsia)
Obstetric haemorrhage (antepartum)
Obstetric haemorrhage (postpartum)
Obstructed labour
Ruptured uterus
Pregnancy-related sepsis (antepartum)
Pregnancy-related sepsis (postpartum)
Severe anaemia
Pre-existing medical conditions exacerbated by pregnancy
Accidents/injuries
Other specific obstetric causes
Other specific NON-OBSTETRIC causes
Cause not possible to determine from verbal autopsy
Other significant conditions contributing to death:
Anaemia
Severe malnutrition
HIV
Maternal age <15 years
Maternal age >35 years

**Table 3.** AMANHI list of underlying causes of neonatal deaths and contributing conditions

Underlying cause of neonatal death:
Preterm birth complications
Perinatal asphyxia
Neonatal pneumonia
Neonatal sepsis/meningitis
Neonatal tetanus
Congenital malformations
Neonatal diarrhoea
Accidents/injuries
Other specific perinatal causes
Cause not possible to determine from verbal autopsy
Other conditions contributing to neonatal death:
Term low birthweight (small for gestational age)
Prematurity
Maternal condition leading to neonatal death:
Pregnancy-induced hypertension (pre-eclampsia)
Pregnancy-induced hypertension (eclampsia)
Obstetric haemorrhage (antepartum)
Obstructed labour
Ruptured uterus
Maternal infection affecting the baby
Pre-existing medical conditions exacerbated by pregnancy
Accidents/injuries
Other obstetric complications (malpresentation, cord prolapse)
Other specific maternal conditions
No identifiable maternal conditions



**Table 4.** AMANHI list of types and underlying causes of fetal deaths (stillbirths) and contributing conditions

<b>Maternal/foetal underlying condition:</b>
Congenital malformations
Pregnancy-induced hypertension
Gestational diabetes
Antepartum haemorrhage
Maternal infections that can affect the foetus
Maternal medical conditions (diabetes, epilepsy, etc.)
Maternal accident/injury
Obstructed labour
Other obstetric complications (malpresentation, cord prolapse)
Other specific perinatal causes
Cause not possible to determine from verbal autopsy
<b>Other conditions contributing to the stillbirth:</b>
Small-for-date baby
Multiple pregnancy
Post-date (>10 months)
Maternal age <15 years
Maternal age >35 years
Obesity
Severe malnutrition
Smoking, alcohol or drug abuse

fetal death and, for the latter, whether it was ante- or intrapartum. All physicians also assign immediate and antecedent causes of deaths for each VA death certificate and specify co-existing significant pathologies/conditions that might have contributed to the death. They draw a flow diagram to explain the link between UCOD and the antecedent and immediate cause(s).

#### AMANHI verbal autopsy software and quality control of the coding process.

A customized software platform was developed by the Community Empowerment Laboratory (Lucknow, Uttar Pradesh, India), in collaboration with WHO/MCA to facilitate the COD assignment. The software helps to coordinate and manage the coding process. It has in-built algorithms to automate the assignment of forms to physicians and for the consensus-building process (Figure 1). Its user interface groups clinical signs and symptoms on the VA form according to physiological systems or/and stages of pregnancy. It also provides physicians with the template to construct the flowchart on the mechanism of the death and mandates them to complete a death certificate for each death, providing the list of UCODs in a drop-down menu. As a monitoring tool, site coordinators have a visual display of the frequency of agreement between each physician and the final UCOD for every form they code and this is used as proxy index to guide refresher training needs of physicians.

#### Quality monitoring

AMANHI-specific quality control procedures include physical presence of study supervisors to directly observe 5% VA interviews as they are being conducted in the field.

They then provide prompt feedback on fieldworker performance. Also, immediately after collection on the field, data are manually checked for completeness and consistency before transmission for data entry. The WHO/MCA sends experts on 6-monthly site visits to monitor quality of implementation. AMANHI mandates every site to submit monthly progress report and transmit all collected data every quarter for quality review and feedback.

#### Sample size considerations

Approximately 263 000 pregnant women will be enrolled into the mortality study across the 11 sites: about 126 000 from sub-Saharan Africa and 137 000 from South Asia. Sample size considerations were based on maternal mortality, given the rarity of this outcome. Estimated regional MMRs for sub-Saharan Africa and south Asia, pooled from the included countries, were 435 and 290 per 100 000 livebirths respectively (Table 5). With these sample sizes, AMANHI would have more than 90% power, at the 5% significance level, to detect all-cause mortality with a precision of  $\pm 8\%$  for sub-Saharan Africa and  $\pm 10\%$  for south Asia, with a higher precision for the pooled sample across all sites. The study will also have adequate power to quantify any single cause that accounts for at least 20% mortality (within  $\pm 15\%$ ). Considerations for country-specific samples sizes are shown in Table 5. With relatively more common outcomes such as stillbirths and neonatal deaths these sample sizes will guarantee highly precise mortality rate estimates overall and for regions and countries.

#### Data management

Data are collected using paper-based forms or tablet-based software with the exception of Zambia where field monitors collected data using forms designed in the TeleForms® system (HP, Cambridge, UK). After supervisors in Zambia review forms for completeness, they scan them, enter and

**Table 5.** Site specific sample size for all cause maternal mortality

STUDY SITE	SAMPLE SIZE	ESTIMATED MATERNAL MORTALITY RATIO/100 000 LIVE BIRTHS	RELATIVE PRECISION
<b>Sub region-Sub-Saharan Africa:</b>			
Democratic Republic of the Congo	20 000	670	$\pm 17\%$
Ghana	32 000	250	$\pm 22\%$
Kenya	22 000	400	$\pm 21\%$
Tanzania (2 sites)	27 000	360	$\pm 20\%$
Zambia	25 000	590	$\pm 16\%$
<b>Sub-Saharan Africa (pooled)</b>	<b>126 000</b>	<b>435</b>	<b><math>\pm 8\%</math></b>
<b>Sub-region-South Asia:</b>			
Bangladesh	19 000	200	$\pm 32\%$
India (2 sites)	90 000	325	$\pm 11\%$
Pakistan (2 sites)	28 000	240	$\pm 22\%$
<b>South Asia (pooled)</b>	<b>137 000</b>	<b>290</b>	<b><math>\pm 10\%</math></b>

export all the data into an Access database for management. Narratives are transcribed in the language of collection or directly into English, French, Swahili, Hindi or Urdu. Close-ended questions are double-entered independently by two clerks into appropriate software with in-built range and consistency checks. The double-entry checks against entry errors. All data are saved to a dedicated password-protected server and transferred quarterly to the WHO/MCA for further consistency checks.

### Data analysis

All analyses will be conducted using Stata statistical software [18]. Simple tabulations will be done to describe the overall burden, timing and causes of deaths—maternal, still-birth and neonatal. Estimates will also be generated from the sub-sample of women who were also part of the prospective morbidity follow-up.

### Ethical clearance and informed consent

The AMANHI mortality study received ethical clearance from institutional review boards in the participating countries, host institutions of principal investigators (including Johns Hopkins University, University of Kinshasa, London School of Hygiene and Tropical Medicine and Boston University) and the WHO. Informed consent is obtained from all respondents to the VA interviews.

## IMPORTANCE OF THE AMANHI MORTALITY STUDY

The AMANHI Mortality study is one of the first to generate improved estimates of the burden and timing of maternal, fetal and neonatal deaths in sub-Saharan Africa and south Asia from empirical data systematically collected in a large prospective cohort of women of reproductive age. More critically, it will make substantial contributions to global knowledge on the causes of these deaths. These improved estimates will inform policy, interventions and investment decisions to reduce these deaths.

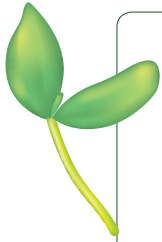
Availability of robust data are critical to intervention design and implementation. In resource-limited settings, allocation of scarce resources requires evidence-based decision-making which must be informed by reliable data [4,19]. Current evidence is derived from estimates from statistical models based largely on cross-sectional data, often facility based and generated using different methodologies and with varying definitions of outcomes. As a result of biases in the data, estimates from these models are difficult to validate, limiting stakeholder buy-in and adversely affecting their use in planning, intervention design and policy decision-making [4,12,20].

The AMANHI mortality study has many strengths. It is a population-based prospective study which followed up a large cohort of women of reproductive age at the community level. Data were also collected from the facilities women attended for deliveries and medical emergencies. This will therefore reduce selection biases that might have resulted from using only facility-based data. Perhaps the greatest strength is the harmonised implementation across all 11 study sites. With the use of common tools and definitions of variables and outcomes, AMANHI collected context-relevant but uniform data across all sites. This validates the pooling of the data across the sites to allow for analyses on rare outcomes.

The AMANHI approach to assigning causes of deaths strategically addresses many of the drawbacks in the use of physicians including drain on their time and subjectivity. The AMANHI VA coding software reduced physician coding time from 90 minutes to less than 20 minutes per verbal autopsy. This reduced time addresses concerns by some advocates that physician times should be better spent in actual service delivery [15,21–23]. Besides, whilst automated computer algorithms have the potential to dramatically improve the speed and efficiency of classifying causes and reducing cost [24], incorporating physician's knowledge of the local context, terminologies and their interpretations in evaluating the causes of deaths is an additional advantage that computer-based algorithms may not have. Furthermore, the use of the ICD principles, centralised accreditation process, automation of the form assignment to physicians and other quality control mechanisms improved the transparency and objectivity of the process. The provision of a limited list of causes and their operational definitions also reduced the occurrence of false discordance between physicians due to typographical errors.

One major limitation of the AMANHI mortality study is generalizability of the results. Data were collected in defined parts of the respective countries; at sites systematically selected for newborn health interventions because of high mortality rates. It is plausible that mortality rates in the study areas might not truly represent all regions of the participating countries. However, estimates from AMANHI will be compared to prevailing estimates for countries. Differences may result from several factors such as quality of data but will challenge the status quo.

The need for robust empirically generated data to inform policy and planning in LMICs is long overdue. By generating data from a very large cohort of women across eleven countries in these two geographic areas with the highest mortality burden, AMANHI will provide very precise estimates of mortality, their timing and causes to inform researchers and policy-makers on improved methods for assigning cause of death in women and children.



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# Shifting chronic disease management from hospitals to primary care in Estonian health system: analysis of national panel data

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**Background** Following independence from the Soviet Union in 1991, Estonia introduced a national insurance system, consolidated the number of health care providers, and introduced family medicine centred primary health care (PHC) to strengthen the health system.

**Methods** Using routinely collected health billing records for 2005–2012, we examine health system utilisation for seven ambulatory care sensitive conditions (ACSCs) (asthma, chronic obstructive pulmonary disease [COPD], depression, Type 2 diabetes, heart failure, hypertension, and ischemic heart disease [IHD]), and by patient characteristics (gender, age, and number of co-morbidities). The data set contained 552 822 individuals. We use patient level data to test the significance of trends, and employ multivariate regression analysis to evaluate the probability of inpatient admission while controlling for patient characteristics, health system supply-side variables, and PHC use.

**Findings** Over the study period, utilisation of PHC increased, whilst inpatient admissions fell. Service mix in PHC changed with increases in phone, email, nurse, and follow-up (vs initial) consultations. Healthcare utilisation for diabetes, depression, IHD and hypertension shifted to PHC, whilst for COPD, heart failure and asthma utilisation in outpatient and inpatient settings increased. Multivariate regression indicates higher probability of inpatient admission for males, older patient and especially those with multimorbidity, but protective effect for PHC, with significantly lower hospital admission for those utilising PHC services.

**Interpretation** Our findings suggest health system reforms in Estonia have influenced the shift of ACSCs from secondary to primary care, with PHC having a protective effect in reducing hospital admissions.

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Estonia, a Baltic state with a population of 1.3 million people [1], has introduced comprehensive health system reforms following independence from the Soviet Union in 1991. The reforms (**Box 1**), which were aimed at improving population health, providing financial risk protection to citizens, enhancing user satisfaction and ensuring financial sustainability, centred on strengthening primary health care (PHC), introduction of a national health insurance system, and consolidating the number of hospitals [2].

**Box 1.** Key reforms and policy changes in the Estonian Health System 2005–2012

**2006:** Quality bonus system implemented in PHC to promote disease prevention and management of selected chronic conditions [2]; Family nurse services also expanded.

**2008:** Nationwide e-health system (integrated electronic health records, e-prescriptions, digital imaging, and laboratory tests, allowing information exchange between clinical, research and managerial professionals, with data confidentiality governed by strict protection laws, whilst providing patients access and control of their records [3]) launched to improve efficiency by reducing paperwork and duplication.

**2009:** Adoption of the Primary Health Care Development Plan that emphasized comprehensive service provision in PHC, prevention, chronic disease management, and improvements to access and care continuity [3]; Health service tariffs reduced by 6% due to economic crisis; maximum waiting times for outpatient specialist visits extended from four to six weeks; outpatient specialist care given higher priority over inpatient care to contain expenditure [2].

**2010:** Amendment to decree on prescribing and dispensing drugs requiring pharmacies to provide patients with the cheapest generic drug; Expansion of the role of family nurses to provide consultations and counselling to key groups, including chronically ill, pregnant women and healthy neonates. School nurses provide all school health services and immunizations. Midwives can prescribe in certain cases and operate individual practices.

**2011:** Health service payment tariffs increased by 1% in general, and by 3% in PHC to encourage higher use of PHC and lower use of hospitals.

**2012:** Tariffs increased to pre-crisis level, with the differential between PHC and hospitals introduced in 2011 maintained; Centralization of planning and regulatory functions, with PHC management functions centralized from country governors to the National Health Board; Amendment to Health Insurance Act to strengthen the gatekeeping function of PHC by reducing the number of directly accessible specialties in outpatients; Age-adjusted capitation payment scheme strengthened to motivate family doctors to treat more patients with chronic conditions and improve management of chronic conditions.

Family medicine was established as a specialty in Estonia in 1993, and in 1997 all citizens were required to register with a family physician, who were established as independent providers or from 2008 employed by municipalities [4,5]. The family medicine model placed PHC at the centre of the health system to improve quality, gatekeeping and care-coordination [6,7], and to address inefficiencies inherited from the Soviet-style hospital-centred health system, by reducing excessive referral and inpatient admissions to hospitals [6].

Estonia transitioned to an insurance-based financing model in 1991 with the creation of regional sickness funds [6], followed by the establishment of the independent Estonian

Health Insurance Fund (EHIF) in 2001 as the national agency responsible for purchasing health care and contracting with health care providers [3]. From its inception, the EHIF implemented a purchasing strategy that prioritised outpatient care over inpatient hospital care through contracting targets and by reallocating funding [3]. Other supply-side changes aimed at improving service quality and efficiency included introduction of clinical guidelines [8], and using new provider payment mechanisms (capitation and of pay-for-performance [P4P] in PHC, and diagnosis-related groups (DRGs) in hospitals).

Strong PHC is associated with more equitable and accessible health care, greater efficiency, reduced emergency care, and better health outcomes [9,10], though few national-level empirical studies exist [10]. Analysis of the Estonian health system reforms offers, therefore, the opportunity to assess the countrywide effect of introducing family medicine centred PHC on health service utilisation, and specifically on the management of chronic conditions. Nationwide individual level data on health care utilisation has been collected by the EHIF since 2000/2001. Data on health system supply-side variables (including health care providers and professionals) and demographic and socio-economic variables allow us to investigate the nationwide effect of health system changes after controlling for other factors influencing health service utilisation.

We examine how the Estonian health system reforms have affected service utilisation across 2005–2012 in family medicine clinics and outpatient departments, and admissions to hospital for selected ambulatory-care sensitive conditions (ACSCs); conditions which should be effectively managed in PHC [11,12]. In a health system with appropriate access to [13] and effective provision of [14] PHC, hospital admissions for ACSCs should largely be avoidable. Study of Estonia is timely, as PHC is critical for achieving universal health coverage (UHC) [15], for creating a patient-centred health systems, and for efficient and effective management non-communicable diseases (NCDs) [16,17].

## METHODS

The study used data from the EHIF administrative data set, which contains patient level records of all PHC, outpatient and inpatient contacts. While the EHIF data has been collected since 2000/2001, data completeness was achieved in 2005 when quality assurance of the data set was standardised. Therefore, the study period is limited to 1 January 2005 to 31 December 2012.

For the period 2005 and 2012, the EHIF data set contains 35.6 million PHC records, 22.2 million outpatient records and 1.7 million inpatient records, covering 1.1–1.2 million patients per year and all health care utilisation episodes for Estonian citizens.

The EHIF uses an electronic invoicing system with controls that ensure all submitted invoices have appropriate patient data, diagnoses and other relevant information related to the contact with the health system. In addition, EHIF uses a retrospective data quality analytical reporting system to identify systematic outliers that are not possible to detect during invoicing. As providers are paid for the services they provide, there is unlikely to be under-reporting, and electronic fraud and quality checking mechanisms ensure data reporting and coding quality.

Seven ACSCs were selected for the analysis: asthma, chronic obstructive pulmonary disease (COPD), depression, Type 2 diabetes, heart failure, hypertension, and ischaemic heart disease (IHD). These ACSCs, which are well-established in the literature and have been used in earlier studies [14,18], account for a proportionally high disease burden in Estonia [19]. We included depression in our list of ACSCs—a relatively prevalent mental health condition that accounts for a high burden of illness and disability [16], with high levels of hospital admissions [20], and common in patients with multi-morbidity [21].

Records for all episodes of care for patients aged 15 years and older, with a primary diagnosis of the seven ACSCs were extracted from the EHIF database. In the database, diagnostic information is coded using the international classification of diseases, 10<sup>th</sup> revision (ICD-10) [22]. All episodes of care with the following ICD 10 codes were eligible for inclusion: asthma (J45), COPD (J44.9), depression (F32), diabetes (E11), heart failure (I50), hypertension (I10, I11–I15) and IHD (I20 & I25).

For all episodes of care, the start and end date of the health care invoice, age, gender, the county of residence of the patient, and the primary diagnosis are recorded. For PHC episodes, details on the service provider (family physician or family nurse) and type of consultation (new vs follow-up, preventive, home visit, telephone or email consultation) are also available.

We obtained data on county level health system and demographic variables from the Statistics Estonia website [23] and the Health Statistics and Health Research Database [24]. These data included total population (by age group); the number of doctors and nurses (full-time equivalents (FTEs)) working in family doctors' offices; number of hospitals and hospital beds; number of family doctor offices; employment rate (individuals aged 15–64 years); and mean yearly disposable income.

To explore changes in PHC provision, we investigated changes in the total number of doctors and nurses per population, as well as PHC practice patterns over time. We analysed PHC practice patterns for ACSCs by service provider (family doctor vs nurse), type (new episode, follow-

up or preventative), and location (office, home, phone/email).

For analysis of national trends in health service utilisation, the total number of yearly health service contacts for all patients in each diagnosis group was aggregated for primary, outpatient; and inpatient care. Utilisation trends were summarized for each health condition using age-standardised service utilisation rates per 100 000 population. We also compared the proportional distribution of service use between different services for each health condition analysed.

For analyses using patient level data, a data set of patient-year observations was created. Unique patient identification numbers in EHIF allow for patients to be followed in time and across primary and secondary care levels. Therefore, the resulting patient-year data was a longitudinal (panel) data set rather than a multi-year cross-section. Panel data has advantages over cross-sectional data, as the analysis can be used to exploit both inter-individual differences and intra-individual dynamics, and as it allows for more accurate inference of model parameters, controlling the impact of omitted variables, uncovering dynamic relationships and providing micro foundations for aggregate data analysis [25]. Each observation in the data set included information on the age and county of residence of the patient in that year and the total number of PHC, outpatient, and inpatient contacts for the selected ACSCs. Multimorbidity was defined as the number of different diagnoses (of the seven ACSCs analysed) for the patient recorded in primary, outpatient or inpatient care in the given year.

Trends in patient-level utilisation patterns for primary, outpatient, and inpatient care were examined by patient age, gender, specific conditions and multimorbidity status (one, two, three, and four or more recorded conditions). While we only present summary statistics for the earliest and latest year of data for each stratum, we tested the statistical significance of yearly trends using basic linear regression models, which are reported in *P*-values in text and in tables.

For patient level multivariate analyses, the outcome of interest is the probability of an inpatient admission in a given year, for patients that had at least one health care contact for any of the seven ACSCs. Given the panel and nested structure of the data set (patients are 'clustered' in counties), the appropriate model of analysis is a multi-level regression, with county level random effects, and robust standard errors [26], to control for intra-cluster correlation. The model specification is:

$$\Pr(y_{i,j,t} = 1 | x, z; u_j) = H\left(\beta_0 + \gamma_t \text{year} + \sum_{i=1}^n \beta_{it} x_{it} + \sum_{\delta=1}^n \delta_{j,t} z_{j,t} + u_{ij}\right)$$

where  $H(\cdot)$  is the logistic cumulative distribution function, mapping linear predictor to the probability of an admission ( $y_{i,j,t} = 1$ ) with  $H(v) = \exp(v)/(1 + \exp(v))$ . The regression co-

efficient  $\gamma$  provides the estimate for the yearly trend in the probability of an inpatient admission, adjusted for patient level explanatory variables ( $x_{i,t}$ : age, gender, and number of conditions) and access to care as measured by county level supply side variables ( $z_{j,t}$ : number of hospitals, beds, PHC centres and doctors in PHC per 1000 population, nurse to doctor ratio in PHC, and log average disposable income in the county).

Using patient level data, we also explored the association between PHC visits and rate of inpatient admissions by patient age, gender and multimorbidity status for 2005 and 2012. For each subgroup of patients, we report the rate of inpatient admissions for patients who had no PHC visits for the seven ACSCs and those who had at least one PHC visit. We provide the logistic regression estimates of the crude and adjusted odds of inpatient admission, for patients who had at least one PHC visit relative to those who did not in the same year. All regression results have robust standard errors controlling for county level clusters.

## RESULTS

Between 2005 and 2012, 552 822 unique patients accessed health services for at least one of the seven selected ACSCs. The total number of patient years covered by the study was 2 257 347. The number of patients accessing health services per year ranged from approximately 260 000 to 300 000, corresponding to 22.0–27.0% of Estonian population aged 15 years and older. Around 63.2% of the patients using health services was female, and the mean age of the patients was 63.3 years.

Approximately 76.7% of the patients presented to services with only one ACSC in a given year, 19.2% had two ACSCs and 4.1% had three or more ACSCs. Hypertension was the most frequent condition in PHC contacts for ACSCs in a given year, with 75.4% of all patients having at least one PHC contact due to hypertension, followed by IHD and diabetes (14.3% and 12.2%, respectively).

The total number of contacts (PHC, outpatient and inpatient) for the seven ACSCs increased from 936 365 in 2005 to 1 247 522 in 2012. The majority of health care contacts occurred in PHC and at outpatient clinics. In 2005, 77.8% of the total contacts were in PHC, 20.0% in outpatients and 2.2% in inpatients. By 2012, the relative proportion for PHC visits had increased to 81.1% of total contacts, while outpatient visits declined to 17.5%, and inpatient admissions fell to 1.4% (**Table 1**).

PHC consultations for ACSCs rose by 38.8%, from 728 885 in 2005 to 1 011 906 in 2012. More than 90% of consultations took place in family doctors' offices, with the proportion decreasing from 93.9% to 85.2% of PHC consultations during the study period. Home visits as a percentage of all PHC contacts also declined (3.3% to 1.3%). There was a six-fold increase in the use of phone consultations in PHC from 20 000 calls in 2005 to 135 000 in 2012 (2.8% to 13.4%), and email consultations, which have been recorded since 2010, rose to 907 in 2012 (**Figure 1** and **Figure 2**).

There were small differences in the type of visit by patient gender, age group and condition. In 2012, patients who were aged greater than 75 years were more likely to have home visits (3.2%) or phone consultations (15.1%) than patients in other age groups, whereas younger patients were more likely to have email consultations. Patients with a diagnosis of heart failure were most likely to have a home visit (5.0%), whereas patients with asthma and depression used phone/email consultations more frequently than patients with other conditions (14.2% and 14.0%, respectively).

Between 2005 and 2012, new consultations decreased by 16.6% (from 233 044 to 194 293) and follow-up consultations increased by 41.5% (from 360 454 to 510 120). The proportion of follow-up consultations among episodes of care in family doctors' offices increased from 55.3% to 70.8%.

While the number of family physicians per capita stayed relatively constant during the study period, the number of full-time equivalent (FTE) nurses in family doctors' offices increased by 26.7% from 0.49 to 0.63 per 1000 popula-

**Table 1.** Total contacts (consultations and hospitalisations) for seven selected conditions (2005–2012) and distribution by primary, outpatient and inpatient care.

	2005	2006	2007	2008	2009	2010	2011	2012
Total contacts*	936 365	973 896	1 031 422	1 181 308	1 137 760	1 179 355	1 202 887	1 247 522
Age-standardised rate†	91 888	95 221	100 366	114 349	109 454	112 718	114 157	117 516
<b>Percentage of contacts by service tier:</b>								
PHC	77.8	77.1	77.9	78.6	79.1	80.4	80.2	81.1
Outpatient	20.0	20.6	20.0	19.5	19.2	18.0	18.3	17.5
Inpatient	2.2	2.2	2.1	1.8	1.7	1.6	1.5	1.4

PHC – Primary Health Care

\*Includes all consultations and hospitalisations.

†Per 100 000 population.



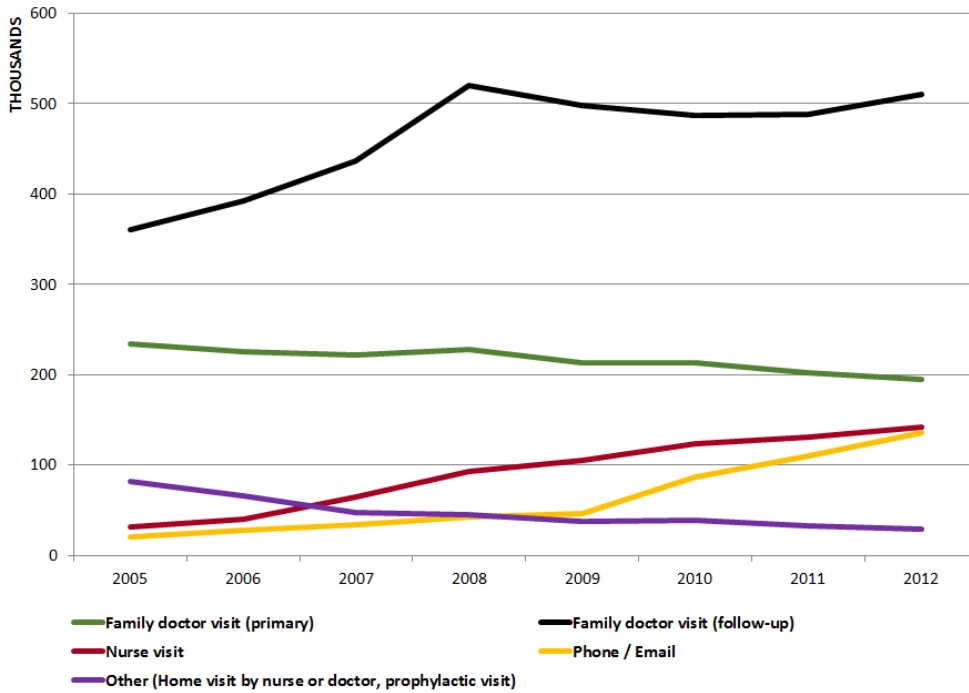


Figure 1. Total number of consultations in primary health care by type.

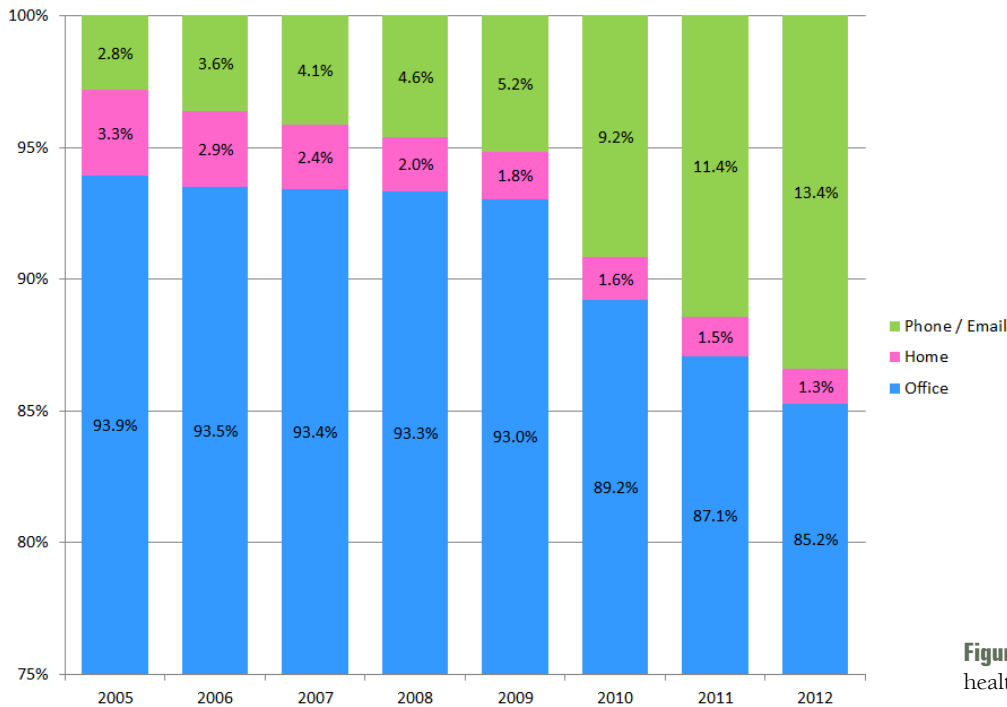
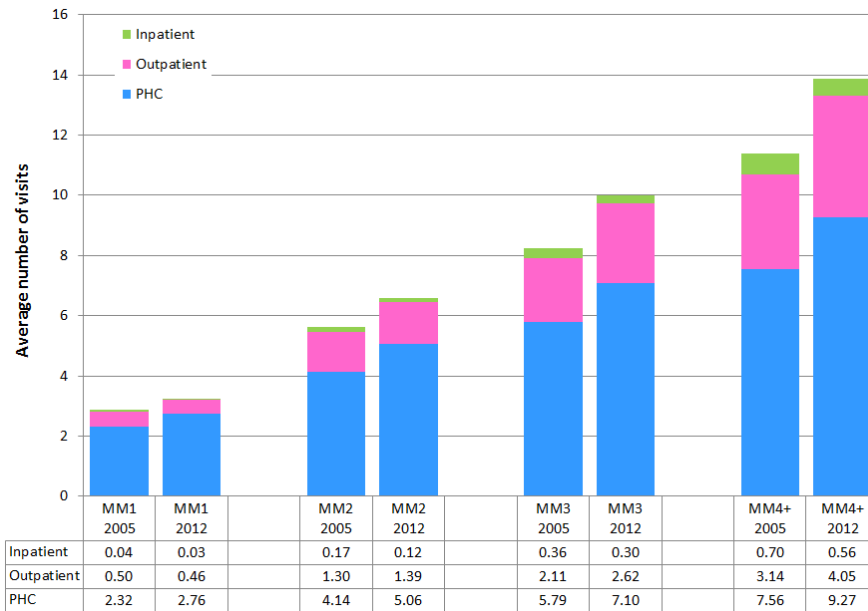


Figure 2. Proportion of primary health care consultations by type.

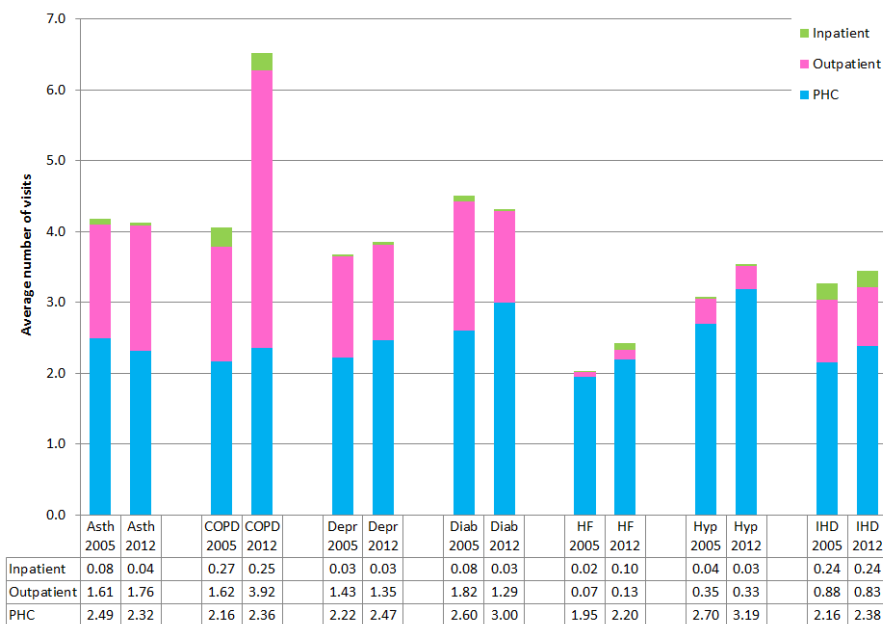
tion. Nurse consultations increased four-fold, from 34 253 to 145 348. Patients with hypertension, diabetes and heart failure were more likely to be consulted by a nurse as compared with patients with other ACSCs.

Among patients that accessed PHC for any of the ACSCs, the average number of visits per patient was 2.8 in 2005, increasing to 3.4 visits in 2012. Average number of outpatient visits remained stable at 0.72 per patient, however. A decreasing

number of patients had at least one inpatient admission during the year: 16 541 patients (6.4%) in 2005 and 13 674 (4.6%) in 2012. The average number of inpatient admissions per patient decreased from 0.079 to 0.056 between 2005 and 2012. Females had higher number of PHC visits on average, while males had higher outpatient consultations and inpatient admissions in both 2005 and 2012 (Figure S1 in Online Supplementary Document).



**Figure 3.** Number of visits in primary, outpatient and inpatient care, by multimorbidity group, 2005 and 2012. MM1 – 1 multi-morbidity, MM2 – 2 multi-morbidities, MM3 – 3 multi-morbidities, MM4+ – 4 or more multi-morbidities.



**Figure 4.** Average number of visits in primary, outpatient and inpatient care, by condition, 2005 and 2012. Asth – asthma; COPD – chronic obstructive pulmonary disease; Depr – depression; Diab – diabetes; HF – heart failure; Hyp – hypertension; IHD – ischemic heart disease.

The average number of visits to PHC and hospitals rose with increasing age and multi-morbidity, with the highest inpatient admission rate observed for patients that had four or more ACS conditions in a given year, and in particular for those aged 55 and above. (Figure 3, Table 2, and Figure S2 in Online Supplementary Document). Healthcare utilisation varied by condition: patients that had at least one health contact in a given year with a primary diagnosis of diabetes or hypertension utilised PHC services more frequently than patients with other diagnoses. Average number of outpatient visits was higher for patients with diabetes, COPD, asthma and depression, and rose significantly for patients with COPD in 2012, whereas patients with IHD or COPD had more frequent inpatient admissions (Figure 4).

Age standardised rates for total health service contacts were 91.9 per 1000 population in 2005 and 117.5 per 1000 population in 2012. PHC utilisation rate was highest (by a significant proportion) for patients with hypertension, followed by diabetes in 2005 and IHD in 2012 (Figure S3 in Online Supplementary Document). Rates of outpatient visits were also highest for patients with hypertension and diabetes (Figure S4 in Online Supplementary Document). Inpatient admission rates were highest for IHD and hypertension in both years (Figure S5 in Online Supplementary Document).

The utilisation levels between the three service elements for each ACSC vary (Figure 5). During the study period, of the seven ACSCs, more than 85% of service utilisation

**Table 2.** Average number of inpatient admissions, by age and multimorbidity (MM) group, 2005 and 2012

Age, year	Number of patients	MM1		MM2		MM3		MM4+	
		%*	Mean	%*	Mean	%*	Mean	%*	Mean
15–44, 2005	32 603	94.3	0.023	5.4	0.082	0.3	0.162	0.0	0.429
15–44, 2012	34 120	93.8	0.019	5.9	0.057	0.4	0.108	0.0	0.417
45–54, 2005	36 624	84.8	0.034	13.6	0.148	1.4	0.312	0.1	0.667
45–54, 2012	39 114	85.6	0.018	13.0	0.082	1.4	0.175	0.1	0.571
55–64, 2005	55 050	78.3	0.038	18.5	0.179	2.9	0.365	0.4	0.724
55–64, 2012	69 122	78.4	0.022	18.3	0.102	2.9	0.266	0.4	0.627
65–74, 2005	70 603	71.8	0.045	23.2	0.177	4.4	0.366	0.7	0.712
65–74, 2012	73 284	73.4	0.028	21.6	0.125	4.2	0.303	0.7	0.553
75+, 2005	63 335	66.9	0.049	26.4	0.175	5.9	0.367	0.9	0.690
75+, 2012	83 799	68.6	0.038	24.8	0.143	5.6	0.321	1.0	0.550

MM1 – 1 multi-morbidity; MM2 – 2 multi-morbidities; MM3 – 3 multi-morbidities; MM4+ – 4 or more multi-morbidities

\*Percentages shown are of total admissions for that age-group and year.

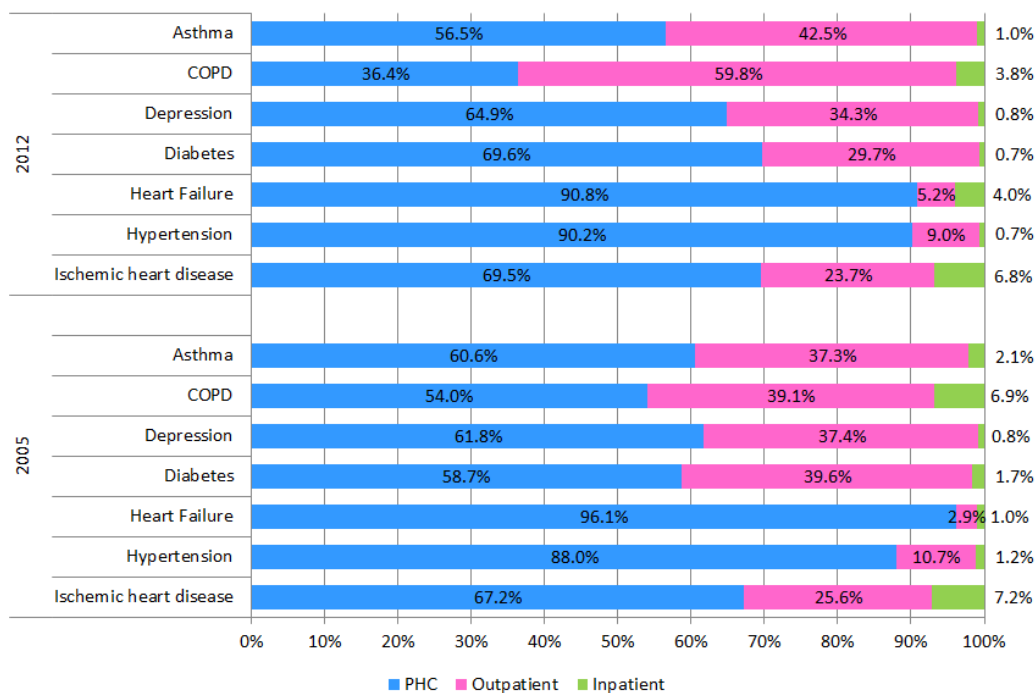
for heart failure and hypertension was in PHC; followed by IHD, depression, and diabetes (63–68%), asthma and COPD (57% and 41% respectively).

Across all gender, age and multimorbidity groups, average number of PHC visits increased between 2005 and 2012 ( $P < 0.01$ ) and inpatient admissions decreased ( $P < 0.01$ ) (Table 3). Patterns of outpatient visits varied by groups: outpatient utilisation for patients aged 75+ ( $P = 0.001$ ) and patients with three ACSCs rose ( $P = 0.03$ ), but declined for those aged for 45–54 ( $P = 0.01$ ) and for patients with one ACSC only ( $P = 0.002$ ).

Service utilisation trends for average number of condition-specific contacts for patients with a primary diagnosis of a condition in a given year also varied. Average number of PHC visits increased for all ACSCs except asthma. Outpa-

tient visits increased for heart failure and COPD, yet declined for diabetes and hypertension. The number of inpatient admissions decreased for asthma, COPD, diabetes and hypertension, but increased for heart failure.

The age-standardised rate for total health service contact increased by 27.9% during the study period from 91 888 to 117 516. For PHC and outpatient services, total utilisation for ACSCs increased by 32.0% (from 72 491 to 95 720) and 16.4% (from 17 347 to 20 193) respectively, whereas age-standardised inpatient admissions rates declined by 21.8% from 2051 to 1604. Yearly trends in PHC utilisation rates were significant for all ACSCs except COPD and depression, with PHC utilisation falling for IHD and heart failure ( $P < 0.001$ ) and rising for asthma, diabetes and hypertension ( $P < 0.001$ ). Outpatient utilisation rates were



**Figure 5.** Distribution of utilization of total consultations and hospital admissions for seven selected conditions between primary health care (PHC), outpatient, and inpatient services (2005 and 2012).

**Table 3.** Annual trends in utilisation measures by selected patient characteristics, univariate linear regression model

	PHC VISITS	OUTPATIENT VISITS	INPATIENT VISITS
<b>Gender:</b>			
Male	Increase ( $P=0.001$ )	No change ( $P=0.57$ )	Decrease ( $P<0.001$ )
Female	Increase ( $P=0.001$ )	No change ( $P=0.41$ )	Decrease ( $P<0.001$ )
<b>Age:</b>			
15–44	Increase ( $P=0.001$ )	No change ( $P=0.48$ )	Decrease ( $P=0.004$ )
45–54	Increase ( $P=0.01$ )	Decrease ( $P=0.01$ )	Decrease ( $P<0.001$ )
55–64	Increase ( $P=0.004$ )	No change ( $P=0.56$ )	Decrease ( $P<0.001$ )
65–74	Increase ( $P=0.001$ )	No change ( $P=0.46$ )	Decrease ( $P<0.001$ )
75+	Increase ( $P<0.001$ )	Increase ( $P=0.004$ )	Decrease ( $P=0.002$ )
<b>Multimorbidity:</b>			
1	Increase ( $P=0.001$ )	Decrease ( $P=0.002$ )	Decrease ( $P<0.001$ )
2	Increase ( $P<0.001$ )	No change ( $P=0.18$ )	Decrease ( $P<0.001$ )
3	Increase ( $P<0.001$ )	Increase ( $P=0.03$ )	Decrease ( $P=0.002$ )
4+	Increase ( $P<0.001$ )	No change ( $P=0.29$ )	Decrease ( $P<0.001$ )
<b>Condition-specific, mean visits per patient:</b>			
Asthma	No change ( $P=0.06$ )	No change ( $P=0.55$ )	Decrease ( $P<0.001$ )
COPD	Increase ( $P=0.01$ )	Increase ( $P=0.05$ )	Decrease ( $P=0.02$ )
Depression	Increase ( $P=0.005$ )	No change ( $P=0.74$ )	No change ( $P=0.12$ )
Diabetes	Increase ( $P=0.004$ )	Decrease ( $P<0.001$ )	Decrease ( $P<0.001$ )
Heart failure	Increase ( $P=0.001$ )	Increase ( $P=0.001$ )	Increase ( $P<0.001$ )
Hypertension	Increase ( $P=0.001$ )	Decrease ( $P=0.03$ )	Decrease ( $P=0.001$ )
IHD	Increase ( $P=0.02$ )	No change ( $P=0.78$ )	No change ( $P=0.41$ )
<b>Condition-specific, utilisation rates per 100 000 population:</b>			
Asthma	Increase ( $P<0.001$ )	Increase ( $P=0.002$ )	Decrease ( $P<0.001$ )
COPD	No change ( $P=0.29$ )	No change ( $P=0.06$ )	Decrease ( $P=0.01$ )
Depression	No change ( $P=0.15$ )	No change ( $P=0.20$ )	No change ( $P=0.11$ )
Diabetes	Increase ( $P<0.001$ )	No change ( $P=0.07$ )	Decrease ( $P=0.01$ )
Heart failure	Decrease ( $P<0.001$ )	Increase ( $P=0.003$ )	Increase ( $P<0.001$ )
Hypertension	Increase ( $P<0.001$ )	Increase ( $P=0.02$ )	Decrease ( $P=0.04$ )
IHD	Decrease ( $P<0.001$ )	Decrease ( $P<0.001$ )	Decrease ( $P<0.001$ )

PHC – primary health care; COPD – chronic obstructive pulmonary disease; IHD – ischaemic heart disease

comparable during the study period for COPD, depression and diabetes, decreased for IHD and increased for all remaining ACSCs. Inpatient admission rates increased for heart failure and decreased for asthma, COPD, diabetes, hypertension and IHD. The significance of yearly trends in age-standardised inpatient admission rates remained in multivariate, county-year panel regressions with county random effects, adjusting for demographics and disease burden (% of patients over 65 years of age, % of patients with three or more ACSC), supply side variables (number of hospitals, beds, PHC centres and doctors in PHC per 1000 population, nurse to doctor ratio in PHC) and socio-economic factors (disposable income, employment rate) (Table S1 in **Online Supplementary Document**).

For diabetes, depression, IHD and hypertension there is a shift towards greater utilisation in PHC (**Figure 5**). For diabetes PHC utilisation increased from 58.7% of total episodes in 2005 to 69.6% in 2012, whereas outpatient and inpatient episodes fell from 39.6% to 29.7% and 1.7% to 0.7%, respectively. There was a similar, albeit smaller, shift in the proportional utilisation of PHC for depression, IHD and hypertension. For depression, PHC utilisation rose from 61.8% to 64.9%, IHD from 67.2% to 69.5% and hypertension from

88.0% to 90.2% of total, with concomitant reductions in the share of utilisation in outpatient and inpatient episodes.

Conversely, COPD utilisation in PHC as a proportion of total episodes decreased from 54.0% in 2005 to 36.4% in 2012, inpatient episodes declined from 6.9% to 3.8% whilst outpatient episodes grew from 39.1% to 59.8% of total. For heart failure, utilisation of PHC as a proportion of total fell from 96.1% to 90.8% while inpatient and outpatient proportions rose from 1.0% to 4.0% and 2.9% to 5.2%, respectively. For asthma, share of outpatient episodes increased, while that for PHC and inpatient admissions fell.

Using patient-year level data, we applied the multivariate regression model to examine the probability of inpatient admissions for patients that accessed health services in a given year for any condition, controlling for patient characteristics and availability of services in the county of residence (**Table 4**). The overall time trends were significant, with the probability of inpatient admissions declining in the study period (odds ratio OR 0.932, 95% CI 0.927, 0.936).

The odds of inpatient admission was higher for males, and increased with age and multimorbidity: patients over 65

**Table 4.** Multivariate regression model of inpatient admissions (multi-level logistic regression with county random effects and robust standard errors, n=2 257 347 patient-year observations)

	OR	L 95% CI	U 95% CI	P-VALUE
	0.932	0.927	0.936	<0.001
<b>Patient characteristics:</b>				
Female	0.603	0.596	0.611	<0.001
<b>Age group:</b>				
15–44	1.000	–	–	–
45–54	1.344	1.301	1.388	<0.001
55–64	1.622	1.575	1.671	<0.001
65–74	1.974	1.918	2.032	<0.001
75+	2.413	2.345	2.484	<0.001
<b>Multimorbidity:</b>				
1	1.000	–	–	–
2	4.317	4.261	4.374	<0.001
3	10.049	9.860	10.241	<0.001
4+	20.065	19.320	20.839	<0.001
<b>Regional characteristics:</b>				
Number of hospitals	0.179	0.026	1.223	0.079
Number of beds	1.011	0.985	1.037	0.424
FTE doctors in FM	1.056	0.855	1.305	0.610
Ratio of nurses/doctors in FM	0.955	0.858	1.063	0.402
Disposable income (log)	1.224	1.154	1.297	<0.001
Random effects (county)				
<i>var(cons): 0.255 (se 0.051)</i>				

OR – odds ratio, L 95% CI – lower 95% confidence interval, U 95% CI – upper 95% confidence interval, FTE – full-time equivalent; FM – family medicine

years of age were two times more likely to have an inpatient admission as compared with patients 15–44 years of age (Age 65–74 OR 1.97, 95% CI 1.91, 2.03; Age 75+ OR 2.41, 95% CI 2.35, 2.48). Patients with four or more ACSCs were 20 times more likely to have an inpatient admission than patients with a single ACSC (95% CI 19.3, 20.8). In counties with higher average income, the likelihood of inpatient admissions was higher. Other county level variables, such as hospitals, beds and number of physicians per capita were not statistically significant.

In 2005, among the patients who had any health contact with the seven ACSCs, 8.2% did not have any PHC contact (had only outpatient or inpatient contact) for these conditions, declining to 6.7% in 2012. The proportion of patients who did not have any PHC contact was higher for males and decreased by age and multimorbidity groups. Those who did not have any PHC contact were more likely to have an inpatient admission than patients with at least one PHC contact (0.121 vs 0.059; adjusted OR 0.20, 95% CI 0.15, 0.29). This association held for 2012, as well as for all patient gender, age and multimorbidity groups (Table 5).

**Table 5.** Inpatient admissions, by primary care attendance in the same year

	Number of patients	% No. PHC contact	INPATIENT ADMISSIONS RATE		ODDS OF INPATIENT ADMISSIONS WITH AT LEAST ONE PHC CONTACT*	
			No PHC contact	1+ PHC contact	Crude OR (95% CI)	Adjusted OR† (95% CI)
ALL 2005	258 215	8.2	0.121	0.059	0.45 (0.36, 0.57)	0.20 (0.15, 0.25)
ALL 2012	299 439	6.7	0.107	0.041	0.36 (0.31, 0.42)	0.13 (0.11, 0.16)
<b>By gender:</b>						
Males 2005	82 280	10.0	0.140	0.074	0.49 (0.40, 0.61)	0.22 (0.17, 0.27)
Males 2012	112 930	7.8	0.128	0.050	0.36 (0.31, 0.42)	0.13 (0.11, 0.17)
Females 2005	163 810	7.3	0.107	0.051	0.45 (0.35, 0.57)	0.18 (0.13, 0.23)
Females 2012	186 509	6.1	0.091	0.036	0.37 (0.31, 0.44)	0.13 (0.10, 0.16)
<b>By age group:</b>						
15–44, 2005	32 603	22.3	0.047	0.018	0.38 (0.30, 0.48)	0.31 (0.24, 0.40)
15–44, 2012	34 120	20.2	0.042	0.012	0.28 (0.24, 0.34)	0.22 (0.18, 0.28)
45–54, 2005	36 624	11.1	0.084	0.041	0.46 (0.40, 0.54)	0.32 (0.26, 0.39)
45–54, 2012	39 114	9.0	0.068	0.021	0.29 (0.25, 0.34)	0.18 (0.15, 0.21)
55–64, 2005	55 050	8.0	0.113	0.056	0.46 (0.36, 0.59)	0.28 (0.21, 0.38)
55–64, 2012	69 122	6.1	0.092	0.034	0.34 (0.31, 0.39)	0.19 (0.16, 0.22)
65–74, 2005	70 603	5.1	0.185	0.068	0.32 (0.25, 0.43)	0.19 (0.13, 0.26)
65–74, 2012	73 284	4.2	0.159	0.046	0.26 (0.20, 0.33)	0.13 (0.09, 0.19)
75+, 2005	63 335	3.1	0.378	0.078	0.14 (0.10, 0.19)	0.06 (0.04, 0.09)
75+, 2012	83 799	2.9	0.307	0.061	0.15 (0.12, 0.19)	0.07 (0.05, 0.09)
<b>By multimorbidity:</b>						
MM1, 2005	197 950	10.1	0.114	0.026	0.21 (0.16, 0.26)	0.16 (0.13, 0.20)
MM1, 2012	230 954	8.3	0.099	0.016	0.15 (0.12, 0.17)	0.11 (0.09, 0.13)
MM2, 2005	49 976	2.4	0.237	0.133	0.50 (0.40, 0.61)	0.47 (0.40, 0.56)
MM2, 2012	56 367	1.8	0.229	0.097	0.36 (0.29, 0.44)	0.32 (0.27, 0.39)
MM3, 2005	8 986	0.8	0.306	0.262	0.81 (0.58, 1.11)	0.78 (0.56, 1.07)
MM3, 2012	10 399	0.8	0.481	0.212	0.29 (0.21, 0.40)	0.28 (0.20, 0.39)
MM4+, 2005	1 303	0.2	0.667	0.448	N/A‡	N/A‡
MM4+, 2012	1 719	0.1	<0.001	0.370	N/A‡	N/A‡

PHC – Primary Health Care, MM1 – 1 multi-morbidity, MM2 – 2 multi-morbidities, MM3 – 3 multi-morbidities, MM4+ – 4 or more multi-morbidities, OR – odds ratio

\*ORs derived from logistic regression model for the subgroup, with any inpatient admissions as the dependent variable, and any PHC attendance in the same year as the explanatory variable. Reference group: patients with no PHC contact (OR=1).

†Adjusted ORs also control for age groups and multimorbidity for subgroups by gender; gender and multimorbidity for age subgroups; and gender and age for multimorbidity subgroups.

‡There are less than 5 cases in the subgroup, regression results not available.

## DISCUSSION

The results indicate increasing overall utilisation of health care services in 2005–2012 for the seven ACSCs analysed. For these seven ACSCs, there was increased utilisation of PHC, with a concomitant fall in inpatient admissions. These trends were observed for all patients, but the utilisation rates rose with age and particularly, with multimorbidity.

The observed trends varied by condition. For asthma, diabetes and hypertension, PHC utilisation as a proportion of total number of contacts rose. Inpatient admissions fell significantly for all conditions except for heart failure. The results point to a shift in care towards PHC—particularly for diabetes and hypertension.

Across the period of analysis, the nature of PHC provision changed: there was an increase in follow-up consultations in PHC as the predominant share of visits, as well as an increase in the number and proportion of consultations with nurses and those using phone and email.

The fall in referral to inpatient admission and outpatient departments has been coupled with increasing numbers of appointments for follow-up consultations in PHC, indicating increased management of these conditions in PHC setting.

High levels of admissions for ACSCs frequently indicates inadequate co-ordination between elements of the health system, and is an indicator of poor overall quality of PHC [27] – particularly for continuity of care [28,29]. There is evidence that better quality PHC, through attainment of financial quality indicators, leads to reductions in hospitalisations for certain ACSCs [30] including diabetes [31–33], COPD [34], but not heart disease [35]. There is also evidence that case management of only high-risk patients with chronic illness at the PHC level may not lead to reduced secondary care admissions in all contexts [36]. Increased access to PHC could potentially decrease emergency admissions [37], and improvements in PHC quality suggest potential cost savings through reduced emergency admissions and outpatient visits [38]. Reductions in admissions of ACSCs in Estonia may be indicative of improvements in the overall quality and continuity of PHC for all patients.

In Estonia, the observed changes in utilisation have been mediated mainly through supply-side changes, such as the introduction of family medicine, and nurses working in family medicine centres, alongside financial changes introduced by the EHIF. Specialist outpatient care was prioritised over inpatient care, with the introduction of a quality bonus system [39,40] and clinical guidelines in PHC, and in response to the 2009 financial crises [41], containment of specialist care growth and reduction of inpatient care [42,43]. Demand side interventions included a visit fee for specialist care while PHC was kept free at the point of service delivery [3].

In spite of significant shifts, a recent study has noted challenges faced by Estonian health system, with high levels of specialist care and long hospital stays. Financial incentives to increase hospital care and lack of capacity to transfer care out of specialist settings were noted as the main reasons promoting hospital use, but inadequacies in PHC were also identified as a contributing factor to high levels of hospital and specialists use [44].

Worldwide, NCDs and multi-morbidity are rising rapidly [45]. Estonia is no exception. Patients with multi-morbidity have higher health system utilisation [16,46]. In Estonia, multimorbidity prevalence increases with age [47], as risk factors and chronic disease accumulate over the years [48]. In Estonia multimorbidity was associated with significantly high levels of outpatient and inpatient utilisation [49]. Patients with four or more ACSCs were 20 times more likely to have an inpatient admission than patients with a single ACSC. In our data, patients with multimorbidity accounted for 59.4% of PHC visits [50].

Multimorbidity is a major challenge to health systems, and prevailing approaches that focus on a single disease lead to fragmented care [51]. PHC has a central role in managing NCDs and multimorbidity [47,52], which require, effective co-ordination and care-continuity across all levels of care [53]. Integrated care that enables interventions across multiple levels of the health system with “connectivity, alignment and collaboration” [54] can help effective management of multimorbidity [55].

Our analysis shows that patients were significantly less likely to have an inpatient admission if they had any PHC visit in the given year, suggesting a protective effect of PHC consultations.

We use an observational study design and do not set out to demonstrate causality on the impact of health system reforms on health service utilisation, but where possible we use a comprehensive data set with robust methods to control for confounders to produce plausible evidence [56]. Although there is potential from error from data quality, the nature of the nationwide comprehensive data set – based on invoicing with built in controls and record validation checks – ensures our findings are reliable.

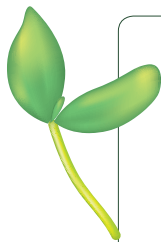
The comprehensive and detailed data used in this analysis has enabled robust analysis to provide deeper understanding of health care utilisation trends in Estonia. As all patient consultations and admissions are recorded, a complete analysis of the country was possible. The EHIF database has in-built quality checks and is subject to retrospective quality analysis to ensure reliable data. Each inpatient admission and outpatient visit is linked to reimbursement so data undergo scrutiny. In PHC—paid by a mixture of capitation, fee-for-service and performance related pay—phy-

sicians report activities to EHIF, and the data are checked to confirm reporting. The nationwide size and completeness of the data set, and regular quality checks mean potential reporting errors should be small.

The seven ACSCs used to examine changes in health care utilisation over time – all of which are high prevalence conditions that are likely to be sensitive to changes in service availability and quality, and represent a subset of all the conditions encountered in Estonia. Whilst we demonstrate changes in these seven ACSCs, there is the potential that concurrently changes in other conditions may negate the positive impacts concluded in this study. While this is a potential, these seven conditions represent a large burden of disease for Estonia and are important in their own right as major NCDs that require effective management and co-ordination, and are good indicators of PHC quality.

Our analysis of multi-morbidity drew on only the seven ACSCs we had data for, whilst previous studies have recommended examining greater than 12 chronic diseases to report two or more concurrent diseases [57]. However, we have not attempted to report a prevalence of multimorbidity, but merely used the measure as a subgroup analysis, therefore we consider these methods adequate for this purpose. Furthermore, our analysis included depression which is likely to be particularly important in multimorbidity management and outcomes [21].

Notwithstanding limitations, the study provides compelling evidence of the positive effects of family-medicine centred health system reforms on expanding PHC utilisation and reducing hospital inpatient admissions for key NCDs – important for many countries globally that have committed to providing UHC and have to efficiently manage the rising burden of chronic illness.



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**Competing Interests:** All authors have completed the ICMJE uniform disclosure form at [http://www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available upon request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years, no other relationships or activities that could appear to have influenced the submitted work.

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# Expansion of health insurance in Moldova and associated improvements in access and reductions in direct payments

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**Background** Moldova is the poorest country in Europe. Economic constraints mean that Moldova faces challenges in protecting individuals from excessive costs, improving population health and securing health system sustainability. The Moldovan government has introduced a state benefit package and expanded health insurance coverage to reduce the burden of health care costs for citizens. This study examines the effects of expanded health insurance by examining factors associated with health insurance coverage, likelihood of incurring out-of-pocket (OOP) payments for medicines or services, and the likelihood of forgoing health care when unwell.

**Methods** Using publically available databases and the annual Moldova Household Budgetary Survey, we examine trends in health system financing, health care utilization, health insurance coverage, and costs incurred by individuals for the years 2006–2012. We perform logistic regression to assess the likelihood of having health insurance, incurring a cost for health care, and forgoing health care when ill, controlling for socio-economic and demographic covariates.

**Findings** Private expenditure accounted for 55.5% of total health expenditures in 2012. 83.2% of private health expenditures is OOP payments—especially for medicines. Healthcare utilization is in line with EU averages of 6.93 outpatient visits per person. Being uninsured is associated with groups of those aged 25–49 years, the self-employed, unpaid family workers, and the unemployed, although we find lower likelihood of being uninsured for some of these groups over time. Over time, the likelihood of OOP for medicines increased (odds ratio OR=1.422 in 2012 compared to 2006), but fell for health care services (OR=0.873 in 2012 compared to 2006). No insurance and being older and male, was associated with increased likelihood of forgoing health care when sick, but we found the likelihood of forgoing health care to be increasing over time (OR=1.295 in 2012 compared to 2009).

**Conclusions** Moldova has achieved improvements in health insurance coverage with reductions in OOP for services, which are modest but are eroded by increasing likelihood of OOP for medicines. Insurance coverage was an important determinant for health care costs incurred by patients and patients forgoing health care. Improvements notwithstanding, there is an unfinished agenda of attaining universal health coverage in Moldova to protect individuals from health care costs.

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Moldova is the poorest country in Europe. Following independence from the Soviet Union in 1991, Moldova experienced rapid economic decline and has faced economic challenges since, hampering government efforts aimed at health system strengthening, financial sustainability, and universal health coverage (UHC) [1,2] – the sustainable development goals (SDGs) for health [3].

The economic downturn in Moldova led to health system funding shortages, reductions in service provision, increased out-of-pocket payments for users [4], and a rise in tobacco and alcohol use. Life expectancy at birth fell from 69 years in 1989 to 66 years in 1995, and the health burden from infections (particularly tuberculosis) and chronic illness rose [5,6]. Adverse economic conditions led to emigration, with the resident population of Moldova falling from 3.62 million in 2003 to 3.56 million in 2013 [7]. In 2006, around 20% of the population lived on less than US\$ 2 (purchasing power parity) a day [8], while gross domestic product (GDP) per capita was US\$ 1967 in 2011 – the lowest in geographical Europe [5]. The GDP has increased from US\$ 1.3 billion in 2000 to US\$ 7.3 billion in 2012 [9], but approximately one quarter comes from remittances from Moldovan population working abroad [8].

The government of Moldova has embarked on health system reforms aimed at rationalising excess hospital capacity [6], reducing service duplication and developing primary health care (PHC) [4] in order to improve health outcomes, provide financial protection and achieve financial sustainability. *The Health Sector Strategy for 1997–2003* [4] set out plans to develop an efficient, effective, responsive and equitable health system [10–12]. Following the 1994 Constitution, which guaranteed a right to health, a state-funded free health service package was introduced in 1999 [4,6], followed by the Law on Mandatory Health Insurance (MHI) in 2001, and the establishment of the National Health Insurance Company (CNAM) in 2004 [4].

The MHI is compulsory for Moldovan citizens – and aims to provide complete insurance coverage – but in reality individuals may choose their own insurance or not to purchase any [4]. Certain individuals (non-working groups including students, children, pensioners, disabled etc.) receive insurance coverage without payment covered by the government [4]. MHI coverage entitles individuals to a benefits package of covered services – including selected primary and secondary care services, emergency care, and dental services. In 2009, primary care services were extended, free of charge, to all irrespective of insurance status, and in 2012, services covered by the benefit package were further extended [4]. Nonetheless, many medicines are not covered and patients incur informal payments due to limited financing of the benefit package [4,13]. The *National Health Policy 2007–2021* [14] was followed by the

*Healthcare Development Strategy 2008–2017* [15] which, alongside wider health system reform, specifically aimed to expand insurance coverage through financial incentives and mandating an insurance policy when renewing government issued licenses [4].

Earlier studies highlight the significant burden of OOP incurred for hospital services (mostly due to informal payments) and for medicines [13] (**Box 1**). This study uses routine administrative data on insurance coverage and health care utilization, and household surveys to explore the effect of health system reforms on OOP, and applies robust econometric methods to analyze the likelihood of being uninsured, incurring an OOP for medicines or health services, or forgoing health care by socio-economic and demographic characteristics.

### Box 1 Health System Financing in Moldova

**Trends in health system financing:** Total health expenditure (THE) as a percentage of GDP rose from 8.1% in 2002 to 11.72% in 2012. While higher than the EU average of 9.61% in 2012, the absolute level of health expenditure per person (PPP\$) is the lowest in Europe at US\$ 344, compared with the EU average of US\$ 3307 [5].

In 2012, health expenditure from public sources was 45.5% of THE compared to the EU average of 76.0%, illustrating the large role private sources play. Public sector expenditure on health as a proportion of total government expenditure rose from 11.7% in 2007 to 13.3% in 2012 – similar to the EU average of 15.2% [5].

The majority of private health expenditures (83.2% in 2012) is OOP and has risen from 79.9% in 2003. Pharmaceutical expenditures accounted for 72% of the OOP payments in 2010 [16].

**Purchaser–provider split:** In 2003, the creation of CNAM introduced a purchaser–provider split in Moldovan health system by separating health financing and service delivery. CNAM is responsible for direct contracting of hospitals and PHC providers, and for 85% of the government expenditure on health [17]. Of this expenditure, around 49% was spent on hospitals, 29% on PHC, 9% on ambulance services, 7% on specialized outpatient care, 4% on compensated outpatient medicines, and 2% on complex health care services (2011 data), with little variation in these proportions since 2007 [17].

**Geographical variation in health system financing:** Health-care spending across regions (rayons) has been uneven, with per capita funding across rayons in 2003 differing by a factor of 4.6. Urban rayons received a substantially greater share of funds due to concentration of hospital and specialist care. Following financial reorganization in 2004 that centralised pooling of funds with CNAM, in 2010 the difference fell to 3.8 [17].

## METHODS

### Analytical framework

This study uses a health systems framework [16,17] to guide the analysis (**Box 2**). The framework builds on earlier approaches used to analyze health system reforms [18,19]. The national Healthcare Development Strategy 2008–2017 follows a similar structure to the health systems framework used in the study, enabling analysis of the changes in the health system goal of financial protection following health system reforms aimed at expanding insurance coverage and exploring the association of insurance

#### Box 2 Health System Framework used for analysis

**Health system functions:** We identify four key health system functions which the policy makers can modify to achieve health system goals: (i) **governance and organization** – the policy and regulatory environment, stewardship function of the ministry of health and its relationship with other levels of the health system, and structural arrangements for insurers/purchasers, health care providers and market regulators; (ii) **financing** – how the funds are collected, funds and risks pooled, finances allocated within the health system and how health care providers are remunerated; (iii) **resource management** – how physical, human and intellectual resources are generated and allocated, including their geographic and needs-based allocation; and (iv) **service delivery** that includes both public health services and individual health services provided within the community, PHC, hospitals, and other health institutions. Health services are produced using governance and organization, financing and resource management functions.

**Health system objectives:** We define four objectives which the policy makers need to balance in relation to individual and public health services: **equity** (including access and use of services by different population groups), **efficiency** (efficient allocation of resources to right interventions and producing them at low cost), **effectiveness** (the extent to which interventions provided are evidence based and safe) and **responsiveness** (of care providers to user needs, including choice of providers).

**Health system goals:** There are three health system goals in our framework which the system aims to achieve. The first goal is **health**, both the level and distribution of population health as measured by morbidity and mortality. The second goal is **financial protection**, for which we examine the level and distribution of health expenditures (targeting of health insurance), levels of health insurance coverage, and levels of financial protection (out of pocket expenditures, and catastrophic health expenditures) for different population segments. The third goal is **user satisfaction**, specifically the satisfaction of the population with the health system.

coverage with service utilization, OOP payments incurred and forgone health care.

### Data sources

Two main sources of data were used for the years 2006–2012. First, publically available datasets from the Moldovan National Center for Health Management (CNMS) were collected. CNMS collates data from public health care provider reports. We extracted health service utilization information relating to number of hospitalisations, average number of visits per person, and emergency calls per 1000 residents.

Second, the monthly Household Budget Survey (HBS) was used. The HBS is based on an internationally validated survey and is undertaken by the Moldovan National Bureau of Statistics (NBS) [7]. The HBS is nationally representative and is undertaken through two-stage sampling based on regional areas and a random selection of households. Approximately 5500 households (15 000 individuals) are surveyed annually on a wide range of questions relating to the economic situation of the household and individuals. Responses for the years 2006–2012 were obtained from the NBS. We selected questions relevant to this analysis including demographic, socio-economic, health and health care-related questions. Our outcome variables of interest were calculated from survey questions: “If individuals currently have health insurance”; “if individuals paid for any service (inpatient or outpatient) either formally or informally when using care in the last four weeks”, and “if you were unwell in the last four weeks, but did not use healthcare”. Because of issues of non-response (up to 40% in some years), the age and gender distribution of the HBS was compared to national population data (from NBS [7]) showing high similarity.

### Analysis

Using the health system analytical framework [14,15], we examine elements of financial protection in the context of the health system objectives. Equity is a key health system objective for this analysis. We examine equity in insurance status, OOP payments, and foregone health across demographic groups. We demonstrate the interactions between insurance status and equity in other financial protection elements such as OOP. Additionally, we also explore the health system objectives of responsiveness in terms of preferred health care provider, effectiveness through forgone health care, and efficiency in terms of national utilization trends. We triangulate these findings to understand how factors contributing to financial protection are being met.

### Descriptive analysis

CNMS data on health care utilization are shown over time. Individual responses on preferred of health care provider,

for those with health care use in the last four weeks, were stratified by provider and year.

For insurance coverage, CNMS data was compared with individual HBS responses (stratified by employed status and age groups) over time.

Insurance coverage trends were compared between individual HBS responses and from administrative data (CNMS) sources. Furthermore, we stratified the insurance status of the respondents in the HBS by occupation and age group.

The percentages of individuals reporting OOP payments were described by consultative services, inpatient services and drugs, and by each year. Mean incurred costs by individuals were shown. Additionally, mean costs were compared to average monthly earnings.

### Logistic regression

We employed logistic regression to calculate the likelihood of: being uninsured, incurring an OOP for medicines or any health care service from health care used in the last four weeks, and not using (foregoing) health care when reporting a health problem in the last four weeks. Logistic regression was employed as the most appropriate method for binary outcomes.

Covariates from the HBS survey were used to control for and highlight explanatory factors. We included in all models: age group (0–17 years, 18–24, 25–34, 35–49, 50–59, 60–74 and 75+); gender; chronic disease status (yes or no); employment status (employed, self-employed (non-agriculture), self-employed (agriculture), unpaid family worker, unemployed (including those not of working age); and educational attainment (pre-school or no education, primary, secondary, and college or university). We also included year (2006–2012) to look for time trends.

For the regressions on the likelihood of an OOP and forgone health care, we included disability (yes or no) and uninsured (yes or no) as covariates. Additionally, for the regressions on the likelihood of an OOP we included first choice of health care provider (family doctor's office, home visit, polyclinic (health center), hospital or other (eg, pharmacy). For the regression of foregone health care, we only examined the years 2009–2012, as the question was not in earlier surveys. Analyses were carried out at the individual level, with adjustments for the clustered nature of the survey. All individual responses were included for analyses, except the likelihood of being uninsured. The regression was restricted to those aged over 18 and under the age of 60 years, as individuals outside these ages are eligible for free insurance coverage. We report adjusted odds ratios and 95% confidence intervals. Interaction terms between covariates and year (linear trends) were additionally tested.

## RESULTS

**Table 1** shows the descriptive statistics, which categorises the respondents by socio-economic and demographic covariates, and additionally overall responses to key variables of interest.

### Service utilization

We examined average health care utilization rate at the national level and preferred first contact provider from HBS respondents. The health care utilization rate at the national level rose between 2006 and 2012 (**Table 2**), with the hospitalization rate (per 100 residents) increasing from 16.7 in 2006 to 18.4 in 2012 and the average number of outpatient visits per person rising from 6.02 to 6.45. These numbers are broadly in line with European averages (of 18.04 hospitalisations and 6.93 outpatient visits per person in 2012) [5].

Responses in the HBS from individuals who sought health care in the last four weeks show the majority sought health care in former polyclinics (centers that in majority of cases include both family doctors and out-patient specialists) (48.0% in 2012) with family doctor offices (32.6%), home visits (8.9%) and hospitals (5.2%). These trends have remained fairly constant since 2003 (**Figure 1**).

### Insurance coverage

Approximately 75% of HBS from individuals respondents reported having health insurance during the period 2006–2012 (**Table 3**). National statistics suggest rising coverage of health insurance from 76.1% to 80.3%. In 2012, only 60% of the working age population (18–59 years) had insurance coverage, with the self-employed and those working in family business having lower coverage levels: 24% of self-employed agriculture workers, 57.8% of self-employed non-agriculture workers, and 53.8% of unpaid family workers had insurance. In 2012, the main reasons for being uninsured were unemployment (27.9%), cost (26.2%), “they would pay for healthcare anyway” (13.9%), working informally (13.1%), “belief that it would not be needed” (8.5%) and working abroad (8.1%).

The odds of not having health insurance were examined using multivariate logistic regression (**Table 4**). Age was an important determinant of being uninsured, with those aged 25–43 and 35–49 years of age, respectively, 2.9 (OR=2.898,  $P<0.001$ ) and 2.3 times (OR=2.261,  $P<0.001$ ) more likely to be uninsured than those aged 18–24 or 50–60 years of age.

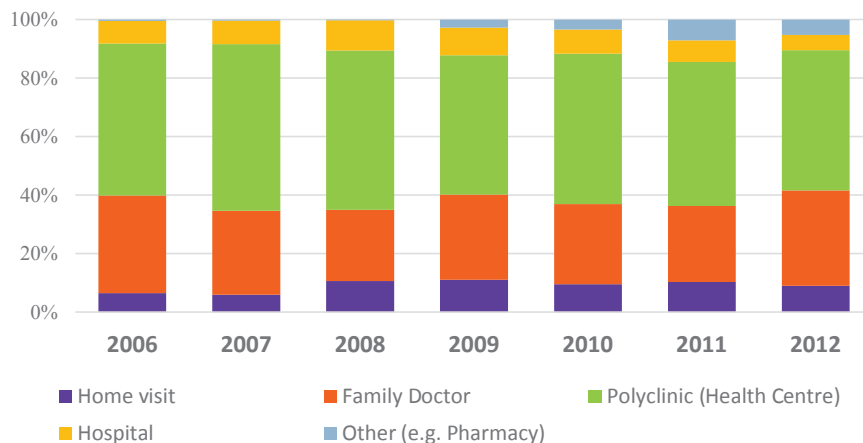
Females were less likely to be uninsured than men (OR=0.599,  $P<0.001$ ), as were those with chronic health conditions (OR=0.303,  $P<0.001$ ). All categories of employment were substantially more likely to be uninsured

**Table 1.** Numbers and percentage distribution of Household Budget Survey (HBS) respondents by year (2006–2012), socio–economics and demographics, and key variables of interest

	2006		2007		2008		2009		2010		2011		2012	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<b>Age group (years):</b>														
0–17	4560	28.2	4507	27.2	4383	26.7	3974	26.4	3703	25.8	3577	24.4	3424	24.5
18–24	1488	9.2	1626	9.8	1539	9.4	1509	10.0	1303	9.1	1319	9.0	1203	8.6
25–34	1771	11.0	1871	11.3	1780	10.8	1684	11.2	1607	11.2	1728	11.8	1589	11.4
35–49	3299	20.4	3186	19.2	3152	19.2	2870	19.1	2702	18.8	2627	17.9	2467	17.7
50–59	2311	14.3	2514	15.2	2601	15.8	2345	15.6	2273	15.8	2440	16.7	2352	16.8
60–74	2027	12.5	2063	12.4	2124	12.9	1910	12.7	2072	14.4	2151	14.7	2174	15.6
75+	707	4.4	822	5.0	841	5.1	774	5.1	719	5.0	817	5.6	765	5.5
<b>Sex:</b>														
Male	7477	46.3	7666	46.2	7514	45.8	6960	46.2	6692	46.5	6720	45.8	6428	46.0
Female	8686	53.7	8923	53.8	8906	54.2	8106	53.8	7687	53.5	7939	54.2	7546	54.0
<b>Chronic condition:</b>														
Yes	3861	23.9	4112	24.8	4303	26.2	3993	26.5	4253	29.6	4038	27.6	4241	30.4
No	12302	76.1	12477	75.2	12109	73.8	11073	73.5	10126	70.4	10621	72.5	9733	69.7
<b>Employment status:</b>														
Employed	4339	26.9	4525	27.3	4540	25.5	4061	25.2	3849	25.0	3987	27.2	3681	26.3
Self-employed non-agriculture	516	3.2	428	2.6	475	2.7	473	2.9	440	2.9	526	3.6	480	3.4
Self-employed agriculture	2661	16.5	3048	18.4	2892	16.2	3037	18.9	3393	22.1	4095	27.9	4339	31.1
Unpaid family worker	350	2.2	354	2.1	242	1.4	252	1.6	244	1.6	295	2.0	288	2.1
Unemployed	8297	51.3	8234	49.6	9671	54.3	8265	51.4	7453	48.5	5756	39.3	5186	37.1
<b>Education:</b>														
Pre-school or none	2365	14.6	2378	14.3	3682	20.7	3140	19.5	3039	19.8	2043	13.9	1943	13.9
Primary	2351	14.6	2307	13.9	2253	12.6	1965	12.2	1750	11.4	1711	11.7	1516	10.9
Secondary	8249	51.0	8503	51.3	8497	47.7	7971	49.6	7735	50.3	7832	53.4	7705	55.1
College or university	3198	19.8	3401	20.5	3388	19.0	3012	18.7	2855	18.6	3073	21.0	2810	20.1
<b>Disabled:</b>														
No	15303	94.7	15676	94.5	15519	87.1	14135	87.9	13501	87.8	13710	93.5	13027	93.2
Yes	860	5.3	913	5.5	2301	12.9	1953	12.1	1878	12.2	949	6.5	947	6.8
<b>Uninsured:</b>														
No	12390	76.7	12656	76.3	12718	71.4	11368	70.7	10879	70.7	11116	75.8	10593	75.8
Yes	3773	23.3	3933	23.7	5102	28.6	4720	29.3	4500	29.3	3543	24.2	3381	24.2
<b>First choice provider:</b>														
Home visit	157	6.6	137	6.0	210	10.7	251	11.0	220	9.5	251	10.3	219	8.9
Family doctor office	792	33.3	656	28.7	479	24.4	665	29.2	633	27.4	633	26.0	799	32.6
Polyclinic health center†	1235	52.0	1302	57.0	1071	54.5	1084	47.6	1185	51.3	1201	49.3	1176	48.0
Hospital	185	7.8	185	8.1	202	10.3	216	9.5	193	8.4	181	7.4	127	5.2
Other (eg, pharmacy)	7	0.3	5	0.2	3	0.2	62	2.7	77	3.3	172	7.1	128	5.2
<b>Sought health care in last 4 weeks:</b>														
Yes	2376	14.7	2285	13.8	1965	13.0	2278	15.1	2308	16.1	2438	16.6	2449	17.5
No	13787	85.3	14304	86.2	13202	87.0	12788	84.9	12071	84.0	12221	83.4	11525	82.5
<b>Any out-of-pocket for drugs:</b>														
No	11692	72.3	12003	72.4	13116	73.6	11610	72.2	10797	70.2	10245	69.9	9584	68.6
Yes	4471	27.7	4586	27.6	4704	26.4	4478	27.8	4582	29.8	4414	30.1	4390	31.4
<b>Any out-of-pocket for services:</b>														
No	15632	96.7	16097	97.0	17199	96.5	15626	97.1	14935	97.1	14280	97.4	13562	97.1
Yes	531	3.3	492	3.0	621	3.5	462	2.9	444	2.9	379	2.6	412	3.0
<b>Foregone health care*:</b>														
No	–	–	–	–	–	–	2190	63.7	1607	57.0	2376	62.1	2333	57.4
Yes	–	–	–	–	–	–	1250	36.3	1214	43.0	1453	38.0	1733	42.6
Number of respondents (N)	16163		16589		17820		16088		15379		14659		13974	

\*This question was not asked in the years prior to 2009.

†Polyclinics include family doctors and out-patient specialists, especially in larger cities and urban centers.



**Figure 1.** Choice of health care provider for individuals who sought medical care in the last four weeks (2006-12). Shows responses from individuals who sought healthcare in the last four weeks and their first preferred healthcare provider. Those seeking care at a hospital are likely underestimated due to the infrequency of events and small samples employed. Polyclinics include family doctors and out-patient specialists, especially in larger cities and urban centres.

than those employed. The self-employed, and unpaid family workers were all more than 20 times more likely to be uninsured. The unemployed were 5 times more likely (OR=4.915,  $P<0.001$ ). All categories of education were more likely to be uninsured than those with only pre-school or no-education with primary, secondary, and college or university educated individuals 7.7, 6.1 and 3.2 times more likely to be uninsured.

Over time, there was no evidence of a trend in change in likelihood of being uninsured. Models with interactions with time (results not shown) suggest that the likelihood of being uninsured declined over time for those with chronic conditions (compared to those without), females (compared to males), and the self-employed (agriculture) and unpaid family workers (compared to employed). There was an increased likelihood in being uninsured for the unemployed over time (compared to other employment categories).

**Table 2.** Healthcare utilization (2006–2012) [20]\*

	2006	2007	2008	2009	2010	2011	2012
Hospitalizations per 100 residents	16.7	17.2	17.8	18.0	18.1	18.5	18.4
Average number of visits per person	6.0	6.2	6.3	6.3	6.5	6.4	6.5
Emergency calls per 1000 residents	266.3	281.4	282.7	301.9	282.7	279.5	271.1

\*Includes responses from individuals who sought health care in the last four weeks and their first preferred health care provider. Those seeking care at a hospital are likely be underestimated due the infrequency of events and small samples employed. Polyclinics include family doctors and out-patient specialists, especially in larger cities and urban centers.

**Table 3.** Insurance coverage national and occupational groups (2006–2012) [7,20]

	2006	2007	2008	2009	2010	2011	2012
From the National Household Budget Survey (individuals):							
National coverage	76.7	76.3	77.5	75.5	75.7	75.8	75.8
By occupation:							
- Employed	83.3	85.7	87.1	85.2	84.6	84.9	84.1
- Self-employed (non-agriculture)	19.8	17.1	20.2	18.8	22.3	22.6	24.0
- Self-employed (agriculture)	32.1	37.3	39.1	41.3	45.7	54.7	57.8
- Unpaid family worker	37.4	37.3	41.3	41.3	52.9	51.9	53.8
- Unemployed*	92.7	90.3	76.9	78.2	78.4	90.7	91.1
By age group (years):							
0–18	98.3	99.2	98.8	98.5	98.7	98.4	98.2
18–24	62.8	59.7	64.5	59.4	61.5	58.6	58.9
25–34	50.3	48.4	50.0	48.8	47.5	51.6	46.8
35–49	56.1	55.5	57.0	53.9	53.5	52.9	54.6
50–60	66.4	67.1	69.0	66.8	66.7	67.6	66.6
60–74	98.1	98.5	97.6	96.9	95.6	96.7	96.7
75+	100.0	100.0	99.9	99.7	99.9	99.9	99.6
From administrative data sources:							
National coverage	76.1	76.2	77.7	80.0	78.6	79.3	80.3

\*Includes those not of working age.

**Table 4.** Multivariate regression results on likelihood of being uninsured for individuals aged 18–60 years (2006–2012)\*

	AOR	P-VALUE	95% CI
Age group:			
18–24 (Ref)	1.000		
25–34	2.898	<0.001	2.682–3.130
35–49	2.261	<0.001	2.102–2.433
50–60	1.033	0.409	0.957–1.115
Sex:			
Male (Ref)	1.000		
Female	0.599	<0.001	0.575–0.623
Chronic disease:			
No (Ref)	1.000		
Yes	0.303	<0.001	0.285–0.323
Employment status:			
Employed (Ref)	1.000		
Self-employed (non-agriculture)	24.339	<0.001	21.729–27.262
Self-employed (agriculture)	27.381	<0.001	25.631–29.249
Unpaid family worker	23.781	<0.001	20.583–27.476
Unemployed	4.915	<0.001	4.590–5.262
Education:			
Pre-school or none (Ref)	1.000		
Primary	7.170	<0.001	4.170–12.327
Secondary	6.047	<0.001	3.866–9.459
College or university	3.182	<0.001	2.029–4.990
Year:			
2006 (Ref)	1.000		
2007	1.108	0.016	1.019–1.204
2008	0.997	0.949	0.916–1.085
2009	1.079	0.088	0.989–1.177
2010	1.008	0.860	0.921–1.103
2011	0.933	0.133	0.852–1.021
2012	0.920	0.074	0.840–1.008
No.	59 151		

AOR – Adjusted Odds Ratio, 95% CI – confidence intervals

\* $P < 0.001$ . Cluster robust standard errors used.

### Private and out-of-pocket expenditure

Around 15% of HBS respondents who sought health care reported a payment for consultative services and 2% for inpatient care in 2012 (Table 5) compared with 20% and 3% in 2006 respectively. The average costs for both consultative services and medicines had increased since 2006.

**Table 5.** Percentage of individuals reporting costs for health care services and average costs incurred (2006–12) [7]

	2006	2007	2008	2009	2010	2011	2012
Of those who sought health care in the last 4 weeks, the percentage incurring costs (formal and informal) for:							
Consultative services*	20.3%	19.7%	23.9%	18.4%	16.9%	13.8%	14.9%
Inpatient services	2.9%	3.4%	4.7%	2.7%	3.1%	2.2%	2.3%
Drugs	82.6%	83.6%	84.1%	86.5%	88.3%	91.1%	89.2%
Average costs incurred (in Moldovan Lei) for:							
Consultative services	132	161	169	190	195	249	215
Inpatient services	711	1548	1132	1284	1065	2343	833
Drugs	175	221	254	258	290	271	269

\*Consultation services include: consultations, analyses, diagnoses, treatments, physiotherapies and medical examinations; Inpatient services including treatment, admission, advice, analysis, interventions, surgery. The results include total costs for formal and informal payment (for consultative and inpatient services). Only small numbers of individuals used hospital services or reported inpatient costs meaning there may be variation across years.

The factors affecting the likelihood of an OOP payment for both medicines and health care services were analyzed separately using multivariate logistic regression (Table 6).

Although low numbers and fluctuations in reported costs make conclusions difficult, there appears to be only modest reductions in costs incurred relative to average monthly earnings over time (Table 7).

### Out-of-pocket payment for drugs

Older individuals (aged over 50 years), who sought health care in the last four weeks, were more likely to incur a cost than those aged under 34 years. Females were 13% more likely to pay (OR = 1.133,  $P = 0.013$ ), while those with chronic conditions were nearly 1.9 times as likely to incurring a cost (OR = 1.911  $P < 0.001$ ).

Unpaid family workers and the unemployed were less likely to incur costs for medicines, as were those with primary and secondary education. Those without health insurance were 1.3 times more likely (OR = 1.297,  $P = 0.004$ ) to incur an OOP for medicines compared to than those with insurance. Individuals were only less likely to incur a cost for medicines at hospitals or other services (such as pharmacies).

Over the period 2006–2012, the odds of incurring a cost for medicines have increased (up to 1.8 times more likely to incur a cost in 2011 (OR = 1.772,  $P < 0.001$ ) compared to 2006. The only significant interaction with time (results not shown) was insurance status with those without insurance increasingly more likely to pay for medicines OOP over time.

### Out-of-pocket payment for health care services

Individuals who sought medical care in the last four weeks and incurred OOP payments (informally or formally) for consultative or inpatient services showed different trends to costs for drugs. Older individuals and those under 18 were least likely to incur a cost than those aged



**Table 6.** Odds of incurring out-of-pocket expenditure for either drugs or health care services for those who sought medical care in last four weeks\*

	DRUGS			HEALTHCARE SERVICES		
	AOR	P-Value	95% CI	AOR	P-value	95% CI
<b>Age group (years):</b>						
0–17 (Ref)	1.000			1.000		
18–24	0.732	0.016	0.568–0.943	1.432	0.006	1.107–1.854
25–34	0.747	0.030	0.575–0.972	1.256	0.081	0.972–1.622
35–49	1.133	0.338	0.878–1.463	1.112	0.396	0.870–1.420
50–59	1.575	0.001	1.219–2.036	0.818	0.106	0.640–1.044
60–74	2.074	<0.001	1.650–2.607	0.564	<0.001	0.450–0.708
75+	1.976	<0.001	1.513–2.579	0.336	<0.001	0.252–0.448
<b>Sex:</b>						
Male (Ref)	1.000			1.000		
Female	1.133	0.013	1.026–1.251	1.083	0.081	0.990–1.185
<b>Chronic disease:</b>						
No (Ref)	1.000			1.000		
Yes	1.911	<0.001	1.691–2.160	1.296	<0.001	1.160–1.448
<b>Employment status:</b>						
Employed (Ref)	1.000			1.000		
Self-employed non-agriculture	0.936	0.734	0.641–1.368	0.999	0.993	0.736–1.355
Self-employed (agriculture)	0.867	0.118	0.725–1.037	0.884	0.112	0.759–1.029
Unpaid family worker	0.610	0.006	0.427–0.871	1.016	0.929	0.717–1.440
Unemployed	0.811	0.013	0.689–0.956	0.903	0.155	0.785–1.039
<b>Education:</b>						
Pre-school or none (Ref)	1.000			1.000		
Primary	0.671	<0.001	0.551–0.818	1.112	0.345	0.893–1.385
Secondary	0.708	0.002	0.571–0.877	1.238	0.066	0.986–1.555
College or university	0.817	0.104	0.640–1.042	1.391	0.008	1.088–1.777
Disabled	1.066	0.478	0.893–1.274	0.634	<0.001	0.542–0.741
Uninsured	1.297	0.004	1.088–1.546	3.833	<0.001	3.307–4.443
<b>First contact health care provider:</b>						
Family doctor office (Ref)	1.000			1.000		
Home visit	1.021	0.848	0.824–1.265	0.415	<0.001	0.324–0.531
Polyclinic (health center)	0.820	0.056	0.668–1.005	2.723	<0.001	2.192–3.381
Hospital	0.722	0.010	0.563–0.926	7.205	<0.001	5.667–9.161
Other (eg, pharmacy)	11.400	<0.001	4.595–28.282	0.081	<0.001	0.034–0.191
<b>Year:</b>						
2006 (Ref)	1.000			1.000		
2007	1.041	0.624	0.886–1.223	0.870	0.101	0.737–1.027
2008	1.071	0.432	0.902–1.271	1.266	0.005	1.072–1.495
2009	1.226	0.019	1.034–1.454	0.922	0.335	0.782–1.087
2010	1.418	<0.001	1.191–1.687	0.866	0.093	0.732–1.024
2011	1.772	<0.001	1.469–2.138	0.707	<0.001	0.594–0.842
2012	1.422	<0.001	1.189–1.700	0.873	0.116	0.736–1.034
N	16 099			16 099		

AOR – adjusted odds ratio, 95% CI – 95% confidence intervals

\* $P < 0.001$ ; 675.12,  $P < 0.001$ . Cluster robust standard errors used.**Table 7.** Average reported health care costs compared to average monthly earnings [7]\*

	2006	2007	2008	2009	2010	2011	2012
Average monthly earnings (Lei)†	1697	2065	2530	2748	2972	3042	3386
Comparison of average reported health care costs as a proportion of average monthly earnings:							
Consultative services	7.8%	7.8%	6.7%	6.9%	6.6%	8.2%	6.4%
Inpatient services	41.9%	75.0%	44.7%	46.7%	35.8%	77.0%	24.6%
Drugs	10.3%	10.7%	10.1%	9.4%	9.8%	8.9%	8.0%

\*Caution is needed in interpretation due to low numbers reporting inpatient costs.

†Monthly earnings include any earning from salaries and employment, and other forms of income, averaged over all employees. It is adjusted for annual inflation.

18–24. Those with chronic conditions were 1.3 times more likely to pay (OR=1.296,  $P<0.001$ ), but those with disability were nearly 40% less likely to pay (OR=0.634,  $P<0.001$ ).

Uninsured individuals were 3.8 times (OR=3.833,  $P<0.001$ ) more likely to incur an OOP payment for health services. There was no difference between employment categories while only those with college or university education were more likely to pay (OR=1.391,  $P=0.008$ ).

Those using hospitals and polyclinics respectively were 7.2 times (OR=7.205,  $P<0.001$ ) and 2.8 times (OR=2.723,  $P<0.001$ ) more likely to incur a cost than at family doctor offices. Home visits were less likely to incur a cost than family doctor office (OR=0.415,  $P<0.001$ ).

There was a general decline in the likelihood of incurring an OOP expenditure cost for services, although the difference was not significant every year. The only interaction with time (results not shown) was age with those aged 50–60 years having an increased likelihood of incurring a cost over time compared to other ages.

### Foregone health care utilization

Using multivariate logistic regression the likelihood of not visiting a health care provider when being sick in the last four weeks was examined (Table 8). Older individuals were more likely not to seek health care with those 75 years or more 2.4 times (OR=2.379,  $P<0.001$ ) more likely than 0–24 year-olds. Females were 9.8% less likely to forego care (OR=0.902,  $P=0.003$ ).

Employed and self-employed (non-agriculture) individuals were most likely to not seek health care when sick. The disabled were less likely to forego health care when sick (OR=0.819,  $P<0.001$ ). Those without insurance were 1.7 times (68%) more likely not to seek health care when sick (OR=1.680,  $P<0.001$ ).

Over time there was an increasing likelihood of forgoing health care when sick with individuals on average 1.3 times (30%) more likely in 2012 than 2009. There were no significant interactions between covariates and time suggesting the increasing trend in likelihood of foregoing health care applies to all individuals.

## DISCUSSION

Our results indicate that aspects of financial protection in Moldova are improving, albeit slowly, but with different trajectories for certain demographic groups.

Health service utilization has gradually increased from to 6.45 visits per person in 2012—now in line with the European average of 6.93—and while the majority of individuals use some form of PHC (former polyclinics or family doctor

**Table 8.** Results from multivariate logistic regression on odds of not utilizing health care when unwell\*

	AOR	P-VALUE	CI
<b>Age group (years):</b>			
0–17 (Ref)	1.000		
18–24	1.267	0.063	0.987–1.626
25–34	1.342	0.016	1.056–1.704
35–49	1.680	<0.001	1.358–2.078
50–59	1.878	<0.001	1.521–2.318
60–74	2.008	<0.001	1.656–2.435
75+	2.379	<0.001	1.972–2.872
<b>Sex:</b>			
Male (Ref)	1.000		
Female	0.902	0.003	0.841–0.966
<b>Chronic disease?:</b>			
No (Ref)	1.000		
Yes	1.059	0.244	0.962–1.165
<b>Employment status:</b>			
Employed (Ref)	1.000		
Self-employed non-agriculture	0.967	0.803	0.742–1.260
Self-employed (agriculture)	0.793	<0.001	0.706–0.891
Unpaid family worker	0.716	0.037	0.522–0.981
Unemployed	0.859	0.014	0.761–0.969
<b>Education:</b>			
Pre-school or none (Ref)	1.000		
Primary	1.156	0.104	0.970–1.378
Secondary	0.989	0.907	0.825–1.186
College or university	0.875	0.180	0.719–1.064
<b>Disabled</b>	<b>0.819</b>	<b>&lt;0.001</b>	<b>0.732–0.916</b>
<b>Uninsured</b>	<b>1.680</b>	<b>&lt;0.001</b>	<b>1.483–1.902</b>
<b>Year:</b>			
2009 (Ref)	1.000		
2010	1.320	<0.001	1.174–1.484
2011	1.070	0.231	0.958–1.195
2012	1.295	<0.001	1.163–1.443
N	14 156		

AOR – adjusted odds ratio, 95% CI – 95% confidence intervals

\* $P<0.001$ . Cluster robust standard errors used.

offices), there has been little change over time in utilization levels for PHC services. The inefficient hospital network [21] needs to be rationalised to encourage greater use of PHC services and to develop a more efficient and effective health system.

The challenging economic environment is slowing efforts to improve financial protection—particularly in terms of equity. Our finding that insurance coverage is still not universal—impacting accessibility of services—particularly in older individuals, unemployed, agriculture workers and those of working age is in line with earlier studies [22]. Our findings illustrate that despite the government efforts to expand coverage through financial incentives to purchasing coverage and as a requirement during certain license renewals, not enough progress has been made.

Limited public finances for health are misallocated due to slow progress in tackling the inefficient hospital network

which reinforces inequitable provision of health care services [21], and limits the ability of the government to further incentivise insurance coverage and expand the benefit package. Although overall there was no significant improvement over time in insurance coverage, the finding that particular groups—the self-employed (agriculture) and unpaid family workers—had reduced likelihood of being uninsured suggests attempts to expand coverage to these groups are having some success.

Our findings confirm earlier studies [13] that reveal the large burden OOP payments—particularly for medicines. Our results indicate the likelihood of incurring a payment has increased over time for medicines, but declined for health care services. Notably insurance status is a strong determinant of likelihood of incurring an OOP payment. The fact that many medicines are not covered by the MHI package [4] is clearly contributing to OOP burdens. The high average cost for drugs, which has increased since 2006, is resulting in the unaffordability of medicines and high prices in both the public and private sectors [23]. Financial protection is still not being met in terms of access to medicines, but on the other hand, we see that efforts to curtail informal payments and reduce OOP in services have had some success. Earlier studies in Moldova suggest that cost as a reason for not seeking care when experiencing a health problem has fallen, but is still a major factor especially in poorer income groups [13].

The finding that health care is still being foregone suggests the minor improvements for some groups in insurance coverage and OOP for services, are not translating to improvements in health care utilization. Individuals are increasingly likely to forego health care—notably the uninsured, older, and certain groups of employed individuals. Challenges in expanding insurance coverage are clearly impacting on health care utilization, but health care utilization is also likely to be affected by the limited benefit package, health service quality and non-financial barriers to access [4]. Evidence indicates health insurance is key to protecting individuals against OOP payments and promoting health care utilization [24,25], although for those in the informal sector the effects may be weaker [26].

### Strengths and limitations

The HBS only provides limited insight into financial protection in Moldova over time. As a survey, certain populations—eg, traveling communities or homeless—will be not represented. The high non-response rate (~40%) raises the issue of reliability of the survey, although the concordance of results with earlier studies and representativeness of age and sex distributions could mean the impact of the high non-response rate is low. There are also potential issues of recall or selective reporting possible. There are lim-

itations in the questions asked in the survey. For example, we do not know individuals' utilization patterns of health care—only if they have used a health care provider in the last four weeks. Healthcare utilization could confound the results reported here. None—the-less, while we must acknowledge certain groups (eg, those with chronic conditions, older people or the disabled) are likely to use health care more, true financial protection should be equitable across groups. Further research into the exact costs and fees incurred by individuals and explanatory demographic variables is also needed.

Other data sources employed—including CNMS—are from administrative sources that may be prone to errors and issue of data quality. Additionally, as administrative data are only from public facilities, this study is not able to analyze private providers in the health system.

The analyses undertaken may also introduce potential errors. Logistic regression identifies associations through predictive probabilities between groups and outcomes, but cannot prove causality. Our results must be interpreted with this limitation in mind. Additionally, assumptions about grouping of outcomes—including OOP from informal and formal sources and between different services—may obscure finer trends and patterns, but due to small sample size it was not possible to analyze these subgroups separately. Even so, we use multiple covariates not to just examine potential inequities between demographic groups, but also to control for potential effects and elucidate clearer associations than descriptive trends. This allows us to identify whether it is age or employment status, for example, which is the stronger determinant of an outcome. Furthermore, we take into account the clustered nature of the survey design further strengthening the validity of our findings.

### CONCLUSIONS

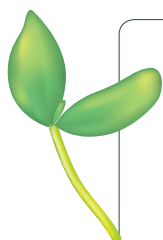
There is clear evidence that many elements of financial protection are not being met in Moldova. While in some areas—insurance coverage and OOP for services—there is slow improvement, but the increase in OOP for medicines counteracts the improvements observed. Healthcare is potentially being foregone due to limited protection from costs. Progress toward UHC is an integral to the SDGs [3], and removing financial barriers to access is key to attaining UHC. To reduce financial access barriers the Moldovan government should focus on three areas: further expansion of health insurance coverage, tackling costs of medicines and health care services, and improving the efficiency of health system financing. The first, further expansion of insurance coverage and access to services centers, can be achieved by further targeting of coverage to the uninsured, by utilizing incentives (both financial and using legal re-

quirements), and by streamlining the enrolment process [27]. Our results indicate that these efforts in the past may have had only small gains, and marginal returns may be low. Alternatively, building upon the expansion and free entitlement to primary care services for all in 2009, insurance coverage could be extended free of charge maintaining inputs from taxation and insurance premiums. Moldova must weigh up the marginal costs of targeted insurance premiums vs expanding free entitlement on the pathway to UHC.

Second, costs for medicines and services could be reduced by: i) introducing regulations to prevent informal payments and to regularise formal cost-sharing [28]; ii) increasing, through allocated funding and legal powers, the powers of the Moldovan Medicines and Medical Devices Agency (MMDA) and CNAM, in procuring medicines, negotiating prices, and regulating quality, to reduce costs for those who

purchase drugs and the cost burden of medicines in the benefit package [23,29]; iii) strengthening the provision of PHC, where the majority of health needs can be dealt with cost-effectively, in resource allocations for both services and medicines [28].

Third, health system financing trends indicate that although Moldova commits a proportion of public sources to health in line with EU averages, the actual amount is very low. The government fiscal space for increased funding of health system could be improved by: (i) increasing tobacco and alcohol taxes—which will not only reduce consumption and tackle the health burden of these substances, but generate revenues for the government, (ii) optimizing and consolidating the inefficient hospital sector (iii) investing in new infrastructure using EU development financing and private sector funding to improve health system efficiency.



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**Authors' contribution:** RA and JH conceived the study and guided the analysis and writing. SD assisted with data collection and analysis. TH compiled the data and undertook analysis. All authors contributed to the writing of the final manuscript.

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# Ebola research funding: a systematic analysis, 1997–2015

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**Background** The latest outbreak of Ebola in West Africa overwhelmed the affected countries, with the impact on health extending far beyond Ebola-related deaths that have exceeded 11 000. The need to promptly mobilise resources to control emerging infections is widely recognized. Yet, data on research funding for emerging infections remains inadequately documented.

**Methods** We defined research investment as all funding flows for Ebola and/or Marburg virus from 1997 to April 2015 whose primary purpose was to advance knowledge and new technologies to prevent or cure disease. We sourced data directly from funding organizations and estimated the investment in 2015 US dollars (US\$).

**Results** Funding for Ebola and Marburg virus research in 1997 to 2015 amounted to US\$ 1.035 billion, including US\$ 435.4 million (42.0%) awarded in 2014 and 2015. Public sources of funding invested US\$ 758.8 million (73.1%), philanthropic sources US\$ 65.1 million (6.3%), and joint public/private/philanthropic ventures accounted for US\$ 213.8 million (20.6%). Prior to the Ebola outbreak in 2014, pre-clinical research dominated research with US\$ 443.6 million (73.9%) investment. After the outbreak, however, investment for new product development increased 942.7-fold and that for clinical trials rose 23.5-fold. Investment in new tools to control Ebola and Marburg virus amounted to US\$ 399.1 million, with 61.3% awarded for vaccine research, 29.2% for novel therapeutics research such as antivirals and convalescent blood products, and 9.5% for diagnostics research. Research funding and bibliometric output were moderately associated (Spearman's  $\rho=0.5232$ ,  $P=0.0259$ ), however number of Ebola cases in previous outbreaks and research funding ( $\rho=0.1706$ ,  $P=0.4985$ ) and Ebola cases in previous outbreaks and research output ( $\rho=0.3020$ ,  $P=0.0616$ ) were poorly correlated.

**Conclusion** Significant public and philanthropic funds have been invested in Ebola and Marburg virus research in 2014 and 2015, following the outbreak in West Africa. Long term, strategic vision and leadership are needed to invest in infections with pandemic potential early, including innovative financing measures and open access investment data to promote the development of new therapies and technologies.

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The 2014 Ebola outbreak in West Africa is the largest recorded in history, infecting almost 30 000 individuals by January 2016 and killing over 11 000 people [1].

The challenge with emerging infections is managing uncertainty, as there are many unknown epidemiological and pathophysiological factors. Glob-

al surveillance systems are incomplete [2], and health systems responses among interdependent countries vary, putting at risk countries bordering others where the response is weak [3]. Experience responding to the HIV, SARS and Avian Influenza H5N1 epidemics suggests that the cost of inaction, and delayed response to emerging infections, can be significant to human health, the global economy, security and stability [4].

The Ebola outbreak epitomises a largely failed global response, with delayed action by leading international agencies. Weak health systems, a lack of information and all but absent surveillance systems in West Africa among Ebola-affected countries have hampered efforts to control the current outbreak. The lack of a licensed vaccine or effective therapeutic drugs has contributed to the uncontrollable surge in cases and inability to control Ebola transmission beyond traditional infection control practices.

As with infection control measures and strong health systems, research and development (R&D) plays an important role in mitigating risk from emerging infections. Funding for R&D in global health and infectious diseases has risen since 2000 [5]. However, several studies from the US [6], United Kingdom (UK) [7], Spain [8], Australia [9] and Norway [10] suggest low levels of R&D funding and a lack of reliable data for neglected diseases and low-income settings [11]. Research also indicates a paucity of funding for other conditions for which there is no sizeable market, for example women during pregnancy and neonates [12,13].

More recently, studies have presented systematic analysis of public and philanthropic financing of infectious disease research in the UK to show a predominant focus on pre-clinical and laboratory research across a wide range of infections and crosscutting disciplines such as diagnostics, therapeutics, and vaccines [7]. Research funding, however, was not well aligned to disease burden and followed colonial ties rather than need [14]. To our knowledge, there have been no studies quantifying funding for filovirus research.

We present the first systematic analysis of global funding for research and emergency response for Ebola and Marburg virus infections. The primary purpose of the study is to quantify global research funding for filovirus research prior to, and following, the largest recorded outbreak of Ebola virus.

## METHODS

Measures of research investment were sourced directly from funding organizations, data on disease burden from the Global Burden of Disease Study 2012, and bibliometric impact from the Elsevier Scopus database. The study forms

part of a wider project entitled RESIN: Research Investments in Global Health. A full list of keywords, definitions, categories, sources of funding and data sets are available online (<http://www.researchinvestments.org/ebola>) and in Appendix S1 of the **Online Supplementary Document**.

We included studies that focused on Ebola infection in humans, or animal studies with a clear zoonotic component. For completeness, we also screened and systematically analyzed research investments for Marburg virus and Cuevavirus, two other related filoviruses, as funding for these viruses are often joint. No studies on filovirus Cuevavirus were identified, and it was therefore excluded from the scope of this analysis.

## Data sources and collection

We sourced information from websites, funding organization databases, and the published literature. Data from the UK, European Union (EU) and the US were included for the period of 1997 to 16 April 2015, which represented a 12-month period following the announcement of the outbreak by the WHO. Variables collected included study title, abstract, website, grant type, funding awarded, name and gender of the principal investigator, host institution, year of award and projected duration of project.

In the UK, research funding organisations included the UK Medical Research Council (MRC), the Wellcome Trust, the UK Department for International Development (DFID); in the EU organisations included the European Commission, the European Centre for Disease Prevention and Control (ECDC); and in the US organisations included the National Institutes of Health (NIH), Congressionally Directed Medical Research Programmes (CDMRP), Bill and Melinda Gates Foundation, Paul G. Allen Foundation, Burroughs Wellcome Fund, Doris Duke Charitable Foundation, Howard Hughes Medical Institute, Donaghue Foundation, Ellison Medical Foundation, Arcus Foundation, and the Roy Carver Charitable Trust. The organisations selected represented the leading infectious disease and public health research funders in the respective regions. Variables collected included financial disbursements, project title, website, donor organization, recipient organization, recipient country, and year of award.

## Data management

All grant funding amounts were reported in 2015 US dollars (US\$). All awards were adjusted for inflation and converted to US dollars, using the mean exchange rate in the year award (<http://www.oanda.com>). Grants were not modified according to levels of overheads applied to the award. For multi-center studies, the distribution of funding was accounted for, where openly available. Unfunded studies, or studies without a clear funding amount, were excluded.

Private sector sources of funding were excluded, as data was not openly available. Channels without a robust data source were excluded from the final analysis.

Data were collected over a period of 7 months, from October 2014 to April 2015. The study title, abstract, and website were used to filter and categorise research studies. All research studies were reviewed by two or more co-authors. Each research award was allocated to one of five R&D categories along with the research pipeline: preclinical research, phase 1, 2, or 3 clinical trials, product development, public health research, and cross-disciplinary research. Public health research included surveillance, epidemiology, modeling, bioinformatics, and operational research. Cross-disciplinary studies were large-scale projects, with significant funds to facilitate two or more subprojects to work in parallel. Duration of research studies was also estimated. Top 3 donors were ranked for each recipient organization.

### Statistical analysis

Microsoft Excel 2011 (Microsoft, Seattle WA, USA) was used to categorise the research studies and generation of

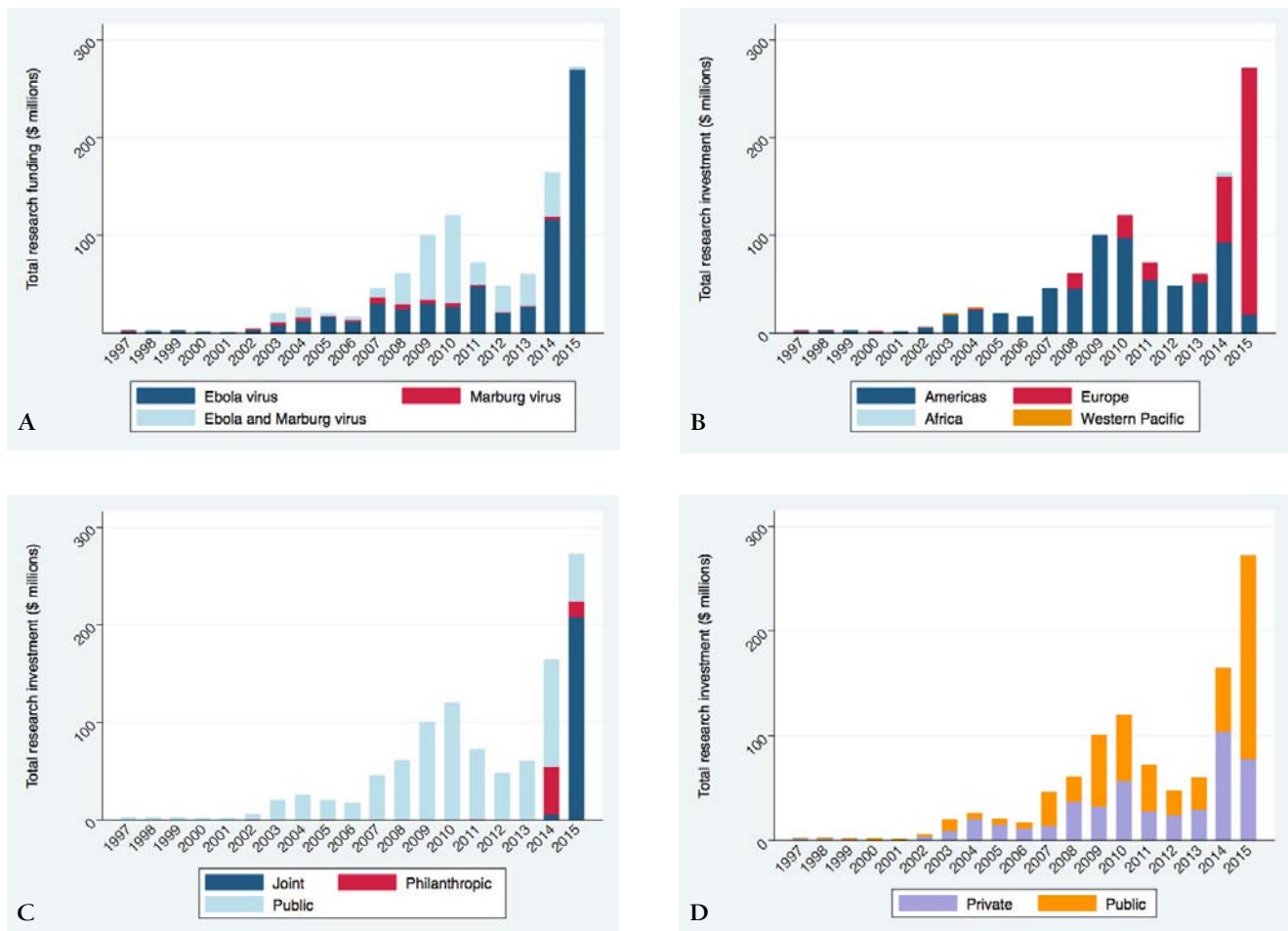
tables. Statistical analysis and generation of figures and graphs were generated using Stata (version 11.2) (STATA Corp LLP, College Station, Texas, USA). Simple regression analyses were reported using Spearman's rank correlation coefficient ( $\rho$ ), to assess the degree of correlation between research investment, disease burden, and bibliometric impact. We used fold differences to compare total investment, number of studies, mean and median grant size.

### Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## RESULTS

**Figure 1** shows the total research investment in Ebola and Marburg virus from 1997 to 2015 in US\$, disaggregated by virus, location of award, source of funding, and recipient of funding, respectively.



**Figure 1.** Total and proportionate investment in research funding by filovirus (A), by geographical location of lead research institution (B), by source of funding (C), and by recipient of funding (D), in 2015 US\$, 1997–2015.



The total research funding awarded over the 18-year time period was US\$ 1.035 billion, including US\$ 435.4 million (42.0%) disbursed in 2014 and 2015 during the West Africa Ebola outbreak. Ebola virus received US\$ 652.4 million (63.0%), Marburg virus received US\$ 34.9 million (3.4%) and cross-cutting filovirus research received US\$ 348.3 million (33.6%).

Relative contributions by Ebola and Marburg virus changed substantially over time, with significant increases in 2003 (from US\$ 5.2 million in 2002 to US\$ 19.4 in 2003), in 2007 (from US\$ 16.5 million in 2006 to US\$ 45.7 million in 2007) and in 2014 (from US\$ 59.6 million in 2013 to US\$ 164.0 million in 2014) respectively (**Figure 1**).

There is clear dominance in research funding awarded by the US, with large rises in 2014 and the 1st quarter of 2015. Large proportions of global research funding are invested in institutions in the European Union, such as the UK with a total of US\$ 152.5 million, Germany with a total of US\$ 66.0 million, and France with a total of US\$ 49.4 million over the 15-month period January 2014–April 2015. Institutions in the US were awarded a total of US\$ 110.1 million during the same time period, predominantly in 2014 (83.2%) (**Table 1**).

Public sources of funding accounted for the majority of total investment in Ebola and Marburg research with US\$ 758.8 million (73.1%). Philanthropic sources awarded US\$ 65.1 million (6.3%), and joint public–philanthropic or public–private funding accounting for US\$ 213.8 million (20.6%), including a further US\$ 90.8 million by the European Commission (**Table 1**).

Publicly funded institutions received a total of US\$ 346.7 million (33.5%) research funding. Private, for profit institutions received a total of US\$ 233.6 million (22.6%) and philanthropic, non-profit institutions received a total of US\$ 455.3 million (44.0%). In other words, for every US\$ 1 invested by a public funding source, a public institution received US\$ 0.46. For every US\$ 1 invested by a private funding source, a for-profit organization received US\$ 2.03, and for every US\$ 1 invested by a philanthropic funding source, a non-profit organization received US\$ 7.00. Universities received the largest investment in Ebola and Marburg virus disbursements with US\$ 579.1 million (55.9%) followed by Research Institutions with US\$ 296.0 million (28.6%) and biopharmaceutical companies with US\$ 229.3 million (22.1%).

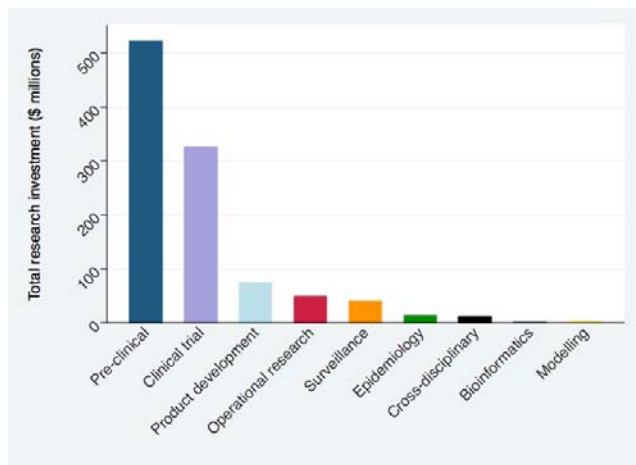
**Figure 2** shows the research investment according to type of research along the R&D pipeline between 1997–2015. Prior to the outbreak, pre-clinical research dominated research with US\$ 443.6 million (73.9%) investment. Per annum investment prior to the Ebola outbreak in West Africa, annual research funding was US\$ 35.3 million over a period of 17 years. Following the outbreak, annual research funding increased 9.5-fold to US\$ 337.1 million.

In 2014 and 2015, a 942.7-fold increase in product development and 23.5-fold increase in clinical trials was observed (**Table 2**). Analyzing data from 1997–2013, there was a moderate association between research funding and research output ( $\rho=0.5232$ ,  $P=0.0259$ ), however Ebola cases in previous outbreaks and research funding ( $\rho=0.1706$ ,  $P=0.4985$ ) and Ebola cases in previous outbreaks and research output ( $\rho=0.3020$ ,  $P=0.0616$ ) were

**Table 1.** Investments by public, private and philanthropic funders for Ebola research

	FUNDING AWARDED, US\$	%	TYPE OF ORGANIZATION	FUNDING RECEIVED, US\$	%	RATIO INVESTMENT:AWARD
<b>Public funding:</b>	756 792 968	73.1	<b>Public institution:</b>	346 738 377	33.5	1:0.46
NIH/NIAID	651 044 589	62.9	University	291 139 730	28.1	
European Commission	93 822 622	9.1	Research Institute	212 219 525	20.5	
German government	4 996 424	0.5	Public Health Institute	63 925 988	6.2	
CDC PHPR	4 634 854	0.4	<b>Non-profit organization:</b>	455 291 509	44.0	1:7
CDMRP	2 232 070	0.2	University	287 955 319	27.8	
<b>Philanthropic funding:</b>	65 064 309	6.3	Research Institute	80 249 373	7.7	
Gates Foundation	52 713 304	5.1	Public Health Institute	60 059 515	5.8	
Wellcome Trust	11 085 919	1.1	NGO	20 765 944	2.0	
Burroughs Wellcome Fund	601 000	0.1	Hospital	6 261 358	0.6	
Ellison Medical Foundation	263 200	0.0	<b>For-profit organization:</b>	233 591 124	22.6	1:2
Paul G. Allen Foundation	170 416	0.0	Biopharmaceuticals	229 370 939	22.1	
Arcus Foundation	121 832	0.0	Research Institute	3 491 497	0.3	
Roy Carver Charitable Trust	108 638	0.0	Technology	728 688	0.1	
<b>Joint funding:</b>	213 763 733	20.6				
EFPIA	114 980 222	11.1				
European Commission	90 797 873	8.8				
Wellcome Trust/DFID/MRC	8 048 047	0.8				
<b>Total Ebola research funding</b>	<b>1 035 621 010</b>	<b>100</b>				

CDMRP – Congressionally Directed Medical Research Programme, CDC PHPR – CDC Office of Public Health Preparedness and Response, NIH – National Institutes of Health, NIAID – National Institute of Allergy and Infectious Diseases, EFPIA – European Federation of Pharmaceutical Industries and Associations, DFID – UK Department for International Development



**Figure 2.** Total investment in Ebola and Marburg research by R&D pipeline, in 2015 US\$, 1997–2015.

poorly correlated (**Figure 3**). Investment in innovative technologies for Ebola and Marburg virus amounted to US\$ 399.1 million, with 61.3% awarded for vaccine research, 29.2% for novel therapeutics research such as antivirals and convalescent blood products, and 9.5% for diagnostics research (**Table 3**).

## DISCUSSION

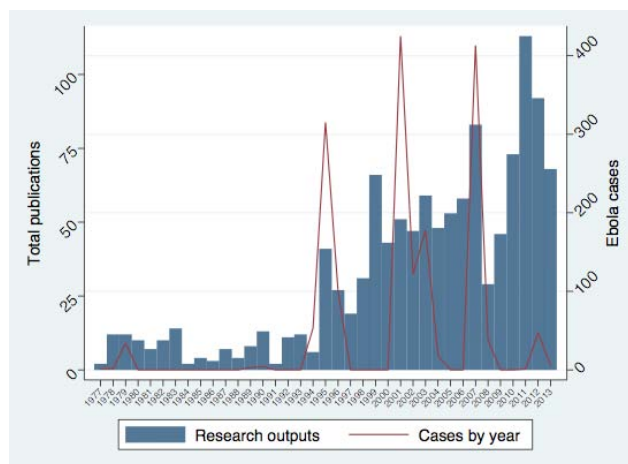
### Implications of mapping research funding

Emerging infections have the potential to disrupt the global economy and global health, mobilising significant resources over short periods of time. In an effort to learn from the latest Ebola outbreak in West Africa and prevent the next epidemic, data on current investments, coupled with data on disease burden and efficacy of interventions, may

provide an enabling environment to strategically allocate scarce resources [15].

We demonstrate significant public and philanthropic funds have been invested in Ebola and Marburg virus research in 2014 and 2015.

Evaluating the impact of R&D is not only good science, but also a social imperative. The responsibility to invest appropriately lies both with researchers, and with funding organisations. Policymakers must work closely with the scientific and funding communities to facilitate channels that provide both the flexibility and the strategic resources to alleviate the burden of emerging infections. Evidence-informed investment is key to allocating resources wisely and fairly. Our analyses provide a first step in aggregating and describing the trends with Ebola and Marburg viruses, in



**Figure 3.** Research bibliometrics output over time with total Ebola cases per annum between 1977–2013.

**Table 2.** Investment in R&D pipeline by focus of Ebola research

	1997–2013			2014–2015			Fold difference
	US\$	%	Per annum	US\$	%	Per annum	
<b>Preclinical:</b>	443 570 456	73.9	26 092 380	78 755 577	18.1	60 972 060	2.3
Host–pathogen	255 676 031	42.6	15 039 767	21 317 338	4.9	16 503 746	1.1
Non–human primates	204 216 041	34.0	12 012 708	16 560 952	3.8	12 821 382	1.1
<b>Clinical trials:</b>	116 942 041	19.5	6 878 944	208 852 606	48.0	161 692 340	23.5
Phase 1	116 942 041	19.5	6 878 944	153 285 276	35.2	118 672 472	17.3
Phase 2–3	–	–	–	55 567 330	12.8	43 019 868	–
<b>Product development:</b>	1 015 328	0.2	59 725	72 726 099	16.7	56 304 077	942.7
<b>Cross–disciplinary:</b>	11 057 065	1.8	650 416	–	0.0	–	–
<b>Public health research:</b>	27 581 023	4.6	1 622 413	75 120 815	17.3	58 158 050	35.8
Surveillance	19 840 535	3.3	1 167 090	20 260 954	4.7	15 685 900	13.4
Epidemiology	6 329 902	1.1	372 347	5 795 974	1.3	4 487 206	12.1
Modeling	501 655	0.1	29 509	433 870	0.1	335 899	11.4
Bioinformatics	908 931	0.2	53 467	224 085	0.1	173 485	3.2
Operational research	–	–	–	48 405 932	11.1	37 475 560	–
<b>Subtotal</b>	600 165 913	100	35 303 877	435 455 097	100	337 126 527	9.5
<b>Total research funding</b>	<b>1 035 621 010</b>						

**Table 3.** Investment in innovation in Ebola research by type of institution

	VACCINES		DIAGNOSTICS		THERAPEUTICS		Total	%
	US\$	%	US\$	%	US\$	%		
Research Institute	108615512	44.4	7832065	20.6	21464466	18.5	137912043	34.6
Biopharmaceuticals	93932058	38.4	9861635	25.9	27752433	23.9	131546126	33.0
University	30429464	12.4	20046125	52.6	60181420	51.7	110657009	27.7
NGO	11667539	4.8	–	–	1376869	1.2	13044408	3.3
Hospital	–	–	–	–	5466616	4.7	5466616	1.4
Public Health Institute	–	–	369008	1.0	94611	0.1	463619	0.1
<b>Subtotal</b>	<b>244644573</b>	<b>61.3</b>	<b>38108833</b>	<b>9.5</b>	<b>116336415</b>	<b>29.2</b>	<b>399089821</b>	<b>38.5</b>
<b>Total research funding</b>	<b>1035621010</b>							

an effort to develop more sensitive methods to evaluate the public health impact of supported research.

What the Ebola crisis in West Africa has demonstrated is the immense repercussions of an outbreak on the stability and social cohesion of a society. The spread of the outbreak is linked to the under-developed and under-resourced health systems preexisting within these countries, but also the imbalance between investments in the diseases that affect individuals in wealthier countries over those living in low-income settings [16].

### Proposals for research strategy

New approaches for research during a new epidemic or pandemic are critical, and useful examples include the 2009 NIHR “Rapid Response” research funding for influenza [17], and the 2011 NIHR “Sleeping grants” where protected funding will be activated in the event of a new pandemic [18].

A portfolio of research along the R&D value chain (extending from preclinical and laboratory science, phase 1 and phase 2 clinical trials, large-scale phase 3 and phase for clinical trials, translational studies and evaluations) is required to address the greatest challenges in global health. Investing in the progression and links between these different types of research is essential in order to build on early stage research findings, and translate breakthroughs in the laboratory into reality in health systems where translation and uptake of innovations remains a challenge [19,20]. Operations research is critical to understand how innovations can be effectively scaled up [21,22].

Encouragingly, the scope and volume of potential Ebola diagnostics, therapies and vaccines is broadening (**Box 1**).

R&D should also extend beyond vaccines, diagnostics, and antivirals, however. Research into novel, digital surveillance systems is also warranted. Surveillance systems are essential to detect outbreaks of emerging infections, and to mitigate their health, security and economic effects, in all countries [27,28]. The International Health Regulations (IHR) confers responsibilities to WHO member states to

**Box 1** Summary of current research for Ebola diagnostics, therapies and vaccines.

Research is currently under way to investigate the therapeutic potential of favipiravir (Toyama Chemical, Japan) and convalescent whole blood and plasma treatment [23]. Clinical trials in Liberia of brincidofovir (Chimerix; NC, USA) with Médecins Sans Frontières and the Wellcome Trust were discontinued due to paucity of numbers recruited. Should these front-runners fail to show promise, 10–15 pre-qualified products may become the next candidates. Zmapp (Mapp Biopharmaceuticals; CA, USA) was not selected as part of the early research candidates due to availability issues.

Efficacy trials for an Ebola vaccine have begun in February 2015, 14 months after the estimated start of the outbreak, using a randomized ring vaccination design adopted with the smallpox eradication campaign [24]. In clarifying their position, Gavi, the Vaccine Alliance, has approved US\$ 300 million spending on vaccine procurement and US\$ 90 million on strengthening immunisation systems [25]. The overarching aim is to enable vaccine development for emerging infections by recognizing the lack of market potential, building laboratory and outbreak investigation capabilities in country, create repositories of potential agents and catalog immunological properties, and develop vaccine vectors. Two candidates exist: GlaxoSmithKline's ChAd3–ZEBOV and Merck's rVSV–Ebov. Further preclinical vaccine candidates include Johnson & Johnson's recombinant vector regimen, a recombinant nanoparticle vaccine by Novavax, a recombinant influenza vaccine developed by the Russian Ministry of Health, a Venezuela equine encephalitis replicon Ebola vaccine developed by the US Army Medical Research Institute for Infectious Diseases, and possibly a further vaccine developed by the Chinese Army. The imperative to invest in emerging infections or diseases with high mortality rates lies in the fact that suboptimal evidence may be generated during an outbreak, due to the urge to develop therapies without randomized controlled trials. Randomization is essential in Ebola drug trials, as it is with cancer trials [26]. An assumption that a therapy will be effective is inappropriate for generating evidence, and harm may be the price of introducing this bias. Strategic health investment can go a long way to ensuring sufficient innovation in science is being fostered, preventing a reliance on insufficient and potentially wasteful products toward the end of the R&D pipeline.

develop surveillance systems to detect and respond to public health emergencies, although many are not ready [29]. IHR provides a mandate for global surveillance, a safety net to detect disease outbreaks if they are not detected and/or reported by countries. Responsive health systems and global collaboration is critically important if these infections are to be rapidly contained [30,31]. In 2002, the Global Public Health Intelligence Network, developed by the Public Health Agency of Canada, openly alerted the global health community to SARS 2 months prior to the WHO. In 2014, HealthMap sounded the alarm to an outbreak of unknown etiology in Guinea 9 days before the WHO. Recent work has further highlighted the density of Google Trends searches for Ebola in West Africa, despite inadequate Internet coverage in the region [32]. These factors together highlight the need for research into digital systems for global health security.

### Limitations and scope

The primary limitation to this work is the difference in quality of research funding, compared with emergency response funding. Although public and philanthropic research funding is, on the whole, well documented and often openly accessible online, there are clear quality concerns with emergency response funding. For instance, it is difficult to verify disbursements and pledges for emergency response, and this is a notable problem with the latest Ebola outbreak. As published in the *Lancet Global Health* – the tools “for tracking resources in a crisis are not fit for purpose” [33]. Despite the challenges with emergency response funding, it is important to document the openly published information, systematically analyze the data and start a discussion on next steps in tracking resources during a crisis. We need a robust financial platform to monitor and evaluate investments – with the capacity to cross-talk with research funding commitments. With the re-emergence of Zika virus in the Americas, this needs to occur without delay.

There are also limitations to analyzing global expenditure data search, elaborated in greater detail in a recent article by Young and colleagues [34]. The first is the challenge of comparing data collected from different countries. The Frascati manual attempts to provide some guidance on the data collection and currency adjustments for R&D [35]. Despite some clear guidance, two recent studies highlight the ongoing difficulties with methodology and subsequent impact on interpretation, particularly due to discrepancies in data conversion [36–38]. The second is the lack of indices to convert health R&D expenditure to a single, commonly used currency [38]. One of the main reasons this is important is the comparative difference in the costs of input for R&D in different settings [39]. There are two possible ways of converting to a common currency: current exchange rates, and GDP purchasing power parities (PPPs)

[40]. The Frascati manual recommends GDP PPPs, and current exchange rates may underestimate the contributions of countries such as India and China, by overstating the costs of R&D. The third is the need to adjust investment over time, in order to account for the potential role of inflation. There is currently no index specific for health R&D and the Frascati manual advocates for using the GDP price index, with the limitation that is not specific for R&D. The special R&D deflator is an index adopted by the US National Institutes of Health and may be adopted for high-income settings [41]. Using this index for settings with high inflation will overestimate respective contributions, and vice versa. The fourth challenge relates to the need first to deflate data in national currency, then to convert the adjusted data to a common currency using a selected base year [42]. Altering data using another mechanism may skew the data inappropriately and alter the comparability between settings. Fifth, our study is likely to underestimate research funding, partly due to the lack of openly available data from the pharmaceutical industry. Sixth challenge relates to difficulties in ascertaining the right proportion of a grant allocated to a specific disease, when there are multiple research sites and conditions researched, which is not uncommon for co-infection studies.

### Strategic coordination of research funding

A Global Observatory on health R&D has been proposed by member states of the sixty-sixth World Health Assembly in 2013 to “provide a mechanism to monitor and analyse relevant existing information on health R&D, including resource flows, product pipelines, and research outputs, with a view to contributing to the identification of gaps and opportunities for health R&D and to inform priority-setting for new R&D investments based on the public health needs of the world’s poorest countries” [43,44].

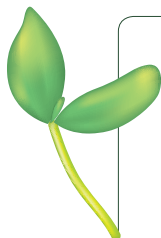
A clear, open source repository for R&D investment data could address the problem by showing the funding landscape of both clinical and non-clinical studies in real time [45]. Gaps in the data highlight the need for a global health R&D observatory. Innovations in reporting will help improve priority setting to address burden of disease in low- and middle-income settings. Interpreting disease burden data in the context of R&D funding data are an essential step in the equitable allocation of health investments. Whether the observatory should be run by the WHO or by another institution or consortium, however, remains for debate.

### CONCLUSIONS

Over 20 years after a landmark publication by the Institute of Medicine, emerging and re-emerging infectious diseases continue pose a serious threat globally to human and ani-

mal health, security and economy [46]. Health and financial resources need to be allocated and available swiftly during a pandemic or emerging infectious disease outbreak to ensure appropriate control. The global health community needs to develop an evidence-base for health research and policy, in particular around priority setting

for health R&D, decision making for funding, evaluating innovation and research pipelines, assessing research outputs and networks, and forecasting future needs and corresponding investment. Strategic funding is required for inter-pandemic research, pre-pandemic research and established pandemic research.



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**Authorship declaration:** JRAF designed the study, managed the research project, undertook data analysis, contributed to the interpretation of the data, and drafted the article. AmL, DTS, ArL and JVDO assisted with data collection and analysis. MGH and RA made significant contributions to developing methods for data analysis, interpreting the data, and writing the article. All authors reviewed and approved the final version. JRAF is guarantor of the paper.

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# Health system resilience: Lebanon and the Syrian refugee crisis

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**Background** Between 2011 and 2013, the Lebanese population increased by 30% due to the influx of Syrian refugees. While a sudden increase of such magnitude represents a shock to the health system, threatening the continuity of service delivery and destabilizing governance, it also offers a unique opportunity to study resilience of a health system amidst ongoing crisis.

**Methods** We conceptualized resilience as the capacity of a health system to absorb internal or external shocks (for example prevent or contain disease outbreaks and maintain functional health institutions) while sustaining achievements. We explored factors contributing to the resilience of the Lebanese health system, including networking with stakeholders, diversification of the health system, adequate infrastructure and health human resources, a comprehensive communicable disease response and the integration of the refugees within the health system.

**Results** In studying the case of Lebanon we used input–process–output–outcome approach to assess the resilience of the Lebanese health system. This approach provided us with a holistic view of the health system, as it captured not only the sustained and improved outcomes, but also the inputs and processes leading to them.

**Conclusion** Our study indicates that the Lebanese health system was resilient as its institutions sustained their performance during the crisis and even improved.

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Lebanon is a country in the Middle East with a population of 4.2 million people [1]. Since the 1970s, Lebanon has endured repeated shocks to its health system, including wars, massive population displacement, economic downturns and political instability, which have produced a country that has been without a president for two years [2]. In addition to the persistent political instability, Lebanon has been housing half a million Palestinian refugees since 1948. The most immediate challenge facing Lebanon, however, is the Syrian refugee crisis.

Since 2011, following the escalation of the devastating war in Syria, there has been a large and ongoing influx of Syrian refugees to Lebanon. By the end of 2015 the numbers of refugees had reached 1.5 million, in addition to 53 000 Palestinians returning from Syria [3,4]. The new refugees represent a 30% increase in Lebanon's pre-crisis population, resulting in the highest refugee density of any country worldwide since 1980 [5]. The refugees from Syria have not been placed in formal camps, but are dispersed



across Lebanon in houses among the Lebanese population, while 17% is residing in informal tented settlements [6].

The unprecedented influx of refugees has placed a considerable burden on the Lebanese government, society and economy, which are facing many other challenges. For example, while the Gross Domestic Product (GDP) of Lebanon grew by 8% in 2010, it fell sharply to 1.5% in 2013 [7], constraining the government's ability to continue financing the expanding population needs in the presence of stagnant economic growth.

A refugee crisis of such a large magnitude is a severe shock to the health system, and threatens continuity of service delivery, destabilizing governance and limiting access to care [8]. To date, however, the Lebanese health system (**Box 1**) has been able to accommodate and adjust to the refugee crisis [11].

Resilience is the ability of a health system to sustain or improve access to health care services while ensuring long-term sustainability [12,13]. A resilient system has high tolerance to uncertainty and relies on a variety of resources in its response to shocks [14,15]. Despite calls for strengthening policy capacity in this important area [16,17] resilience of health systems to external and internal shocks remains understudied [18,19].

Lebanon is currently facing an acute crisis [20] due to an unprecedented influx of refugees from Syria with multiple health needs, which has placed a rapid and an unprece-

ded demand on the health system [21,22]. The extraordinary situation of the refugee crisis offers a unique setting to study resilience of Lebanon's health system to an external shock, combined with internal shocks due to economic and political instability.

## METHODS

The aim of this study is to assess the resilience of the Lebanese health system in the face of an acute and severe crisis and in the context of political instability.

While many conceptual frameworks for resilience exist [23] there is no unified definition of health system resilience, or an established method to measure it [24]. One framework offers 5 dimensions to assess the potential of health system resilience to an emerging crisis, but a standardized set of internationally accepted indicators for these dimensions have yet to be developed and tested empirically [25]. For the purpose of this study, we have used the following working definition of a resilient system: "a resilient system has the capacity to absorb change due to external or internal shocks, maintain original functions and ensure long-term sustainability" [26–29].

When studying the resilience of the Lebanese health system we drew on insights from studies of health systems that have faced refugee crises – studies which have considered the ability of a health system to maintain service delivery, prevent major outbreaks and sustain improvements in population level outcome indicators including utilization, service coverage, morbidity and mortality rates, as measures of success [30–33]. The indicators used in these earlier studies are in line with the definition of resilience we have used. This definition stresses the ability of a system to reorganize and adapt to change while maintaining original functions and ensuring long-term sustainability [26–28].

The study employs a case study approach and draws on data from multiple sources. We use an input–process–output/outcome model of a health system [30], where inputs, processes and outputs measure the capacity of the health system while outcomes measure its performance [30]. This approach allows for a comprehensive and holistic analysis of the Lebanese health system and offers enough flexibility to capture both the contextual characteristics of the system and factors in place during the acute crisis that have affected the health system response and resilience.

The study, which took place from January 2014 to July 2015, consisted of two main components: a literature review on resilience and how to measure it, and analysis of secondary data to document the impact of the refugee crisis and the health system response in Lebanon.

For the literature review, we undertook a search using the following databases: OVID Medline, the Cochrane Library,

### Box 1. Lebanese health system – a brief overview

The health system in Lebanon is a public–private partnership with multiple sources of funding and channels of delivery. Almost one half of the population is financially covered by the National Social Security Fund (NSSF), an autonomous public establishment or by other governmental (civil servants cooperative and military schemes) or private insurance. All those schemes provide financial coverage with variable patient copays. The non-adherents are entitled to the coverage of the Ministry of Public Health (MoPH) for secondary and tertiary care at both public and private institutions. Palestinian refugees are covered through the United Nations Relief and Work Agency for Palestinian refugees (UNRWA) for their health care services [9].

Although the MOPH does not cover ambulatory care services, it provides in kind support to a national network of primary health care (PHC) centers all over Lebanon [2]. The centers provide consultations with medical specialists at reduced cost, as well as medicines for chronic illness and vaccines funded by the ministry of health [2].

Around 68% of the primary health care centers in the national network are owned by NGOs while 80% of hospitals belong to the private sector [2]. The strong presence of the private sector in service delivery has led to an oversupply of hospital beds and technology [2]. While there is an oversupply of physicians, there is a shortage of nurses [10].

and Health Systems Evidence. In addition, we searched gray literature databases such as Reliefweb, MedNar, OAIS-TER, Open DOAR, PROSPERO and OpenGrey.

Local data were obtained from multiple sources, namely the Lebanese Ministry of Public Health database which included data on service utilization, human resources, immunization coverage, and epidemiological surveillance. We also used national health accounts data (that uses the System of Health Accounts 1.0) and maternal mortality observatory data. The MOPH information systems and the maternal mortality observatory data sets are designed to incorporate ongoing assessment and reporting related to displaced Syrians, including for immunization coverage, disease surveillance and utilization of health services in addition to maternal and child mortality. Other sources included statistics from the Lebanese Ministry of Finance, Bank of Lebanon and the Central Administration for Statistics (CAS), UN agency publications, World Bank assessments, and international and local NGOs publications.

## RESULTS

### Health system inputs and processes

**Human resources.** The fluctuating pattern in the number of physicians started before the Syrian Refugee crisis as a result of a mismatch in supply and demand, with persistent oversupply [34]. By contrast, the number of nurses working in Lebanese health system increased steadily and was not affected by the Syrian crisis [34]. The steady rate of increase in number of nurses occurred as a result of deliberate MOPH policies, such as the establishment of a career path for nurses, financing of training of more nurses by the Lebanese university, supporting the bridging between vocational and academic training, and increasing nursing wages in the public sector [2].

**Financing.** In 2013–14, there was no substantial change in patterns of public spending on health, the budget of the MOPH, and all public funds rose at the same rate of yearly increase as in the preceding years [1,35]. However, throughout the crisis, the levels of funding from international donors were erratic and far below the amounts required to meet the health needs of the refugees. For example, in 2013, less than 50% of funding requirement was met [36], declining in 2014 to 33% of the funding amount needed [4]. The funds from international donors are managed by United Nations (UN) agencies and are channeled through different international and local NGOs. The MOPH was not a recipient of these funds but worked with international entities to influence effective application of the funds to priority areas and populations.

Throughout the crisis, the Lebanese health system was able to sustain the level of financing of services at primary–, sec-

ondary– and tertiary–care levels. The MOPH contracts with primary health care centers were maintained. The MOPH was able to uphold and improve its contracting terms with private hospitals by including performance measures in the contracts to achieve required service volumes at specified quality levels. Additionally, all the public funds and private insurance companies continued to provide cover to their respective beneficiaries, notwithstanding delays in reimbursement.

Despite financial constraints, the MOPH managed to increase its expenditure on drugs, which helped to effectively meet the higher demand that arose in recent years [1]. This expenditure of funds to increase expenditure on drugs was coupled with collaboration with different donors in order to direct external funds to priority areas.

For Syrian refugees, primary care has been partly subsidized by the United Nations High Commission for Refugees (UNHCR). However, for secondary care the financial assistance provided by UNHCR has been limited to vulnerable groups, and for life-threatening conditions with co-payments provided by refugees [36]. The limited financing of secondary care services has resulted in a major gap in service coverage, however leading to heavy financial burden on refugees seeking secondary and tertiary care services [36].

**Governance.** At the start of the crisis, there was no clear government policy regarding the displaced Syrian population. While the MOPH began to offer displaced Syrians the same immunization schedule and primary health care services offered to Lebanese citizens, UNHCR and other relief agencies sought to create their own delivery channels and their own mechanism of financing coverage which operated in parallel to the existing health system. The parallel systems established by international agencies led to fragmentation and poor coordination of the health system response to the refugee crisis. In the absence of a clear government policy, the fragmentation of health system governance prompted the MOPH to call upon international agencies to consider a more integrated approach to planning, financing and service delivery by embedding refugee health care within the national health system. To develop an integrated approach, the MOPH established a steering committee that includes major international and local partners to guide the response. The steering committee, led by the MOPH, develops strategic plans and coordination mechanisms and monitors the response [4]. All partners in the refugee health response including MOPH, UN agencies, international and local non-governmental organisations (NGOs) held regular meetings and set up yearly response plans such as the “Lebanon crisis response plan”. These response plans detailed all funding sources, activities performed and coordination efforts. These plans were regular-

ly updated and tracked, and the results were shared in dissemination workshops and on the websites of these partners. The inclusive model of governance, based on participation, transparency and accountability, was critical in mounting an effective emergency response and in creating health system resilience, and in establishing an effective surveillance system (**Box 2**).

During the crisis, the participation of the private sector and civil society, and networking with different donors, international stakeholders and UN agencies was not only important for health system governance but also for the development of multi-sectoral health strategies. Examples of successful partnerships included the engagement of the primary health care national network and private hospitals in health care delivery to mount a unified and effective response [37].

**Service provision.** Provision of health care has been sustained at all levels throughout the crisis. Primary health care centers and hospitals from both public and private sectors have remained operational. Health programmes, such as those for epidemiological surveillance, immunization, medication for chronic illnesses, tuberculosis, HIV/AIDS and reproductive health, among others, are functioning effectively [38]. Other programs, such as the accreditation of primary health care centers and integration of non-communicable disease management within primary health care, progressed as planned despite the crisis [38].

### Box 2. Surveillance of refugees

The registration of Displaced Syrians began in January 2012 by the UNHCR. By 6th May 2015, UNHCR had temporarily suspended new registrations as per Government of Lebanon's instructions. The highest influx occurred in 2013, with the number of Displaced Syrians reaching around 1 200 000 by end of 2014. The number of Displaced Syrians had declined by 31st October 2015 to 1 075 637.

In response to the rapid rise in demand for human health resources, the MOPH, in collaboration with UNHCR, WHO and UNICEF, recruited a limited number of health workers to strengthen its surveillance system and emergency response capability and to cater for the needs of Displaced Syrians living in the informal tented settlements, in addition to a limited number of administrative employees at central and peripheral levels. A total of 92 new staff was recruited in PHC, in dispensaries' and in public hospitals. Due to financial constraints, however, this number diminished gradually to 42 by the end of 2015. Retention of the remaining staff will largely depend on the evolution of the crisis.

Embedded in each program of work were a set of monitoring and evaluation tools that made the stretched activities run smoother. Each program approached the crisis as if they were dealing with an enlarged population of 30%. Immunization activities, PHC services, and secondary care provision were all maintained and effectively expanded while monitoring and maintaining quality standards.

Nationwide vaccination campaigns for polio and measles have been routinely conducted as needed, and services provided to all those in Lebanon irrespective of nationalities [39]. These immunization campaigns were conducted in accordance with the district physicians, municipalities, civil society and schools. Community health workers, including volunteers from universities and schools, participated in the door-to-door immunization campaigns [38]. Additionally, the epidemiological surveillance program was able to sustain and even enhance its functions, including measurement and monitoring disease burden, detecting outbreaks, investigating emerging infections and implementing early warning and response system [4]. Staff trainings were conducted by MOPH health experts and adequate precautionary measures were taken at airports and seaports against pandemic threats, such as Ebola and MERS Coronavirus [39,40].

In addition to the primary care centers across Lebanon that were providing health services for Syrians refugees and the public health response, at the hospital level, UNHCR contracted with public and private hospitals to provide for registered Displaced Syrians selected secondary care services, covering 75% of the fees [41]. The additional services financed by UNHCR enabled the MOPH to maintain the functioning of existing units to meet the needs of displaced Syrian refugees while allocating additional dedicated health workers for those living in informal tented settlements [6].

### Health system outputs and outcomes

**Health service utilization.** Since 2013, the number of primary health care centers in the national network as well as the number of beneficiaries steadily rose [38]. In 2014, the total beneficiaries of the primary health care network exceeded 1.2 million, compared to about 700 000 in 2009 [38]. These beneficiaries include both Lebanese and Syrian nationals. In 2014, Syrian nationals made up around 35% of the beneficiaries for the primary health care national network [38].

Private and public hospitals continue to deliver quality services. While the MOPH has sustained its coverage of hospital admissions for uninsured Lebanese, admissions for insured Lebanese have not been disrupted by the Syrian refugee crisis [1] (**Figure 1**). Meanwhile, the proportion of Syrian beneficiaries in Rafic Hariri Governmental University Hospital has continued to increase from 2% in 2010 to 33% in 2014 (**Figure 2**) [42].

In terms of immunization coverage, vaccination rates for measles and diphtheria, pertussis and tetanus (DPT) are considered important indicators of health system performance [43]. The vaccination campaigns achieved high vaccination rates for both Lebanese and Syrian beneficiaries [38] (**Figure 3**).

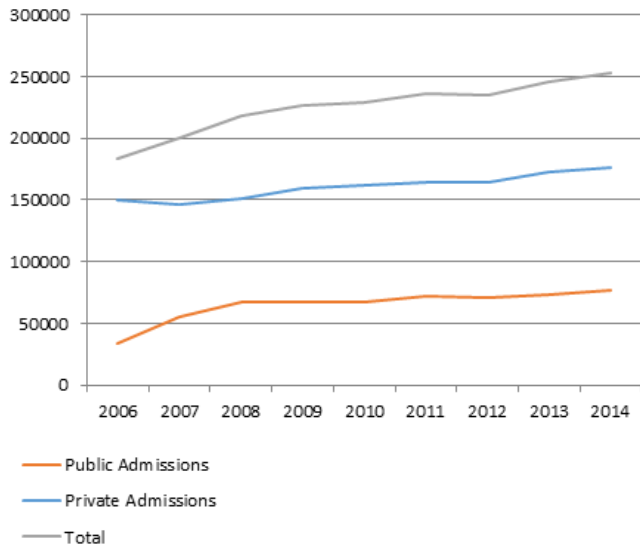


Figure 1. Hospital admissions by 2006–2014.

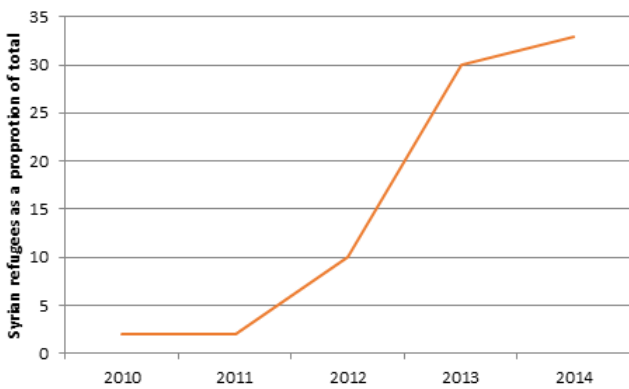


Figure 2. Utilization of hospital services in public hospitals 2010–2014.

**Health expenditures.** To ensure uninterrupted financial coverage, the MOPH developed and implemented a reform strategy in 1998 to rationalize health expenditures targeting the high financial burden on households. This strategy resulted in lower out of pocket expenditures from 60% in 1998 to 34% in 2013, at the peak of the Syrian crisis [2,35,44].

**Morbidity and mortality.** Despite political instability, Lebanon has achieved the health related Millennium Development Goals (MDGs 4, 5 and 6) [7]. Infant Mortality Rate (IMR) fell sharply from 33.5 per 1000 live births in 1996 to 8 per 1000 live births while Under 5 Mortality Rate (U5MR) declined from 36.5 per 1000 live births in 1996 to 9 per 1000 live births in 2013 [45]. Similarly, the maternal mortality ratio decreased from 140 per 100 000 live births in 1990 to 16 in 2013 [45–47]. Child and Maternal Mortality Observatory data confirm the downward trend in these indicators over the recent years [1,45,46].

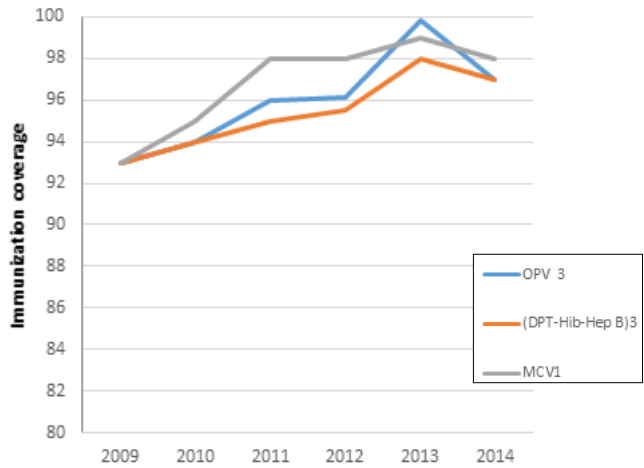
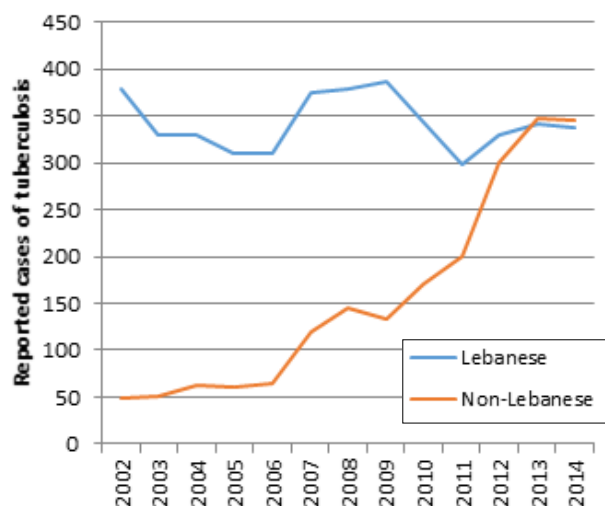


Figure 3. Polio, DPT (diphtheria, pertussis and tetanus) and measles vaccination rates in Lebanon, 2009–2014.

**Prevention of outbreaks of infections.** The influx of Syrian refugees has increased the risk and exposure to communicable diseases, including those that previously did not exist in Lebanon [23]. Communicable diseases, such as polio, measles and waterborne infections, are considered the greatest public health risks in refugee situations [48]. Outbreak prevention and control, therefore, represent an important measure of the resilience of a health system.

Lebanon effectively managed several outbreaks including for measles. In 2013, the number of reported measles cases was 1760, compared to 29 cases in 2015 [49]. The spread of Leishmaniasis, an infection which was previously not noted in Lebanon, was also avoided despite the existence of its vector, the sand fly, in North Lebanon and the Bekaa, and the presence of infected Syrians as a human reservoir [49]. The number of Leishmaniasis cases fell substantially between 2013 and 2015 (1033 to 32 cases), with only three Lebanese citizens contracting the disease during the crisis [49]. Additionally, Lebanon was able to stay polio-free despite reemergence of the disease in Syria [38]. The MOPH ensured that the vaccination campaigns reached the maximum number of children by conducting school field visits, by having an MOPH vaccination team at every UNHCR refugee registration entry point, by coordination with the MOPH officers at district level, and primary care centers and by providing door-to-door coverage. Syrian refugees have also received routine immunizations and other vaccinations, such as polio and measles through the vaccination campaigns spearheaded and coordinated by the MOPH, UNICEF and WHO. As for cholera, and despite it being considered a public health threat in Lebanon by WHO due to the refugee crisis, Lebanon was cholera-free from 2013 to 2015 [49].

Case notification rate of tuberculosis (TB) in Lebanon had been declining until 2011. In 2012, the case notification



**Figure 4.** Reported cases of tuberculosis in Lebanon among Lebanese and Non-Lebanese persons 2002 to 2014.

rate increased by 27%, however [50] (**Figure 4**). This increase was attributed to a rapid rise in the number of Syrian refugees, as only 48% of notified TB cases was among non-Lebanese [50]. Early detection, isolation, and treatment of TB cases in specialized centers and hospitals among the displaced populations prevented an outbreak in host communities [51]. In 2014, the treatment success rate was 76%, with one half of the TB cases receiving treatment completely cured [51].

## Discussion

Our findings indicate that the health system in Lebanon was able to maintain service delivery for both refugees and Lebanese citizens, prevent communicable diseases and sustain improvements in morbidity and mortality levels in the presence of major external and internal shocks, despite relatively limited increase in system inputs. The health system was “able to adapt to change and retain functionality” of governance, financing and service delivery “while maintaining achievements” [26–28]. As the crisis evolves, the resilience of health care service delivery in Lebanon will be continuously monitored, as the health system comes under increasing pressure.

The resilience of the Lebanese health system could be attributed to four major factors. First, networking with the multitude of partners in the health sector [52] and the mobilization and support of regional and global partners, were at the core of the response to the Syrian refugee crisis. This integrated approach was evident in the refugee response plan that was developed by key actors and implemented by a wide array of service providers, including from the private and public sectors and NGOs [25]. Additionally, the Lebanese health system was able to draw upon diverse

sources of funding and multiple conduits for service delivery. Although multiple financing sources and service providers can lead to fragmentation, good governance based on a public private partnership helped to secure a constant stream of funds, primarily through both reallocation of resources and internal resource mobilization, which allowed patients to bypass government bureaucracy and partially compensate for the delayed and scarce international aid. Integration and smart dependency achieved in Lebanon is a key feature of resilient health systems [25].

Second, adequate infrastructure and sufficient supply of health human resources was vital in absorbing the additional numbers of refugees. Resilient health systems have the ability to tap in to excess capacities for an optimal health response during a crisis [25,53]. Lebanon, which had a diverse set of providers also had an oversupply of hospital beds and technology that was used to meet the increased demand during the crisis [2,54]. An adequate supply of a committed and responsive workforce is a precondition for resilience [25,53]. In Lebanon, the health workforce is well accustomed to crisis situations [55]. This experience ensured a regular supply of health human resources that catered to both refugee and Lebanese populations.

Third, a comprehensive communicable disease response helped combat outbreaks, a major health priority during a refugee crisis [48]. The Ebola crisis in West Africa has highlighted the importance of epidemiological surveillance as part of an “aware” system in outbreak control [25,53]. In Lebanon, the primary health care department, along with the epidemiological surveillance unit, played an important role in ensuring effective and ongoing surveillance. Widespread immunization campaigns, with augmented community engagement activities, were employed in a timely manner and synchronized with regional levels to achieve high coverage rates. Effective immunization coverage, coupled with the early warning and response system, allowed for prevention and control of the spread of communicable diseases.

Fourth, integration of refugee health care within the national health system, made possible by the settlement of refugees within Lebanese communities rather than camps, was also an important factor. Although this approach may have been problematic for the host communities, it reduced administrative and set-up costs, and enabled more responsive service delivery. It also shifted the burden to several geographic areas in Lebanon and to several different players in the Lebanese health system. The benefits of the integrated health system approach over the approach, which creates multiple parallel service delivery and financing systems, have been documented in other refugee crises [56].

Our findings suggest a resilient response by the Lebanese health system to the refugee crisis. Despite the limited resources and the turmoil caused by the war in Syria, Lebanon

has been able to cope with an unprecedented influx of refugees, maintain improvements in mortality and morbidity outcomes in the country and achieve the MDG targets.

Our observations in a real empirical setting lead us to suggest a revised definition of resilience of health systems: “Resilience is the capacity of a health system to absorb internal and external shocks, and maintain functional health institutions while sustaining achievements.” We believe that this revised definition describes a real life and tested experience of resilience in an unprecedented setting.

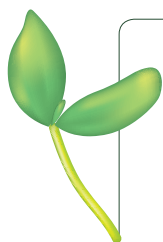
We identified four major factors that enabled resilience: (i) networking with stakeholders (ii) diversification of the health system that provided for adequate infrastructure and health human resources (iii) a comprehensive communicable disease response and (iv) the integration of refugees into the health system. A question that remains unanswered is the longer-term sustainability of the current response. Although, thus far, Lebanon has sustained achievements in morbidity and mortality levels, the magnitude and the chronic nature of the crisis continues to pose a threat to the health system.

The study has three main strengths. First, to our knowledge, this is the first study to investigate the resilience of a health system during an ongoing major refugee crisis. Sec-

ond, the use of the input–process–output–outcome model to analyze the data and to categorize the health system resilience has helped to frame the system as a whole, and shed light on the possible contributing factors to achieving resilience. Third, the study used multiple sources of information, including the public, private, civil society and humanitarian sectors, to provide a comprehensive view of the Lebanese health system.

Several limitations are also acknowledged. First, the literature lacks a rigorous and scientifically validated method for measuring and proving resilience in health systems. We used a model that included several dimensions of resilience identified from published and gray literature, in addition to health system performance indicators which we considered to be important measures relating to resilience. Second, the study was limited by the availability of data on the dispersed refugee population and the ongoing influx of refugees. Third, the dynamic nature of the refugee situation means data need to be regularly updated.

Notwithstanding limitations, however, our study contributes to an area of global importance and helps empirically to illuminate effective response from a health system that has shown resilience in spite of the most severe refugee crisis of recent times experienced anywhere in the world.



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# Age or health status: which influences medical insurance enrollment greater?

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**Background** The New Cooperative Medical Scheme (NCMS) for peasants implemented in 2003 and the Urban Resident Basic Medical Insurance (URBMI) for the urban unemployed implemented in 2007 have many similarities. They both apply the financing mode of individual premiums plus government's subsidies, and the voluntary enrollment. The Chinese government plans to integrate these two systems and build a unified basic medical insurance system for the unemployed in order to achieve the medical equity and increase the general health level. Thus, to analyze the main influencing factors of the enrollment of the urban unemployed and rural residents is very important for improving the system and securing the stability of the system during the transition.

**Methods** The study uses data from the China Health and Nutrition Survey (CHNS) and adopts logistic regression models to test which factors influence the enrollment of the URBMI and the NCMS under the background of rather high enrollment rate of Chinese basic medical insurances and strong fiscal support of the Chinese government, especially whether health status or age influences enrollment of these two insurances greater.

**Results** There is indeed some adverse selection in the URBMI and the NCMS. Whether the individual has chronic diseases have significant influence on enrollments of both the urban unemployed and rural residents, while whether the individual got ill in last four weeks just influences enrollments of the urban unemployed. Age influences enrollment greater than health status. The older the insured are, the larger the enrollment rates are.

**Conclusion** Because of the active support for basic medical insurances of the Chinese government, the enrollment performance of the urban unemployed and rural residents has already changed. When implementing the new policy, the government should pay attention to the willingness to enroll in and the change of enrollment performance of the insured. Therefore, under the policy of voluntary enrollment, every coordinated province and city should enlarge the proportion of young people to insuring group, optimizing the age structure, and the financing proportion of governments and individuals should be measured properly. With the increasing of governments' subsidies, the proportion of individual's premiums should also be increased.

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The Urban Employee Basic Medical Insurance (UEBMI), the Urban Resident Basic Medical Insurance (URBMI) and the New Cooperative Medical Scheme (NCMS) compose Chinese basic medical insurance system. The UEBMI for urban employees which was built in 1998 adopts the compulsory enrollment and its premiums are contributed by both of employees and their companies, while the NCMS for rural people in 2003 and the URBMI for urban unemployed in 2007 adopt the voluntary enrollment and their funds are raised by multi-channel financing – individual contributions combining with higher governmental subsidies, which shows the great differences between the UEBMI, and the NCMS and the URBMI.

As for voluntary medical insurance, many scholars have pointed out that voluntary membership can make these schemes vulnerable to adverse selection [1-4], which may result in the opposite problem of too little coverage and thus under consumption of medical care [5,6]. Voluntary medical insurance has the potential disadvantage of not nurturing the principles of mutual support and the health care costs will increase at the same time [7]. However, some other researches show that premium subsidies for medical insurance may mitigate adverse selection and lead to excessive coverage and excessive spending on medical care [8].

The NCMS and the URBMI, using voluntary enrollment, have many similarities. Both of them have achieved a great success and exert an important effect on satisfying people's demands for medical security and increasing people's health level. However, with the development of social economy, the negative sides of separating these two system have appeared, like re-enrolling or re-financing. To solve these problems, the State Council of the People's Republic of China has released A Guideline on the Integration of Basic Medical Insurance for Urban and Rural Residents which pointed that the solution should begin with the improvement of the policies and the government would propel the integration of the URBMI and the NCMS and build a unified basic medical insurance system for the unemployed in the whole country gradually [9]. This medical insurance must cover all the insured of the URBMI and the NCMS, ie, it must cover all the urban and rural residents except employees. Since there are big differences in the insured group, the financing modes and the payment modes between the URBMI and the NCMS, the unified basic medical insurance for the unemployed will face a lot of challenges. The first problem to be solved is about enrollment [10]. Only if the government instructs the residents who are eligible to insure continually for a long term, can the financing of the unified basic medical insurance be stable and sustainable.

Although the total enrollment rate of the three basic medical insurance maintains higher than 95% now, the re-en-

rolling rate is about 10% [11]. The actual enrollment rate of the medical insurances for the unemployed in 2014 was only 67.46%. That is to say, there some people do not enroll in any insurance, while the other people enroll in two or more medical insurances, which shows a great difference in enrollment performances of residents. Therefore, under the background of integration of the URBMI and the NCMS, because of the voluntary enrollment and a rather high enrollment rate, it is important for forecasting the structure of the insuring group and calculating the medical insurance fund to study the influencing factors of enrollment of medical insurance for the unemployed, which is also the first consideration when the government makes policies of the insurance.

Nowadays, most of scholars' researches about influencing factors of enrollment focus on people's health status and ability to pay [12,13]. Based on previous studies, the study holds the opinion that although the influencing factors of enrollment are various, under the background of strong aged tendency of population, the key factors are health, ability to pay, and age. Meanwhile, due to the "inclusive policies" in China, people's premiums only take a small part of insurance financing. Therefore, the object of this study is not ability to pay but the influences of health status and age on insurance enrollment, and the comparison between them.

As for the research of the influences of health status on insurance enrollment, there are great differences between the results of them. Many studies show that the insurance market is facing serious adverse selection, especially in the insurance market of voluntary enrollment. People in poor health may have greater willingness to enroll in medical insurances [14–17]. However, other studies show that there is not a significant relationship between health status and enrollment rate. Thus there is not a severe adverse selection in insurance market [18–20]. In addition, some studies revealed that there exists a positive selection in insurance market [21,22]. Then, how health status influences insurance enrollment rate in the market of the URBMI and the NCMS is a problem that needs to be studied in the further researches.

However, as for the researches of the influences of age on insurance enrollment, the results are in agreement that people's age influences the insurance enrollment significantly. The older the people grow the more willingness they may have to [23–25]. In addition, many research results indicate that education and marital status also have significant influences on the enrollment.

Obviously, although international and domestic scholars concentrate their research on different influencing factors of insurance enrollment, there are close connections between them. Most of these researches show that people's

health status and age have significant influences on medical insurance enrollment. Nowadays, under the background that China has gradually entered the aging society and the basic medical insurance rate is at a high level, it is meaningful to research which influencing factors can influence the enrollment better. The study is based on the voluntary enrollment policy and high enrollment rate, deeply researching whether age or health status influences medical insurance enrollment greater and further analyzing the reasons. It uses logistic regression model with the latest data of CHNS in 2011 to evaluate the influences of health status and age respectively on the enrollment of the NCMS, the URBMI, and the medical insurance for the urban and rural unemployed, then to analyze the change of enrollment performances after the expansion of the medical insurances. Finally, the study offers suggestions for the integration of the URBMI and the NCMS.

## DATA AND METHODS

Employing binary logistic regression model, the study analyzes the influencing factors of enrollment performance, especially health status and age, which influences the enrollment of the URBMI and the NCMS greater. The study tests whether it is a severe adverse selection in the URBMI and the NCMS, and with the aged tendency of population, whether age influences the enrollment greater.

The study adopts cross-sectional data of 2011 from the China Health and Nutrition Survey (CHNS), and its official website is <http://www.cpc.unc.edu/projects/china>. The China Health and Nutrition Survey (CHNS), an ongoing open cohort, international collaborative project between the Carolina Population Center at the University of North Carolina at Chapel Hill and the National Institute for Nutrition and Health at the Chinese Center for Disease Control and Prevention (CCDC), was designed to examine the effects of the health, nutrition, and family planning policies and programs implemented by national and local governments and to see how the social and economic transformation of Chinese society is affecting the health and nutritional status of its population. Their data from both urban and rural areas in 12 provinces and cities, which mainly cover aspects of demographics, employment status, income, demands of health services, health status, etc. are representative enough.

The number of cases which are included in the survey of medical insurance of 2011 in the CHNS is 15638. The study first eliminates individuals who enroll in the UEBMI and free health care. Then, according to the family register, the study divides registered urban and rural residents into two groups, and regards whether the individual enrolls in the URBMI and the NCMS as the dependent variables re-

spectively. Finally, it eliminates the samples which lack main variables and gets 10992 samples including 3761 samples of urban residents and 7231 samples of rural residents to do regression analysis. By analyzing variables, especially health-related variables and age, and studying whether these variables influence enrollment significantly, the study investigates the enrollment mechanism of the inclusive URBMI and NCMS.

## Variables

The enrollment of the URBMI and the NCMS can be influenced by many factors. Considering data from the CHNS, the research objective and research needs, the study decides whether the individual enrolls in the medical insurance for the unemployed – whether the urban residents who do not enroll in the UEBMI and free health care enroll in the URBMI, whether the rural residents enroll in the NCMS or whether residents enroll in one of these two insurances—to be the dependent variable. The dependent variable is a binary variable, which means that it has two values, enrolling as 1, not enrolling as 0. There totally 10992 people are analyzed. The amount of people who enroll in the insurances is 8902, which shows the enrollment rate of the URBMI and the NCMS in 2011 was 81.0%, not a high number. Among them, the amount of urban residents is 3761 and there are 2291 people covered by the URBMI, leading to the enrollment rate of 60.9%; the amount of rural residents is 7231 and there are 6611 people covered by the NCMS, getting the enrollment rate of 91.4%. Generally speaking, the enrollment rates of the URBMI and the NCMS are rather different. Therefore, it is important for improving the basic medical insurance for the unemployed based on the voluntary enrollment to compare the enrollment performances of people enrolling in these two insurances and analyze the main causes of the differences.

The independent variables are classified into three categories: health consciousness and health status, controlled variables, and age. The variables in health consciousness and health status include whether the individual received health care in last four weeks, whether the individual got ill in last four weeks and whether the individual has chronic diseases. The controlled variables includes education, per capita income of their family for a year, whether the individual is on the jobs, living districts, gender, and nationality.

The health consciousness is measured by whether the individual received health care in last four weeks. It is acknowledged that people with higher health consciousness are more likely to avoid risk and choose to enroll in medical insurances. However, in the data of the CHNS, there is

no direct indicator for preferences in risk avoiding. Referring to the conventional practices in international empirical literatures of health economics [26], the study uses individual health behaviors to reflect their preferences in risk avoiding, which means that people who want to avoid risk will pay attention to health care and purchase medical insurances. Finally, it chooses whether the individual received health care (such as physical examination, visual examination, blood test, test of hypertension, cancer screening, etc.) in last four weeks as the indicator.

The study regards whether the individual got ill in last four weeks and whether the individual has chronic diseases as the indicators of health status and predicts the expected size of medical needs by actual and hidden health problems. In the field of medical insurance, the adverse selection is shown as people with poor health status are more willing to enroll in the insurances, ie, their enrollment rate is higher. Because it was hard to know their health status and medical needs when respondents chose enrollment performances in the survey of CHNS, the study considers whether the individual got ill in last four weeks as the expected medical needs and whether the individual has chronic diseases as the actual medical needs. As for whether the individual has chronic diseases, according to the questionnaires, if an individual has been diagnosed as any one or more of hypertension, diabetes, myocardial infarction, stroke, neoplasm, fracture and asthma, he will be considered to have chronic diseases.

Among the controlled variables, the income is divided based on the quartile of the per capita income of their family for a year. Since the income of urban residents and of rural residents have a big difference and the individual financing levels of the URBMI and of the NCMS are also different, the study divides the per capita income of their family for a year of urban residents and of rural residents into quartiles and does regression analyses respectively. As for district, the Jiangsu Province, the Shandong Province, the Beijing City and the Shanghai City are classified as the East; the Henan Province, the Hubei Province and the Hunan Province are classified as the Middle; the Guangxi Zhuang Autonomous Region, the Guizhou Province and the Chongqing City are classified as the West; the Liaoning Province and the Heilongjiang Province are classified as the Northeast.

The evaluation method of the variables and descriptive statistical results are shown in **Table 1**.

On the basis of characteristics of the URBMI and the NCMS, any urban residents without formal employment, including children, the elderly, and other unemployed urban residents, can enroll in the URBMI, while the rural residents, taking family as a unit, can enroll in the NCMS

voluntarily. When doing a further analysis, among the group covered by the URBMI, 26.4% of them are minors; 34.2% of them being older than 55, 72.2% of them having no jobs; and for rural residents, the limits of natural resources and economic conditions restraint their medical needs to some degree. Most of these residents are the vulnerable group and their health should be secured by medical insurances.

In the social medical insurance system, the relative departments of the government will not investigate individuals' health status like commercial insurance companies. Therefore, the health information of the insured cannot be observed by the insurers, which exacerbates the information asymmetry. Under the policy of voluntary enrollment, if the individuals having different health risks enjoy the same insurance price, when the insurer offers insurances with different security levels, the individuals having higher health risk will choose to enroll in the insurance with higher security level (with low out-of-pocket). Because both the URBMI and the NCMS are designed as enrolling voluntarily and are of single security mode, if there are severe adverse selections in these two medical insurances, the results of the logistic regression analyses will perform as the enrollment rate of the high-risk individuals are higher and whether the individuals enroll in the insurance is related with the level of risk significantly. If age influences enrollment greater than health status, then under the condition of other fixed variables, when put age into the model, the coefficients of health status will decrease much, and the influences of health status on enrollment will not be significant even.

## RESULTS

The study does a simple cross-tabulation analysis of the independent variables as whether the individual got ill in last four weeks, whether the individual has chronic diseases, whether the individual received health care in last four weeks and age. The results are shown in **Table 2**. Finally, adopting the binary logistic regression model, it takes whether the individual enrolls in the medical insurances as the dependent variable and put the independent variables into the logistic analysis. The results are shown in **Table 3** and **Table 4**.

### Cross-tabulation analysis of health status and age, and enrollment

To reflect the relationship between whether the individual enrolls in the URBMI as well as the NCMS and health status as well as age, **Table 2** shows the cross-tabulation analysis of health consciousness, health status, age and whether the individual enrolls in the medical insurances.

**Table 1.** The descriptive statistics of enrollment of the medical insurances for the urban unemployed and rural residents

INDEPENDENT VARIABLES AND DEFINITION	THE URBAN UNEMPLOYED			THE RURAL RESIDENTS			MERGING		
	Rate (%)	Mean	Standard deviation	Rate (%)	Mean	Standard deviation	Rate (%)	Mean	Standard deviation
<b>Receiving health care in last four weeks:</b>									
Yes=1	9.40	0.094	0.292	5.10	0.051	0.221	6.60	0.066	0.248
No=0	90.60			94.90			93.40		
<b>Having chronic diseases:</b>									
Yes=1	20.80	0.208	0.406	16.00	0.16	0.366	17.60	0.176	0.381
No=0	79.20			84.00			82.40		
<b>Getting ill or injured in last four weeks:</b>									
Yes=1	19.50	0.195	0.396	14.60	0.146	0.354	16.30	0.163	0.369
No=0	80.50			85.40			83.70		
<b>On the job:</b>									
Yes=1	27.80	0.278	0.448	54.60	0.546	0.498	45.40	0.454	0.498
No=0	72.20			45.40			54.60		
<b>Education:</b>									
Elementary school or below=1	43.20	1.637	0.607	60.10	1.409	0.512	54.30	1.487	0.557
Middle school or high school=2	49.90			38.90			42.70		
College or above=3	6.90			1.00			3.00		
<b>Income:</b>									
Low-income=1	25.00	2.499	1.118	25.00	2.499	1.118	25.00	2.499	1.118
Lower-middle-income=2	25.10			25.00			25.00		
Upper-middle-income=3	24.90			25.00			25.00		
High-income=4	25.00			25.00			25.00		
<b>Gender:</b>									
Male=1	44.70	1.553	0.497	46.70	1.533	0.499	46.00	1.54	0.498
Female=2	55.30			53.30			54.00		
<b>Nationality:</b>									
Han nationality=1	93.30	0.933	0.251	85.70	0.857	0.35	88.30	0.883	0.322
National minority=0	6.70			14.30			11.70		
<b>District:</b>									
East=1	47.50	1.944	1.029	19.70	2.48	0.985	29.20	2.297	1.032
Middle=2	18.90			28.90			25.40		
West=3	25.30			35.10			31.70		
Northeast=4	8.30			16.30			13.60		
<b>Age:</b>									
0-17.99=1	26.40	4.036	2.226	19.00	4.277	2.035	21.60	4.194	2.105
18-24.99=2	4.70			4.20			4.30		
25-34.99=3	7.70			7.80			7.80		
35-44.99=4	11.80			16.20			14.70		
45-54.99=5	15.40			18.80			17.60		
55-64.99=6	18.30			19.70			19.20		
65-=7	15.90			14.20			14.80		

**Table 2.** The cross-tabulation analysis of health consciousness, health status and enrollment

HEALTH CONSCIOUSNESS AND HEALTH STATUS	URBMI			NCMS			MERGING		
	Number of people	Number not enrolling (%)	Number enrolling (%)	Number of people	Number not enrolling (%)	Number enrolling (%)	Number of people	Number not enrolling (%)	Number enrolling (%)
Getting ill or injured in last four weeks	734	252 (34.3)	482 (65.7)	1059	89 (8.4)	970 (91.6)	1793	190 (10.6)	1603 (89.4)
Not getting ill or injured in last four weeks	3027	1218 (40.2)	1809 (59.8)	6172	531 (8.6)	5641 (91.4)	9199	1152 (12.5)	8047 (87.5)
Having chronic diseases	781	254 (32.5)	527 (67.5)	1155	83 (7.2)	1072 (92.8)	1936	187 (9.7)	1749 (90.3)
Not having chronic diseases	2980	1216 (40.8)	1764 (59.2)	6076	537 (8.8)	5539 (91.2)	9056	1155 (12.8)	7901 (87.2)
Receiving health care in last four weeks	354	125 (35.3)	229 (64.7)	372	47 (12.6)	325 (87.4)	726	102 (14.0)	624 (86.0)
Not receiving health care in last four weeks	3407	1345 (39.5)	2062 (60.5)	6859	573 (8.4)	6286 (91.6)	10266	1240 (12.1)	9026 (87.9)
Older than 55	1286	380 (29.5)	906 (70.5)	2455	129 (5.3)	2326 (94.7)	3741	253 (6.8)	3488 (93.2)
Younger than 55	2475	1090 (44.0)	1385 (56.0)	4776	491 (10.3)	4285 (89.7)	7251	1089 (15.0)	6162 (85.0)

URBMI – Urban Resident Basic Medical Insurance; NCMS – New Cooperative Medical Scheme

**Table 3.** The results of logistic regression analysis of influences of whether the individual got ill or injured in last four weeks on enrollment

INDEPENDENT VARIABLES AND DEFINITION	URBMI			NCMS			MERGING		
	Model I	Model II	Model III	Model I	Model II	Model III	Model I	Model II	Model III
<b>Receiving health care in last four weeks (no=0):</b>									
Yes=1	1.189	0.377	0.195	-0.462‡	-0.34†	-0.362†	-0.216*	0.539	0.159
<b>Getting ill or injured in last four weeks (no=0):</b>									
Yes=1	0.253‡	0.265‡	2.503	0.316	0.603	0.356	0.211†	0.324‡	2.107
<b>On the job (no=0):</b>									
Yes=1		-0.231‡	-0.197†		1.103‡	0.786‡		1.026‡	0.771‡
<b>Education (elementary school or below = 1):</b>									
Middle school or high school=2		0.303‡	0.356‡		-0.11	-0.098		-0.23‡	-0.312‡
College or above = 3		-0.065	0.243		-1.034‡	-0.895‡		-1.265‡	-1.246‡
<b>Income (low-income = 1):</b>									
Lower-middle-income = 2		0.245†	0.248†		0.221*	0.248*		0.882	1.114
Upper-middle-income = 3		0.431‡	0.429‡		-0.009	0.035		1.567	0.8
Upper-income = 4		0.613‡	0.567‡		-0.247†	-0.232*		1.432	0.791
<b>Gender (male = 1):</b>									
Female = 2		0.124*	2.523		0.146*	0.043		0.146†	0.724
<b>Nationality (national minority = 0):</b>									
Han nationality = 1		0.366	0.202		-0.586‡	-0.601‡		-0.653‡	-0.67‡
<b>District (east = 1):</b>									
Middle = 2		-0.22†	-0.24†		0.188	0.196		0.329‡	0.314‡
West = 3		-0.794‡	-0.795‡		0.487‡	0.605‡		-0.013	0.075
Northeast = 4		-0.536‡	-0.63‡		-0.098	-0.082		-0.176*	-0.209†
<b>Age (0-17.99 = 1):</b>									
18-24.99 = 2			-0.47†			0.612‡			0.425‡
25-34.99 = 3			-0.327*			0.197			0.238*
35-44.99 = 4			0.102			0.665‡			0.584‡
45-54.99 = 5			0.413‡			0.883‡			0.95‡
55-64.99 = 6			0.573‡			1.131‡			1.394‡
65- = 7			0.75‡			1.089‡			1.108‡
Constant	0.396‡	0.231†	0.078	2.395‡	2.224‡	1.79‡	1.956‡	2.16‡	1.803‡

URBMI – Urban Resident Basic Medical Insurance; NCMS – New Cooperative Medical Scheme

\*Significant at 90% confidence level.

†Significant at the 95% confidence level.

‡Significant at the 99% confidence level.

It can be seen from **Table 2** that the enrollment rates of people with different health consciousness, different health status and different ages are distinct. As for the URBMI which has a rather low enrollment rate, the enrollment rate of people who got ill in last four weeks, have chronic diseases, received health care in last four weeks or are older than 55 are higher than it of people who did not and are not; as for the NCMS which has a high enrollment rate, the enrollment rate of people with poor health status and it of good health status have little differences, but people older than 55 are more willing to enroll in the insurance. Merging data of the URBMI and the NCMS, the difference is smaller than the data only of the URBMI. What should be paid attention to is that the data in **Table 2** also report that whether received health care in last four weeks, as the variables reflecting health consciousness, influences enrollment rate slighter than health status, while age influences enrollment rate greater than health status.

The results of cross-tabulation analysis in **Table 2** only explain that there are differences in enrollment rates of people with different health consciousness, health status and ages from the perspective of percentage. It need further analysis by logistic regression model to explore whether there is connection between enrollment and health status, health consciousness and age, how strong the connection is and which variable influences the insurance enrollment greater.

### Influences of whether the individual got ill in the last four weeks on insurance enrollment

In the logistic regression model, the likelihood-ratio is applied to test and backward stepwise manner is applied to filter variables. If the variable's significance level is smaller than 0.05, it will be analyzed continually, but if its significance level is larger than 0.10, it will be excluded. The influences of whether the individual got ill in last four weeks

**Table 4.** The result of logistic regression analysis of influences of whether the individual has chronic diseases on enrollment

INDEPENDENT VARIABLES AND DEFINITION	URBMI			NCMS			MERGING		
	Model I	Model II	Model III	Model I	Model II	Model III	Model I	Model II	Model III
<b>Receiving health care in last four weeks (no=0):</b>									
Yes=1	1.406	0.143	0.195	-0.5‡	-0.392†	-0.362†	-0.218*	0.41	0.078
<b>Having chronic diseases (no=0):</b>									
Yes=1	0.358‡	0.254‡	2.278	0.259†	0.37‡	0.67	0.327‡	0.43‡	0.181*
<b>On the job (no=0):</b>									
Yes=1		-0.234‡	-0.197†		1.093‡	0.786‡		1.025‡	0.762‡
<b>Education (elementary school or below = 1):</b>									
Middle school or high school=2		0.291‡	0.356‡		-0.104	-0.098		-0.237‡	-0.307‡
College or above = 3		-0.071	0.243		-1.025‡	-0.895‡		-1.275‡	-1.238‡
<b>Income (low-income = 1):</b>									
Lower-middle-income = 2		0.228†	0.248†		0.234*	0.248*		1.085	1.014
Upper-middle-income = 3		0.416‡	0.429‡		-0.003	0.035		1.585	0.811
Upper-income = 4		0.592‡	0.567‡		-0.24†	-0.232*		1.044	0.832
<b>Gender (male = 1):</b>									
Female = 2		0.126*	2.523		2.547	0.043		0.149**	0.653
<b>Nationality (national minority = 0):</b>									
Han nationality = 1		0.536	0.202		-0.592‡	-0.601‡		-0.645‡	-0.666‡
<b>District (east = 1):</b>									
Middle = 2		-0.219†	-0.24†		0.214*	0.196		0.346‡	0.303‡
West = 3		-0.779‡	-0.795‡		0.517‡	0.605‡		0.031	0.065
Northeast = 4		-0.56‡	-0.63‡		-0.086	-0.082		-0.188*	-0.214†
<b>Age (0-17.99 = 1):</b>									
18-24.99 = 2			-0.47†			0.612‡			0.432‡
25-34.99 = 3			-0.327*			0.197			0.247*
35-44.99 = 4			0.102			0.665‡			0.605‡
45-54.99 = 5			0.413‡			0.883‡			0.99‡
55-64.99 = 6			0.573‡			1.131‡			1.459‡
65- = 7			0.75‡			1.089‡			1.193‡
Constant	0.372‡	0.248†	0.078	2.359‡	2.232‡	1.79‡	1.936‡	2.121‡	1.808‡

URBMI – Urban Resident Basic Medical Insurance; NCMS – New Cooperative Medical Scheme

\*Significant at the 90% confidence level.

†Significant at the 95% confidence level.

‡Significant at the 99% confidence level.

on insurance enrollment are shown in **Table 3**. Model I only estimates influences of whether the individual got ill in last four weeks and whether the individual received health care on insurance enrollment and broadens the pre-supposition of the model gradually. Model II adds controlled variables that are whether the individual is on the job, education, income, gender, nationality, district, etc. Model III adds the variable of age on the basis of Model II.

It can be seen from Model I and Model II in **Table 3** that as for people insuring the URBMI and merging people insuring the URBMI and the NCMS, not considering other independent variables, whether the individual got ill in last four weeks influences insurance enrollment significantly. In addition, the enrollment rate of people who got ill in last four weeks is higher than it of people who did not get ill in last four weeks, while whether the individual got ill in last four weeks does not influence people just involving in the NCMS much.

The regression results of Model III show that after adding the variable of age, whether the individual got ill in last four weeks, which has influenced insurance enrollment significantly in Model I and Model II, does not influence it much yet. That is to say, age influences individuals on enrollment greater than whether the individual got ill in last four weeks.

### Influences of whether the individual has chronic diseases on insurance enrollment

Using the same method, the results of influences of whether the individual has chronic diseases on insurance enrollment are shown in **Table 4**. Model I estimates influences of whether the individual has chronic diseases and whether the individual received health care in last four weeks on insurance enrollment. The variables put into Model II and Model III are totally the same as the variables in last part.

Model I and Model II in **Table 4** show that whether the individual has chronic diseases influences whether the indi-

vidual enrolls in the insurances significantly. People with chronic diseases are more willing to enroll in the insurances than people without them.

Similar to the situation happened to whether the individual got ill in last four weeks, when adding the variable of age, the previous significant variable in Model I and Model II – whether the individual has chronic diseases – are not significant anymore. However, regarding merging residents, whether the individual has chronic diseases still has a statistically significant influence at the 10% level. Age influences enrollment greater than the individual's actual health status (whether the individual has chronic diseases) toward urban unemployed and rural residents.

### Summary

Analyzing **Table 3** and **Table 4**, the results show that the adverse selection exists in the URBMI and the NCMS. Compared with the adverse selection in the NCMS, the adverse selection in the URBMI is more evident but not severe. Whether the individual got ill in last four weeks and whether the individual has chronic diseases influence the enrollment of the URBMI significantly and people having gotten ill in last four weeks or having chronic diseases are more willing to enroll in the insurance; whether the individual got ill in last four weeks has no significant influence on the NCMS, but whether the individual has chronic diseases has, which is performed as the enrollment rate of rural residents who have chronic diseases is higher than those who do not have.

What should be noticed is that when we put the variable of age in the analysis, the influences of whether the individual got ill in last four weeks on the enrollment rates of urban residents, rural residents or urban and rural residents together are not significant, and the influences of whether the individual has chronic diseases on the enrollment rates of urban residents and rural residents are also not significant, but the level of influences on the enrollment rates of urban and rural residents together is still in 10% which is significant. Whether to take actual health status or to take expected health status as the variable indicating health status, the influences of age on insurance enrollment are similar and are greater than the influences of health status. In another word, in the market of the URBMI and the NCMS, there are not severe adverse selection. In addition, the results of **Table 3** and **Table 4** show that the enrollment rate will increase with age growing.

Above all the samples in this study, 20% of urban samples and 13% of rural samples were students, in addition, some samples were preschool children. For these samples, their enrolment decisions were made by their parents, thus it may have some influences on the final results and conclusion. Although this study cannot reveal the influences of

parents on the enrolment willingness of these samples, it verified that age and health status were the main reasons that influence students and preschool children's enrolment willingness.

## DISCUSSION

### Easing adverse selection and changing enrollment performances of residents by inclusive policies

According to the data from the CHNS of 2011, under the policy of voluntary enrollment, the URBMI and the NCMS in China cover a great range of people. Though there are problems of adverse selection in these two basic medical insurance markets, they are not severe. Age influences insurance enrollment greater than health status (whether the individual got ill in last four weeks and whether the individual has chronic diseases). The older the group are, the higher the enrollment rate is. The study considers that it is related to the inclusive design of the system for one thing, and changes of enrollment performances of the urban unemployed and rural residents for another thing.

In the market of the URBMI and the NCMS, the central government offers large subsidies. After the start of the new health-care reform in 2009, governments at all levels committed 850 billion yuan to medical field in the first three years, mainly to support five reforms including construction of basic medical security system. As for the construction of medical security system for the whole population, the government has spent over 680 billion from 2009 to 2012 to subsidy the URBMI and the NCMS. The increase of fiscal subsidy per capita in the URBMI are always larger than the increase of individual premiums, leading to a higher proportion of government subsidies to financing per capita, from 60.8% in 2009 to 79.3% in 2014. The ratio of government subsidies to individual premiums is close to 4:1, which means that the actual individual financial burdens are not heavy. The massive fiscal supports stimulate people's willingness to enroll in the medical insurances and develop the coverage of the insurances effectively, which may be the reason why there is no severe adverse selection in the market of basic medical insurances in China.

Analyzing **Table 1** and **Table 2**, at present, the self-care consciousness of the urban unemployed and rural residents is still very low. The percentage of the urban unemployed who received health care in last four weeks is only 9.4%, while it of rural residents is only 5.1%. The percentage of individuals who received health care in last four weeks is similar to the percentage of individuals who enroll in the health care. Because of weak self-care consciousness, when the urban unemployed and rural residents decide whether



they insure or not, their health status and medical needs will not influence their decisions. They pay more attention to their ages and potential health risks. In the process of developing basic medical insurances in China, under the background of large financial subsidies from Chinese government and high general enrollment rates of the insurances for the urban unemployed and rural residents, the enrollment performances of them may change. With age growing, the potential health risks and medical needs increase and the urban unemployed and rural residents are more sensitive to age. Therefore, they choose to enroll in the medical insurances.

### **Optimizing the structure of insuring group and increasing anti-risk ability of medical insurance funds**

The results of the study show that although age influences insurance enrollment greater than health status, the enrollment performance that the enrollment rates increase with age growing will go against optimizing the structure of insuring group. With the growing aged tendency of population, the general enrollment rate of Chinese basic medical insurances for the urban unemployed and rural residents can maintain stable or even higher, but it also results in an unreasonable structure of insuring group. If the reimbursement level of these insurances raises continually, the burden of the medical insurance funds must be increased, which brings about a danger to them. To optimize the structure of insuring group, there must more young adults be appealed to enroll in the insurances, and then, the basic medical insurances exert the effect of social assisting and risk sharing under the law of great number.

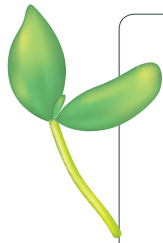
Learning from the practices in China, the great input of government cannot keep the sustainability of the basic medical insurances. After the new reform of medical system, medical expenditures in our country increase rapidly, causing the growth rate of expenditures of medical insurance funds higher than the growth rate of income of it. In some provinces, the income of their medical insurance funds cannot pay out the cost of the funds and the insurance funds are dangerous. To keep the insurance funds from risks, the Ministry of Human Resources and Social Security of the People's Republic of China and the Ministry of Finance of the People's Republic of China has investigated in 2009 and suggested that only the fund can satisfy the financial demand of six to nine month, can the medical insurances be well

operated. The data from the Ministry of Human Resources and Social Security of the People's Republic of China show that compared with it of 2013, the length of payable months of 2014 in 22 provinces become shorter. There are six provinces that the length of payable months is shorter than six months. The medical insurance funds in many regions are in danger and the sustainability of social medical insurances face a great challenge. In addition, the policies of the insurance that integrate the URBMI and the NCMS for urban unemployed and rural residents will follow the principle: the financing standard should be the lower one; the reimbursement level should be the higher one; the range of pharmaceuticals should be the larger one, which increases the expenditures of the medical insurance funds [27]. Therefore, it should keep the fund resources stable, optimize the financing structure, enlarge the coverage of the insurance, enlarge the medical insurance fund, and increase the anti-risk ability of the fund.

### **CONCLUSION**

The results of the study show that although both of the URBMI and the NCMS apply the policy of voluntary enrollment, the problems of adverse selection in them are not severe. Age influences people's enrollment of medical insurances. The older the insuring group are, the higher their enrollment rate is. This enrollment performance is just like adverse selection which goes against the sustainability of the medical insurances.

Analyzing from the perspective of actuarial studies, when people with different ages and different health status enroll in the medical insurance simultaneously and continually, the security function of insurance fund can be exerted and the insurance fund can be operated sustainably. However, based on the analyses above, it can be known that the older the individual is, the greater the willingness to enroll in the insurance is and also the higher the enrollment rate is. With the growing aged tendency of population, this will be more and more evident. Therefore, under the background of integrating the URBMI and the NCMS together, every provinces and cities should increase the proportion of young adults in the market of medical insurance and optimize the structure of insuring group. Moreover, the financing of government and individual should be divided properly. When the government's subsidies increase, the proportion of individual's premiums should also be raised.



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**Competing interests:** All authors have completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author). The authors declare no competing interests.

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# Causes of death in children younger than five years in China in 2015: an updated analysis

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**Background** Substantial progress in reducing the child mortality rate has been made globally in the last two decades. However, for China, the number of children dying from preventable diseases is still very large. It is important to have regularly updated information on the distribution of causes of death (COD) in children to inform policy and research. In this study, we aim to estimate the COD spectrum in children younger than five years old from 2009 to 2015 with a focus on the year 2015 and to provide an updated COD prediction model for China.

**Methods** Updated data of under-five mortality rates (U5MRs) and the number of live births at national and provincial levels were obtained from United Nation's Inter-agency Group for Child Mortality Estimation (UN IGME), Institute for Health Metrics and Evaluation (IHME), and United Nations Population Division (UNPD). Then, we conducted a systematic review across four Chinese and English bibliographic databases and identified high-quality community-based longitudinal studies of COD in children younger than five years in China. We developed a number of single-cause models to predict the number of child death for main COD in different age groups at both national and provincial levels. The jackknife procedure was applied to construct the 95% Uncertainty Ranges (URs).

**Results** From 2009 to 2015, the under-five mortality rates have declined by 37.1%. The leading causes of death in 2015 were preterm birth complications (17.4%), birth asphyxia (15.2%), congenital abnormalities (14.1%), accidents (13.5%) and pneumonia (12.4%) for children under five years old. The COD spectrum varied substantially across Chinese provinces with different development levels. The leading cause in children under five years in the wealthier provinces (with lower U5MRs) was congenital abnormalities (up to 18.9%), while in the poorer provinces (with higher U5MRs), pneumonia was the dominant COD (up to 23.4%).

**Conclusions** This study updates and validates the accuracy of the findings of our previous COD study and proposes a new modelling method to predict proportions for the most common causes of child death in China. These updated COD estimates suggest that current strategies to reduce child mortality should prioritise action on neonatal deaths and target interventions against the top COD according to the local COD spectrum. Special attention should also be given to reducing differences between Chinese provinces and regions with differing development levels.

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Child health is widely regarded as a public priority for every nation [1,2]. The under-five mortality rate (U5MR), which estimates the probability of dying between birth and the fifth birthday (usually expressed per 1000 live births) [3], is a useful indicator that measures not only the level of child health, but also the overall development of a society [4,5]. Since the adoption of the Millennium Development Goals (MDGs) by 189 member states of United Nations (UN) in September 2000 [6,7], substantial progress has been made towards improving global child survival [8].

China has made impressive progress in reducing child mortality in the 21st century and it could, therefore, serve as a model to many other low- and middle-income countries (LMIC) [7,9]. Despite the progress, gaps remain with inequities/disparities by socioeconomic status and geographical locations (rural vs urban). The newly launched UN's Sustainable Development Goals (SDGs) framework calls for an end to preventable deaths of newborns and children under five years of age by 2030 [10]. For a populous and diverse country like China, this goal is still challenging: the total number of children who died before their fifth birthday is still very large [11]. In addition, there are also large disparities in child mortality rates between the rich and the poor, as well as between the urban and the rural regions of the country [12–14].

Targeted efforts are required immediately to address the growing inequalities by the year 2030 [10,15]. Information on causes of death (COD) is important for targeted health policy development and continuous monitoring of the progress in reducing child mortality [16]. However, a complete and universal coverage of civil registration and vital statistics (CRVS) system for providing detailed information on COD has not been achieved in China. Still, sample-based longitudinal registration systems, based on representative surveillance sites, have been in use for some time. They gradually became the most valuable resource for understanding national-level child mortality patterns [17,18]. Other relevant sources include surveillance systems, household surveys and censuses. They can also be used as additional information to the CRVS system to provide reasonably reliable data for the entire Chinese population [19,20]. A detailed description of the relevant systems for providing mortality data and COD information in China can be found in Table S1 in **Online Supplementary Document**.

The two main sources on child death statistics in China are the National Maternal and Child Mortality Surveillance system (MCMS) and the National Maternal and Child Health Annual Reporting System (MCHARS). One of the main aims of MCMS is to monitor the COD in children under five years of age. An important property of MCMS is that it was designed to be representative for the entire nation, or for the three large regions at best, but not for individual

provinces or counties. MCHARS has an advantage of covering the whole population of China with substantial density, so it could potentially provide U5MR estimates at the level of specific provinces, but it does not collect COD data in children [21].

To investigate the underlying COD in children under five years of age in China, a study conducted by Rudan, Chan et al. [22] estimated the COD distribution in children under five years in China between the years 2000 and 2008. Based on the information extracted from 206 multi-cause studies, they estimated proportions of different causes at the level of each province and nationally [22]. Since then, this study has been widely adopted as the most relevant source on the causes of child mortality in China [23,24]. However, that study was based on studies that were published between 2000 and 2008, and it now requires an update [1,24,25]. The year 2015 marks an appropriate time for updating the progress with the completion of MDG-4 on child mortality reduction.

The aim of this study was to conduct a new systematic analysis on COD in Chinese children based on all informative studies published in the Chinese and English literature and any other sources from 2009 onwards. The newly obtained information was used to update our estimate of the causes of child deaths in China in the period 2009–2015 and to advance our methods of estimation.

## METHODS

### Data sources

In this study, we used the national-level U5MR estimates from the UN's Inter-agency Group for Child Mortality Estimation (UN IGME), which are largely based on the data from MCMS, as reported in the latest "China Health and Family Planning Statistical Yearbook" (former China Health Statistics Yearbook). The yearbook is considered the most reliable source of the estimates of national-level U5MR, but for our assessment, we also require province-level U5MRs. For the purpose of this study, we used province-level U5MRs for the year 2013, published by Wang and colleagues [26]. We picked these estimates over possible alternatives, such as MCHARS source, because we conducted a plausibility test that compared all available estimates [27]. We concluded that the estimates by Wang et al. [26] were the most plausible because they made an attempt to adjust for the likely under-reporting in MCHARS data [26,28] and then estimated the provincial U5MRs for the year 2013 based on the corresponding national total numbers of child deaths.

In terms of assessing the number of live births in China for each year, previous studies on China's child mortality often

used the estimates from the National Bureau of Statistics of China (NBS) [22,29]. In recent years, however, the United Nations Population Division (UNPD) estimates of live births in China, as well as those from the UN IGME, have started to converge very closely to NBS estimates from China. For this reason, our study was based on live births estimates that were made available from the UNPD and the UN IGME's.

## Systematic review

To develop epidemiological models to predict the cause-specific proportions of deaths in children, a systematic review was conducted in 2015 according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines using a PRISMA checklist [30]. The following electronic databases were searched: China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database for Chinese Technical Periodical (VIP) and PubMed. The search terms and strategies that were used are presented in Table S2 in **Online Supplementary Document**). All titles, abstracts and keywords were examined, and full texts of potentially relevant papers were obtained for final assessment.

In the assessment procedure, we used the selection procedures that the Child Health Epidemiology Reference Group (CHERG) advised, which came as a result of a decade-long work of this group of international experts on the questions of child mortality estimation [31]. Only the community-based, longitudinal, multi-cause studies that were mutually independent in terms of the population were included in this systematic review and analysis. This is because studies conducted at hospital sites tend to have poor representativeness of the surrounding general population, especially for children in poor rural areas where the access to hospitals is not universal [32,33]. Moreover, studies conducted retrospectively introduce recall bias, so we only included longitudinal, prospective studies. Single-cause studies tend to overestimate the reported cause, so we excluded studies that only reported a single cause, or that didn't give any breakdown by cause. Furthermore, we applied some additional criteria to ensure the quality of included studies. Uncertainties and disagreements in the study selection were resolved through discussions between the two reviewers and a consensus that was achieved in all cases. The detailed inclusion and exclusion criteria are listed in **Table 1**.

All extracted data was stored in the final standardized data abstraction form, which included three parts:

1. Characteristics of the study: authors, publication year, study setting, population type (urban or rural), surveillance period, quality control method and frequency;
2. Mortality data: the number of live births, overall number of deaths and overall mortality rates for neonates, post-

neonatal infants, 1–4 years old children and all 0–4 years old children;

3. COD data: Most eligible studies reported the COD data based on the national unified MCMS “child death report card” (see Table S3 in **Online Supplementary Document**). Therefore, we included all pre-set causes in the data extraction form.

## Statistical analysis

The statistical procedures for estimating the proportional causes of child death in China for the years 2009–2015 included the following steps:

(i) Firstly, we acquired the information on national- and province-level U5MRs and the number of live births from UN IGME, IHME, and UNPD, to develop the “envelopes” for the total number of child deaths in China in the years 2009–2015;

(ii) Secondly, based on studies derived from the systematic review, we developed three statistical models that predicted the proportion of deaths that occur in the neonatal (<1 month), postneonatal infant (1–12 months), 1–4 years (12–59 months) period, to create the “envelopes” for these particular age groups. Within each age group, we further developed statistical models that assigned COD to all deaths based on information from independent studies acquired through the systematic review. All the models were based on the best performing model below:

$$\ln(\% \text{ Criterion variable}) = \alpha + \beta \times (\ln U5MR) + \gamma \times (\ln U5MR)^2$$

where the criterion variable was either the proportional contribution of the specific age group, or the specific COD. This model was chosen after an exhaustive pilot-testing of the performance of different models to address different COD (see Table S4 and Figure S1 in **Online Supplementary Document** for more details);

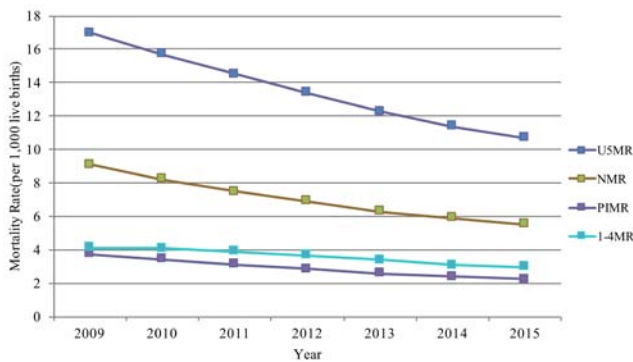
**Table 1.** Eligibility criteria for selection of studies in the systematic review

Inclusion criteria
1. Community-based study of the COD in children aged 0–4 years
2. Multi-cause studies
3. Studies with more than 100 observed deaths
Exclusion criteria
1. Multiple publications of the same data from the same study
2. Studies with no breakdown of deaths by cause or age
3. Studies with no reported numerical estimates
4. Unclear study design (prospective/retrospective) or unclear definitions
5. Retrospective studies
6. Studies where no overall U5MR was reported
7. Studies with inconsistencies between reported methods and presented results
8. Studies based on CDC death monitoring system
9. Studies with clear calculation mistakes or logical mistakes

(iii) Thirdly, we estimated the COD structure in children in China for each of the years from 2009 to 2015 at both national and provincial levels. The jackknife procedure was applied to construct the 95% Uncertainty Ranges (URs). The procedures are described in detail in Table S5 in **Online Supplementary Document**. All statistical analyses were performed in R Studio (version 0.99.486) built on R (version 3.2.2).

## RESULTS

According to the estimates of UN IGME [34], from 2009 to 2015, the neonatal mortality rates (NMRs), postneonatal infant mortality rates (PIMRs), 1–4 years mortality rates (1–4MRs) and U5MRs have declined by 39.6% (from 9.1 to 5.5 per 1000 live births), 40.4% (from 3.8 to 2.2 per 1000 live births), 28.5% (from 4.1 to 3.0 per 1000 live births) and 37.1% (from 17.0 to 10.7 per 1000 live births), respectively (**Figure 1**). In 2015, the provincial estimates



**Figure 1.** Trends in mortality rates (per 1000 live births) in China during 2009–2015 in neonates, post-neonatal infants, 1–4 year-old children and children under five years.

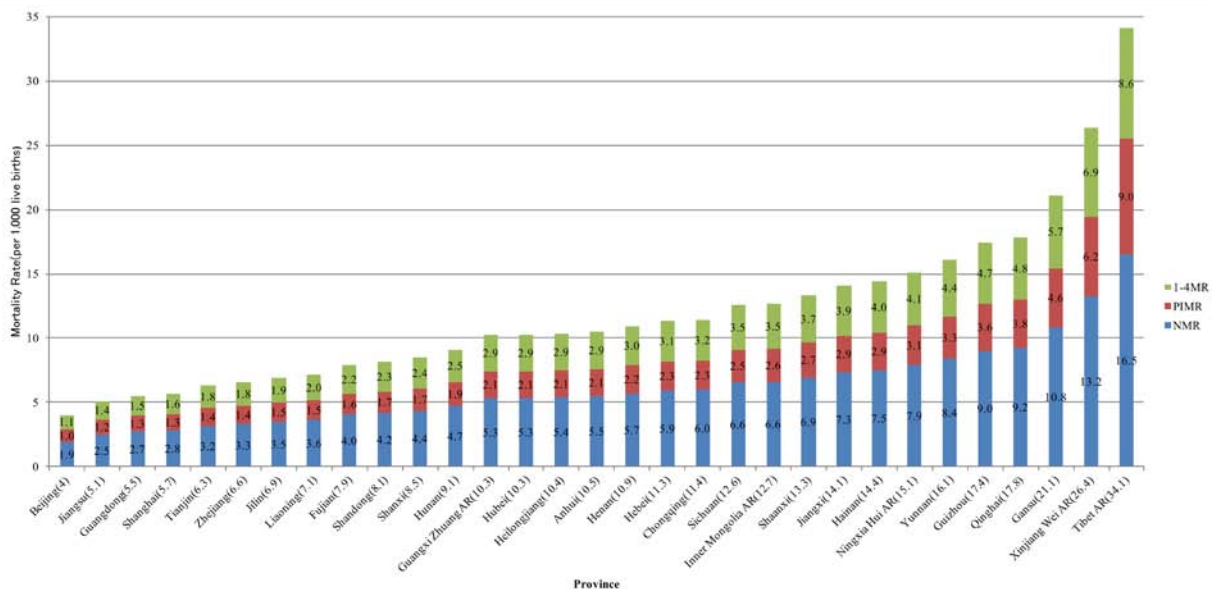
of U5MR, NMR, PIMR and 1–4MR are shown in **Figure 2**. U5MR was the lowest in Beijing and the highest in Tibet, whereas NMR, PIMR and 1–4MR had the same geographical trend as U5MR. U5MRs in China had an inverse relationship with economic development (based on Gross Domestic Product (GDP) per capita). Provinces with higher GDP per capita had lower U5MRs, such as Beijing and Shanghai, while provinces with lower GDP per capita had higher U5MRs, such as Xinjiang and Tibet (**Figure 3**).

## Systematic review

Through a literature search, a total of 81 079 citations were identified. After removing 35 247 duplicates, 44 367 apparently irrelevant citations by title and abstract review, and 49 citations with no sufficient information on methods and results, a total of 1416 articles with full-texts were reviewed to assess their eligibility. According to the study criteria, a total of 1128 publications were excluded and 288 publications were included (**Figure 4**).

A summary of the main characteristics of the 288 included studies is shown in **Table 2**. The detailed information on the included studies can be found in Table S6 in **Online Supplementary Document**. The geographic distribution of the 288 studies included 212 different locations in 30 provinces, municipalities and autonomous regions in China (except Tibet Autonomous Region, Hong Kong Special Administrative Region, Macao Special Administrative Region and Taiwan) (**Figure 5**).

All the statistical models were based on those 288 studies. The detailed description of our models can be found in Table S7 and Figures S2–S3 in **Online Supplementary Document**.



**Figure 2.** Child mortality rates in 31 provinces in China in 2015. Provinces are ranked according to under-five mortality rates (recorded in x-axis label).

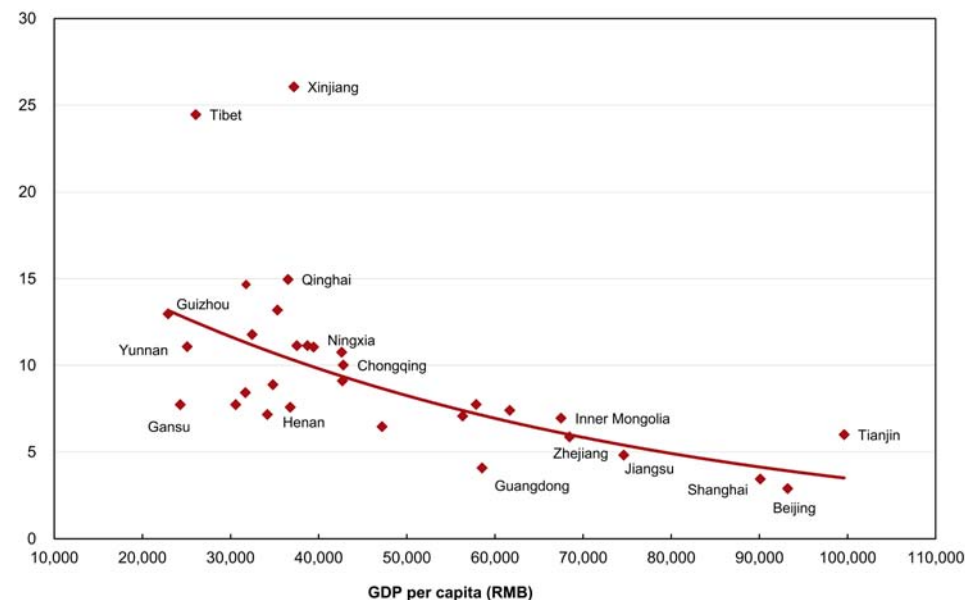
**Table 2.** Characteristics of the included studies

CHARACTERISTICS OF STUDY (TOTAL N = 288)	NUMBER OF STUDIES (%)
<b>Year published:</b>	
2009	51 (17.7)
2010	36 (12.5)
2011	48 (16.7)
2012	61 (21.2)
2013	47 (16.3)
2014	45 (15.6)
<b>Setting:</b>	
Urban	45 (15.6)
Rural	17 (5.9)
Both	226 (78.5)
<b>Number of observed deaths:</b>	
101–500	146 (50.7)
501–1000	56 (19.4)
1001–2000	38 (13.2)
2001–3000	20 (6.9)
3001–4000	11 (3.8)
>4000	17 (5.9)
<b>Number of live births:</b>	
<10000	11 (3.8)
10001–30000	95 (33.0)
30001–60000	73 (25.3)
60001–100000	38 (13.2)
100001–150000	15 (5.2)
>150000	56 (19.4)
<b>Reported U5MR (per 1000 live births):</b>	
<5.0	15 (5.2)
5.1–10.0	113 (39.2)
10.1–15.0	84 (29.2)
15.1–20.0	35 (12.2)
>20.0	41 (14.2)
<b>Surveillance time (year):</b>	
<5	69 (24.0)
5–9	167 (58.0)
10–14	50 (17.3)
>15	2 (0.7)
<b>Conducting quality control:</b>	
Yes	219 (76.0)
Unknown	69 (24.0)

## Main causes of child deaths in China

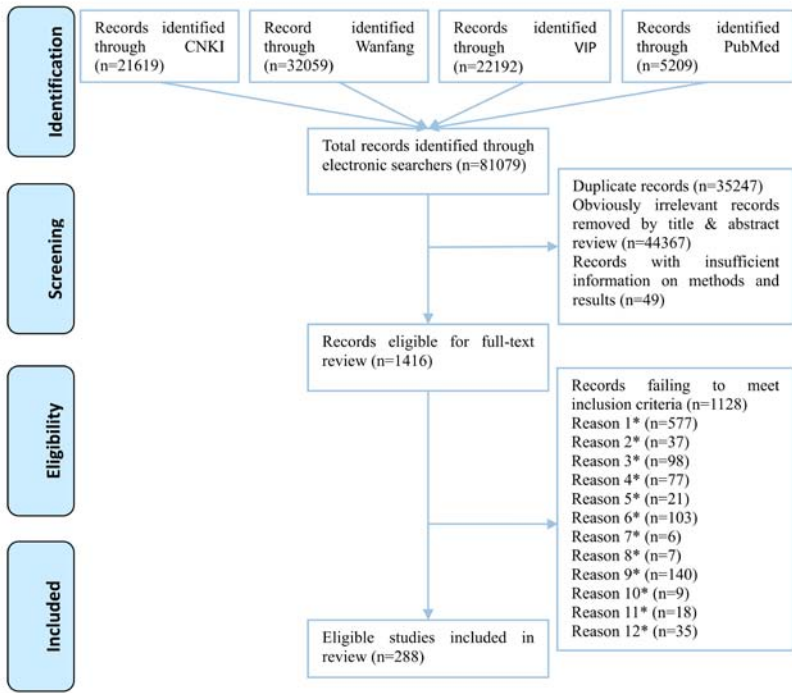
The main COD in under five years old children are shown in **Figures 6** to **7**. In the period between 2009 and 2015, the proportions of deaths due to infectious causes – pneumonia and diarrhea – fell substantially among the children under five years of age (**Figure 6**, panel a and **Figure 7**, panel a), leading to an overall reduction of U5MR. Pneumonia decreased from 16.4% (95% UR=16.3–16.6%) to 12.4% (95% UR=12.3–12.5%), and diarrhea from 5.3% (95% UR=4.9–5.5%) to 3.2% (95% UR=2.9–3.4%). In addition, the proportion of birth asphyxia also fell slightly (from 16.1% [95% UR=16.0–16.2%] to 15.2% [95% UR=15.1–15.3%]), while the proportion of preterm birth / low birth weight rose slightly (from 16.7% [95% UR=16.6–16.8%] to 17.4% [95% UR=17.3–17.5%]). The proportion of congenital abnormalities increased much faster: from 10.6% (95% UR=10.5–10.8%) to 14.1% (95% UR=13.9–14.3%). The proportions of neonatal sepsis and sudden infant death syndrome (SIDS) also showed an increase in this time period (from 1.1% [95% UR=0.9–4.7%] to 1.6% [95% UR=1.3–2.4%], and 5.8% [95% UR=5.5–6.2%] to 6.6% [95% UR=6.2–6.9%], respectively). The proportion of accidents fluctuated around 13.5%, with no apparent increasing or decreasing trend. In 2015, the leading COD in children under five years of age were preterm birth / low birth weight (17.4%) and birth asphyxia (15.2%). In addition, congenital abnormalities (14.1%), accidents (13.5%) and pneumonia (12.4%) also contributed substantially.

The changes in the distribution of the main COD in neonates from 2009 to 2015 are shown in **Figure 6**, panel b. From 2009 to 2015, the proportions of deaths attributable to neonatal causes – birth asphyxia, preterm birth / low

**Under-five mortality rate (deaths per 1,000 live births)**

**Figure 3.** GDP per capita and under-five mortality rate in 31 provinces in 2013 (source: [35]).





**Figure 4.** PRISMA flow diagram. Reason 1: Papers that were not community-based study of the COD in children aged 0–4 years; Reason 2: Papers that were not multi-cause studies; Reason 3: Papers with less than 100 deaths observed; Reason 4: Multiple publications of the same study; Reason 5: Papers with no breakdown of deaths by cause or age; Reason 6: Papers with no reported numerical estimates; Reason 7: Studies where design (prospective/retrospective) and definitions were not clear; Reason 8: Studies that were retrospective in design; Reason 9: Papers where no (overall) U5MR was reported for the study site; Reason 10: Papers with inconsistency between reported methods and presented results; Reason 11: Studies based on CDC death monitoring system; Reason 12: Papers with calculation mistakes or logical mistakes.

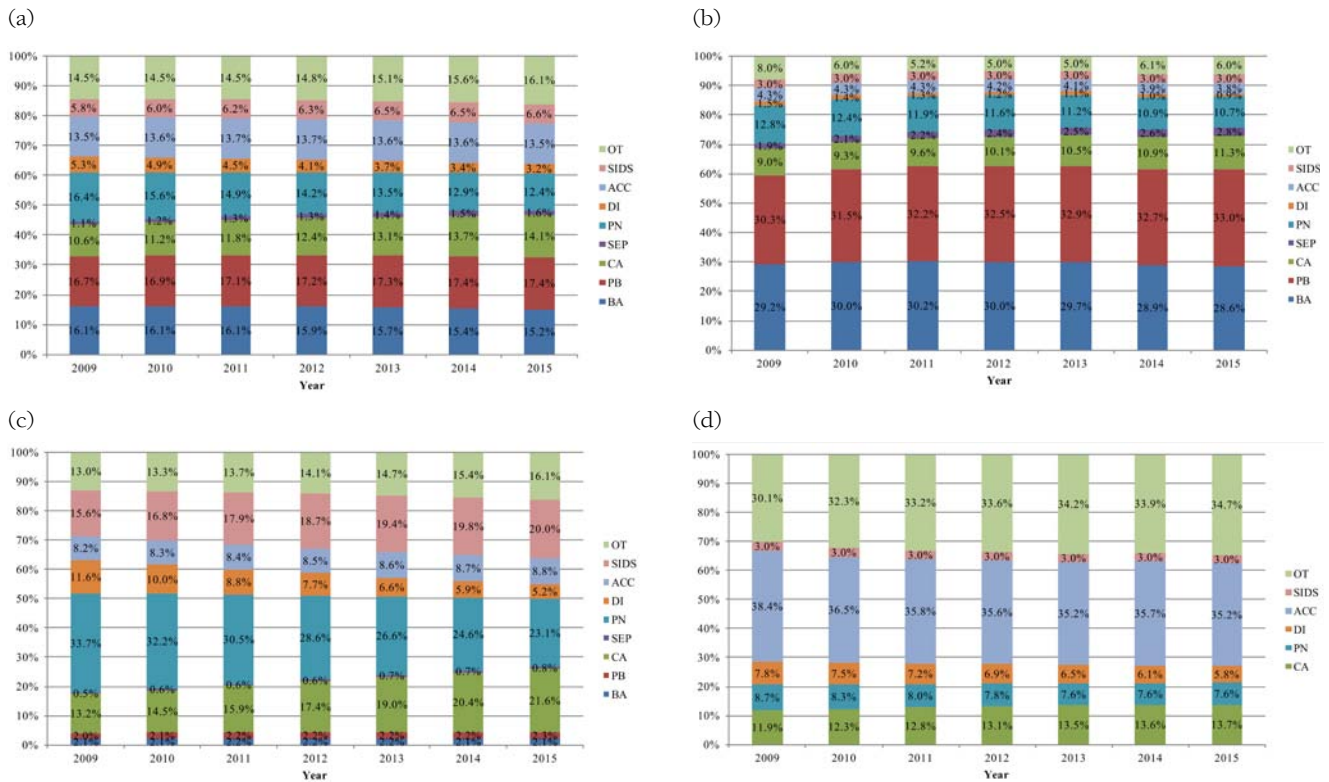


**Figure 5.** Geographic distribution of the included studies. Note: The classification of East, Central and West was based on MCMS categories according to geography and economic development of each province [36].

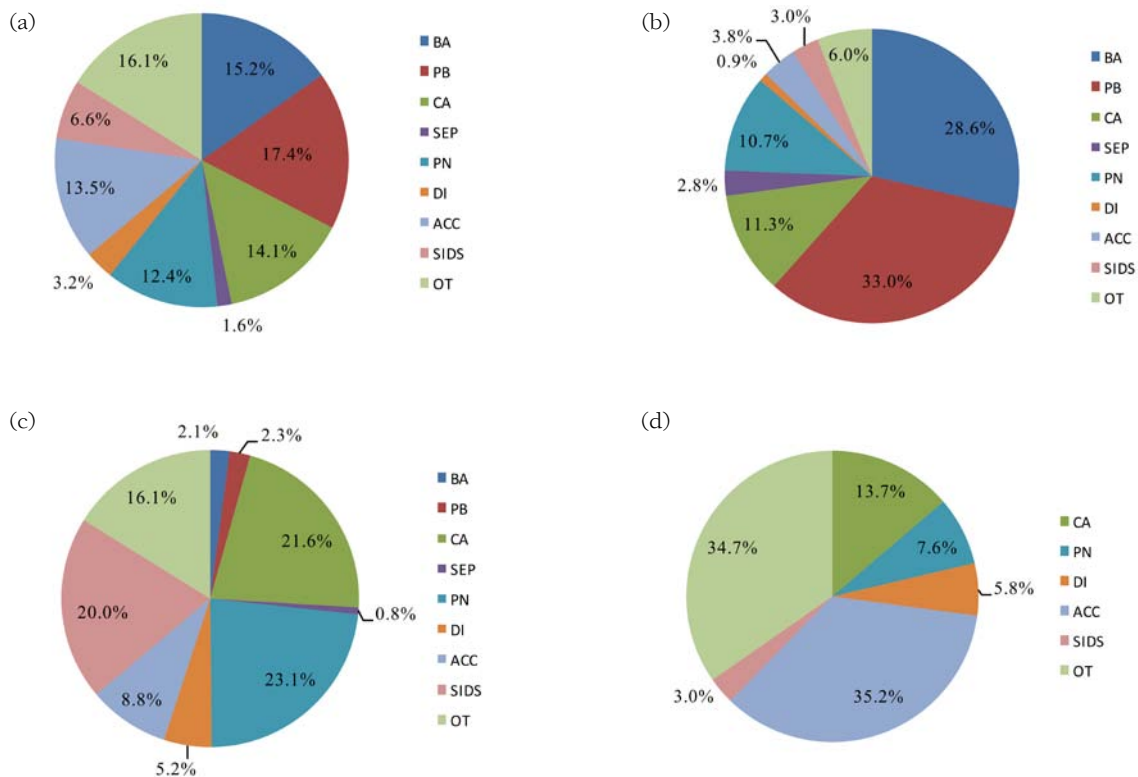
birth weight, and neonatal sepsis – accounted for more than half of all the deaths. The proportional contribution of preterm birth/low birth weight and neonatal sepsis gradually increased from 30.3% to 33.0% and 1.9% to 2.8%, respectively. The proportion of birth asphyxia declined slightly during this period – from 29.2% to 28.6%. Infectious causes – pneumonia and diarrhea – continued to decrease, from 12.8% to 10.7%, and 1.5% to 0.9%, respectively. The proportion of congenital abnormalities increased from 9.0% to 11.3%, while the proportion of accidents decreased from 4.3% to 3.8%, and the proportion of SIDS

was fairly constant around 3.0%. In 2015 (**Figure 7**, panel b), preterm birth / low birth weight and birth asphyxia contributed more than half of the neonatal deaths, accounting for 33.0% and 28.6%, respectively. Congenital abnormalities (11.3%) and pneumonia (10.7%) were also the main causes that accounted for more than 10% of all neonatal deaths.

The changes in the distribution of the main COD in post-neonatal infants from 2009 to 2015 are shown in **Figure 6**, panel c: from 2009 to 2015, the proportions of infec-



**Figure 6.** Causes of child deaths in China, 2009–2015. (a) Children under five years; (b) Neonates; (c) Post–neonatal infants; (d) 1–4 year–old children; BA – Birth asphyxia, PB – Preterm birth and low birth weight, CA – Congenital abnormalities, SEP – Neonatal sepsis, PN – Pneumonia, DI – Diarrhea, ACC – Accidents, SIDS – Sudden infant death syndrome, OT – Other.



**Figure 7.** Proportional distributions of main COD in neonates, post–neonatal infants, 1–4 year–old children and children under five years in China in 2015. (a) Children under five years; (b) Neonates; (c) Post–neonatal infants; (d) 1–4 year–old children; BA – Birth asphyxia, PB – Preterm birth and low birth weight, CA – Congenital abnormalities, SEP – Neonatal sepsis, PN – Pneumonia, DI – Diarrhea, ACC – Accidents, SIDS – Sudden infant death syndrome, OT – Other.

tious causes – pneumonia and diarrhea – declined substantially, from 33.7% to 23.1%, and from 11.6% to 5.2%, respectively. At the same time, the proportions of congenital abnormalities and SIDS increased from 13.2% to 21.6%, and 15.6% to 20.0%, respectively. The proportions of neonatal sepsis and accidents also rose slightly – from 0.5% to 0.8%, and from 8.2% to 8.8%, respectively. Other neonatal causes – birth asphyxia and preterm birth / low birth weight, remained relatively low, contributing to about 2.0% of all post–neonatal deaths during this period. In 2015 (Figure 7, panel c), most post–neonatal deaths were caused by pneumonia (23.1%), congenital abnormalities (21.6%) and SIDS (20.0%). Other important causes were accidents (8.8%) and diarrhea (5.2%).

The changes in the distribution of the main COD in the children 1–4 years of age from 2009 to 2015 are shown in Figure 6, panel d. From 2009 to 2015, the proportions of congenital abnormalities continued to increase, from 11.9% to 13.7%, while the other main causes – accidents and diarrhea – both declined, from 38.4% to 35.2%, and from 7.8% to 5.8%, respectively. The proportion of pneumonia declined from 8.7% to 7.6% and then remained at this level. The proportion of SIDS was around 3.0%. This trend of predominant reduction in the main causes resulted in the proportion of “other” causes increasing from 30.1% to 34.7%. In 2015 (Figure 7, panel d), accidental deaths became the dominant COD (35.2%) among children aged 1–4 years. Congenital abnormalities (13.7%), pneumonia (7.6%) and diarrhea (5.8%) also contributed substantially. Another dominant category was “other” (34.7%), accounting for more than one third of the deaths in 1–4 year–old children. We noticed that this category mainly included tumors and meningitis.

The spectrum of causes of child deaths in 31 Chinese provinces (ranked by U5MRs) in 2015 is shown in Figure 8. In 2015, U5MR ranged from 4.0 per 1000 live births in Beijing to 34.1 per 1000 live births in Tibet. Correspondingly, the leading causes in children under five years (Figure 8, panel a) in the wealthier provinces (with lower U5MRs) were congenital abnormalities, preterm birth / low birth weight, and birth asphyxia, while in the poorer provinces (with higher U5MRs), the proportions of infectious diseases were still the dominant COD, especially pneumonia. Among neonates (Figure 8, panel b), the distributions of COD between the wealthier and the poorer provinces were quite similar, with birth asphyxia and preterm birth / low birth weight being the top two causes. The proportions of congenital abnormalities were higher in the wealthier provinces than in the poorer provinces, where pneumonia was still one of the leading causes. Among post–neonatal infants (Figure 8, panel c), the spectrum of causes changed dramatically with the level of development: congenital abnor-

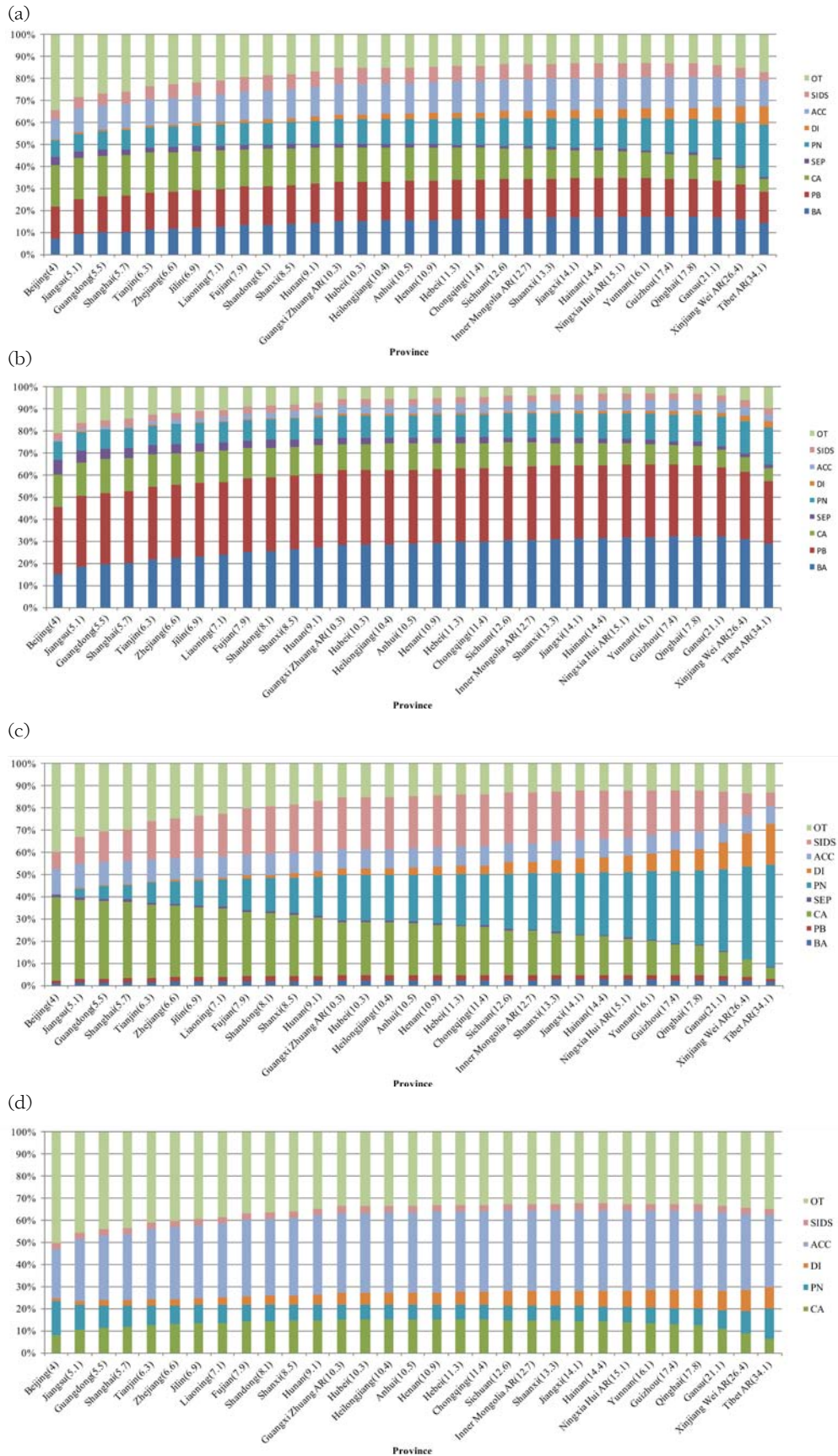
malities were a dominant cause in the wealthier provinces, while pneumonia dominated in the poorer provinces. Among the children aged 1–4 years (Figure 8, panel d), accidents were the leading COD in every province, while the poorer provinces were still observing a large burden of child deaths from diarrhea.

## DISCUSSION

With the primary aim of this study being related to estimating proportions attributable to different COD, the spectrum of COD in children in China in the period 2009–2015 has been successfully defined in our analysis. This study was based on the most recent comprehensive review of independent studies of causes of child mortality in Mainland China and it provided an update to the previous estimates of COD in children in China in 2008 by Rudan and Chan [22]. The relationship between COD in children and overall U5MR proved to be a useful approach to predict the main COD based on overall mortality [37,38]. Through a systematic review of relevant local community–based epidemiological studies, the leading causes were successfully assessed, and they were very consistent with the previous papers in terms of cause–specific time trends between 2000 and 2015. Within the current global context of determining increasingly accurate COD estimates for children globally, our modelling–based analysis serves as an example of estimation of COD in countries where primary COD data are scarce, but the secondary data are abundant.

Preterm birth complications have been the leading COD in children under five years in China over the past seven years continually, the increasing trend of neonatal sepsis was consistent with the rise in the proportion of complications of preterm birth. This temporal change could perhaps also be explained by the rising rate of caesarean sections in China [39–41], especially of the induction/elective caesarean sections [42,43]. Nevertheless, the increase of caesarean section rate can bring overall benefits and reduce neonatal mortality, as it reduces the occurrence of birth asphyxia [44,45]. The large share of deaths that still occur in the neonatal period highlights the importance of initiating health interventions at the start of life, priorities should be set to enhancing the capacity for antenatal care and early recognition of neonatal diseases among both parents and postpartum care professionals, especially in rural poor areas.

From 2009 to 2015, the overall decrease of U5MR could have mainly been contributed to a substantial decline in deaths attributable to infectious diseases, particularly childhood pneumonia and diarrhea. According to an analysis from National Surveillance System, the decline in pneumonia deaths in China can be largely explained by a rapid economic growth, increasing access to child health care and



**Figure 8.** Proportional contributions of common causes of child deaths in 31 provinces in China in 2015. Provinces are ranked according to under-five mortality rates (recorded in x-axis label); (a) Children under five years; (b) Neonates; (c) Post-neonatal infants; (d) 1–4 year-old children; BA – Birth asphyxia, PB – Preterm birth and low birth weight, CA – Congenital abnormalities, SEP – Neonatal sepsis, PN – Pneumonia, DI – Diarrhea, ACC – Accidents, SIDS – Sudden infant death syndrome, OT – Other.

antibiotic treatment, improvement in child nutrition (such as breastfeeding and nutrients supplementation), and health promotion [46]. These may also be important contributors to another infectious disease – diarrhea. However, our analysis confirmed that in China diarrhea was not such a common COD among children under five, in comparison to some other developing countries [47]. This may be partly explained by the common Chinese cultural practice of eating cooked food and drinking boiled water and some other hygiene practices [48]. Another feature is that infectious diseases were most relevant as the COD in post-neonatal infant period, this implies that special attention should be given to post-neonatal infants when expanding effective preventive and curative interventions among vulnerable children.

The burden of congenital abnormalities increased in relative terms during the period of 2009 to 2015, with a trend to replace birth asphyxia and become the most significant cause of child deaths in China in the future years. In 2015, congenital abnormalities have become the third most common COD in children under five years nationally and the leading COD in several economically highly developed provinces. However, for a broad cause of congenital abnormalities, primary prevention can only be effective when the understanding of causes is clear. Major factors affecting the prevalence and distribution of congenital abnormalities should be understood, with more efforts diverted to revealing the situation of congenital abnormalities in detail, to provide the basis of targeted policy.

The importance of accidents as a cause of child deaths has drawn much attention worldwide, and also in China [49,50]. Among all types of accidents, drowning has long been recognized as a very important cause [50,51]. This suggests that prevention strategies focused on child drowning should be made a national policy priority. In addition, other major accidental causes include accidental asphyxia, traffic accidents and falls. The national, and even provincial estimates of the breakdown of deaths due to accidents, can increase the universal awareness of the harm of accidents and provide the basis for policy-making on a large scale.

The relative burden of mortality due to SIDS was the worst among post-neonatal infants. The reasons for SIDS have long been regarded as unexplained, and it's quite difficult to distinguish between SIDS and accidental asphyxia as a direct COD, especially in cases of sleep-related infant deaths. In MCMS, there's no preset category of SIDS for estimating the actual burden. However, the high prevalence of preterm births and culturally highly prevalent practices of all-night bed sharing (particularly with newborns and infants) make it plausible that SIDS is generally classified into the preset category of accidental suffocation [52,53], which includes situations such as being smothered by a

quilt, accidentally crushed by mother when she turned over, suffocated with mother's nipple in mouth, or abnormal objects in the trachea, etc. The uncertainty about coding of SIDS makes it difficult to try to understand more about this important COD.

In this study, the rigorous criterion of retaining only the “multi-cause” studies has ensured that the reported sum of COD attributable to each cause was adding up to 100% in all studies. This avoided the potential problem of the sum of all single-cause estimates adding up to more than 100% of the known number of total deaths (“envelope”), which can occur when single-cause models are primarily relied upon [23,54]. Also, a very large number of child deaths observed across 288 independent studies, which exceeded 350000, is certainly much larger than the maximum observable number of deaths within MCMS system over the same period of time. This gives our study a considerable statistical power to estimate the proportions for different COD with substantial precision, and to supplement the observations from the MCMS system. Another very important feature of this study, which provides further evidence for its strength and accuracy, is that the cause-specific estimates for the year 2009 matched very nicely the corresponding estimates for the year 2008 from the previous study [22], although the two studies were based on two entirely different and non-overlapping data sets, both of them acquired through a systematic review of Chinese literature in two different time periods: 2000–2008 and 2009–2015. A remarkable consistency between the two sets of estimates in two studies on their bordering point (2000 to 2009) leads us to a conclusion that the current study provides, in essence, a successful replication of the results presented in the previous study.

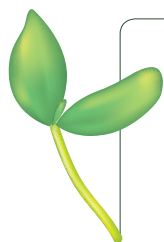
Nonetheless, there are several limitations in this study. First, for the modelling method, although the applied model was based on the best available information from high-quality studies, the model may still be biased because of unmeasured characteristics of the study population from each individual study. This is especially the case wherever the vast majority of the included studies were from the Eastern provinces, few from the Western provinces and there were hardly any studies from Tibet. In order to specify the most comprehensive and robust association between the proportions of COD and overall U5MR, a number of additional covariates should be considered, such as the local socio-economic development level, vaccination rate, etc. Second, for the purpose of defining the distribution of COD, this study only focused on a limited number of selected leading causes. This is especially true for a large category of causes such as “accidents” and “congenital abnormalities”. Third, the estimates of SIDS in this study were based on the contribution of accidental suffocation, where

an over-estimation may exist and further research should be conducted to find out the real contributors to accidental suffocation. In addition, misclassification may have occurred when there was no clinical diagnosis or treatment before death, even though a detailed interview with the parents or main guardians were conducted to identify the factors attributing to the child death, the low specificity of verbal autopsies may lead to an underestimation of some specific causes, especially those relying on medical diagnosis (eg, infectious diseases, tumor, and nervous system disease) [46,55].

The updated COD estimates can serve as the basis for making child health and development-related policies, especially at a local level, where the model-based analyses are the only solution that is presently available for predicting COD in children. The model-based analyses in this study could now be readily used to conduct national and provincial estimates in all cases where MCMS primary data are not available for analysis. Even if the MCMS data are available locally, the predictive models should still have merit as a supplementary information source, especially when estimating local (provincial) distributions of COD, where MCMS data are either absent or lack representativeness. However, the estimates in this study should only be considered to represent an approximation of the true picture of the spectrum of causes of child deaths in China. Future

work will be needed to externally validate the estimates presented in this study. This can be achieved by comparing our results with the primary surveillance data from MCMS, which should also help to clarify the large and uncertain “other” cause, especially for children aged 1–4 years old, where the unknown “other” has become the second dominant cause and had the tendency to become the first in the following years. The newly developed GATHER guidelines (Guidelines for Accurate and Transparent Health Estimates Reporting) should also assist in improving health estimates world-wide, and this study is one of the first examples of adoption of these guidelines [56].

Finally, despite all major advantages, development and improvement of statistical models of COD distribution should never become the ultimate focus of research on child mortality. Substantial efforts should be made to collect sufficient amount of locally informative data [24]. In China, the data presently available in MCMS are only representative nationally or regionally, but they do not allow province-level or county-level COD estimates. More attention should be focused on improving the availability and quality of CRVS, MCMS and MCHARS data resources in China and their combining in order to estimate overall and cause-specific mortality rates, which can then provide an improved picture of the causes of child deaths in China at all levels.



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**Authorship declaration:** IR, HC and KC conceptualized and designed the study, PS and XL prepared the data. ET and PS conducted the analysis. PS and IR wrote the manuscript. LL, YC and RB critically reviewed the manuscript. All authors have read and approved the final manuscript as submitted.

**Declaration of interest:** I. Rudan and H. Campbell are editors-in-chief of the *Journal of Global Health*. To ensure that any possible conflict of interest relevant to the journal has been addressed, this article was reviewed according to best practice guidelines of international editorial organizations. The author completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author). The authors declare no competing interests.

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# Preventing delayed diagnosis of cancer: clinicians' views on main problems and solutions

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**Background** Delayed diagnosis is a major contributing factor to the UK's lower cancer survival compared to many European countries. In the UK, there is a significant national variation in early cancer diagnosis. Healthcare providers can offer an insight into local priorities for timely cancer diagnosis. In this study, we aimed to identify the main problems and solutions relating to delay cancer diagnosis according to cancer care clinicians.

**Methods** We developed and implemented a new priority-setting approach called PRIORITIZE and invited North West London cancer care clinicians to identify and prioritize main causes for and solutions to delayed diagnosis of cancer care.

**Results** Clinicians identified a number of concrete problems and solutions relating to delayed diagnosis of cancer. Raising public awareness, patient education as well as better access to specialist care and diagnostic testing were seen as the highest priorities. The identified suggestions focused mostly on the delays during referrals from primary to secondary care.

**Conclusions** Many identified priorities were feasible, affordable and converged around common themes such as public awareness, care continuity and length of consultation. As a timely, proactive and scalable priority-setting approach, PRIORITIZE could be implemented as a routine preventative system for determining patient safety issues by frontline staff.

Timely cancer diagnosis improves patient survival and quality of life [1]. Delayed diagnosis is a major contributing factor to lower cancer survival in the UK compared to a number of European countries [2,3]. The outcomes of an 1 in 3 people in the UK, estimated to develop cancer during their lifetime, are significantly affected by a large national variation in timely cancer diagnosis [4,5]. Delayed cancer diagnosis accounts for 5 to 10 000 premature deaths in England and an extra £150 million of the NHS spending annually [2,6].

In the UK, primary care providers play an important role in cancer care pathway as the first point of contact for patients. Cancer is mostly diagnosed on presentation to primary care, upon screening as an incidental finding or after an emergency presentation [5]. Patients diagnosed in primary care are referred to specialists for further diagnostic workup and treatment. Diagnostic delays occur because of late patient presentation, problems at the primary (from presentation to referral) or secondary care

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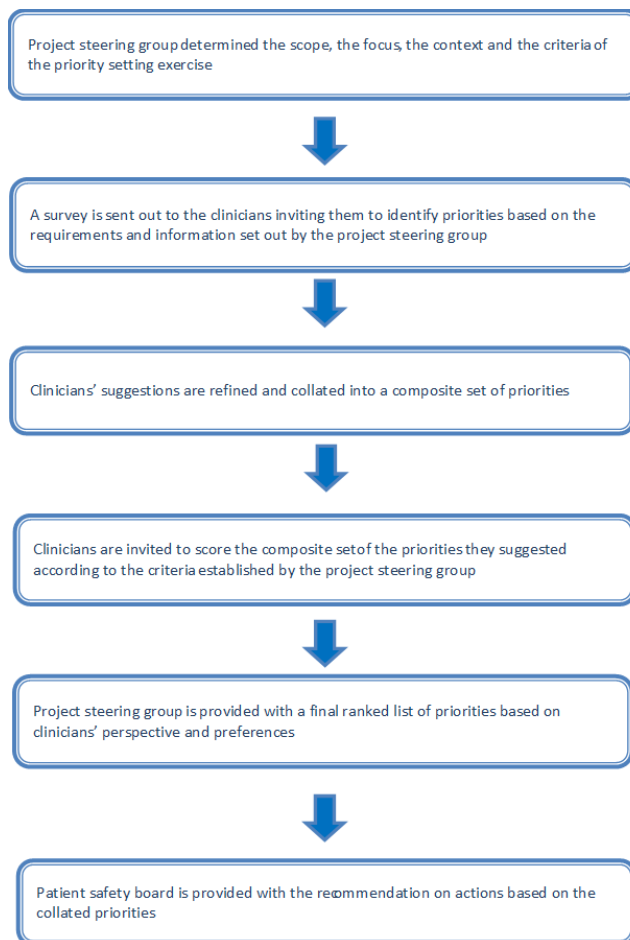
level (from referral to final diagnosis) and during screening [7].

Delayed diagnosis of cancer has been extensively researched, particularly with the launch of “Evidence for a National Awareness and Early Diagnosis Initiative” (NAEDI) [5]. However, the UK is still faced with significant regional differences in timely cancer diagnosis [8]. A nationwide, consistent implementation of available evidence alone could lead to a better chance of survival in 20 000 people [8]. Regional differences in the UK cancer outcomes call for safety policies informed by a local prioritization of the effective interventions. Although existing research identifies a number of contributing factors to delayed cancer diagnosis, it is unclear which patient safety interventions would have the highest yield and should be given precedence. Clinicians offer unmatched, first-hand insight into the health care service delivery and can help in establishing a consensus on priorities for timely cancer diagnosis [9–11]. Furthermore, clinicians’ engagement is essential for successful implementation of patient safety interventions. The UK’s new national patient safety programme and the recent Institute of Medicine report on improving diagnosis in health care call for the inclusion of clinicians in identifying high-priority areas for patient safety and timely diagnosis. [12,13]. In this study, we aimed to identify cancer care clinicians’ priorities for prevention of delayed diagnosis of cancer in North West London.

## METHODS

We adopted a definition for delayed diagnosis as “a diagnosis that was unintentionally delayed while sufficient information was available earlier” [14].

We developed and implemented the PRIORITIZE method, an adaptation of the Child Health and Nutrition Research Initiative (CHNRI) approach, to determine the main problems and solutions relating to delayed diagnosis of cancer [15–17] (**Figure 1**). The CHNRI methodology invites international research experts to nominate priorities for research and has been used extensively to inform policymakers, funding bodies and international organizations. PRIORITIZE is designed to reveal priorities for health care services delivery as seen by clinicians using two complementary angles: problems and solutions. The final output of this approach is presentation of the top priorities categorized according to level of implementation: a) actions for clinicians b) actions for health care organisations and c) actions for health system custodians (**Figure 1**). This study is a service evaluation as well as a quality and safety improvement initiative and therefore did not require ethics or governance approval according to the UK’s Health Research Authority guidance [18,19].



**Figure 1.** PRIORITIZE methodology flow diagram

At the study outset, the project steering group (Imperial College Health Partners’ Patient Safety Board) decided to focus on two topics relating to cancer care patient safety: medication safety and delayed diagnosis. This paper describes the findings related to delayed diagnosis of cancer. The project steering group also determined the most pertinent criteria to guide the prioritisation of the collated suggestions, ie, scoring of problems and solutions (**Box 1**).

In the first phase of the study, we developed an open-ended questionnaire for clinicians to identify the main problems and solutions relating to delayed diagnosis in cancer care. The questionnaire was piloted on a smaller sample of primary care physicians and trainees and amended accordingly. The final questionnaire was distributed in both paper-based and online version and disseminated via email lists, snowballing (participants were asked to forward the survey to colleagues), and visits to several general practices in North West London (Text S1 in **Online Supplementary Document**). We targeted oncology consultants, general practitioners, trainees, nurses and pharmacists. The collected ideas were examined using content analysis with open coding to categorise the free-text responses. Suf-

**Box 1.** Scoring criteria for prioritization of collated suggestions**For problems****Frequency:** This patient safety threat is common**Severity:** This patient safety threat leads to high rates of mortality, morbidity and incapacity**Inequity:** This patient safety threat affects lower socio-economic groups or ethnic minorities more than other groups**Economic impact:** The consequences of this patient safety threat are costly to the health care system**Responsiveness to solution:** This incident is amenable to a solution within 5 years**For solutions****Feasibility:** The implementation of this solution is feasible**Cost-effectiveness:** This solution is cost-effective**Potential for saving lives:** This solution would save lives

ciently similar suggestions were merged and collated into composite set of priorities.

In the second phase, we created a prioritization matrix consisting of collated priorities and statements outlining prioritization criteria (Box 1 and Text S2 in **Online Supplementary Document**). Next, we invited clinicians to categorize the priorities according to the prioritization criteria using four options: score of 1 for 'Yes – I agree with this statement', score of 0 for 'No – I do not agree with this statement', score of 0.5 for 'Unsure – I am unsure whether or not I agree' and no score (blank) for 'Unaware – I do not feel sufficiently familiar or confident to score this suggestion' (Text S2 in **Online Supplementary Document**). As the scoring process took about an hour to complete, we offered a token payment to the participants in a form of a GBP 50 voucher. From the initial cohort of primary care clinicians, we arbitrarily invited clinicians to perform scoring of the priorities.

The scores for the suggested priorities were computed as the mean of scores for each of the criteria (ie, five criteria for problems and three for solutions) and ranged from 0 to 100. The Kappa statistic was deemed an inappropriate test to determine inter-rater agreement in this study due to the sample size, the non-standardised categorical nature of data, the option of blank response to some statements and the number of our different criteria used for scoring. Instead, we evaluated the inter-rater agreement using the average expert agreement (AEA). The AEA is the proportion of scorers selecting the mode (the most common score) for each research question. The AEA does not provide information on statistical significance of any differences between scorers, but is pertinent to decision makers as it gives an indication of the degree of agreement between clinicians in terms of priorities. The AEA was calculated using the following formula (**Figure 2**), where q is a question that experts

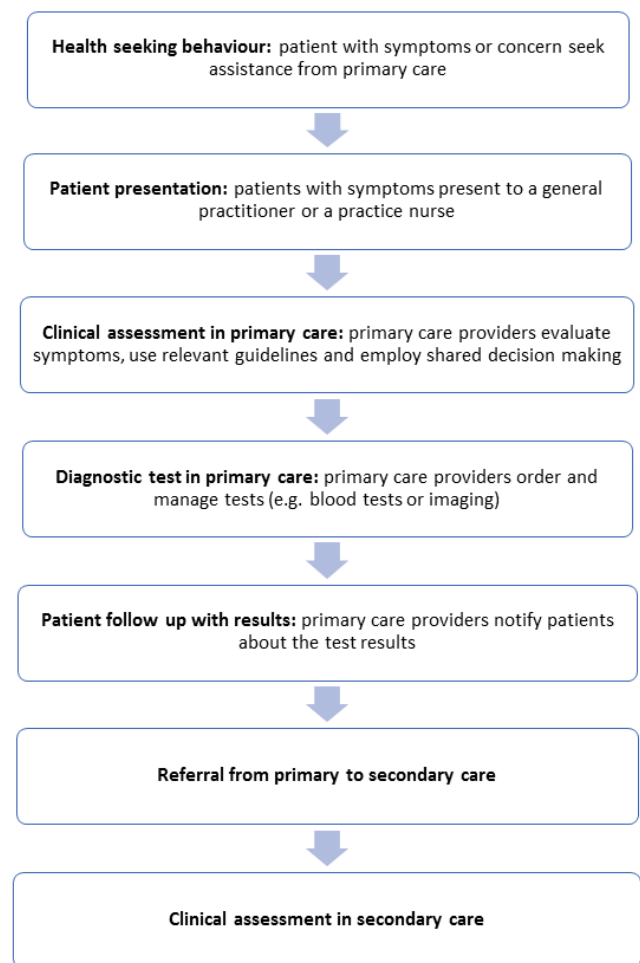
are being asked to evaluate competing patient safety threats (in this case problems leading to delayed diagnosis of cancer), ranging from 1 to 5 for problems and 1 to 3 for solutions.

$$\text{AEA} = \frac{1}{5} \times \frac{\sum \frac{N(\text{scorers who provided the most frequent response})}{N(\text{scorers})}}{q=1}$$

$$\text{AEA} = \frac{1}{3} \times \frac{\sum \frac{N(\text{scorers who provided the most frequent response})}{N(\text{scorers})}}{q=1}$$

**Figure 2.** Formula for calculating average experts agreement; q is a question that experts' are being asked to evaluate competing patient safety threats.

Diagnosis is a multistep process that is influenced by the provider, the patient and the health system [20,21]. In accordance with the patient cancer care pathway in the UK developed by the National Patient Safety Agency (**Figure 3**),



**Figure 3.** The primary care cancer pathway in the UK (based on "National Patient Safety Agency. Delayed diagnosis of cancer: thematic review, 2010").

we employed an adapted version of a four–dimension model of delays in cancer diagnosis consisting of: 1. Patient delay – from the onset of symptoms to patients' first presentation, 2. Primary care delay – from the first presentation in primary care to the referral for further care or diagnostic investigation, 3. Referral delay – from the referral for further care or diagnostic investigation to being seen in secondary care, 4. Secondary care delay – from being first seen in secondary care to diagnosis and 5. Screening delay – from being screen to being diagnosed [22,23]. In our analysis, we used an extensively referenced framework categorizing the diagnostic errors into system, cognitive and patient–related factors [14,24]. In addition, solutions were categorized in terms of the type of organizational interventions to decrease the diagnostic errors they addressed, ie, technique, personnel changes, staff educational interventions, structured process changes, technology–based intervention and additional review (Text S3 in **Online Supplementary Document**) [25]. To this framework, we added an additional category focused on patient education and empowerment.

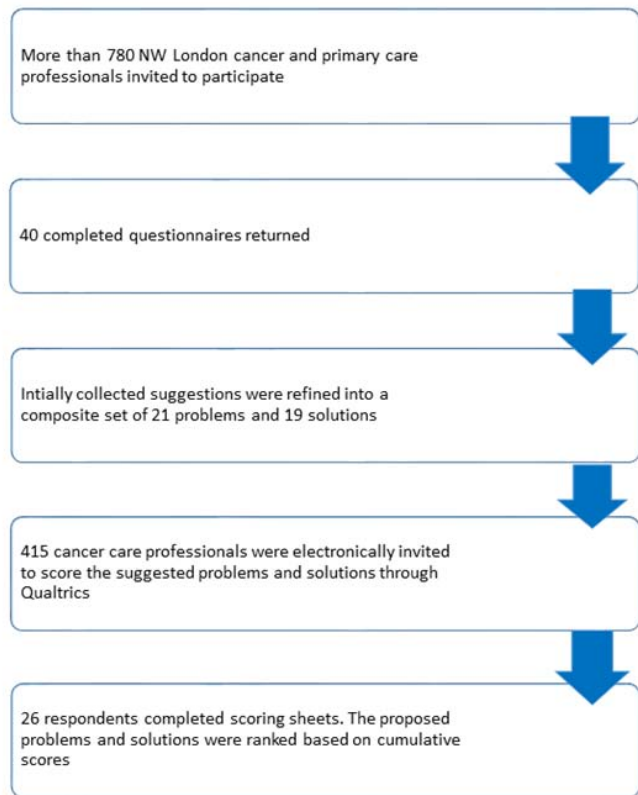
## RESULTS

In the first phase, we invited >780 cancer care clinicians and received 40 completed questionnaires, mostly by oncology consultants (n = 15, 37.5%) and trainees (n = 15, 37.5%) (Text S4 in **Online Supplementary Document**). 93 problems and 65 solutions relating to delayed diagnosis were thematically merged into a set of 21 distinct problems and 19 solutions. In the second phase, we invited 415 cancer care clinicians from the initial cohort to score the composite list of suggestions and received 26 fully completed scoring sheets (**Figure 4**).

The top ranked problems leading to delayed diagnosis of cancer according to clinicians are lack of patient awareness of cancer symptoms, poor continuity of care and delays in referrals to secondary care (**Table 1**). The highest ranked solutions to delayed cancer diagnosis are public awareness campaigns on common symptoms of cancer, better adherence to referral guidelines and improved communication between general and oncology teams in hospitals (**Table 2**).

Most of the top ten problems addressed system–level issues and organization of care (eg, lack of care continuity, short GP consultations leading to inappropriate history taking and examination, delays in ordering and processing referrals and poor access to diagnostic testing) (**Table 1**). Clinicians considered referrals from primary to secondary care as the most liable to the problems leading to delayed cancer diagnosis (Table S5 in **Online Supplementary Document**).

Patients' lack of cancer symptom awareness and the consequent late presentation, poor continuity of care and referral



**Figure 4.** Participants' flow diagram.

delays were considered top problems leading to delayed diagnosis in cancer care (Table S5 in **Online Supplementary Document**). Patients from lower socio–economic groups or ethnic minorities were considered most likely to use other health care services not designed to diagnose cancer. Proposed cognitive–related problems focused mostly on GPs ignoring or overlooking cancer alarm symptoms due to patients' comorbidities, an unusual presentation and in patients with the low risk of cancer. Clinicians considered diagnostic lapses by midwives, introduction of lower–threshold referrals and more inclusive screening as least important problems leading to delayed diagnosis of cancer. Errors at the hospital system level, such as referrals being lost or misallocated were also ranked very low.

Overall, proposed solutions focused on the organisational changes with the aim of improving the referral process and the access to diagnostic testing as well as educational interventions aimed primarily at general practitioners (Table S6 in **Online Supplementary Document**). The most cost–effective solutions according to the clinicians are public awareness campaigns on common symptoms of cancer to ensure early presentation. Rapid referrals from primary care to hospitals were considered a solution most likely to save lives. The most feasible solution according to clinicians are longer consultations to ensure full examination and his-

**Table 1.** Clinicians-identified top ten problems leading to delayed diagnosis of cancer\*

RANK	PROPOSED PROBLEM LEADING TO DELAYED DIAGNOSIS OF CANCER CARE	PRIORITY SCORE	TYPE OF FACTOR LEADING TO DIAGNOSTIC ERROR	TYPE OF DELAY TO CANCER DIAGNOSIS
1	Lack of patient awareness of cancer symptoms mean that they do not attend for advice and investigation in a timely manner	82.5	Patient-related	Patient delay
2	Poor continuity of care for patients leads to symptoms being missed and delayed diagnosis	79	System	Patient delay
3	Delays in referrals eg, GPs not following two-week referral guidelines mean that patients are diagnosed late in the course of the disease	79	System	Referral delay
4	Patients not having a GP mean that they may use other services such as the Emergency Department which are not designed to detect or diagnose cancer and hence present late	78	Patient-related	Patient delay
5	GPs not having enough time mean that they do not take a full history or examine patients fully and miss cancers	78	System	Primary care delay
6	Delays in accessing diagnostics in the community mean that patients wait longer for hospital appointments	76.5	System	Referral delay
7	Patient fears of the diagnosis of cancer mean that they do not seek health advice early in the course of their illness	75	Patient-related	Patient delay
8	Inefficient processes and bureaucracy in hospitals leads to delays in processing referrals and arranging appointments	69.5	System	Referral delay
9	Co-morbidities make it more difficult to diagnose cancer as the symptoms may be confused with those of other existing illnesses	68.5	Cognitive	Primary care delay
10	GPs ignoring alarm symptoms eg, rectal bleeding leads to delays in diagnosis	68	Cognitive	Primary care delay

\*The table uses clinicians' verbatim statements which were only exceptionally reworded for clarity. Clinicians scored problems using the following criteria: frequency, severity, inequity, economic impact and responsiveness to solution (**Box 1**). The scoring options were 1 for "yes" (eg, this problem is common), 0 for "no" (eg, this problem is uncommon), 0.5 for "unsure" (eg, I am unsure if this problem is common) and blank for "unaware" (eg, I do not know if his problem is common). Total priority score is the mean of the scores for each of the five criteria and ranges from 0 to 100. Higher ranked problems received more "Yes" responses for each of the criteria and a higher score.

**Table 2.** Clinicians' identified top 10 solutions for delayed diagnosis of cancer

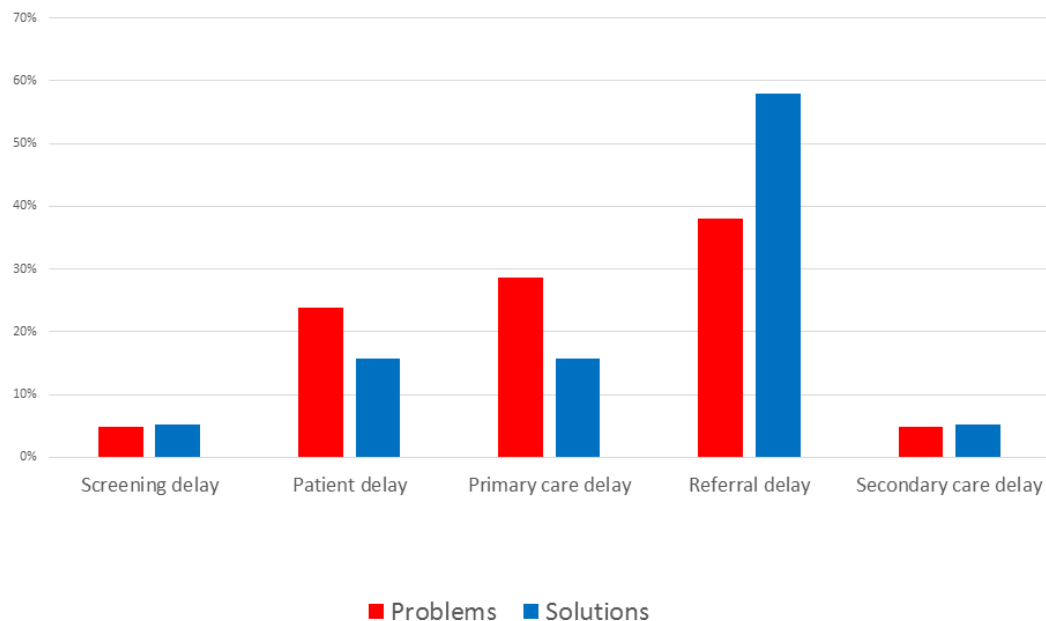
RANK	PROPOSED SOLUTION TO DELAYED DIAGNOSIS OF CANCER	PRIORITY SCORE	CATEGORIES OF ORGANIZATIONAL INTERVENTIONS TO DECREASE DIAGNOSTIC ERRORS	TYPE OF DELAY THE PROPOSED SOLUTION IS AIMED AT
1	Encourage public awareness campaigns on common symptoms of cancer to ensure patients present early in the course of their disease	94.1	Patient education and empowerment	Patient delay
2	Improve adherence to referral guidelines to ensure earlier diagnosis	93.3	Educational intervention	Referral delay
3	Improve communication between general and oncology teams in hospitals to improve the standard of care	93.3	Structured-process change	Referral delay
4	Provide prompt feedback to primary care if delayed diagnosis to encourage learning about incidents	90	Educational interventions	Primary care delay
5	Facilitate rapid referrals from primary care to hospitals	89.2	Structured-process change	Referral delay
6	Improve specialist education for doctors and nurses to ensure better standards of care	89.2	Educational interventions	Secondary care delay
7	Improve funding provided to improve services available and provide quicker access to diagnostics and specialists	87.5	Structured-process change	Referral delay
8	Improve access to GPs for patients to ensure earlier diagnosis	85.8	Structured-process change	Patient delay
9	Improve referral and follow up processes to ensure referrals are not lost	85.8	Structured-process change	Referral delay
10	Ensure sufficient staff available to deal with referrals to ensure no delay in processing referrals	84.1	Personnel change	Referral delay

The table uses clinicians' verbatim statements which were only exceptionally reworded for clarity. Clinicians scored solutions using the following criteria: feasibility, cost-effectiveness and potential for saving lives (**Box 1**). The scoring options were 1 for "yes" (eg, this problem is common), 0 for "no" (eg, this problem is uncommon), 0.5 for "unsure" (eg, I am unsure if this problem is common) and blank for "unaware" (eg, I do not know if his problem is common). Total priority score is the mean of the scores for each of the three criteria and ranges from 0 to 100. Higher ranked solutions received more "Yes" responses for each of the criteria and a higher score.

tory taking. The least important solutions to delayed cancer diagnosis according to clinicians are referring people with a family history of cancer regardless of their symptoms, mandating referral for certain symptoms and tracking patients who do not attend their hospital appointment.

The proposed problems and solutions were interrelated as the majority of the identified problems and solutions ad-

ressed referrals between primary and secondary care and the top priority in both types of suggestions relates to public awareness of cancer (**Figure 5**). The highest ranked suggestions had the highest AEA, ie, there was a stronger consensus among the clinicians regarding to the top suggestions compared to those ranked lower. The lowest ranked suggestions received a significant number of "Unsure" and



**Figure 5.** Comparison of problems and solutions related to delayed diagnosis in cancer care in terms of the diagnostic process breakdown point.

“Unaware” answers through scoring (Table S5 in **Online Supplementary Document**).

## DISCUSSION

Cancer care clinicians in our study identified a range of priorities for timely diagnosis of cancer in North West London. Lack of cancer symptom recognition among patients, poor continuity of care and complex patient presentation were seen as top problems. Raising public awareness, better patient education and easier access to specialist care and diagnostic testing were seen as top solutions. Referrals from primary to secondary care were considered particularly problematic and likely to cause diagnostic delays. Many suggestions were synergistic or interrelated, and focused on common themes, eg, symptom awareness, care continuity, consultation length etc. This agreement among the identified suggestions reaffirmed the importance of certain priorities in the North West London context and conveys a clear message where action is needed. While all identified problems and solutions are important and revealing, their prioritization can support development of customised, locally-relevant policies in the context of limited health care means.

Clinicians in our study considered patient delays (due to symptom unawareness, late or emergency patient presentation and lack of personal GP) a key problem, more likely to affect lower socio-economic groups. This corresponds to the surveys showing that awareness of cancer warning signs is low, especially among young men and lower socio-economic groups [26,27]. In addition, almost a quarter of all cancer patients in England present as emergencies, often

with the later stage of cancers and poorer outcomes [28]. Research shows that poor care continuity, a major problem in our study, hinders timely cancer diagnosis, especially in patients with complex cancer presentation and comorbidities [29,30]. Raising patient awareness through public campaigns, a key solution identified in our study, has been associated with better recognition of symptoms and GP attendance among patients as well with earlier stage lung cancer diagnosis [31,32].

In our study, better adherence to referral guidelines and a quicker access to diagnostic investigations were seen as the top priorities. This is consistent with the recent findings showing that the introduction of “urgent referrals” (seeing a specialist within 2 weeks of presenting to a GP) via National Institute for Health and Care Excellence (NICE) cancer guidelines in 2005 was associated with earlier cancer diagnosis and better patient outcomes [33,34]. And yet, there are still large variations in GP cancer referral rates revealing substantial differences in individual GP thresholds for referring symptomatic patients [35]. Furthermore, instead of mandated “urgent referral”, some patients receive time-consuming diagnostic workup in the primary care setting, leading to later referral for specialist assessment [36]. In our study, clinicians considered rapid referrals to hospitals for certain patients as most likely to save lives which is in fitting with the recent addition of “very urgent referrals” (seeing a specialist within 48 hours of presenting to a GP) to the updated NICE cancer guidelines [37].

## Strengths and limitations

PRIORITIZE is a timely, cost-effective and straightforward answer to calls for engagement of health care staff in patient

safety priority-setting [12]. While existing health care provider surveys on delayed diagnosis define priorities according to their frequency [38,39], PRIORITIZE employs several additional relevant and well-defined prioritization criteria such as severity, equity, economic impact and feasibility. Given the regional inequalities in the UK's cancer care and diagnosis, "one-size-fits-all" approach to development of safety policies and initiatives is unlikely to be successful. PRIORITIZE enables identification of local priorities and implementation of tailored patient safety interventions and policies.

The response rate in our study was low response which may have affected the generalizability of our findings. However, the number of participants in our study corresponds to those in other priority setting exercises involving health care professionals or employing the CHNRI methodology [40–44]. Furthermore, physician surveys, especially those containing open-ended questions and focusing on sensitive topics, are challenging and in general yield low response rates [45–47]. To boost the response rate, surveys of hospital staff on patient safety in general necessitate leadership engagement, intense campaigning, assurance that the employees' feedback will be impactful etc. [48]. Surveys in general recruit a self-selected sample and the participants in our study potentially differed from those who did not take part in this study. Although our findings mirror the relevant literature and the participants had the same eligibility criteria by being a cancer care provider in North West London, there may have been other, unmeasured biases. As most of the participants were oncology consultants or hospital-based trainees, this may have also influenced the choice and ranking of priorities.

While our findings are revealing, this approach is at an early stage and could be improved, eg, providing examples to guide specificity of responses (eg, error producing conditions, errors and adverse events), increasing the response rates or enabling longitudinal data collection. PRIORITIZE also provides opportunities for different types of analysis, inclusion of diverse prioritization criteria (eg, urgency, impact, affordability, execution risk, sustainability etc.) and recruitment of both health care professionals and patients.

### Implications for practice and policy

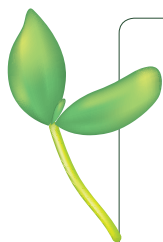
Delayed diagnosis of cancer has been recognized as the key reason for the UK's lower cancer survival rates. Clinician-identified priorities for a timely cancer diagnosis in our study focused on public awareness, patient education and access to specialist care and diagnostic testing. Using a bottom-up approach, in which clinicians drive change, we collated concrete, locally-relevant and affordable sugges-

tions to inform the health care policy on patient safety. Many suggestions showed agreement underscoring the importance of certain priorities. The Patient Safety Board assembled priorities that were synergistic or inter-related (eg, improving adherence to referral guidelines, improving referral and follow up processes to ensure referrals are not lost, ensuring sufficient staff available to deal with referrals, improving the quality of information in patient referrals) to address them with a focused and concerted effort. Our findings are now being used to guide the Imperial College Health Partners' work on the Medicines Optimisation in North West London.

Research shows that clinicians often feel excluded from the development of patient safety policies [49], avoid incident reporting due to lack of anonymity or time [50] and are frequently victimised when pointing out safety issues [51]. PRIORITIZE allows transparent, easy reproducible and anonymous voicing of concerns, suggestions and ideas from many health care providers. It triggers staff feedback and involvement, enables evaluation of the organizational culture and the frontline staff views on the locally-relevant patient safety priorities and ultimately aligns the policies with clinicians' feedback. It also ensures staff calibration, ie, a comparison between the physician's self-assessment and external overall evaluation of the health care system's and the organisational safety threats. We propose exploring whether this priority-setting exercise could be included into the annual staff appraisal process to detect clinicians' perspective on the weaknesses in diagnostic processes in different settings. As a system-wide initiative, PRIORITIZE could increase the awareness of patient safety threats, improve the organisational culture, allow country-wide comparison and implementation of locally tailored-interventions.

### CONCLUSIONS

Clinicians proposed a wide range of implementable, affordable and concrete suggestions for timely cancer diagnosis. The top ranked priorities focused on raising public awareness, patient education as well as better access to specialist care and diagnostic testing. The identified suggestions focused mostly on the delays during referrals from primary to secondary care. While all identified problems and solutions are noteworthy and revealing, their ranking can serve as an aid to policy makers and commissioners of care in prioritization of scarce health care resources. PRIORITIZE is a highly feasible, informative and scalable priority-setting approach, and merits wider exploration with a view of becoming part of a routine pro-active and preventative system for patient safety assessment.



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**Ethics approval:** This study is a service evaluation as well as a quality and safety improvement initiative and therefore did not require ethics or governance approval according to the UK's Health Research Authority guidance [18,19].

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**Authors' contributions:** LTC, CV and JC conceived and designed the study. MEK and NP performed the data collection. LTC and NP analysed the data and wrote the initial draft of the paper. CU, AM, PA, RA, IR, JC and CV participated in the interpretation of the data and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

**Conflict of interest:** The authors completed the Unified Competing Interest form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available upon request from the corresponding author). Prof Paul Aylin reports grants from NIHR, grants from Dr Foster Ltd, grants from Department of Health, during the conduct of the study; non-financial support from Dr Foster Ltd, outside the submitted work; Prof Charles Vincent: carries out occasional consultancy and advisory work on patient safety.

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# Diarrhea no more: does zinc help the poor? Evidence on the effectiveness of programmatic efforts to reach poorest in delivering zinc and ORS at scale in UP and Gujarat, India

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**Background** India has the greatest burden of diarrhea in children under 5 years globally. The Diarrhea Alleviation through zinc and oral rehydration salts (ORS) Therapy program (2010–2014) sought to improve access to and utilization of zinc and ORS among children 2–59 months in Gujarat and Uttar Pradesh (UP), India, through public and private sector delivery channels. In this analysis, we present findings on program's effect in reducing child–health inequities.

**Methods** Data from cross-sectional baseline and endline surveys were used to assess disparities in key outcomes across six dimensions: socio-economic strata, gender, caregiver education, ethnicity and geography.

**Results** Careseeking outside the home for children under 5 years with diarrhea did not increase significantly in UP or Gujarat across socioeconomic strata. Declines in private sector careseeking were observed in both sites along with concurrent increases in public sector careseeking. Zinc, ORS, zinc+ORS use did not increase significantly in UP across socioeconomic strata. In Gujarat, increases in zinc use (20% overall; 33% in the Quintile 5 (Q5) strata and zinc+ORS (18% overall; 30% in the Q5 strata) were disproportionately observed in the high income strata, among members of the most advantaged caste, and among children whose mothers had  $\geq 1$  year of schooling. ORS use increased significantly across all socioeconomic strata for children in Gujarat with diarrhea (23% overall; 33% in Q5 strata) and those with dehydration + diarrhea (33% overall; 38% in Q5 strata). The magnitude of increase in ORS receipt from the public sector was nearly twice that observed in the private sector. In Gujarat, while out of pocket spending for diarrhea was significantly higher for male children, overall costs to users declined by a mean of US\$ 2; largely due to significant reductions in wages lost (–US\$ 0.79;  $P < 0.003$ ), and transportation costs (–US\$ 0.44;  $P < 0.00$ ).

**Conclusions** While significant improvements in diarrhea treatment were achieved in Gujarat, new strategies are needed in UP, particularly in the private sector. If national-level reductions in diarrheal disease burden are to be realized, improved understanding is needed of how to optimally increase coverage of zinc and ORS and decrease contraindicated treatments amongst the most disadvantaged across geographic areas and axes of gender, ethnicity, education and socioeconomic status.

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Diarrhea is one of few infections, which underpins the gap in child survival between the world's poorest and richest countries [1,2]. Despite declines of nearly 50% since 2000, an estimated 578 000 deaths in children under 5 in 2013 were attributed to diarrhea [3]. The majority of deaths due to diarrhea occur in low resource settings; one in four in India alone [3].

Diarrhea is a disease of the poor. Defined by the passing of three or more loose or liquid stools in 24 hours, diarrhea is caused by viruses, bacteria, and/or parasites spread through contaminated food, water, or person-to-person contact resulting from poor hygiene and inadequate sanitation. Vast differentials in sanitation coverage and access to safe water across population sub-groups underscore the differential risk of diarrheal diseases on the poorest children.

In nearly all diarrhea cases, death stems from fluid loss and dehydration. While oral rehydration solution (ORS) – effective in reducing morbidity and mortality due to dehydration – has been used as a mainstay of treatment diarrhea since 1978, its use is limited to only 38% of diarrheal episodes globally and 26% in India [4,5]. Overall use rates mask wide disparities across wealth groups, with only 19% of the poorest and poor in India receiving ORS as compared to 43% in the highest wealth groups [4]. Further disparities in treatment and health outcomes by age, sex, education, and geography have been reported for diarrhea management in Bangladesh [6] and other child health outcomes in India [7].

Zinc supplementation for the treatment of acute diarrhea has been shown to decrease the duration and severity of the diarrheal episodes, rates of hospitalization for diarrhea, and all-cause and diarrhea mortality [8]. As a result, in 2004 the World Health Organization (WHO) and UNICEF amended global guidelines for the management of acute diarrhea to include the recommendation that children receive zinc supplementation for 10–14 days, in addition to ORS and continued feeding [9]. Yet over a decade later, zinc availability remains limited and its use rates unknown, particularly amongst the poorest.

To address persistent gaps in diarrhea treatment in India, the Diarrhea Alleviation through zinc and ORS Therapy (DAZT) program was initiated in 2010 to improve access to and utilization of zinc and ORS among children 2–59 months in 6 of 26 districts in Gujarat State, India and 12 of 75 districts of Uttar Pradesh (UP), India. In this analysis, we present findings related to the effect of DAZT programmatic activities on equity in caregiver knowledge, careseeking, treatment, cost, and diarrheal disease prevalence following zinc introduction.

## METHODS

### Key definitions and terminology

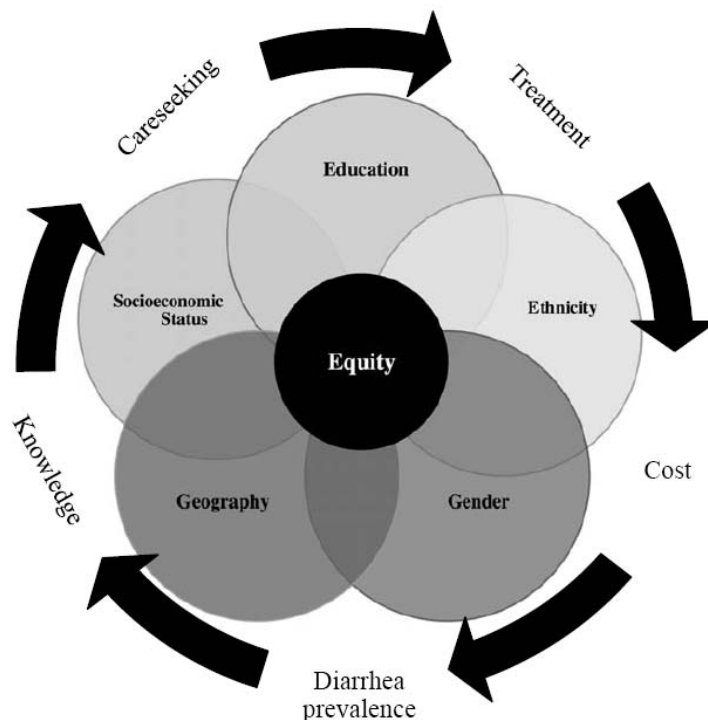
In the context of the DAZT program, we sought to assess horizontal equity (treating like cases of diarrhea alike) by exploring the effects of program activities across population subgroups on key outcomes, including caregiver knowledge of zinc and ORS, careseeking overall and by sector, treatment, and diarrheal disease prevalence [10,11]. Vertical equity (treating unlike cases of diarrhea differently) was explored through analyses of different types of diarrhea (eg, diarrhea with and without dehydration) and the effects on ORS use across population subgroups. In contrast to many analyses, which focus on one dimension of equity defined by socioeconomic status and measured by wealth quintiles [12–14], we additionally considered the distributional impacts according to gender, education, ethnicity and geography at a sub-national level by comparing UP with Gujarat (**Figure 1**). Elsewhere the importance geography at a sub-national level [6] has been noted for diarrhea in Bangladesh. However, the constraints of DAZT program implementation to rural areas at sub-state level limited our inclusion of this added dimension.

### Study sites and context

Gujarat (population 60 million) and Uttar Pradesh (population 199 million) are states in West and Central India, respectively [15]. Project activities were implemented among a population of 41 million (6.3 million under 5 population) across 12 districts of UP and 13 million (2.1 million under 5 population) across 6 districts of Gujarat [15]. With a Gross Domestic Product (GDP) of US\$ 2337, Gujarat ranks among India's top 10 states for economic productivity. By comparison, with a GDP of US\$ 793, UP is second only to Bihar as the worst performing state in India. Economic trends underscore disparities in disease burden, careseeking, and health practices across states. In UP, nearly 1-in-10 children die prior to reaching their fifth birthday; only 30% receive all 3 DTP immunizations, and 23% receive all basic immunizations [4,16]. In Gujarat, for every 1000 live births, 56 children die prior to their fifth birthday [4,16]. While immunization rates exceed those reported in UP, deficits remain with only 61% of children receiving all 3 DTP immunizations and 45% receiving all basic immunizations [4]. Prior to the implementation of DAZT, among children with diarrhea, 58% of children in UP and 57% in Gujarat were taken to a health care provider [4]. In Gujarat, 26% received ORS and 31% unknown drugs as compared to 13% and 47%, respectively, in UP [4].

### Program description

A detailed overview of the DAZT program has been published elsewhere [17]. Project activities sought to improve



**Figure 1.** Framework for assessing the effects of multiple dimensions of equity influencing knowledge, careseeking, treatment, cost and health status for diarrhea.

the availability of and access to ORS and zinc for the management of acute diarrhea through public and provider delivery channels in Gujarat and UP. Public sector activities were concentrated in primary health centers and among community based providers, including Accredited Social Health Activists (ASHAs) and Anganwadi workers (AWWs). Programmatic inputs included training in overall diarrhea prevention and management to district and block level supervisors, as well as facility and community based health providers. To address immediate shortages in supplies, the program provided an initial seed supply of diarrhea treatment kits (DTKs) comprised of two ORS sachets, 10 taste masked zinc tablets, a measuring cup, and an informational leaflet for caregivers.

Private sector activities included work with pharmaceutical companies, homeopathic and alternative medicine associations, to promote zinc and ORS use and ensure product supply among informal and formal private providers in both states. Implementation involved a push and pull strategy. The former sought to change prescription practices among key opinion leaders in the medical community and market ORS and zinc to private providers, while the latter, pull strategy sought to create demand for ORS and zinc amongst private providers. Programmatic inputs included the provision of Information Education and Communication (IEC) materials, and training in diarrhea prevention

and management, including the importance of zinc and ORS, dosage and regulatory guidelines, as well as promotional strategies for effective product placement. DAZT corners were additionally established as informational booths in private clinics and hospitals to create awareness among caregivers and remind providers to prescribe zinc.

### Sampling and study design

The details of the study design and sampling plan are provided in great details elsewhere [18]. Briefly, the evaluation of the DAZT program assumed a prospective, pre–post design with activities primarily comprised of cross-sectional surveys conducted at baseline and endline (**Figure 1**). Surveys assessed household characteristics, caregiver knowledge, care seeking behavior, out of pocket expenditures, and household assets for classifying individuals according into wealth quintiles [18].

A post-hoc power analysis was performed to identify the lowest detectable difference between the wealth groups for the outcome of ORS use among respondents with diarrhea in the past 2 weeks. The analysis was based on a minimum sample size of 84 (least poor at endline for Gujarat) per group, type 1 error of 0.05, and power of 80%. For ORS use with baseline prevalence of 16%, the minimum detectable difference was 18% while for zinc use with baseline prevalence of 2%, the minimum detectable difference was 11%.

## Data analyses

All data analyses were conducted in Stata 13 (StataCorp, College Station, TX, USA). Bivariate analysis was used to analyze demographic and socioeconomic characteristics of included households using  $\chi^2$ -square tests. Principal Components Analysis (PCA) has become the norm for classification of households into wealth categories in low resource settings [19]. Households were classified into wealth quintiles using the PCA technique for each survey round to ensure that the same relative level of economic well-being was assessed across study phases. Wealth quintile 1 (Q1) represents the poorest 20% of households in the survey sample and quintile 5 (Q5) represents the least poor. Multivariable logistic regression analysis was used to address the evaluation question of whether differences in the proportion of respondents differed significantly across socioeconomic strata over time for indicators of disease burden, knowledge of zinc/ORS, careseeking, and treatment practices for diarrhea. To model the prevalence of the various outcome variables and any changes from baseline to end-line surveys a model with an interaction term with time for the variable representing dimension of equity was used: *Probability of outcome for subject i in village j*  $(y_{ij}) = b_0 + b_1(\text{Wealth group}) + b_2(\text{Time}) + b_3(\text{wealth group} \times \text{time}) + b_i(\text{other explanatory variables}) + u_j$  where  $u_j$  is the random effects due to the village level clustering. Similar models were created for the other dimensions of equity – ethnicity, sex and mothers' education. Adjusted means for the outcomes for category of the variable of interest holding the other variables in the models at their mean values are presented. Confidence intervals at 95% are presented.

Concentration curves and indices were used to examine socioeconomic inequalities in the distribution of diarrhea prevalence, careseeking, treatment and cost. Concentration curve plots the cumulative share of the health care utilization (ie, use of zinc) against the cumulative share of households in the population ranked from poorest to richest using asset scores [17,18]. If the concentration curve lies above the 45-degree line (line of equality), then the health care utilization is concentrated among the poor and if the concentration curve falls below the line of equality, then health care utilization is concentrated among the rich [18]. If the concentration curve falls along the line of equality, then health care utilization is equally distributed across groups. Concentration indices (CIs) are obtained from the associated concentration curves as twice the area between a concentration curve and the line of equality. The Relative Concentration Index (RCI) measures the extent to which health care utilization is concentrated among particular social groups. It takes on values between -1, when the population's health care utilization is concentrated among the poor, and +1, when the utilization is concentrated among

the rich. A positive index signifies that the distribution of utilization is higher among the richer groups while a negative index indicates utilization is higher among the poor.

Costs were analysed using linear models without any transformations, even though the data showed skewness to the right and "lumpiness" at 0. Using linear models for cost data are considered acceptable when the primary purpose of the analysis is the estimation of average costs [20]. When analyzing costs associated with diarrhea, we have an issue of selection bias – only subjects with diarrhea can incur costs and costs are zero for those who do not suffer from diarrhea. Use of linear models to only those who suffer diarrhea raises the possibility of sample selection bias. The probability of suffering from diarrhea can be influenced by wealth and demographic characteristics which may also influence costs incurred. It is possible that the wealthier groups suffer fewer episodes of illness and may be under sampled if the sample were restricted to only those who suffered from diarrhea. A Heckman sample selection model helps to use the entire sample by first modeling the probability of diarrhea and then using the probability as a predictor of costs. The selection model is based on the notion that some of the independent variables that predict the probability of suffering from diarrhea are different from the independent factors that are associated with costs. The two-step estimation approach is used when the outcome of interest is an observed continuous variable (cost). To assess differences in mean out of pocket payments for treatment and careseeking across socioeconomic strata prior to and after program initiation, we theorized two interdependent models – first, a probit selection model where

$$\text{Probability of diarrhea } (P_d) = b_0 + b_{\text{Wealth}} + b_{\text{Mother's education}} + b_{\text{number of children in the family}} + b_{\text{type of family}} + \text{error}$$

and the second is a regression model

$$\text{Out of pocket cost } (C) = b_{\text{Wealth}} + b_{\text{program intervention}} + b_{\text{Wealth}} \times b_{\text{program intervention}} \text{ if } P_d > 0$$

and

$$\text{Out of pocket cost } (C) = 0 \text{ if } P_d = 0.$$

We generated mean costs incurred for the different wealth categories and estimated the difference in the costs saved by the intervention. Clustering at the level of the village (Primary Sampling Unit) was accounted for by the use of robust variance estimators based on a first-order Taylor series linear approximation.

## Ethical approval and study status

Ethical approval was obtained from the Johns Hopkins University Bloomberg School of Public Health Institutional Review Board (IRB) and Society for Applied Studies Ethics Research Committee (ERC).

## RESULTS

### Sample characteristics

Baseline and endline household survey data were collected from 4200 and 5080 caregivers in Gujarat and from 3889 and 7853 caregivers in UP, respectively (Figure 2). In both states, household, caregiver, and child characteristics were similar for most parameters assessed (Table 1). In Gujarat, significant differences from baseline to endline were observed in the number of nuclear families (37% vs 32%;  $P < 0.001$ ), the proportion of mothers with greater than 1 year of schooling (51% vs 59%;  $P = 0.01$ ), mean number of children under 5 living in the house (1.46 vs 1.40;  $P < 0.001$ ), and the proportion of households below the poverty line (40% vs 48%;  $P < 0.001$ ). In UP, significant differences in the proportion of mothers with greater than 1 year of schooling (38% vs 51%;  $P < 0.001$ ), mean number of children under 5 living in the house (1.44 vs 1.41;  $P = 0.05$ ), the proportion of children breastfed within the previous 24 hours (67% vs 64%;  $P < 0.001$ ), and the proportion of households below the poverty line (28% vs 22%;  $P < 0.001$ ) from baseline to endline.

### Caretaker awareness of zinc and ORS

Caretaker awareness is often viewed as a predictor for treatment seeking behavior. Variations in awareness of zinc and ORS as well as careseeking overall and by sector for diar-

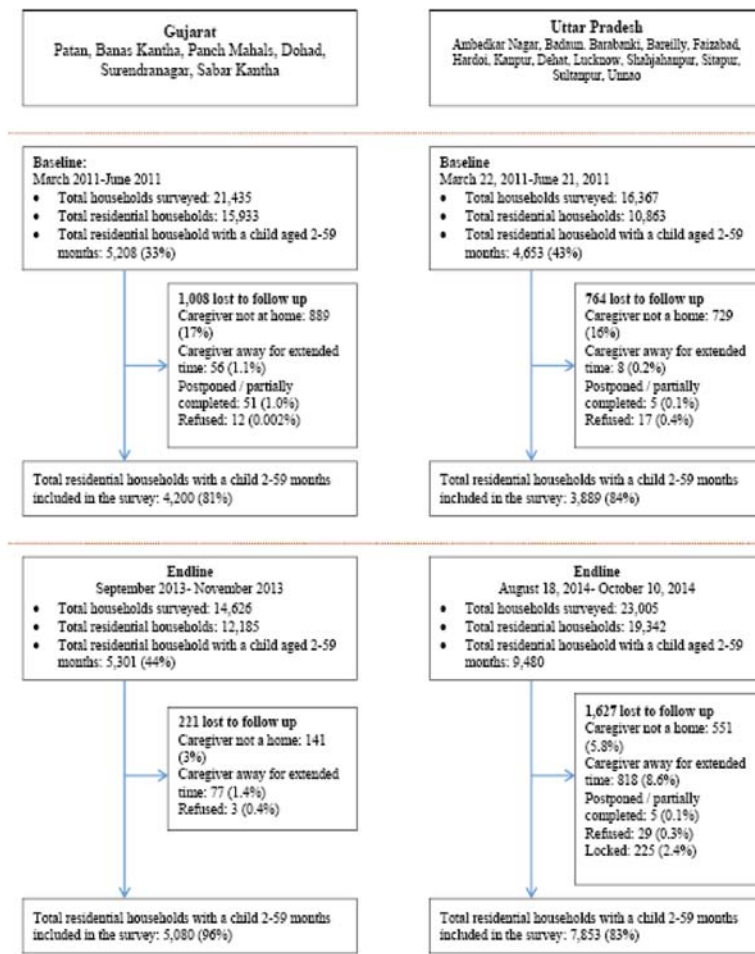
rhea treatment are presented in Figure 3 and Table S1 in Online Supplementary Document. Findings suggest that in contrast to ORS, where nearly all caregivers in UP and half of caregivers in Gujarat reported some baseline knowledge of ORS, baseline awareness of zinc for diarrhea was lower at 6% in UP and 5% in Gujarat. Across socioeconomic strata, a significant 10%–24% increase in zinc awareness was observed over time in Gujarat and 20–36% increase in UP. In both sites, while improvements in zinc awareness were similar by gender and ethnicity, increases were greatest amongst caregivers with  $\geq 1$  year of schooling (Gujarat: 22%  $P < 0.001$ ; UP: 30%  $P < 0.001$ ) and in the Q5 socioeconomic strata (Gujarat: 24%  $P < 0.001$ ; UP: 36%  $P < 0.001$ ). In both sites, concentration indices show a pro-rich bias.

### Diarrhea careseeking

Careseeking outside the home for children under 5 with diarrhea did not increase significantly over time in either site across socioeconomic strata or by maternal education (Figure 3, Table S3 in Online Supplementary Document). In Gujarat, careseeking outside the home increased significantly for male children (8%,  $P < 0.001$ ) and members of other backward castes (12%,  $P < 0.001$ ). Across public and private sectors, the majority of careseeking among children with diarrhea occurred in the private sector. However, declines in private sector careseeking were observed over time from 86% to 75% in Gujarat ( $P < 0.001$ ).

**Table 1.** Demographic and socioeconomic characteristics of included households

CHARACTERISTICS	GUJARAT (95% CONFIDENCE INTERVAL)			UTTAR PRADESH (95% CONFIDENCE INTERVAL)		
	Baseline	Endline	Endline–Baseline P value	Baseline	Endline	Endline–Baseline P value
	March–May 2011 (n = 4200)	October–December 2013 (n = 5080)		March–June 2011 (n = 3889)	August–October 2014 (n = 7853)	
Number of nuclear families	37% (35 to 40%)	32% (30 to 34%)	<0.001	55% (52 to 58%)	52% (50 to 54%)	0.16
No. mothers with $\geq 1$ year of schooling	51% (47 to 56%)	59% (56 to 62%)	0.01	38% (34 to 42%)	51% (48 to 53%)	<0.001
No. children <5 living in this house	1.46 (1.43 to 1.49)	1.40 (1.37 to 1.43)	0.00	1.44 (1.41 to 1.47)	1.41 (1.39 to 1.43)	0.05
Mean number boys	0.76 (0.74 to 0.79)	0.74 (0.72 to 0.77)	0.31	0.74 (73 to 77%)	0.73 (72 to 75%)	0.30
Mean number girls	0.70 (0.68 to 0.73)	0.66 (0.63 to .68)	0.01	0.69 (67 to 72%)	0.68 (66 to 69%)	0.30
Age of the index child (mean in months)	24.3 (23.7 to 24.9)	24.0 (23.4 to 24.5)	0.43	24.7 (24.1 to 25.4)	25.3 (24.9 to 25.6)	0.13
Sex of index child: female	46% (44 to 47%)	44% (42 to 45%)	0.10	47% (46 to 49%)	46% (45 to 47%)	0.25
Proportion of children breastfed in the previous 24 h	58% (56 to 60%)	60% (58 to 62%)	0.21	67% (65 to 69%)	64% (63 to 65%)	<0.001
Below poverty line	40% (37 to 44%)	48% (45 to 51%)	0.00	28% (25 to 31%)	22% (21 to 24%)	<0.001
Religion:			0.17			0.54
–Hindu	95% (92 to 98%)	96% (94 to 97%)		88% (83 to 92%)	86% (84 to 88%)	
–Muslim	4% (2 to 9%)	4% (2 to 6%)		12% (8 to 17%)	14% (12 to 16%)	
–Other	0% (0 to 1%)	0% (0 to 1%)		0% (0 to 0%)	0% (0 to 0%)	
Ethnic group:			0.14			0.86
–Scheduled caste	12% (9 to 16%)	17% (14 to 20%)		35% (31 to 40%)	37% (34 to 40%)	
–Scheduled tribe	31% (24 to 38%)	25% (21 to 31%)		0% (0 to 1%)	0% (0 to 0%)	
–Other backward caste	41% (35 to 48%)	44% (40 to 49%)		48% (43 to 53%)	47% (44 to 50%)	
–Other	16% (12 to 21%)	13% (11 to 16%)		17% (13 to 21%)	16% (14 to 18%)	



**Figure 2.** Sampling for baseline and endline household surveys in Gujarat and Uttar Pradesh (UP), India.

and from 98% to 87% in UP ( $P < 0.00$ ). Declines in private sector utilization were offset by increases in facility and community-based careseeking in both states. In Gujarat, utilization of public sector providers increased significantly irrespective of maternal education, for both male (19%,  $P < 0.001$ ) and female (16%,  $P < 0.001$ ) children, members of the scheduled (23%,  $P < 0.01$ ) and other backward castes (23%,  $P < 0.01$ ), and amongst members of the Q3 (25%,  $P < 0.001$ ), Q4 (20%,  $P < 0.01$ ), and Q5 (24%,  $P < 0.001$ ) socioeconomic strata (Figure 3, Table S2 in Online Supplementary Document). Among public sector providers, increases in careseeking were driven by increased utilization of community based AWWs and ASHAs. In UP, increases in public sector utilization were significant for male children (5%;  $P = 0.035$ ) and members of the scheduled caste (8%;  $P = 0.004$ ). Increases were similarly driven by a modest increase of 1–4% across all socioeconomic strata in community based careseeking from ASHAs and AWWs.

### Treatment among children with diarrhea

In Gujarat, zinc, ORS and zinc+ORS use increased significantly across all subgroups including socioeconomic strata, gender, ethnicity and maternal education (Table 2, Figures S1 and S2, and Table S3 in Online Supplementary Document).

However, the magnitude of increase was lowest among individuals in the Q1 and Q2 socioeconomic strata, members of the disadvantaged scheduled castes and tribe, and among children whose mothers had <1 year of schooling. This trend was similar across both private and public sectors sources for careseeking (Table 2). The magnitude of increase from baseline to endline in the number of caregivers receiving ORS from the public sector (23%, from 8% to 31%) was nearly twice that observed in the private sector (12%, from 18% to 30%). Receipt of zinc was similar across sectors, increasing significantly from 1% to 18% ( $P < 0.001$ ) in the public sector and 3% to 18% in the private sector ( $P < 0.001$ ). Increases in the use of home fluids, antibiotics, and antidiarrheals, coupled with declines in use of unknown tablets, powders, and syrups were observed across all sub-groups from baseline to endline.

In UP, significant increases from baseline to endline across socioeconomic strata in zinc and ORS use were not observed, while the use of antidiarrheals increased significantly from 48% in the Q1 ( $P < 0.001$ ) to 34% in the Q5 ( $P < 0.001$ ) (Table S3 in Online Supplementary Document). When stratified by sector, zinc receipt increased in the private sector (from 4% to 8%;  $P = 0.03$ ) and ORS increased in the public sector (from 1% to 4%;  $P = 0.001$ ).



**Table 2.** Treatment received among children 2–59 month with diarrhea in the preceding 2 weeks by sector

	GUJARAT (95% CONFIDENCE INTERVAL)*			UTTAR PRADESH (95% CONFIDENCE INTERVAL)†		
	Baseline (n=594)	Endline (n=553)	Endline–Baseline Difference	Baseline (n=572)	Endline (n=854)	Endline–Baseline difference
<b>Receipt of zinc – public sector</b>						
Socioeconomic status:						
–Quintile 1	0%	10%	10% (–2 to 21%)	0%	2%	2% (–1 to 4%)
–Quintile 2	1%	9%	8% (2% to 15%)‡	0%	1%	1% (–1 to 3%)
–Quintile 3	2%	18%	16% (8 to 25%)‡	1%	1%	–0% (–3 to 3%)
–Quintile 4	1%	29%	28% (17 to 38%)‡	0%	3%	3% (–0 to 7%)*
–Quintile 5	3%	28%	25% (12 to 38%)‡	0%	3%	3% (–1 to 7%)
Concentration index	0.12 (–0.11 to 0.36), 0.17 (0.00 to 0.34)			0.26 (–0.50 to 1.02), 0.23 (–0.02– to 0.49)		
Gender:						
–Male	1%	21%	15% (9 to 21%)‡	0%	2%	2% (0 to 4%)*
–Female	0%	33%	20% (14 to 26%)‡	0%	1%	1% (–1 to 3%)
Ethnicity:						
–Scheduled caste	2%	12%	14% (7 to 21%)‡	0%	1%	1% (–0 to 3%)‡
–Scheduled tribe	3%	16%	12% (3 to 21%)‡	–	–	–
–Other backward caste	1%	22%	21% (14 to 29%)‡	1%	2%	1% (–1 to 4%)
–Other	0%	25%	24% (10 to 38%)‡	0%	2%	2% (–1 to 6%)
Maternal education:						
–Mothers with <1 year of schooling	3%	20%	17% (10 to 24%)‡	0%	2%	2% (0 to 4%)*
–Mothers with ≥1 year of schooling	1%	17%	18% (12 to 24%)‡	0%	1%	1% (–1 to 3%)
<b>Receipt of zinc – private sector</b>						
Socioeconomic status:						
–Quintile 1	2%	11%	9% (2 to 17%)‡	3%	6%	4% (–1 to 8%)
–Quintile 2	3%	9%	6% (–2% to 14%)‡	3%	9%	6% (–0 to 12%)§
–Quintile 3	2%	18%	16% (7% to 24%)‡	5%	7%	3% (–5 to 10%)
–Quintile 4	3%	22%	19% (9 to 29%)‡	7%	8%	1% (–7 to 9%)
–Quintile 5	4%	33%	28% (15 to 41%)‡	1%	8%	6% (–1 to 14%)
Concentration index	0.11 (–0.21 to 0.44), 0.23 (0.10 to 0.36)			0.04 (–0.18 to 0.25), 0.03 (–0.10 to 0.17)		
Gender:						
–Male	4%	20%	16% (9%– to 23%)‡	4%	8%	4% (–1 to 8%)§
–Female	1%	16%	15% (9 to 20%)‡	3%	7%	4% (–1 to 8%)§
Ethnicity:						
–Scheduled caste	1%	21%	20% (9 to 31%)‡	4%	5%	2% (–3 to 6%)
–Scheduled tribe	2%	12%	10% (4 to 16%)‡	–	–	–
–Other backward caste	4%	19%	15% (7 to 2%)‡	5%	9%	4% (–1 to 9%)
–Other	2%	27%	25% (9 to 41%)‡	3%	9%	6% (–2 to 13%)
Maternal education:						
–Mothers with <1 year of schooling	6%	20%	15% (9 to 21%)‡	2%	7%	5% (1 to 8%)‡
–Mothers with ≥1 year of schooling	0%	16%	16% (10 to 21%)‡	6%	8%	2% (–3 to 8%)
<b>Receipt of ORS – public sector:</b>						
Socioeconomic status:						
–Quintile 1	5%	22%	18% (5 to 31%)‡	3%	5%	2% (–3 to 6%)
–Quintile 2	9%	24%	15% (3%–27%)‡	1%	4%	3% (–1 to 7%)
–Quintile 3	8%	33%	25% (13 to 37%)*	0%	3%	3% (0 to 6%)‡
–Quintile 4	9%	38%	29% (16 to 42%)*	2%	6%	4% (–2%–10%)
–Quintile 5	10%	37%	27% (11%–42%)*	–1%	4%	5% (–0 to 9%)§
Concentration index	0.19 (0.03 to 0.36), 0.04 (–0.06 to 0.15)			–0.17 (–0.58 to 0.24), 0.15 (–0.06 to 0.36)		
Gender:						
–Male	6%	29%	23% (16 to 31%)	1%	4%	3% (1 to 6%)‡
–Female	10%	33%	23% (14 to 32%)	2%	4%	3% (–1 to 6%)
Ethnicity:						
–Scheduled caste	5%	29%	23% (11 to 35%)‡	1%	5%	4% (0 to 7%)‡
–Scheduled tribe	8%	26%	18% (7 to 29%)‡	–	–	–
–Other backward caste	7%	34%	27% (18 to 37%)‡	1%	3%	2% (–1 to 5%)
–Other	13%	36%	23% (6 to 40%)‡	2%	7%	4% (–1 to 10%)
Maternal education:						
–Mothers with <1 year of schooling	7%	30%	23% (15 to 32%)‡	1%	4%	3% (–0 to 5%)§
–Mothers with ≥1 year of schooling	9%	32%	23% (15 to 31%)‡	1%	4%	3% (0 to 6%)‡

Table 2. Continued

	GUJARAT (95% CONFIDENCE INTERVAL)*			UTTAR PRADESH (95% CONFIDENCE INTERVAL)†		
	Baseline (n = 594)	Endline (n = 553)	Endline–Baseline Difference	Baseline (n = 572)	Endline (n = 854)	Endline–Baseline difference
<b>Receipt of ORS – private sector:</b>						
Socioeconomic status:						
–Quintile 1	22%	21%	–1% (–11 to 10%)	26%	23%	–3% (–17 to 10%)
–Quintile 2	17%	19%	2% (–10 to 14%)	22%	25%	3% (–8 to 13%)
–Quintile 3	19%	29%	9% (–5 to 23%)	26%	15%	–11% (–23 to –0%)‡
–Quintile 4	16%	39%	23% (9 to 37%)‡	22%	25%	3% (–11 to 16%)
–Quintile 5	15%	47%	32% (15 to 48%)‡	29%	29%	1% (–14 to 15%)
Concentration index	0.04 (–0.07 to 0.15), 0.16 (0.07 to 0.24)			0.00 (–0.08 to 0.08), 0.12 (0.05 to 0.20)		
Gender:						
–Male	16%	32%	16% (7 to 26%)‡	23%	26%	3% (–5 to 11%)
–Female	20%	28%	7% (–2 to 17%)	27%	19%	–8% (–16 to 1%)§
Ethnicity:						
–Scheduled caste	5%	29%	23% (11 to 35%)‡	23%	23%	–0% (–11 to 10%)
–Scheduled tribe	8%	26%	18% (7 to 29%)‡	–	–	–
–Other backward caste	7%	34%	27% (18 to 37%)‡	26%	21%	–5% (–14 to 3%)
–Other	13%	36%	23% (6 to 40%)‡	23%	29%	5% (–7 to 18%)
Maternal education:						
–Mothers with <1 year of schooling	16%	28%	12% (4 to 20%)‡	22%	18%	–4% (–12 to 5%)
–Mothers with ≥1 year of schooling	20%	31%	12% (2 to 21%)‡	28%	29%	1% (–8 to 9%)

\*Adjusted for type of family, maternal education, number of children, below poverty, and ethnicity.

†Adjusted for type of family, maternal education, number of children, gender, age in mothers, breastfeeding status, below poverty, and ethnicity.

‡ $P < 0.05$ .

§ $P = 0.10$ .

Increases in antidiarrheals was highest amongst female children (43% vs 38% for males), members of scheduled and other castes, and for children of mother's with <1 year of schooling (43% vs 36%). The use of antibiotics was reported by nearly one-third of caregivers at baseline and endline and did not differ significantly across socioeconomic strata over time. Over the same time period, utilization of other treatment, including unknown powders, pills and syrups, declined significantly over time across all income strata and in particular amongst the least poor individuals.

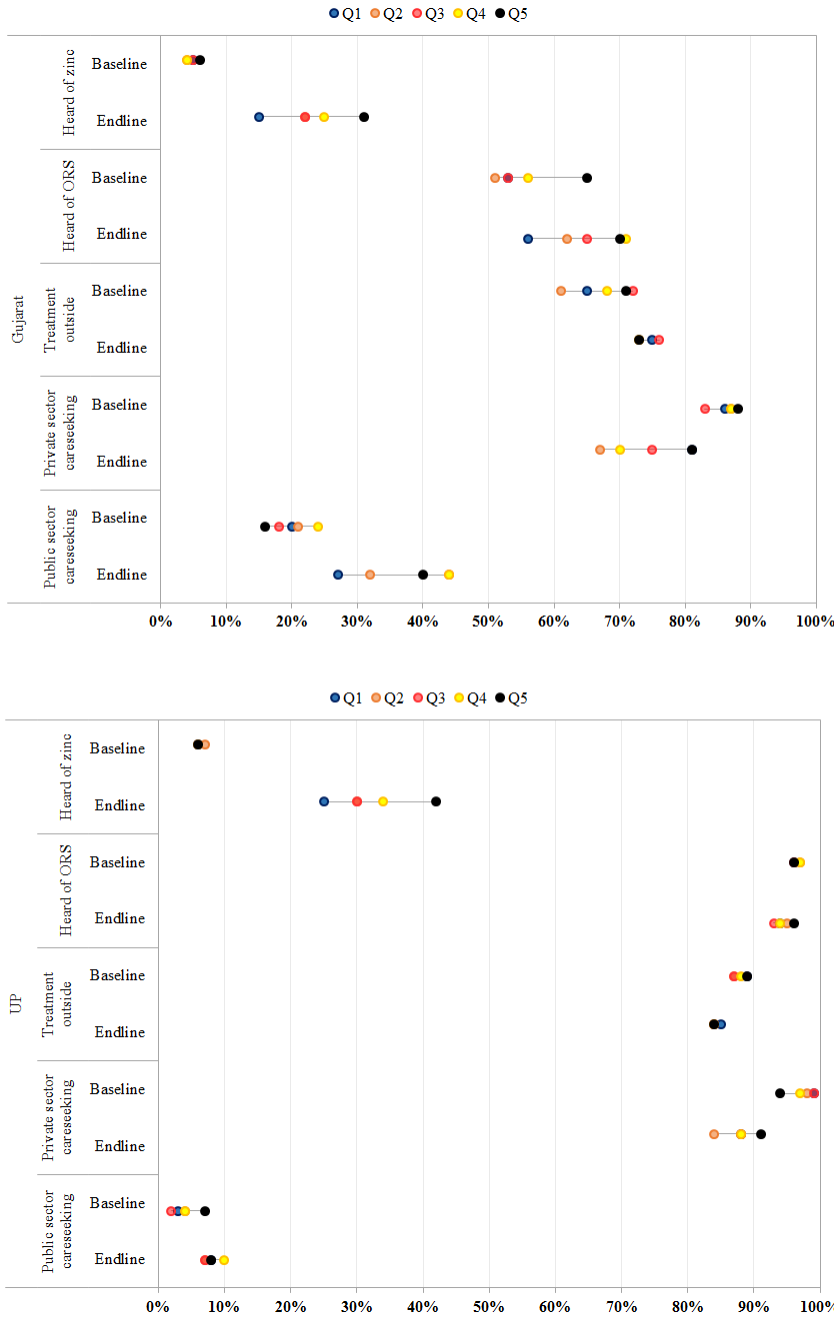
### Treatment among children with severe dehydration and diarrhea

To measure vertical equity and ensure that program activities did not have an adverse effect on the treatment of children with dehydration in addition to diarrhea, we sought to assess changes in ORS use over time in both sites for children with diarrhea alone vs those with dehydration in addition to diarrhea in the preceding 2 weeks (Figure 4). In Gujarat, ORS coverage rates prior to DAZT introduction, were similar for children with diarrhea (16%) and those with dehydration + diarrhea (17%). However, at endline, ORS use increased significantly for children with diarrhea (23%,  $P < 0.001$ ) and those with dehydration + diarrhea (33%,  $P < 0.001$ ). Across socioeconomic strata, the magnitude of increase was highest amongst children in the Q5 income strata in both groups. In UP, ORS use rates for both

children with diarrhea and those with dehydration + diarrhea did not change significantly from baseline to endline across socioeconomic strata.

### Beneficiary costs per patient

Table 3 presents data on the mean out of pocket payments for diarrheal episodes in the preceding 2 weeks in 2014 US dollars by subgroup. In Gujarat, the mean cost among children with diarrhea who sought care declined significantly from US\$ 5.97 to US\$ 4.01 ( $P < 0.001$ ) from baseline to endline and significantly amongst the least poor (–US\$ 4.24,  $P < 0.003$ ). Out of pocket spending was nearly US\$ 1 higher for male children at baseline and US\$ 0.59 at endline. Over time, costs to users declined by a mean of US\$ 2 from baseline to endline, largely as a result of significant reductions in reported wages lost (–US\$ 0.79;  $P < 0.003$ ), and transportation costs (–US\$ 0.44;  $P < 0.00$ ). The magnitude of declines were greatest amongst the least poor for both wages lost (–US\$ 1.57,  $P = 0.005$ ), and transportation (US\$ 0.86,  $P < 0.003$ ) from baseline to endline. Concentration indices similarly suggest a significant pro-rich bias with the greatest reductions in cost occurring amongst the least poor, however, the magnitude of difference across socioeconomic strata decreased at endline. In UP, mean costs for diarrhea treatment among those who sought care did not change significantly over time across socioeconomic strata.



**Figure 3.** Awareness and careseeking for diarrhea in children 2–59 months in Gujarat and Uttar Pradesh (UP), India.

### Diarrhea prevalence

Figure 5 presents data on the differences in the period prevalence of diarrhea in the preceding 24 hours and in the preceding 2 weeks. In Gujarat, the proportion of children with diarrhea in the preceding 24 hours declined significantly across all sub-groups. The magnitude of decline in prevalence in the last 24 hours and 2 weeks was greatest for children in the Q1 and Q2 socioeconomic strata, among the least disadvantaged castes, and with mothers with <1 year of schooling. Despite declines in diarrhea prevalence, concentration indices suggest a pro-poor bias, indicating

higher disease burden amongst the poorest at endline (–0.13, 95% confidence interval (CI) –0.17 to –0.08) vs baseline (–0.04, 95% CI –0.08 to 0.01). In UP, significant declines were observed in the proportion of children with diarrhea in the preceding 2 weeks and 24 hours across all sub-groups, with the exception of the poorest. Concentration indices for diarrhea prevalence in the preceding 2 weeks and 24 hours mirror those for Gujarat and suggest a significant pro-rich bias over time indicating higher disease burden amongst the poorest at endline (–0.01, 95% CI –0.06 to 0.04) vs baseline (0.16, 96% CI 0.12 to 0.20).

**Table 3.** Total costs in USD for diarrhea treatment among those who seek care in the preceding 2 weeks

	GUJARAT (95% CONFIDENCE INTERVAL)			UTTAR PRADESH (95% CONFIDENCE INTERVAL)		
	Baseline (n = 398)	Endline (n = 412)	Endline–Baseline Difference	Baseline (n = 572)	Endline (n = 854)	Endline–Baseline difference
Total cost	5.97	4.01	-1.96 (-3.29 to -0.63)*	4.61	4.99	0.38 (-0.41 to 1.17)
Socioeconomic status:						
–Quintile 1	3.91	3.03	-0.88 (-3.28 to 1.52)	4.83	5.16	0.33 (-1.84 to 2.49)
–Quintile 2	4.55	3.37	-1.17 (-3.61 to 1.26)	3.44	5.11	1.67 (-0.46 to 3.80)
–Quintile 3	7.29	4.05	-3.33 (-5.56 to -0.92)*	5.89	4.3	-1.58 (-3.75 to 0.58)
–Quintile 4	4.25	4.26	0.02 (-2.34 to 2.38)	6.37	6.27	-0.11 (-2.38 to 2.17)
–Quintile 5	8.18	3.94	-4.24 (-7.02 to -1.46)*	4.98	5.77	0.79 (-1.79 to 3.38)
Concentration index	0.10 (-0.00 to 0.19), 0.04 (-0.03 to 0.10)			0.05 (-0.03 to 0.12), 0.07 (0.01 to 0.12)		
Gender:						
–Male	6.46	4.44	-2.01 (-3.54 to -0.49)*	4.38	5.53	1.14 (-0.23 to 2.52)
–Female	5.42	3.85	-1.57 (-3.17 to 0.02)*	4.37	3.48	-0.89 (-2.37 to 0.59)
Ethnicity:						
–Scheduled caste	4.73	4.49	-0.24 (-2.85 to 2.37)	4.86	4.36	-0.50 (-2.19 to 1.19)
–Scheduled tribe	5.83	4.48	-1.36 (-3.32 to 0.60)			
–Other backward caste	5.99	3.12	-2.87 (-4.62 to -1.12)*	4.25	5.19	0.94 (-0.50 to 2.37)
–Other	6.05	4.29	-1.76 (-5.07 to 1.55)	5.29	4.76	-0.54 (-3.07 to 2.00)
Maternal education:						
–Mothers with <1 years of schooling	7.40	4.52	-2.88 (-4.49 to -1.27)*	3.80	4.87	1.07 (-0.29 to 2.43)
–Mothers with ≥1 years of schooling	5.49	4.65	-0.84 (-2.36 to 0.69)	5.87	5.00	-0.87 (-2.38 to 0.64)

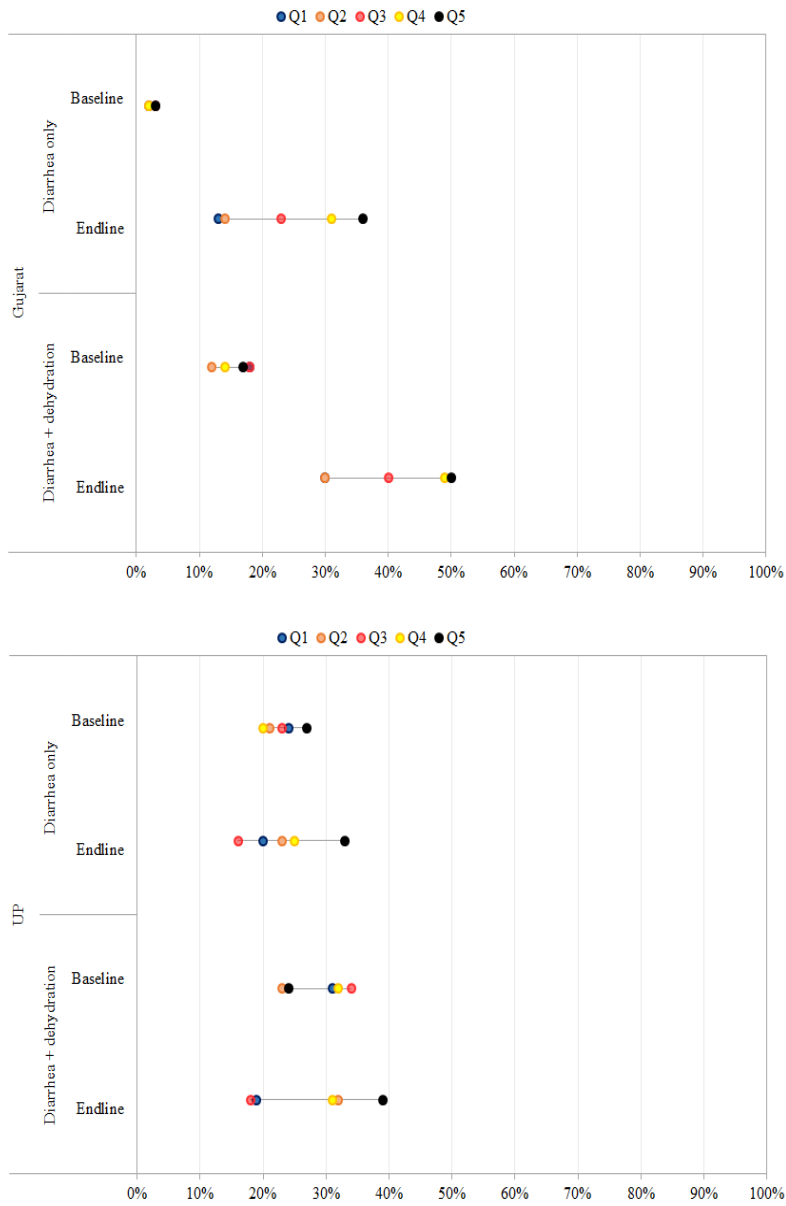
\**P* < 0.05.

## DISCUSSION

Overall study findings suggest that DAZT programmatic activities corresponded to a significant increase in caregiver awareness of zinc in Gujarat (18%, *P* < 0.001) and UP (26%, *P* < 0.001) across all dimensions of equity considered, including socioeconomic strata, gender, ethnicity and caregiver education. Careseeking for diarrhea treatment outside the home did not increase significantly across socioeconomic strata in either state, however, a significant increase was observed in Gujarat for male children, members of other backward castes, and children whose mothers had ≥1 year of schooling. While the private sector constituted over 80% of careseeking in both states, slight declines (~10%) were observed over time coinciding with an increase in public sector utilization (Gujarat: 17% increase from 20%–37%; UP: 4% increase from 4%–8%). Increases in use of zinc, ORS, and zinc+ORS, were only observed in Gujarat despite a longer period of implementation in UP. The magnitude of increase in Gujarat was lowest amongst children in the Q1 and Q2 income strata, female children, members of the scheduled tribe, and children of mothers with <1 year of schooling. Further increases in antibiotic (17–23%) and antidiarrheal (16–24%) use occurred for 4 of 5 socioeconomic strata along with significant increases in the median number of treatments taken. Overall, modest gains in awareness (both sites), and product use (Gujarat only) were disproportionately observed amongst the least poor; suggesting a pro-rich bias and trend towards ‘inverse equity’ reported elsewhere [21].

Study findings fall well beneath the effectiveness of smaller scale efforts to increase zinc and ORS use in Haryana which corresponded to zinc and ORS use in 60% and 59% of diarrhea cases in the preceding 4 weeks after 9 months of implementation [22]. However, findings are similar to those reported from efforts to deliver zinc at scale in Bangladesh through the Scaling Up of Zinc for Young Children (SUZY) Project [23]. SUZY activities in Bangladesh were implemented over a 3-year period (2003–2006) through public and private delivery channels, resulting in increased awareness and zinc use in four populations: city slum, city non-slum, municipal, and rural [23]. Across socioeconomic strata, SUZY activities were similarly associated with a pro-rich bias, reaching a peak of just under 30% among the least poor vs ~7% amongst the poorest at 7–10 months of implementation [23,24]. Amongst the least poor in Gujarat, zinc utilization under DAZT reached a peak of 36% at endline (reflecting a 33% increase from baseline), while ORS use rose from 17% to 50% from baseline to endline. Use rates among the least poor mirror those reported in Bangladesh, suggesting an increase from 2% to 13% from baseline to endline for zinc and 18% to 30% for ORS.

Despite the similarities in the effectiveness of efforts to scale zinc in Bangladesh and Gujarat, programmatic activities in UP did not yield significant improvements in zinc and ORS use. DAZT study findings may be attributed either to a negative confounding due to a worsening of contextual factors or alternatively effect modification [25]. We sought to measure potential confounders and effect modifiers through the household survey as well as efforts during anal-



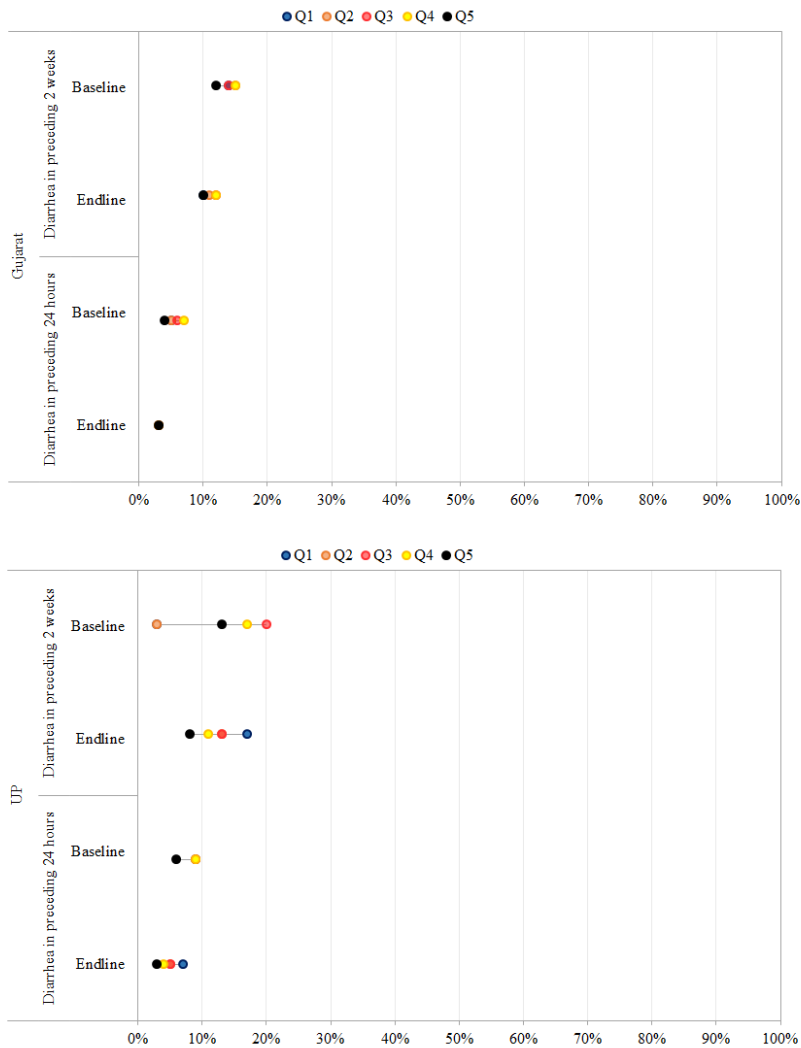
**Figure 4.** ORS use amongst children with diarrhea vs those with dehydration and diarrhea in the preceding 2 weeks at baseline and endline in Gujarat and Uttar Pradesh (UP), India.

ysis to adjust for observed differences in population health status, characteristics, and practices. However, implementation-related effect modifiers were much more challenging to measure and understand, including differences across and within states in the health service characteristics related to supply, availability of human resources, and supervision, as well as the presence of other programs.

In UP and Gujarat, the overwhelming majority of treatment-seeking occurred in the private sector. While private sector engagement has been reported elsewhere in India with much success [22], the scale of prior implementation efforts has been significantly less than that achieved under DAZT. While DAZT programmatic efforts corresponded to the training of thousands of health workers, private sector engagement was not precipitated with a formal census and thus the true de-

nominator from which DAZT-engaged providers were identified remains unknown. Without question, engagement with the private sector is not an easy task – the market is expansive and evolving, and the type and quality of providers varied. However, in the absence of data on the proportion of providers identified, trained, followed-up and prescribing zinc, it remains challenging to ascertain the true supply side coverage of the program. Further challenges associated with village level supply monitoring too hampered efforts to fully capture the depth and breadth of programmatic inputs and their link with outcomes reported here.

DAZT implementation targeted rural areas where access to basic health services as well as adequate water and sanitation facilities were more limited [25]. Even within the rural areas, trends in inverse equity – which postulates that zinc



**Figure 5.** Diarrhea prevalence and incidence in Gujarat and Uttar Pradesh (UP), India.

and ORS uptake would occur first by the wealthiest, leading to increased inequities, before uptake occurs amongst the poorest – were observed [21]. The focus on rural populations limits the generalizability of study findings to other geographic areas and population groups; potentially masking wider disparities likely to occur in more heterogeneous implementation.

There is precedence for our approach to measuring economic poverty through wealth quintiles [7,13,14,25,26]. However, in the case of principal components analyses, the quality of assets are not considered, the first principal component is assumed to be an adequate indicator of socioeconomic status, and ultimately quintiles are produced with variable arrays of asset ownership [14,19,27]. There are further limitations to multiple approaches that operate under an additive assumption [28]. In an effort to address the limitations of measuring equity singularly through the lens of socioeconomic status, we expanded the dimensions assessed to include education, gender, ethnicity and geography, and sought to identify determinants of inequities in

disease burden, careseeking, and practices related to diarrheal diseases. Elsewhere inequities in child health disease burden and management have been reported for gender, ethnicity and education [23,24,29]. Findings from Bangladesh highlighted disparities in the likelihood of receiving zinc based on gender in municipal households (21% for males vs 16% for females,  $P=0.024$ ) [23,24]. Findings from DAZT program activities in Gujarat suggest that overall receipt of zinc is similar for males and female children, however, in the public sector females have a slightly higher use of zinc (33% for women vs 21% for males) and ORS (33% for women vs 29% for males).

An intersectionality perspective would posit that inequities observed are not the result of a single, distinct factor but rather the outcome of the “intersection of different social locations, power relations, and experiences” [28]. Efforts to explore the intersectional inequalities in immunization coverage in India provided important insights into disparities across gender, caste, and place of residence along with wealth [29]. Our inclusion of these parameters and their

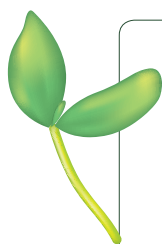
further expansion to include ethnicity and education was intended to provide greater insights into the inequalities observed and generate clearer evidence that can be used to meaningfully intervene and improve programmatic effectiveness [29,30].

Beyond efforts to expand the range of evaluation methods employed and consider alternative underpinning theoretical approaches for assessing inequity, it is worth noting that the metrics for evaluating coverage in diarrheal disease programs can be unforgiving on the program being assessed. The nature of household surveys for diarrhea management necessitates a short recall window of 2 weeks to limit caregiver recall biases. This arguably sets a high programmatic bar to achieve effective product availability and use; requiring adequate product supplies, provider knowledge and willingness to prescribe, coupled with caregiver demand, affordability, and use within the narrow window of time under assessment. The approach adopted by the SUZY program of more frequent cross-sectional surveys may allow for greater insights into ongoing program implementation,

particularly when linked to specific activities (eg, mass media campaigns), while providing insights into variations in coverage over time.

## CONCLUSION

This paper aims to contribute to a growing body of evidence on inequities in child health [7,13,31,32] and in diarrhea [23]. As one of few equity analyses conducted of a diarrhea treatment program at scale, findings provide further evidence suggesting that magnitude of effect observed under efficacy and effectiveness trials wanes as programs are scaled. Inverse inequities in the number of treatments as well as uptake of ORS and zinc were observed in Gujarat, along with increased use of antibiotics and antidiarrheals. If national-level reductions in diarrheal disease burden are to be realized in India, improved understanding of how to optimally increase coverage of zinc and ORS and decrease contraindicated treatments is essential, particularly amongst the poorest [13].



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**Competing interests:** The authors declare that they have no competing interests.

**Authors' contributions:** CFW is the principal investigator of the DAZT Evaluation. AEL and SM are leading economic evaluation activities. CFW led efforts with inputs from ST, SM, LL, and AEL to determine DAZT effectiveness including household and provider surveys. AEL conceived the idea for this paper. AEL and DM conducted the analyses. AEL wrote the first draft of this manuscript with editing and proof reading from all other authors. All authors read and approved the final manuscript.

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