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# Journal of Global Health: The Mission Statement



China managed to reduce its child mortality by two thirds between 1990 and 2006, thus achieving Millennium development Goal 4 nearly a decade before the deadline in 2015 that was suggested by the United Nations. This stunning success, given country's population, was a combined result of economic and social development, clear and progressive health policies, improved nutrition and micronutrient supplementation, development of China's health system, increased coverage and quality of implementation of life–saving interventions such as vaccines and antibiotics.

The *Journal of Global Health* is a peer-reviewed journal published by the Edinburgh University Global Health Society, a not-for-profit organization 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*

# Community–based primary health care: a core strategy for achieving sustainable development goals for health

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A major barrier to the achievement of Millennium Development Goals (MDGs) for reducing maternal and child mortality by three quarters and two–thirds respectively, related to lack of access to care by millions living in abject poverty in rural populations and urban slums [1]. Notwithstanding the challenges, with extraordinary efforts by countries and development partners in the MDG era, child mortality has seen a remarkable decline. Under–five deaths decreased from 12.7 million in 1990 to 5.8 million in 2015 with an increase in the annual rate of under–five mortality reduction from 1.8% over the period 1990–2000 to 3.9% over 2000–2015. However, corresponding progress in reducing neonatal mortality has been less substantial, and the approximate 2.6 million neonates who die every year account for nearly half of all under–five deaths. The annual rate of decrease of neonatal mortality stands at 2.9%, as compared to 4.9% for the 1–59 month age group over this period [2,3].

These gains in global maternal and child health and survival are by no means equal and wide global disparities persist. Sub–Saharan Africa continues to have the highest under–five mortality rate among all regions, with 83 deaths per 1000 live births annually. Although Millennium Development Goal 4 was achieved in some high–mortality countries in Sub–Saharan Africa and South Asia, there are still 58 low– and middle–income countries (LMICs) who are still to reach this target. Barriers to access and equitable care are related to poverty and compounded by lack of trained human resources for health and poorly functional health systems.

In 2015, the world transitioned from the MDGs to the Sustainable Development Goals (SDGs). Although the maternal, neonatal, child and adolescent health issues remain central, the SDGs are all encompassing and the health goal (SDG3) will require close linkages with other contributing SDGs. Although lack of skilled birth attendants and qualified health workers is a large part of the problem, poor health outcomes also related to complex issues such as maternal empowerment, sociocultural taboos, and care–seeking practices and behaviors during pregnancy and child–birth [4]. Given the clustering of maternal and newborn burden of disease in rural settings and among the urban poor we need strategies for promoting community demand as well as appropriate outreach through community health workers and volunteers.

The global evidence base for strategies and interventions for newborn care in community settings has substantially improved, with a range of interventions that can be potentially packaged for delivery at different times during pregnancy, childbirth, and after birth, through various health–care providers, especially community health workers (CHWs). These CHWs were tasked with improving maternal and child health outcomes in a range of research settings and shown to be effective [5]. A fundamental question is whether such concerted interventions especially promotion of behavior–change interventions can be applied in real health systems with busy schedules of health workers and competing priorities. A recent collation of evidence from national programs suggests that this strategy can be effective [6]. Studies evaluating women's groups, frequently supported by community volunteers show consistent benefits on improved maternal and newborn outcomes [7]. These studies also provide strong evidence that community–based

strategies for preventive newborn care substantially improve domiciliary practices, care–seeking patterns, and newborn survival. The case for the scaling–up of strategies for preventive newborn care in community settings with a range of participatory approaches is thus very strong.

Much of the global evidence for community based strategies for care has been collated in systematic reviews with an undue reliance on randomized controlled trials [8]. This supplement collates a vast amount of information from community–based studies of strategies and programs to improve maternal and child health and immunization outcomes, and enhances the evidence in several ways. Dr Perry and colleagues painstakingly collected and reviewed a large body of information from almost 700 reports and studies exploring various aspects of the cumulative experience of community based primary health care globally [9]. The studies comprise of a vast amount of information and while systematic meta–analyses were not performed, the narrative reports demonstrate the effectiveness of various approaches undertaken in disparate geographies and socio–economic settings. These findings are consonant with the findings from a review of community based approaches for primary health care almost a decade ago [10] and the recent evidence synthesis undertaken by the Disease Control Priorities project.

As we move toward accelerating action for achieving the SDGs, the role of community based platforms will become more important. These strategies are needed to ensure that several of the key themes of the SDGs such as reducing inequities and reaching marginalized populations, are achieved within the next 15 years. Some 40 years following the Alma Ata declaration of "health for all", this might yet become a reality.

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# Africa

▶▶ New regional health centers, the Africa Centres for Disease Control and Prevention, will be set up across Africa to tackle health threats. These Centres will partner with the US, EU and China, with technical advice from the WHO. The announcement was made at February's summit of the African Union (AU) in Addis Ababa, Ethiopia, alongside a commitment to make immunisation available across the continent by 2020. Currently, 1 in 5 children in Africa are without access to basic immunisation, while conflict states have experienced a resurgence in diseases like polio. Although immunisation has increased in Africa over the past 15 years, Africa is falling behind on vaccination targets, hampered by hot climates, unreliable electricity, and supply shortages. Fewer than 20 countries fund more than 50% of their immunisation programmes, but as more countries approach middle–income status they will become ineligible for GAVI support for their immunisation programmes. Dr Ngozi Okonjo–Iweala, the chair of GAVI, commended the AU's leadership, and called for sustainable immunisation financing. "Immunisation is one of the smartest investments a country can make in its future. When our children are healthy, our families, communities and countries thrive," said Yifru Berhan Mitke, Ethiopia's health minister. (*The Guardian*, 1 February 2017)

▶▶ In South Africa, miner Bongani Nkala and 55 others have brought a class action against 32 of the world's largest gold mining companies, seeking compensation for up to 500 000 miners who may have contracted silicosis and tuberculosis while working underground. One estimate of the total compensation due is US$ 3.25 billion. Silicosis is an incurable disease caused by inhaling silica particles, and is also a strong risk factor for tuberculosis. In 2016, South Africa's Supreme Court ruled that their application – the largest class action in South Africa's history, and the first concerning an employer exposing workers to harmful quantities of dust underground – could proceed, although the 32 companies are seeking leave to apply and hence delay any compensation payments. The companies are also petitioning against the transferability of compensation from deceased miners to their spouses and families. There are concerns that the appeals process could continue for another 18 months – when many of the claimants are seriously ill and elderly. For the past 100 years, the problem of miners suffering from lung diseases went ignored and uncompensated, and under apartheid was systematically under–reported. Moreover, in order to qualify for compensation, a miner's lung function must be impaired by more than 10%, leading to many cases being rejected – and death certificates recording tuberculosis often missed the underlying cause of silicosis. (*Daily Maverick*, 2 March 2017)

▶▶ By early April, 4637 cases of cerebrospinal meningitis were recorded across Nigeria, killing at least 489 people. This announcement was made at an emergency meeting of northern state governors and traditional rulers, by the country's health minister, Mr Isaac Adewole. Mr Adewole confirmed that so far 823 000 doses of the conjugated Type C vaccine had been delivered to the Federal Government by the UK government, and UNICEF had delivered over 1 million Type A vaccines. He also confirmed that the Federal Government would spend US$ 1 billion to procure vaccines to eradicate meningitis in the 5 most affected states in North Nigeria. He highlighted how the federal government had collaborated with state governments and aid organisations to tackle the outbreak across 26 states, and called for traditional rulers to spread the message on prevention, plus for more investment in health systems at the state level to tackle health challenges. He also called for corruption to be tackled to ensure that funds are properly utilized. (*Premium Times*, 11 April 2017)

▶▶ As countries in Africa urbanise, disease patterns change and more people can afford health care or health insurance, bringing opportunities for private companies. Africa's disease pattern is moving from infectious diseases toward non–communicable diseases, and the WHO estimates that 1 million people will die of cancer each year in Africa by 2030. Moreover, the IFC (the private–sector arm of the World Bank) estimated that US$ 25–30 billion of investment will be required in health care infrastructure up to 2022. These trends are an opportunity for private companies, as African health care systems are generally developing from a low base. GE Healthcare Africa has adapted its business model toward developing innovative financing and training practitioners, and by public–private partnerships to supply equipment. Private equity firms are also investing in African health care companies, eg, Investment Funds for Health in Africa has invested in 12 companies covering care delivery, medical supplies and distribution, plus hospitals and private clinics. In addition, the Egyptian conglomerate the Mansour Group, are consider-

ing expanding into health care. "Nigeria has almost 200 million inhabitants and they have four MRI machines. It doesn't take rocket science to see the opportunity," says Mohamed Mansour, group chairman. (*Financial Times*, 10 May 2017)

▶▶ Biovac, a South African company, and PATH [a global health, non–profit organization] will develop a new vaccine against Group B Streptococcus (GBS) – one of the leading causes of infections in infants. This partnership with PATH, funded by the Bill and Melinda Gates Foundation, makes Biovac one of only 3 companies working on a conjugate vaccine against streptococcus – and the only one in a developing country. South Africa has one of the world's highest incidences of streptococcus infections – up to 3 in every 1000 live births – and deaths can occur in up to 4% of infections, and survivors can face life–long impairments, such as blindness and developmental impairments. Streptococcus can affect all age groups, but newborns are particularly vulnerable because of their immature immune systems. Infections can be prevented by antibiotic treatment given to pregnant women, but this is not available is most resource–limited countries, and is less effective against late–onset GBS. According to Biovac's CEO, Dr Morena 'Makhoana, this is an opportunity for Biovac to not only be a manufacturer but "a true developer of novel vaccines aimed at African and developing–world diseases." (*Daily Trust*, 19 May 2017)

# ▶ Asia

▶▶ According to researchers from Imperial College London, South Korea is set to have the longest life expectancy by 2030, overtaking the current holder, Japan. The average lifespan of Japanese women is forecast to be overtaken by South Korea and France, while Japanese men will drop from 4th to 11th place in the global rankings. South Korean women will be the first to have an average life expectancy of more than 90 years, and men will have an average life expectancy of 84 years. The study authors believe that these developments are mainly due to investments in universal health care, education, childhood nutrition and the rapid scale–up of new medical technologies, underpinned by lower body–mass indices and blood pressure. This highlights South Korea's remarkable transformation from an impoverished, war–torn country 60 years ago into today's modern, technologically–advanced powerhouse. However, a note of caution in interpreting these figures was sounded by Prof Park Eun–cheol, who highlighted that the country's low fertility rate means a very low incidence of child mortality, which affects life expectancy calculations. In addition, nearly 50% of South Koreans aged 65 years or above live in poverty – the highest rate in the OECD. (*Financial Times*, 22 February 2017)

▶▶ After no indigenous cases of malaria for the past 3 years, Sri Lanka was declared malaria–free by the World Health Organization – bringing the number of cases from 264 549 in 1999 to 0 in November 2012. Sri Lanka joins 17 countries that have eliminated malaria, and India plans to join this group by 2030 – in India, 1.06 million people were infected by malaria in 2015, with 242 confirmed deaths. Sri Lanka deployed various tools in its fight against malaria, such as: web–based surveillance, including testing all fever cases for malaria, and monitoring travelers from countries with malaria–transmission; a 24–hour telephone helpline to notify, track and treat malaria patients in isolation to halt the spread of infection; changing emphasis from mosquito–control to parasite control; strengthening public health systems, improved sanitation and transport infrastructure to make health care more accessible; and working in partnership with other stakeholders on disease surveillance, and social, technical and financial support for malaria eradication. (*Hindustan Times*, 5 May 2017)

▶▶ Bangladesh has approved construction of a giant coal–fired power station, and the environmental campaigning organization Greenpeace warns that it could worsen air pollution for millions of people, and cause the early deaths of 6000 people over its lifetime. The plant will be erected on the edge of the world's largest mangrove forest, also threatening the area's fragile ecosystem, as the forest is a barrier against storm surges and cyclones – and violent weather patterns have killed thousands of people in the area. Greenpeace also warns that the plant could render fish unsafe to eat for millions across the Bay of Bengal due to mercury deposits, and devastate the aquatic food chain, as it is projected to discharge nearly 125 000m³ of waste–water into nearby water catchments. Mr Sheikh Hasina, Bangladesh's Prime Minister, defended the project and rejected concerns as being politically motivated. However, it has galvanised street protests in Bangladesh, with campaigners calling for the plan to be scrapped or relocated. (*Arab News*, 5 May 2017)

▸▸ Laos held its first National Conference on Family Planning, as part of its strategy to move away from Least Developed Country Status by 2020. The conference's theme was "investing in family planning for economic prosperity", and was supported by the UN Population Fund. Despite Laos's progress in reducing maternal mortality and improving access to contraception, its rate of maternal deaths remains high (206 per 100 000 births), with correspondingly high levels of teenage pregnancies. Contraceptive use stands at 50%, and 20% of all family planning needs are unmet – with rates much higher in some remote areas. The Laotian government plans to spend US$ 15 million over the next 4 years, focusing on promoting long–acting reversible contraception, increasing the number of midwives, improving capacity at health centers, and campaigns aimed at young people. According to the UN Population Fund's representative, Frederika Meijer, the conference represented a shift from viewing contraception as merely a way of limiting population, toward viewing it as a way of saving lives, and improving quality of life, economic prosperity and development. (*News Deeply*, 19 May 2017)

▸▸ In the first cross–border civilian exchanges since North Korea's 4th nuclear test in 2016, South Korea will allow a civic group to contact North Korea to help fight malaria. The announcement signaled that South Korea's new government may try to re–start civilian aid and exchange programmes as part of improving tense relationships between the countries. The civic group will have email contact with North Korea to offer insecticides, diagnostic kits, mosquito repellants and nets – the first time the group had sent such supplies since 2011. According to the World Health Organization, North Korea had 7010 malaria cases in 2015, compared to 21 850 in 2012, partly due to international anti–malaria aid programmes. Malaria in North Korea's southern–most regions is also a risk for South Korea, as mosquitoes can readily cross the heavily–fortified border. (*ABC News*, 26 May 2017))

# ▸ Australia and Western Pacific

▸▸ Australia was the first country to introduce mandatory plain packaging for tobacco products, and plans to increase tobacco taxes until a packet of cigarettes costs US$ 40. Some Australian states have also introduced stringent anti–smoking measures, such as prohibiting smoking with 10m of a playground, or 4m from the entrance to a public building, and banning smoking on many beaches. This measures are enforced by heavy fines in many places. These measures, combined with anti-smoking campaigns, have caused smoking rates to fall by almost 50% since 1980 – in Australia, the smoking rate is 13% compared to a global average of 20%, and there has been a 23% decrease in hospital admissions for smoking–related illnesses. The Australian government has committed to reducing the percentage of adult smokers to 10%, and Tasmania is discussing a bill to outlaw smoking for those born after 2000. A "culture of shame" around smoking is beginning to emerge in Australia, which also acts as a deterrent. However, smoking is mainly taken up by the poorest in Australia society, so the trend to stigmatise smoking may add a burden of shame to those who are already marginalised. (*BBC*, 30 January 2017)

▸▸ Australia's mosquito–borne Ross River virus (RRV) – the country's most common mosquito–borne disease– was reported in higher numbers in 2016 due to unusually wet weather – and could become a global epidemic. Previously, RRV was believed to be confined to Australia and Papua New Guinea, but there is evidence that it may have spread overseas, with some cases being reported in the South Pacific. This was uncovered when travelers to the South Pacific were infected with RRV despite never visiting Australia or Papua New Guinea – and contrary to the earlier belief that RRV was only transmitted via marsupials, thus self–limiting itself to Australia and Papua New Guinea. This has caused concerns that the virus is self–sustaining, and could become global. RRV is not a deadly disease, but it can be difficult to diagnose as its symptoms are very general (including swollen joints, fever, fatigue and pain), and in 2016 more than 3500 Australians were infected. (*Xinhua*, 23 February 2017)

▸▸ According to a nationwide survey, 1–in–6 unvaccinated children in Australia have been denied treatment because their immunisations were not up–to–date. The findings came from the Melbourne Royal Children's Hospital Child Health Poll, which surveyed nearly 2000 parents of 3500 children. The vast majority of the parents surveyed had their children fully immunised, with 6% were being selectively unvaccinated, and only 1% completely unvaccinated. Federal Health Minister Greg Hunt will refer the findings about care refusal to the Australian Health Practitioners' Regulatory Agency for further investigation.

The President of the Australian Medical Association, Michael Gannon, emphasized that refusing care to anyone, particularly children who cannot choose their immunisation status, was unethical. "No matter what reservations an individual doctor might have, it's not ethical to deny care to an unvaccinated child," he said, although he recognized that individual doctors may need to vary their practice depending on risks to other patients, eg, a child with measles could infect other children in the waiting room. (*Sydney Morning Herald*, 7 March 2017)

▶▶ The Federated States of Micronesia, the Marshall Islands and the Republic of Palau are covered by the Compact of Free Association (COFA) agreements, which puts them under the protection of the US Government. This entitles citizens of these countries to live and work in the USA and currently 6500 people from these nations live in Washington DC, but they currently do not qualify for Medicaid. These nations were the site of more than 60 nuclear tests carried out by the USA between 1946 and 1958, and these tests still adversely affect their citizens' health today. However, a bill is being passed that would help Washington's COFA citizens to pay for insurance under the state health insurance exchange, and would allocate US$ 3.9 million over the next three years to support it. To qualify, a COFA islander has to live in Washington, earn up to 133% of the federal poverty level, and be ineligible for any other state or federal benefits, including Medicaid. Washington State would be required to set up enrolment procedures at the state health insurance exchange, and carry out public outreach. (*Seattle Globalist*, 8 March 2017)

▶▶ There have been a few cases of newborn hemorrhagic disease, caused by a Vitamin K deficiency, due to parents refusing the routine post–birth Vitamin K injection for their babies. Up until the early 1970s, the disease killed 15 newborn babies each year in New South Wales, but the introduction of routine Vitamin K injections at birth virtually eliminated it. However, one baby died in 2013 and another in 2012, and pediatricians have reported regularly having to convince parents to get the Vitamin K shot. It appears that the home–birth and anti–vaccination movement are often involved in falsely persuading parents of the dangers of the Vitamin K injection. (*The Mercury*, 11 March 2017)

# ▶ China

▶▶ A variety of *E coli* bacteria in China has recently evolved resistance to colistin, a key antibiotic of last resort. The gene conferring resistance, mcr–1, was found in 1% of *E coli* bacteria and 1% of *Klebsiella pneumonia* bacteria, which can cause pneumonia, and blood and wound infections. The mcr–1 gene moves easily from host to host, and also across types, eg, *E. coli* and *Klebsiella*. In many countries, the use of colistin is reserved for human use, and in emergencies only. However, it is widely used in China for agricultural purposes, eg, fattening farm animals. China will ban the use of colistin in agriculture from 1 April, licensing it for human use only to deal with the spread of other superbugs in China. It will be required to deal with China's problem of carbapenem–resistant *Enterbacteriaceae* – gut bacteria which are not susceptible to the key antibiotic group of carbapenems. There is a danger than resistance to colistin and carbapenem may converge – although it appears not yet to be a significant problem in China – and that standard medical procedures could become too dangerous to perform. (*Scientific American*, 27 January 2017)

▶▶ China's plan to increase the number of doctors by nearly 40% over the next 5 years is threatened by medical graduates choosing other professions. China needs to rely more on general practitioners, or family doctors, to relieve the pressure placed on underfunded public hospitals from an aging population and the increasing burden of non–communicable diseases such as diabetes. Moreover, the State Council's plan to increase average life expectancy also includes plans for more doctors, and China will need an estimated 140 000 additional obstetricians and midwives after it scrapped its one–child policy to allow couples to have two children. But it may be difficult to recruit doctors in sufficient numbers, as the total number of doctors rose by just 750 000 from 2005–2015, while China produced 4.7 million medical graduates. Low salaries are one factor behind this leakage, as the average doctor's salary is US$ 720/month; another factor is overwork, as doctors will often see up to 12 patients per hour, and can be attacked by patients and their families who are frustrated over medical care. The shortage is particularly acute in the countryside, with a shortfall of 500 000 doctors, and in certain specialties such as pediatrics. (*Financial Times*, 19 January 2017)

▶▶ China has established its first big data research centre for children's health, to improve the health of the country's children by developing a more complete health system for children, focusing on disease

prevention, diagnosis and personalised treatment. It was established by Wuhan University and a Beijing technology firm in central China's Hubei province, and to date has collected information on more than 200 000 children in 70 hospitals across 7 provinces, expanding to 300 hospitals by 2017 and 1000 by 2020. The research centre plans to develop into a national cloud platform for children's health information, offering standards on personalised medical care and clinical treatment. (*Xinhua*, 11 March 2017)

▶▶ China has already experienced remarkable progress in lifting people from poverty – 800 million people over the past 35 years, and the country's government has pledged to effectively eradicate rural poverty by 2020, moving 45 million people above the rural poverty line of US$ 324 per year (ie, the average income of the poorest 5% of rural households, which compares to US$ 1128 for urban households). In recent years, the pace of poverty reduction in China has slowed, from 26 million people a year up to 2000, to 22 million a year from 2000–15. The government now has a target of lifting 10 million people from poverty each year. As the rate of poverty reduction has slowed, its costs have risen – in 2000, it cost approximately US$ 48 per year to lift a person out of poverty, and by 2010 this increased to US$ 150 per year. This illustrates how the people who benefit most from poverty reduction are generally those who are best equipped to do so – those who are left behind are generally harder to reach, and may lack access to roads, electricity and clean water. The cost of lifting those still below the rural poverty line out of poverty is more than US$ 200 a year. However, in 2016 the government exceed its annual target, as 12.4 million rural people left poverty, and its 2017 budget is 30% larger, meaning that at least US$ 1000 has been allocated for each person the government plans to lift out of poverty in 2017. (*Project Syndicate*, 28 March 2017)

▶▶ Yi Fuxian, a demographer working at the University of Wisconsin–Madison, has claimed that Chinese statisticians have overestimated the country's population by 90 million, partly by inflating fertility rates, and that India may have overtaken China as the world's most populous country. He estimates that China's population is 1.29 billion, compared to the government's estimate of 1.38 billion, while India's population is 1.32 billion. This claim was disputed by other demographers, while still accepting the country's very low–birth rate, counter–argue that the government's figures are correct. India's demographers also accept that China has a higher population, but predict that India will overtaken China by 2025. Wang Feng, a demographer at the University of California, dismissed Yi Fuxian's claims; although he believes that the government may have slightly overestimated the country's population, the error is much less than 90 million people. "That is two Spains. It's not possible to be off by that much. That's like one of China's largest provinces not being there," he commented. (*The Guardian*, 24 May 2017)

# ▶ Europe

▶▶ Several countries in Europe, including Switzerland, the Netherlands, Germany, Denmark and Spain, provide "fixing rooms" where users of hard drugs can take drugs under medical supervision, and with clean equipment. Although there are concerns that these facilities could encourage illegal drug use, the managers believe that they prevent drug users from publicly consuming drugs, and prevent fatal drug overdoses. The Skyen facility in Denmark provides harm reduction services, and will support users in cutting down or stopping their drug consumption, if desired. Other countries are following this initiative, with a hospital in Paris housing France's first "fixing room", and Glasgow is planning to open the UK's first "fixing room", looking to countries such as Denmark for inspiration. (*BBC*, 10 Jan 2016)

▶▶ The UK's health secretary, Jeremy Hunt, confirmed that he did not expect the UK to remain within the European Medicines' Agency (EMA) when the UK leaves the EU ("Brexit"). The former UK pharmaceutical regulator, Sir Alasdair Breckenridge, has warned this may led to delays in UK patients getting new drugs, including cancer drugs. The EMA authorises drugs for use across the EU, and companies may be slower in seeking permission in the UK alone if they need to pay for a separate assessment for their product, and the UK market is small compared to the EU. Jeremy Hunt is "hopeful" that the UK can work closely with the EMA, but David Jeffreys, the vice–president of Eisai – a Japanese pharmaceutical company – warns that UK patients could face delays of up to 2 years as the early innovations system will apply first in USA, Japan and the EU. He calls for a co–operation deal with the EMA, although there are risks that the issue may be absorbed into a wider debate on trade terms. A spokeswoman for the UK's Department of Health said

that ensuring the timely access to safe and effective medicines is a priority, and that Brexit is an opportunity to give even faster access to pharmaceutical innovations. (*BBC*, 10 February 2017)

▶▶ With the death of Prof Hans Rosling of the Karolinska Institute and co–founder of Gapminder, the world has lost a unique statistician, global health champion and communicator. The best way to remember Hans Rosling and champion his legacy is to keep push his key messages. His first message is that the world is evolving, and so should our perceptions on countries' places on development pathways. We should ask more questions, and look for answers in evidence–based facts. Second, knowing the past makes it easier to believe in the future, as we grasp humanity's progress in reducing poverty. Third, the rise of populism makes it even more vital to be vigilant and hold politicians accountable for the factual basis for their policy–making. Fourthly, we must share and apply scientific knowledge, especially in new and engaging ways, to make changes. And lastly, we must continue to "close the gap" between the message of statistics and our perceptions of the world. (*Huffington Post*, 17 February 2017)

▶▶ The Netherlands Minister for Foreign Trade and Development Co–operation launched the "She Decides" fund for family planning, to counter the US government's "global gag rule", which prevents non–US NGOs from providing services or information which relate to abortion (including counselling and legal advice), from receiving US government funding for any of their activities. Countries including Sweden, Belgium, Canada, the Netherlands, Finland, Denmark, Australia, Norway and Luxembourg have pledged more than US$ 110 million to the fund, with an additional US$ 20 million from the Bill and Melinda Gates Foundation, and US$ 50 million from an anonymous donor and US$ 10 million from Sir Christopher Hohn. The US application of the "global gag rule" could result in the loss of at least US$ 600 million of US funding, and some agencies believe its overall impact could be US$ 9.5 billion on issues such as HIV, maternal health and vaccinations. According to Alexander De Croo, Belgium's Minister of Development Co–operation, the Sustainable Development Goals could not be achieved without sufficient access to family planning. "We cannot accept that the purely ideological decision of one country … would push millions of women and girls back into the dark ages. We will lead with our actions," he said. (*Devex*, 2 March 2017)

▶▶ Nestlé will remove 10% of sugar from its confectionery products sold in the UK and Republic of Ireland – equivalent to 7500 tonnes each year. The move, following the possibility of a tax on sugary drinks, will lead to Nestlé replacing sugar with higher quantities of existing ingredients, and/or reducing product sizes. It may also involve the company's touted "scientific breakthrough", in which it claims to found a way to re–structure sugar, enabling it to reduce sugar content by up to 40%. Public Health England welcomed the announcement. "Nestlé is the latest household name to commit to making everyday products healthier, and we're delighted that this is just the start of its efforts. This sends a clear message that reducing sugar in food is possible, even in products that are typically harder to reformulate," says Duncan Selbie, the chief executive of Public Health England. (*The Guardian*, 7 March 2017)

# ▶ India

▶▶ According to the National Family Health Survey, the lack of quality neonatal care, especially in rural areas, is the main reason behind India's high neonatal mortality rate. The neonatal mortality rate in urban areas is 29 per 1000 live births, compared to 41 per 1000 live births in rural areas – a total of 650 000 deaths each year. The main causes of death are premature births, infections and asphyxia, and many premature babies who survive suffer from disabilities including cerebral palsy, learning disabilities and respiratory conditions, resulting in physical, psychological and economic stress to the individual and their families. There is a severe shortage of neonatal intensive care units across India, Bhupendra Avasthi of the Surya Mother and Child Hospital, calls for public–private partnerships to set up more neonatal intensive care units in in rural and urban areas. (*Times of India*, 27 March 2017)

▶▶ Attempted suicide and "any act towards the commission" of suicide were repealed as criminal acts by India's government in March 2017. These measures are part of a wider package of mental health reforms, which declares psychiatric care to be a right for all Indian people, along with increased funding. Before the repeal, people who attempted suicide faced a fine and imprisonment rather than support, while their families often had to pay bribes to avoid prosecution; and officials used the attempted suicide laws to lock

up protesters who staged hunger strikes. India's suicide rate is almost double that of the USA's, and it lacks a suicide prevention plan; and measures such as limiting access to poison and tackling the taboos which prevent depressed people from opening up to friends and doctors could help. However, the main challenge lies in improving the lives of young people, where suicide is the leading cause of death, and the suicide rate for women aged 15–29 is more than double that of any other country except Surename. (*Economist*, 30 March 2017)

▶▶ The WHO confirmed that India has eliminated visceral leishmaniasis (also known as kala azar) in 82% of its sub–districts in 2015. The WHO also noted that Bangladesh achieved elimination in 97% of its sub–districts, and 100% of Nepal's sub–districts achieved elimination. The importance of protection against financial risk was also highlighted by the WHO, as 25–75% of households in India, Bangladesh, Nepal and Sudan where some–one is affected by visceral leishmaniasis face some form of financial difficulties in obtaining diagnosis and treatment, even if diagnosis is free. Yaws were also eliminated in India, and the discontinuation of India's Mass Drug Administration programme for lymphatic filariasis must be carefully monitored, while ensuring that de–worming coverage is maintained. The WHO recognizes that India has made significant progress against lymphatic filariasis in 72 sub–districts. India is among the countries with the highest prevalence of neglected tropical diseases (others include Brazil, China, Indonesia and Nigeria), and that 960 million of the 1.59 billion people requiring treatment for these diseases live in lower–middle rather than low–income countries. (*Live Mint*, 20 April 2017)

▶▶ In an attempt to reduce alcohol–related road accidents, India has banned the sale of alcohol within 500m of national and state highlights – a decision that affects shops selling alcohol, bars, restaurants and hotels. Binge drinking, with its resultant social and health problems are a large concern in India, where male drinkers aged over 15 years drank an average of 32.1 L of pure alcohol in 2010, 77% higher than the USA. Road deaths in India are also high, with 146 133 people killed in 2015. Many states ban alcohol entirely, while others are considering the move. The increasing restrictions on alcohol consumption have raised concerns among the drinks industry, who have been investing heavily in India, thanks to its large middle class and its status as the world's largest whisky market by volume. The ban on sales near highways could severely affect tourist areas, eg, 85% of Goa's alcohol shops could close or be forced to move. However, some states and shops are taking steps to circumvent the ban: states which rely on alcohol tax revenues have moved to reclassify highways as roads; and there are reports of shops moving their entrances to force people to travel more than 500m from the highway to enter them. (*Wall Street Journal*, 24 April 2017)

▶▶ According to the latest Global Burden of Disease study, published in *The Lancet*, India continues to perform poorly, ranking at 154 in the study's index of the quality and accessibility of health care, behind countries such as China, Sri Lanka and Bangladesh. Despite India's economic growth, it is failing to meet its health care goals and the gap between its actual and predicted score has widened over the past 25 years. Despite some gains, India performed worse than expected in tuberculosis, diabetes, rheumatic heart disease and chronic kidney disease. More broadly, the study also highlights inequalities in health care access and quality among countries at similar development levels, with China's score of 74, ranking ahead of India's score of 44.8, Sri Lanka scores 73, and Brazil and Bangladesh score 65 and 52 respectively. However, India is slightly ahead of Pakistan, at 43. (*Times of India*, 19 May 2017)

# ▶ The Americas

▶▶ Mayors across the USA have written to Congress on the effects of repealing the Affordable Care Act (ACA, or "Obamacare"), noting that it will be mainly felt at local level. The letter gathered more than 130 bi–partisan signatures, and calls for key provisions within ACA to be retained. These provisions include: insuring children up to the age of 26 years; eliminating lifetime and annual limits; assuring eligibility for insurance coverage even with pre–existing conditions; guaranteeing coverage for pregnancy and breast cancer screening; and providing coverage for preventive services at no additional cost. Martin Welsh, the Mayor of Boston and Chair of the US Conferences of Mayors Health Standing Committee, states that "health is not a privilege, it is a human rights. I am proud that mayors across the country are standing up in a bipartisan effort to improve the ACA, not repeal it." (*Cities Today*, 24 February 2017)

▶▶ Hot tropical air is getting trapped in the narrow concrete alleys in many Latin American cities, causing stifling conditions and potential health problems. It increases the risk of mosquito–borne diseases,

heat exhaustion, stress, and respiratory and cardiovascular conditions – and people suffering from conditions such as heart disease or hypertension are more prone to related complications. Poorer people are at increased risk from these heatwaves, as they may have inadequate water supplies or be further from hospitals. As well as the health impact, stifling air can worsen pollution, boost energy consumption and potentially curb economic activity. The problem of temperate spikes is caused by haphazard urban development, and the heat generated by cars, factories and buildings leading to "urban heat islands". Temperature differentials are greater at night – when stagnant warm air becomes trapped – and may only be a few °C in some areas, but can differ by up to 20°C in others. Initially, urban heat islands were mainly a problem of megacities such as Mexico City and Rio de Janerio, but are rapidly spreading to other cities such as Santiago, Lima and Buenos Aires, and a 2015 study shows an increasing incidence of urban heat islands, coupled with a decline in city winds – and urban temperatures are rising more quickly than global temperatures. Changing building design and materials, improving airflows and planting trees may provide some relief to cities and their inhabitants, and in the longer–term changing the positioning of buildings, providing more green space, and promoting public transport over cars will decrease heat generation and improve air flow. (*Reuters*, 15 February 2017)

▶▶ The WHO confirmed that trachoma has been eliminated as public health problem in Mexico, making it the first country in the Americas (and the third globally, after Morocco and Oman) to eliminate the disease. Trachoma is transmitted by contact with eye bacteria and nasal discharges of infected people, and globally it is the main infectious cause of blindness. In Mexico, trachoma was endemic in 246 communities in the state of Chiapas, affecting over 146 000 people. Action to combat the disease were strengthened in 2004 with the creation of the Trachoma Prevention and Control Program, and strengthening the WHO SAFE strategy (a package of interventions including surgery for advanced cases, antibiotics, and hygiene and environmental improvement measures). Groups of doctors, nurses and technicians worked locally to reduce the number of cases from 1794 in 2004 to none in 2016, allowing Mexico to meet the criteria for elimination of trachoma as a public health threat. To prevent resurgence and maintain elimination, PAHO/WHO recommends continuous monitoring and care delivery to affected patients. (*Outbreak News*, 24 April 2017)

▶▶ With medicine shortages and escalating rates of malnutrition, Venezuela's child mortality rate rose by 30% in 2016, and more than 11 000 babies died. The head of the country's Ministry of Health was fired after these statistics were published. According to the Catholic aid agency, Caritas, child hunger is a "humanitarian crisis" in parts of Venezuela, with 11.4% of children aged under 5 suffering from severe or acute malnutrition, and 48% "at risk" of going hungry. A recent survey of 6500 families found that 75% of adults lost an average of 19 lb [8.6 kg] in 2016 – highly unusual outside of a war zone or an area hit by natural disasters. This crisis is largely man–made; with cash shortages and increasing debts, the government has cut back sharply on food imports. Despite ample fertile land, sunshine, water and cheap fuel, Venezuela's farmers are unable to make up the shortfall, due to the country's highly–inefficient system of agricultural production, with the government acting as producer, processor and distributor. Farmers lack sufficient hard currency to buy imported feed, fertilizers and spare parts, and the domestic production of rice, corn and coffee have fallen by at least 60% in the past decade. Venezuela's currency, the bolivar, has lost 99% of its value in the past 5 years, meaning that a bag of rice worth US$ 1 sells for 6000 bolivars – about a day's wages for the average worker. Farmers are only able to stay in business by breaking the law and selling at market prices, and also face extortions from criminal gangs, demanding money for "protection". (*Washington Post*, 22 May 2017)

▶▶ According to a report by Save the Children, all 10 countries with the highest child homicide rates are in Latin America and the Caribbean, with Honduras having the highest rate. This is fostered by increases in violent criminal activity across the region, which also jeopardises children's schooling and future prospects. Save the Children ranked countries based on indicators on child health, education, labour, marriage, childbirth and violence. The USA ranked relatively poorly, due to wide disparities between states on high–school dropout rates, food insecurity, rates of teenage pregnancies – and in 2015, 5000 children were murdered or committed suicide. "Children have the right to survival, food and nutrition, health and shelter. They also have the right to be encouraged and educated, both formally and informally. And they have the right to live free from fear, safe from violence and protected from abuse and exploitation," said Save the Children. (*NBC News*, 31 May 2017)

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# ▶ The Bill and Melinda Gates Foundation

▶▶ In a *Project Syndicate* article, Bjørn Lomborg praised the Bill and Melinda Gates Foundation's strategy of focusing on three specific investment areas (vaccination, contraception and nutrition), all of which generate high returns. Eg, expanding vaccination programmes by US$ 1 billion/y to prevent childhood pneumonia and diarrhea would save 1 million lives each year, with each US$ 1 invested generating US$ 60 of human welfare. Likewise, achieving near–universal access to contraception would prevent 150 000 maternal deaths and 600 000 children from being orphaned, with a resultant boost to economic growth from the demographic dividend – generating US$ 120 for every US$ 1 invested. And improving children's nutrition in the first 1000 days of life can return benefits of US$ 45 per US$ 1 spent, rising to US$ 166 in some countries. He contrasts this approach with the UN's Sustainable Development Goals (SDGs), which cover these areas, but they are buried within scores of other detailed and off–topic topics such as sustainable tourism and inner–city garden access for disabled people – ie, worthy issues, but not necessarily the most vital ones and do not provide signposts for the most vital investments. He recognizes that the BMGF can focus on what works best and, unlike governments, does not face competing priorities and taxpayers' sentiments. However, focusing on what works best saves lives – the previous Millennium Development Goals encapsulated 8 simple, clear goals, and have saved at least 21 million lives. (*Project Syndicate*, 14 February 2017)

▶▶ The Cambridge MA firm Affinivax, with key support from the Bill and Melinda Gates Foundation, has been working on the first clinical trial of a successor to Pfizer's pneumococcus vaccine Prevar 13, which had US$ 6 billion turnover in 2016. Affinivax has abandoned the traditional conjugation pathway for the vaccine development, but instead uses a Multiple Antigen Presentation System, that allows the new vaccine to cover a full spectrum of 90 strains of pneumococcus instead of the 13 strains covered by Prevnar 13. Moreover, the vaccine's efficacy is boosted by using its proteins to elicit B and T cells responses, instead of being used as a carrier. Although Affinivax has not formally declared a timeline for the clinical trials, it has completed preclinical trials and is finalising its Good Manufacturing Practice plans. (*Endpoint News*, 28 February 2017)

▶▶ A Bill and Melinda Gates Foundation–funded project to set up a Faecal Sludge Treatment Plan (FSTP) in India's Trichy district has been challenged by the Woraiyur–Pandamangalam and Thamalavarabuyam Villages Agriculturists' Association. FSTPs remove, treat and dispose of faecal sludge, and the purified water from the cleaning process can be used for irrigation and the sludge for fertiliser. The plant, which has received US$ 5.5 million of funding from the Foundation, has been challenged on the grounds that it violates the city's master plan, planning consent was granted in secret, and tendering protocols were not followed. The Association filed a Public Interest Litigation petition, and the court directed the commission of Trichy to file a counter–argument. (*Times of India*, 7 March 2017)

▶▶ The Bill and Melinda Gates Foundation has committed US$ 80 million to close gender data gaps, and in *The Wire India*, Katherine Hay of the BMGF's India office argues that data are essential for measuring progress on gender equality goals. Data allows us to know where the problems are, to better understand them and to solve them. She highlights the high rate of infant mortality in Bihar, where 4.2% of babies will die by their first birthday. This figure breaks down into 3.6% of boys and 5% of girls dying by their first birthday – a huge gap with no biological foundation. The data also uncovers other gaps, such as birth and death registration – better registration would have thrown up this gap much earlier. Data can also help reveal why fewer girls are surviving, eg, different immunisation rates, poorer nutrition, or lower care seeking and levels of spending. Understanding the gap can present solutions, arising from evaluations what has worked elsewhere. This allows funds to be directed toward effective programmes, although data are lacking on what works well at scale. Evidence from data will help policy–makers in India, and elsewhere, to drive change and tell them how to do better. (*The Wire India*, 8 March 2017)

▶▶ In an interview with BBC News, Bill Gates commended pharmaceutical companies for their role in donating drugs to combat neglected tropical diseases. Globally, 1 billion people were treated for at least one tropical disease in 2015, and companies have donated 7 billion treatments since 2012. Every year, 170 000 people die from neglected tropical diseases, but their biggest impact lies in the resultant disabilities. Speaking from a meeting in Geneva, where new commitments of US$ 812 million from govern-

ments, drug companies and charities were made to continue the fight against neglected tropical diseases, Mr Gates highlighted some of the campaign's successes. These include substantial falls in lympathic filariasis and sleeping sickness, and the near–elimination of guinea worm. He expressed confidence that pragmatism will prevail on maintaining the USA's strong development aid budget, and has already had talked with President Trump on the US's critical role in progress on HIV, malaria and reproductive health, and how strong health systems can stop pandemics. He lauded the UK government's recent announcement that it would double support for fighting neglected tropical diseases, saying "the UK is a critical donor. As somebody who's very measurement–oriented, I find that partnering with the UK on these health–related areas is a great way to spend money and lift these countries up." (*BBC*, 19 April 2017)

# ▶ The GAVI Alliance

▶▶ GAVI, along with Google.org, and the Bill and Melinda Gates Foundation, are providing funding to Nexleaf Analytics, a Los Angeles–based start–up that produces wireless sensors and data analytics tools such as ColdTrace – a remote temperature monitoring technology that protects vaccines. The funding is part of GAVI's INFUSE scheme, to accelerate support in Innovation for Uptake, Scale and Equity in Immunisation. With this funding, Nexleaf will develop an analytics framework, gathering data from the countries its technology reaches, to share data with governments seeking to make evidence–based decision–making. The main attraction with Nexleaf's approach is how it prioritises data to drive decision–making and ensuring that data are actionable and useful, rather than the technology itself. This is part of GAVI's strategy of innovating to strengthen health systems, in this case modernising cold chains. "A lot of new technologies for gathering data are either on the market or in development, from smart fridges to temperature monitors. Our experience working with everyone from nurses in clinics to national ministries of health, and with making the real time data available in formats that servce them, is what Nexleaf brings to the table," said Martin Lukac, co–founder and chief technology officer of Nexleaf. (*Devex*, 18 January 2017)

▶▶ GAVI and Deutsche Post DHL announced a global partnership to help improve vaccine supply chains in GAVI–supported countries, to overcome the constraints placed by outdated supply chains. Deutsche Post DHL's logistical expertise in health care and life–sciences, combined with its global transportation network, will help to make vaccine supply chains more efficient, helping to increase coverage, reduce vaccine wastage and protect availability and potency – ultimately saving lives. It is essential to improve supply chains, as vaccine volumes grow and weak health systems struggle to cope with expanded immunisation programmes. Kenya will be the first country to trial the new partnership, with its Ministry of Health testing a dedicated transportation management solution to distribution vaccines throughout the country. The partnership dovetails with GAVI's strategy of forming clusters of private–sector alliances to address coverage and equity bottlenecks, accelerating progress and achieving lasting impact. "Robust vaccine supply chains are a vital part of building strong health systems, so that children, parents and communities can be reached wherever they live with life–saving vaccines. DHL's expertise in healthcare delivery and its footprint in sub–Saharan Africa will help the partnership develop and test new innovative solutions aimed at increasing the health impact in GAVI–supported countries," said Seth Berkley, CEO of GAVI. (*Global Trade Magazine*, 29 January 2017)

▶▶ Results for Development, a not–for–profit organization based in Washington DC, USA, released its new resource guide to provide practical advice for low– and middle–income countries (LMICs) who are planning on mobilising resources for their immunisation programmes. The guide, *Immunization Financing: A Resource Guide for Advocates, Policymakers and Program Managers,* offers 26 briefs, including 8 case studies, to assist countries in providing sustainable financing of immunisation. The guide is an update to the current *Immunization Financing Toolkit,* published by the World Bank and GAVI in 2010. Its publication is timely as many countries have pledged to increase domestic financing for vaccines and immunisation delivery, new vaccines are being developed, and many countries experiencing economic growth are moving from GAVI support toward full domestic financing of their immunisation programmes. (*allafrica.com*, 21 February 2017)

▶▶ GAVI is supporting the introduction of new coolers and refrigerators that run on solar power to keep vaccines cold. Dr Orin Levin, Director of Vaccine Delivery at the Bill and Melinda Gates Foundation, and the BMGF's focal point of engagement with GAVI, highlighted Ghana's success in being the first country in Africa to introduce pneumococcal and rotavirus vaccines, thereby jointly tackling two of the biggest killers of the world's children – pneumonia and diarrhea. He notes that Ghana's leadership in this area will pave the way for other African and Asian countries to follow suit. He commended Ghana for its strong partnership between communities and local health workers, adding that "vaccination programmes work best when health workers, traditional leaders and parents are all actively involved and understand the value of vaccines and the importance of bringing kids in on time." He was speaking at the celebration of this year's Vaccination Week, which coincided with the first anniversary of the Ministerial Conference on Immunisation in Africa and the ground–breaking Addis Declaration on Immunisation (ADI). (*Ghana News Agency*, 12 May 2017)

▶▶ In an op–ed piece in the *New York Times*, GAVI's CEO, Seth Berkley, wrote of the potential global health threat posed by yellow fever, as Brazil faces an unusually large outbreak, with 715 confirmed cases, 820 suspected cases and 240 confirmed deaths. To date, these cases have been in remote, sparsely populated areas, but if it spreads to urban areas, it would be very difficult to contain. Yellow fever is transmitted by certain mosquito species, and kills more than 30 000 people each year. There is a real risk that it could spread to previously unaffected areas, such as Asia, where the presence of mosquitos and 1.8 billion un-vaccinated people in a densely–populated region is a potentially catastrophic combination. Cities in Brazil are intensively vaccinating their citizens, in the hope of reaching 12 million people by the end of 2017. To meet this, Brazil has been forced to request 3.5 million doses of yellow fever vaccine from the International Co–ordinating Group of Vaccine Provision, financed by GAVI. These stockpiles are probably insufficient to meet global demand if there is a major outbreak in cities, where diseases can spread more quickly. Mr Berkley argues that these stockpiles should be the last line of defense, and that better outbreak prevention is vital, in the case of yellow fever via improved mosquito control and immunity against yellow fever through routine immunisation and pre–emptive vaccination campaigns. Preventative approaches can be highly effective, but in order to work, first we must recognize that there is a problem. (*New York Times*, 15 May 2017)

# ▶ The World Bank

▶▶ According to the World Bank's Global Economic Prospects report, global economic growth in 2016 was dampened by sluggish performance from the US economy and recession in large commodity–dependent economies, as growth faltered from 2.7% in 2015 to 2.3% in 2016. The Bank forecast a return to 2.7% growth in 2017, supported by the "ripple effect" of US tax cuts and public expenditure promised by the Trump presidency on other developed economies – provided that they are not undermined by aggressive US trade policies pledged during his election campaign. Moreover, rising oil prices are expected to help Brazil, Russia and Nigeria – leading commodity exporters – to move from recession back to growth in 2017. It forecast lower growth rates for the UK economy, as uncertainty over Brexit drags on business and consumer confidence. (*The Guardian*, 10 January 2017)

▶▶ The launch of risk–sharing insurance in East Africa is expected to increase the update of agriculture insurance as premiums start to fall. The facility, from the Global Index Insurance Facility (GIIF), and the African Reinsurance Corporation (Africa Re), aims to support regional underwriters to create affordable insurance products, which will enable farmers to be more resilient against external shocks, such as crop failures arising from drought. Across East Africa, uptake of insurance schemes is low, due to existing methods of risk–mitigation and expense – premiums range from 7–15% of the sum insured. The new risk–sharing facility aims to decrease premiums to 4%. According to Mr Makhtar Diop, World Bank Vic President for Africa, insurance expansion is critical for small farmers to build resilience against the impact of climate change. "It is the poor and vulnerable who are the most affected by climate change and natural disasters, and insurance is a critical tool to help protect their livelihoods," he said. GIIF is managed by the World Bank, with funding from the EU, Japan and the Netherlands. (*allafrica.com*, 3 March 2017)

▶▶ The UK's Department for International Development (DfID) plans to spend half its budget on fragile states and regions; and the World Bank plans to double to US$ 14 billion the money allocated to fragile

states over the next 3 years. Up to 33% of the war–scarred Central African Republic's GDP will comprise World Bank assistance. The accepted wisdom is that aid should be directly at poor, well–governed countries where aid may not be squandered. However, as countries such as India and Vietnam pull more of their people out of poverty, there are fewer such countries and the most acute need is with fragile states with barely–functioning governments. These fragile countries are a regional threat, and if they can be stabilized their neighbors will also benefit. However, it is easy to waste aid money in these places where corruption and mismanagement are rife and infrastructure investments can be destroyed by conflict. Their own systems can be undermined by donors setting up parallel welfare systems, and rich countries often wait until situations become calamitous before rushing in with expensive food aid, when it is often better to give people cash. Another, more intelligent way, is to provide substantial peace–keeping forces to allow the countries to develop and build infrastructures peacefully. Donors could provide risk insurance or subsidies to help private firms enter dangerous markets, and allow governments to set their own spending priorities but channel spending through whatever organisations work in any given area. These are new ideas and could well fail, but may inform future models for fixing failing states. (*Economist*, 16 March 2017)

▶▶ The World Bank has cut its forecasts for sub–Sahara Africa's economic growth in 2017, from 2.9% to 2.6%, which is in line with the International Monetary Fund. The region's resource–reliant economies, and all commodity exporters, continue to be affected by the slump in prices, which although stabilized remain subdued. South Africa's credit rating has been downgraded to junk status, and its economy grew by 0.3% in 2016 – the slowest since 2009. The region's other large economies – Nigeria and Angola – are projected to have faltering economic growth following sharp slowdowns in 2016. However, the World Bank anticipates a rebound, with the region posting growth rates of 3.2% and 3.5% in 2018 and 2019 respectively, although rising interest rates in developed economies and tighter access to finance, sluggish improvements in commodities and a move toward protectionism could threaten this. The Bank also emphasizes the importance of closing Africa's infrastructure gap – almost US$ 100 billion a year – narrowing it could add up to 2.6% to the region's GDP each year. (*Public Finance Internation*, 20 April 2017)

▶▶ According to the International Labour Organisation (ILO), 40 million jobs per year must be created to keep pace with the growth in the global working–age population. The World Bank notes that the pace of job creation is not keeping pace with the estimated number of entrants into the labour market – between 600 million and 1 billion up to 2030. Economic growth is intrinsic to the Sustainable Development Goals, and is essential for eliminating hunger, improving health care and access to education. Young people make up a large proportion of the world's unemployed, and the rate is often higher among women. It can be difficult for governments to create work – jobs supported by wage subsidies can disappear when subsidies end, and employers can shed existing workers to recruit subsidised workers. Other tools, such as job guarantees whereby the state promises to hire unemployed workers, are expensive and do not address the structural causes of unemployment. Governments also face the challenge of technologies such as robotics and artificial intelligence wiping out millions of jobs, and there are concerns that governments are unprepared for the impact of the digital economy on the nature of work over the next 10–15 years. (*Financial Times*, 20 April 2017).

# ▶ United Nations

▶▶ Two UN peacekeepers have been kidnapped in the central Kasai region of the Democratic Republic of the Congo (DRC), with one worker being confirmed as Michael Sharp, a US citizen, and the other as Zaida Catala, a Swedish citizen. They were among a group of UN experts investigating DRC conflicts, and their kidnappers have not yet been identified. In the preceeding week, a Uruguayan peacekeeper was shot and wounded in the same region, which has fallen victim to a rebellion since September 2016 after government forces killed Kamwina Nsapu, a tribal chief and militia leader. The violence spread to neighboring provinces, leaving at least 400 people dead. Zeid Ra'ad Al–Hussein, the UN High Commissioner for Human Rights, confirmed that three mass graves have been discovered in the area. The UN has almost 19 000 troops deployed in the DRC, its largest and costliest peacekeeping mission. The UN Secretary General, Antonio Guterres, asked the Security Council to send an additional 320 UN police to the DRC, after a deal to end the dispute of the presidential election stuttered. (*Al Jazeera*, 13 March 2017)

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▶▶ The UN Security Council unanimously renewed its US$ 1.2 billion peace–keeping mission to the Democratic Republic of the Congo (DRC) for another year, albeit at reduced numbers. This renewal comes amid warnings that violence is spreading across the DRC ahead of elections. The resolution authorises the replacement of some troops with better–trained specialist units, and enables the force to intervene anywhere in the DRC if needed, and not just in the volatile east. It also calls for a dialogue between the UN and the DRC government to develop an exit strategy. The UN is pressing DRC's government to honor a power–sharing deal with the opposition ahead of this year's election, as violence in the central Kasai region has spilled over into neighboring provinces, leaving at least 400 people dead. There are also reports of violent clashes between Congolese forces and local militia, a large number of deaths, kidnappings and summary executions, all of which could potentially constitute crimes under the International Criminal Court. (*Al Jazeera*, 31 March 2017)

▶▶ According to the UN, war and famine have forced more than 2 million children in South Sudan to flee their homes, creating the most troublesome refugee crisis in the world. More than 1 million children have fled outside South Sudan, while another 1 million are internally displaced. And in a country of 12 million people, nearly 75% of children do not attend school. The UN, the UN High Commission for Refugees and UNICEF also report than more than 1000 children have been killed in South Sudan's civil war, which began 2 years ago following its independence from Sudan. The true figure may be much higher, as there are no accurate figures on deaths from South Sudan. Many of the refugees have fled to Uganda, Kenya, Sudan or Ethiopia – nations who are already struggling to provide enough food and resources for their existing populations. (*IRIN*, 8 May 2017)

▶▶ Nikki Haley, the US Ambassador to the UN, confirmed that she will visit Turkey and Jordan, to check on the welfare of Syrian refugees, to see UN humanitarian work and highlight the US aid response. She plans to talk to government leaders about the effectiveness of US programmes to help refugees, and will visit refugee camps and families, US–funded schools, and witness UN efforts to ship humanitarian aid into Syria from Jordan and Turkey. It will be her first official overseas trip, and follows a bid from President Trump to temporarily ban refugees from entering the US and to cut US funding to the UN and its agencies. "What is happening in Syria and its neighbouring countries is a true humanitarian crisis. But those who accuse the US of heartlessness in the face of this crisis are wrong. No country has provided more in protecting, housing, feeding and caring for Syrian refugees that the US. We have provided nearly US$ 6.5 billion in emergency assistance for Syria since the start of the crisis. With American help, Syria's neighbours have made the difference between life and death for millions of Syrians. The US and UN will continue to do a great deal of heavy lifting for these desperate people," she wrote in a recent *Wall Street Journal* article. (*Business Insider*, 17 May 2017)

▶▶ President Trump confirmed the US's withdrawal from the Paris climate agreement, arguing that it imposes unfair environmental standards on US businesses and workers, and that it is an attack on US sovereignty, although he reiterated his commitment to the trans–Atlantic alliance and to environmental protection overall. The agreement was intended to bind countries together in a co–operative effort to battle climate change. The US is the world's second–largest emitter of greenhouse gases, and its withdrawal is a blow toward limiting greenhouse gases and limiting climate change; under the accord it had pledged to cut its greenhouse gases 26–28% below 2005 levels by 2025 and committed up to US$ 3 billion in aid to developing countries by 2020. Some business leaders critised the decision, claiming it would ultimately harm the economy by ceding future jobs in clean energy and technology to overseas competitors. Mr Trump will stick to the withdrawal process set out in the agreement, which will take nearly 4 years to complete – meaning a final decision on the US withdrawal will be made by American votes in the next presidential election. (*New York Times*, 1 June 2017)

# ▶ UN AIDS and The Global Fund

▶▶ In partnership with civil society, UN AIDS and the US Agency for International Development, Thailand has developed a stigma reduction programme that is gradually being rolled out to all public hospitals. It was launched on 2 March 2017, following the annual Zero Discrimination Day of 1 March. The programme recognizes that the fear of HIV transmission and stigma against people living with HIV hinders access to treatment, care, employment and education, and that tackling this stigma is essential to ending the HIV epidemic. Thailand's related HIV–stigma reduction programme for health–care workers

is one of the most ambitious in the world, and is being adapted and implemented in other South East Asian countries, including Viet Nam. Other countries such as Laos and Myanmar have expressed interest in similar initiatives, and UN AIDS dedicated the 2017 Zero Discrimination Day to eliminating discrimination in health care settings, to overcome barriers to treatment. (*ReliefWeb*, 3 March 2017)

▶▶ According to UNAIDS, 13.9 million people out of the 17 million world–wide on anti–retroviral (ARV) treatment for HIV live in low– and middle– income countries (LMIC). 15 generic manufacturers supply more than 95% of ARVs to LMICs, with 4 suppliers accounting for 83% of the total volume. Moreover, ARVS are largely purchased by 3 buyers – the US President's Emergency Plan for AIDS Relief (PEPFAR), the Global Fund and South Africa – enabling the rapid expansion of HIV treatment and quality assurance. However, it means that these buyers are largely responsible for treatment continuity, limiting drug resistance and introducing better drug treatments. It is argued that coverage for 30 million people by 2030 [part of the UN AIDS 90–90–90 target, whereby by 2020, 90% of all people living with HIV will know their HIV status; 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy; and 90% of all people receiving ART will have viral suppression] must be ensured by these buyers becoming less dependent on a limited number of suppliers, allocating procurement to all suppliers who meet quality standards, and allow excluded or limited suppliers to quickly increase their volume. Eg, PEPFAR procures ARV through annual tenders but the Global Fund and South Africa have 3–year supply contracts, which may be extended and thus exclude other sources – this is hazardous as generic manufacturers of ARVs could switch production to other pharmaceuticals; and all suppliers are vulnerable to supply interruptions and must ensure the continual supply of ARVs to HIV–positive people who have no other treatment options. This over–dependency creates risks because if treatment stops (eg, through breaks in the supply chain), the HIV virus will progress without treatment and there are no treatment alternatives. (*Financial Times*, 16 March 2017)

▶▶ UN AIDS has expressed concern at the HIV prevalence in Karachi, and urged Pakistan's government to devote all available resources to containing it. Mr Mamadou Sakho, UNAIDS Country Director for Pakistan and Afghanistan, reiterated that wider technical and financial support will be available. Mr Sakho noted that HIV is currently concentrated in "at risk" populations, but it may spread and become generalised if it is not tackled within these groups now. Karachi has one of the highest rates of HIV infection in the world, and that the Sindh region has almost 50% of Pakistan's total HIV population. The Sindha AIDS Control Programme (SACP) will establish more treatment facilities in Karachi and Sindha. It also plans family awareness centers, from basic health untis and rural health centers, up to tertiary levels. These new plans will help SACP to achieve 80% coverage in HIV treatment. (*India.com*, 27 April 2017)

▶▶ The Board of the Global Fund met in Kigali, Rwanda, in May and elected Aida Kurtovic as its new Chair. Ms Kurtovic will serve a two–year term as Chair, and she has previously served as the Global Funds' Vice–Chair, as well as being involved in various other capacities. The Board also elected John Simon, the former US ambassador to the African Union, as the incoming Vice–Chair. Opening the board meeting, the Rwandan President Paul Kagame highlighted the importance of strengthening health systems, aligning financial support with countries' strategic health plans, and long–term improvement underpinned by constant learning. Statistics from the Rwandan government shows that Global Fund investments in the country have meant that 175 000 people receive ART treatment for HIV, more than 36 000 cases of TB were detected and treated, and more than 18.1 million insecticide–treated nets were provided to protect families from malaria. (*Xinhua*, 4 May 2017)

▶▶ Botswana – with an estimated 25% HIV prevalence among its adult population – was the first country in Africa to establish an antiretroviral therapy (ART) program, and is close to achieving the UN AIDS's 90–90–90 target. According to research published in *Clinical Infectious Diseases*, there is a significantly–higher incidence of cryptococcal meningitis (CM) among HIV–positive people compared to the general population. This suggests that key populations are developing advanced HIV and associated opportunistic infections, as they are not engaging in care. Botswana's rate of CM among HIV–positive people is similar to pre–ART South Africa, and 30% of Botswana's people aged 10–64 years had not been tested for HIV in 2013, and that its ART program must reach an additional 100 000 people. The study's researchers suggested adjusting the program to fit the needs of specific populations: "to avoid leaving vulnerable individuals behind, differentiated care models should be considered to streamline care for populations with well–controlled disease and focus more intensive resources on those with higher need who are now driving the epidemic," they write. (*Healio*, 24 May 2017)

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# ▶ UNICEF

▶▶ New figures from UNICEF shows that Boko Haram have used 27 children to carry out suicide bombing attacks in the first 3 months of 2017, in Nigeria, Chad, Niger and Cameroon – an increase on the 30 children in 2016. In total, 117 children have been used in suicide attacks since 2014 – 80% of them girls. This move suggests a change in tactics by Boko Haram, as it moves from holding towns and territory toward a guerilla–style insurgency with hit–and–run attacks and improvised explosives. The group systematically kidnaps children – including the 270 girls taken from Chibok, Nigeria in 2014 – who may be forced or deceived into carrying out suicide attacks. It appears that not all of the children are aware of their actions, and the group's strategy of using children in suicide attacks makes it more difficult for returning children to be re–integrated into their communities upon release, as they can be suspected of carrying explosives. (*NPR*, 13 April 2017)

▶▶ According to Robin Nandy, principal adviser and UNICEF's head of immunisation, rapid urbanisation presents a massive challenge in vaccinating the world's poorest children, and increases the risk of rapidly spreading disease outbreaks. More and more unvaccinated children live in urban slums with limited vaccination coverage – especially concerning because disease outbreaks can potentially spread more quickly and infect more people. The UN estimates that 25% of people will live in urban slums by 2030, mainly in Africa and Asia, and the Ebola outbreak shows how quickly outbreaks can spread in cities. The pressure on cities' immunisation services is increased by growing numbers of refugees settling in urban areas – many of whom have not been vaccinated due to weak or crumbling health infrastructures in their conflict–ridden home areas. Each year, around 19.4 million children – many in war–torn areas – miss out on full vaccinations, while weak health systems, poverty and inequality also lead to 1–in–5 of all children aged under 5 years not being immunised. The poorest children are almost twice as likely to die before 5 years of age compared to richer children, and in those countries accounting for 80% of deaths in children aged under 5 years, over 50% of children are not fully vaccinated. Each year, 1.5 million children die from vaccine–preventable diseases. Mr Nandy also expressed concern that recent outbreaks of measles could indicate a resurgence of the disease, causing unnecessary deaths and illness among children. (*Thomson Reuters Foundation*, 26 April 2017)

▶▶ In a report released in May, UNICEF counted 300 000 unaccompanied and separated refugee children globally in 2015 and 2016 – compared to 66 000 in 2010 and 2011. Out of the total, around 100 000 children were trying to cross from Mexico into the USA. Overall, around 200 000 children applied for asylum in 80 countries, including 170 000 lone children – and 92% of children and young people who reached Italy by boat in 2016 traveled alone, compared to 75% in 2015. Some of the children are orphans, others are seeking to join relatives, and the parents of the remainder believed that unaccompanied children would have a greater chance of being allowed to stay. UNICEF called upon the countries where children have sought asylum to provide better services, and not to be placed in adult detention camps. At the G7 summit in May 2017, UNICEF will urge world leaders to protect refugee and migrant children from exploitation, violence and detention, to keep families together, and give children access to education and health care. UNICEF also calls for action on the underlying causes of large–scale migration, and measures to combat xenophobia and discrimination in both transit and destination countries. (*Al Jazeera*, 18 May 2017)

▶▶ UNICEF found that up to 150 children aged under 5 years die in Myanmar each day, despite the reform and reconciliation promoted by Aung San Suu Kyi's one–year government. UNICEF estimates that Myanmar's child mortality rate is 50 per 1000 live births, compared to 4 per 1000 in the UK, nearly 30% of children under 5 suffer from moderate or severe malnutrition, and that more than 50% of all children live below the poverty line. There are disparities across Myanmar, especially among families in war zones unable to reach health clinics; and UNICEF calls for improved humanitarian access to the estimated 2.2 million children affected by violence. UNICEF acknowledges that Myanmar is undergoing an "unprecedented period of change and opportunity", but that progress has been disappointingly slow, and there is a worrying escalation of conflict in more remote border areas. In Rakhine province, 120 000 people who have been displaced by violence live in camps, and UNICEF's humanitarian access to these camps is still highly problematic, although improving slightly. It calls for an end to the laying of landmines, and for landmine clearances to start whenever possible – highlighting that 1–in–3 victims of landmines are children. (*The Guardian*, 23 May 2017)

▶▶ UNICEF's recent study on Thailand's Comprehensive Sexuality Education (CSE) programme found that sex education at secondary level does not equip students with the skills needed to manage their sexuality and sex lives, despite near–universal coverage. Much of the programme's teaching focuses on imparting information, rather than developing critical thinking, and communication and negotiation skills, and important topics such as rights, gender equality and diversity are ignored – risking the development of skewed attitudes toward equality, domestic violence and rights. Effective sex education is vital in reducing Thailand's high rate of teenage pregnancy, and the high rate of sexually–transmitted diseases among young people. The study also found that 41% of male vocational students thought that it was acceptable for a husband to physically punish his wife for adultery, 50% believed that same–sex relationships are wrong, most students did not know basic facts about the menstrual cycle, and only 54% of female students were confident that they could insist on condom use. The CSE programme was found to focus on biology, abstinence on sex before marriage, and preventing unwanted pregnancy, and 50% of teachers did not receive training on delivering CSE. It concludes by recommending that the program's delivery includes all designated topics, that it should foster critical thinking, that each school allocates enough time for it, and that every teacher receives full training in it. (*The Nation*, 1 June 2017)

# ▶ World Health Organization (WHO)

▶▶ The WHO is launching a global initiative to reduce severe and avoidable medication–associated harm by 50% over the next five years. The Global Patient Safety Challenge is the WHO's third patient safety campaign, following the Clean Care is Safe Care and Safe Surgery Saves Lives initiatives. It aims to address health system weaknesses that lead to medication errors and the resultant harm to patients. According to the WHO, medication errors cause at least one death every day and globally injure 1.3 million people each year. As well as the human cost, this places a huge strain on health budgets and families – at an estimated annual US$ 42 billion, or almost 1% of total health expenditure. Preventing errors, which can be caused by fatigued workers, overcrowding, staff shortages, poor training, lack of co–ordination among agencies and wrong patient information, would save lives and money. "Preventing errors and the harm that results requires putting systems and procedures in place to ensure the right person receives the right medication via the right route at the right time," said WHO Director–General Margaret Chan. (*Sun-Star*, 30 March 2017)

▶▶ The WHO is set to update its recommendations for treating postpartum hemorrhage, following the results of a study published in *The Lancet*, which suggests that tranexamic acid could cut deaths by one–third. The study was co–ordinated by the London School of Hygiene and Tropical Medicine, in collaboration with 193 hospitals across Africa and Asia. Each year, 100 000 women die from postpartum hemorrhaging, and it is the biggest cause of death during pregnancy and birth. 77% of maternal deaths occur in just 20 countries, and 1360 mothers per 100 000 die in childbirth in Sierra Leone, compared to 3 maternal deaths per 100 000 in Greece, Poland and Finland. Tranexamic acid prevents clots from breaking down, making it easier for the body to stem bleeding. It was developed by husband and wife team Shosuke and Utako Okamoto in 1960s Japan, but they could not persuade pharmaceutical companies to conduct clinical trials for treating postpartum hemorrhage. Tranexamic acid is cheap – US$ 1 per dose – and is given in a single shot, making it easy to administer. Prof Ian Roberts, one of the study's researchers, admits that making the drug accessible around the world will be a challenge. "When we started the trial, the staff would cry hearing about babies left without their mothers. Making sure the treatment is available everywhere it can save a life is hugely important. We shouldn't have children growing up without a mother for lack of a drug that costs a dollar," he says. (*BBC*, 27 April 2017)

▶▶ The WHO and Somalia's Federal Ministry of Health have launched a preventative oral cholera vaccination campaign, targeting 224 000 people aged over 1 year. The campaign follows a major outbreak of cholera in January 2017, with a total of 31 674 reported cases and 618 deaths, mainly in the South West State. Drought has worsened the cholera outbreak, due to shortages of clean water and sanitation. The campaign does not replace other preventative measures, such as clean water and good hygiene, and is supported by the Global Task Force on Cholera Control, GAVI, UNICEF and other health partners. Dr Ghulam Popal, WHO's representative in Somalia, reiterated WHO's commitment to support cholera response efforts in Somalia. "We are working with health authorities at all levels and humanitarian partners to limit this outbreak," he said. (*Outbreak News*, 7 May 2017)

▶▶ According to the WHO, improvements in data collection have led to nearly 50% of global estimated deaths being registered with a cause in 2015, compared to 33% in 2005. This means that 27 million of the world's 56 million deaths were registered with a cause in 2015. Several countries, including China and Turkey, have made significant progress in data collection, and Iran has moved from recording the cause of death in only 5% of cases in 1999 to 50% in 2015. Recording the causes of death enables countries to develop and implement more effective health systems, and address the underlying causes of mortality. The WHO is working with countries to strengthen their health information systems and improve data quality. (*Reuters*, 17 May 2017)

▶▶ The WHO announced the appointment of its next director general, Tedros Adhanom Ghebreyeus, who will take over from Dr Margaret Chan. His 5–year term will begin on 1 July, and he will be the first WHO director–general from Africa. The election coincides with a deterioration in the WHO's reputation over its handling of the 2014 Ebola outbreak. Mr Ghebreyesus is a former health and foreign affairs minister, and according to his application, as Ethiopia's health minister he oversaw the creation of 3500 health centers and 16 000 health posts, contributing to falls in child mortality, HIV infections, and malaria and tuberculosis deaths. In a pre–election speech, Mr Ghebreyeus spoke of his background of "knowing survival cannot be taken for granted, and refusing to accept that people should die because they are poor." (*Time*, 23 May 2017)

# ▶ Demography

▶▶ Cuba's economy has long been stunted by its isolation from the outside world, and its reliance on partners which have themselves collapsed (eg, the Soviet Union and Venezuela). Improving relations with the US had helped boost economic growth, but Venezuela's economic crisis led to official figures showing a fall of 0.9% fall in Cuba's GDP. Raul Castro, Cuba's president has called for a more welcoming attitude to foreign investment and increased local production to replace imports to support the country's economy. However, any attempts to boost economic growth could be arrested by Cuba's stagnating population growth. Its population has reached a peak of 11 million, and is projected to fall due to an ageing population and a birth–rate below the replacement level. This has been exacerbated by improved US relations, as a wave of migrants left Cuba over the past 2 years, and many young Cubans plan to leave due to a lack of opportunities at home. This trend could intensify if the government pursues painful policies to counteract a contracting economy. (*Business Insider*, 7 January 2017)

▶▶ The percentage of UK women working into their 70s has doubled in the last 4 years, nearly reaching the same level as men, with 5.6% women stopping work after the age of 70 in 2012. This rose to 11.3% (or 150 000 women) in 2016 as increases in longevity, worries over pension income and desires to stay active has pushed up workforce participation rates among older women. An estimated 15.6% of men stopped working in their 70s in 2016. This trend is underpinned by legislation to end age discrimination and more flexible working patterns. Often, women have shortfalls in their pension provisions due to career breaks to raise children. Although continuing to work later in life is beneficial if by choice, employers risk demotivated and unproductive workforces if workers are forced to work by a lack of pension provision. Recently, the UK government launched a strategy to encourage the over–50s to consider a second career to extend their working lives. "Staying in work for a few more years can make a significant difference, not only to someone's income but also their physical and mental health," says Damian Green, the UK's Work and Pensions Secretary. (*BBC*, 22 March 2017)

▶▶ Nearly 20 years ago, world leaders launched a new initiative to get new and underused vaccines to the world's poorest people, at a time when millions of children died each year from vaccine–preventable diseases. This was the start of the GAVI Alliance, which has saved more than 7 million lives as child mortality has plummeted in most countries worldwide. Today, argues Dr Ngozin Okanjo–Iweala, the Chair of GAVI, the world is facing an equally acute need – 800 million children who do not have access to quality education. By 2030, many young people will lack basic secondary–school level skills, which are essential for 21ˢᵗ century jobs. Young people lacking in skills may feel hopeless and turn to violence. Dr Okanjo–Iweala is a member of the Education Commission, a group of countries which works together to ensure that the world's children are all in education – "vaccinating the world against poverty". Their message is that quality education is the strongest antidote to poverty, and they have developed an innovative financing plan for education. This tool would leverage up to US$ 13 billion for education by 2030, working with development backs to coordinate funding and create financing packaging the multiply the impact of donor dollars to fill the funding up between governments and donors. This investment in human capital would strengthen families, communities and countries, making the world more stable and prosperous. (*Thomson Reuters Foundation*, 27 April 2017)

▶▶ For the first time in Canada's history, there are more Canadian citizens aged over 65 years than under 15 years, and from 2011–16 the country had its largest ever–increase in the proportion of senior citizens. This data, from the 2016 census, shows that the number of senior citizens grew by 20%, against an overall 5% population increase. Canada's population of children aged under 15 grew at 4.1%, reflecting lower fertility rates, which are now 1.6 children per woman. In line with increasing life expectancy – currently at 82 years – the number of centenarians grew by more than 40%. As women live longer than men, this increasing longevity means than among people aged over 85 years, there are two women for every man. This changing nature of Canada's demography means that in just over 10 years, nearly 25% of Canadians will be aged over 65 years, with just 16% aged under 15, with resultant effects on tax revenue and health spending; and changing patterns of consumption and housing. While immigration has had a major impact on Canada's population growth, it has had little effect on these trends, partly because immigration has been stable; and also because immigrants arrive as young adults and grow old in Canada. (*National Post*, 3 May 2017)

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▶▶ According to the IMF, Asia's changing demography means that the region is moving from being the biggest contributor to the global workforce, to subtracting millions of people from it. It estimates that population growth with fall to zero by 2050 (with Japan already experiencing negative growth), and that the percentage of working–age people has already hit its peak. This unravelling of Asia's demographic dividend could hamper global and regional economic growth. The IMF highlights how Asia is undergoing accelerated aging compared to Europe and the USA, with aging happening at lower levels of per capita income compared to other developed countries. The speed of change hinders these countries from adapting to change, and they risk being "old before becoming rich." The IMF estimates that Japan's economy could shrink by 1% a year over the next 30 years as a result, and China, Hong Kong, South Korea and Thailand experiencing fall of between 0.5–0.75%, with an overall impact on the world's economy of 0.1% each year. Labour market, pensions and retirement systems reform could help offset these adjustments, and the region's working–age population could be boosted by immigration. The region also needs to improve productivity to offset slowing investment caused by excessive savings rates, the growth of less productive sectors (eg, services), and the declining importance of external trade. (*Bloomberg*, 7 May 2017)

# ▶ Economy

▶▶ From 2000 onwards, the economies of the world's richest and poorer countries have begun to converge, as the latter undergo faster economic growth. Despite this welcome trend, many countries are left behind, including the world's poorest, with the lowest – and diverging – average income growth. The emergence of these trends – convergence overall, but divergence among the poorest countries – is vital to understand global goals on the reduction of extreme poverty. This is shown by the success of the MDG in halving the rate of extreme poverty in developing countries – an example of convergence – even as the number of people living in extreme poverty in fragile states has risen, and the living standards of the very poorest people (the "consumption floor") has barely risen. The poorest countries will face the biggest challenge in achieving the first SDG of ending extreme poverty everywhere. The World Bank has adopted a target rate of 3% for extreme poverty by 2030, but this will mask gaps in poverty rates, with a minority of countries having higher rates, and may continue to diverge and be left behind. There are 30 countries at risk of being left behind (including Malawi, St Lucia, and Zambia). 25 of these countries are relatively small, so risk being overlooked in the World Bank's global poverty monitoring as the 3% target is compatible with several small countries failing to progress (although the Bank stresses the need to reduce poverty everywhere), and collectively they could account for more than 30% of all people living in extreme poverty – 280 million people. 18 out of the 30 are fragile, and 9 are resource–rich. (*Brookings*, 24 January 2017)

▶▶ In 2016, Zimbabwe's central bank began printing a new form of money, the "bond note", which is pegged at US$ parity. Zimbabwe adopted the US$ in 2009 after experiencing disastrous hyperinflation, but queues of citizens waiting to withdraw cash from banks reveal little faith in the government's latest economic plans. Nearly 25% of Zimbabweans rely on food assistance, and 72% live in poverty – in a country with abundant natural resources, a once–booming agricultural sector and abundant human capital. However, much has been squandered during Robert Mugabe's 37–year regime. Mr Mugabe began promisingly in 1980 following independence from Britain, with calls for reconciliation, better education and health care, but degenerated into oppressive and undemocratic rule, bringing the country to its knees through gross economic mismanagement. This began in earnest in 2000, when take–overs of white–owned farms were passed onto many of Mr Mugabe's supporters with no experience of modern farming – causing sharp falls in the country's main export earner. The central bank began printing money to pay off debts and offset higher prices caused by failing farms, leading to severe hyperinflation. At one point, the 100 trillion Zimbabwean dollar was worth US$ 0.40, and ultimately was abandoned, to be replaced by a multi–currency system dominated by the US$. A brief power–sharing arrangement with the country's opposition tempered some of Mr Mugabe's destruction, but this ended in 2013 with his party's resumption of full control. Behind the scenes, the struggle to succeed the 93–year–old president has begun, but without a designated successor the potential vacuum can only add to the country's woes. (*Economist*, 27 February 2017)

▸▸ Intensive animal–raising techniques, where animals are crammed together in small spaces, means that antibiotics are routinely given to healthy animals to prevent the spread of infectious diseases, and to fatten animals. As the demand for meat is set to rise in the large emerging economies, it is estimated that their use will double over the next 20 years, while bacteria evolve resistance to antibiotics. Some experts estimate that drug–resistance bacteria could kill 10 million people by 2050, at a cost of US$ 1 trillion. In economic terms, the use of antibiotics in this context is an example of "the tragedy of the commons", whereby individuals pursuing their own interests ultimately create a collective disaster. Until the 1970s, new antibiotics were regularly discovered to replace those to which resistance had evolved, but new developments have since dried up. It can be argued that the real solution lies in giving drug companies better incentives to develop new antibiotics, such as "advanced market commitment", where donors promise to pay for drugs that do not yet exist, as well as tighter regulation of the use of antibiotics and improved animal welfare to discourage the spread of disease. (*BBC*, 6 March 2017)

▸▸ China has more than 2000 mobile health care apps, covering medical advice, appointment booking and niche services, and tapping into demand by offering convenience in country where clinics are widely distrusted and hospitals are overcrowded as a result. They appeal to consumers who are underserved by government–run facilities, with inadequate access to doctors, particularly in rural areas. These apps cannot charge for booking hospital appointments, and so rely on advertising and referrals to doctors – which can be charged for – to generate income. However, investors are beginning to lose confidence in these companies profitability, and investment dropped by 10% year–on–year in the last quarter of 2016, after a 41% decline in the previous quarter, despite burgeoning user numbers. In line with China's ecommerce sector movement toward bricks and mortar retailing, medical apps are finding tie–ups with hospitals essential to boost revenues, and WeDoctor aims to set up 100 hospitals over the next 3 years; and another app is diversifying into private health insurance. Others have expanded into consumer services, such as over–the–counter medicines or cosmetic procedures like Botox. This move toward diversification is underpinned by fears that medical apps will face further regulations, following the investigation of advertisements on Baidu's search engine for private hospitals offering unnecessary treatments. (*Financial Times*, 9 March 2017)

▸▸ Myanmar's government is considering a change to the law to allow foreign investors to take stakes of up to 35% in the country's banks. Myanmar's banking system is one of the most under–developed in the world, and is unable to support the country's aspiration for fast and inclusive economic development. However, it is one of the fastest–growing banking sectors in Southeast Asia, albeit starting from a very low base. Moreover, the World Bank recently announced plans to work with Myanmar's government to carry out the first audit of the country's banking system in decades, in an attempt to modernise it, and to support economic growth. (*Irrawaddy*, 13 March 2017)

# ▸ Energy

▸▸ Solar power provides a mere 1.3% of the US's electricity, but the labour–intensive nature of the technology's design and manufacturing, plus marketing and installation, means that the industry employs more than 260 000 people. And with the solar industry generating 1–in–50 of all new jobs, it is growing quickly. This is slightly more people than in the natural gas industry, over twice as many as the coal industry, over three times as many as wind energy, and almost five times the number in nuclear energy; and only the oil/petroleum sectors employ more people. Although solar power is growing from a low base, and is in a labour–intensive period of its growth, it is worth considering the implications of these statistics. First, although the jobs growth is welcome, it may keep the solar power prices high, as the industry is labour–intensive. Ultimately, this could deter the spread of clean energy, and may need to be addressed by economies–of–scale and automation. Second, the solar industry still lacks the political leverage of the coal or petroleum industries. It is also relatively concentrated in certain states (eg, California), although it is beginning to fan out across the US. President Trump has previously criticized solar power and the White House energy paper makes no mention of it; but as the industry grows and adds jobs, it will become harder to ignore. (*Vox*, 7 February 2017)

▸▸ According to a report from the Energy and Resources Institute (TERI) in New Delhi, India will not need to build another coal plan after 2025 if renewables continue to fall in cost at their current rate. This

also suggests that its carbon levels could be cut beyond the levels agreed at the recent climate talks in Paris, reducing $CO_2$ emissions by about 600 million tonnes, or 10%, after 2030. This is significant, because India is the world's fastest–growing major polluter and the third–largest emitter of $CO_2$ behind China and the USA, and its ability to curb carbon emissions is vital in capping the rise in global temperatures. Much of its growth in $CO_2$ emissions is driven by increased electricity consumption – 60% of which is provided by coal–fired plants. India plans to build an extra 65 gigawatts of coal–fired capacity in the next few years, although it already has 308 gigawatts of capacity, with 156 gigawatts being the highest amount ever used. According to TERI's research, the coal–fired plants under construction will be built, but no more will be needed after 2025 provided that these conditions are met. First, renewables and battery storage prices must keep falling – if they reduce to 50% of their current prices by 2025, they will be cheaper than coal – entirely feasible at their current rates. Second, the government needs to adopt policies to make it possible for electricity companies to switch quickly between renewables and storage energy, eg, if solar power generation is disrupted by weather conditions, a company should be able to instantly buy replacement power from a stored source, such as batteries. (*Financial Times*, 22 February 2017)

▶▶ Nigeria's parliament voted to pass its 2017 budget more swiftly than previous years, to avoid delays in signing the spending plans into law. President Muhammadu Buhari presented the US$ 23.2 billion budget aims to pull Nigeria out of its first recession for 25 years. The recession was caused by low oil prices and attacks on energy facilities in the Niger Delta oil hub. Financial pressures require Nigeria's government to control the wide–scale corruption and loose tax policy that allows many to siphon off the country's oil production, hide their wealth and avoid paying taxes. According to government figures, only 214 people pay US$62 232 in taxes, despite a high number of extremely wealthy people who benefit from the country's oil reserves, and is one of the lowest rates of taxation in the world. (*Reuters UK*, 30 March 2017)

▶▶ Peat, despite aromatically flavouring whiskey, and being agreeable and cheap to burn, is one of the dirtiest fuels in use, emitting 23% more $CO_2$ than coal. It has been used for fuel in Ireland for at least 1000 years, and today produces 6% of the country's energy – indeed, Ireland is unusual among developed countries by burning it on an industrial scale. However, Ireland is beginning to turn to other energy sources, including another it also possesses in abundance – wind. Galway Wind Park, scheduled to open later in 2017, will generate 169MW of power at its peak capacity – 3% of Ireland's average needs. This is the latest development in Ireland's growing use of wind power, tripling over the past 10 years to reach 3GW of capacity, and overall renewable energy accounts for 25% of Ireland's electricity consumption, and further wind capacity is being planned. Wind power is difficult to manage and unpredictable, and other countries export excess power that takes their grids beyond the point of stability. Ireland already has two connections to the UK, and the Irish power company, Eirgrid, is planning to expand energy exports into continental Europe. Ireland could potentially meet its entire domestic energy demand from wind power by 2030, with surplus for export – and Bord na Móna, the body responsible for Ireland's peatlands, plans to stop cutting peat for energy in the same year. (*The Economist*, 22 April 2017)

▶▶ In April, Germany set a new record for renewable energy, as at one point energy produced from renewable sources nearly obliterated coal and nuclear power, producing nearly 85% of the country's total energy. Germany, under its Energiewende initiative, is moving away from fossil fuels and nuclear energy, and plans to transition to low–carbon energy generation by 2050. The success of this policy is shown by April's record – on 30 April, electricity prices fell into negative figures as renewable sources fed so much power into Germany's grid that supply exceeded demand. Coal use also fell to a record low at the same time, producing under 8 GW of energy – well under their maximum output of 50G, and most plants were only operational between 3–4 pm. Germany's nuclear power plants – which will be phased out by 2022 – were also operating at reduced capacity. Germany's Energiewende plan requires that at least 80% of all power to be generated from renewable sources by 2050, with intermediate targets of 35–40% by 2025; and 55–60% by 2035. (*The Independent*, 5 May 2017)

# ▶ Environment

▶▶ According to the environmental organization International Rivers, Laos's plan to push ahead with its Pak Beng dam on the Mekong River, along with related projects, could cause 6700 people to be re–located, and 25 villages in Laos and 2 villages in Thailand being directly affected. This is contrary to gov-

ernment claims that only 1000 people will be affected, all of whom will be compensated. This project is part of a proposed cascade of 11 dams on the main river, but environmental experts claim that building so many dams on the Mekong River could turn it into a series of interconnected lakes, affecting fisheries, sediment and hydrological flows. Most of the 912 megawatts of energy generated by the dam would be exported to Thailand. Dr Daovong Phonekeo, director–general of Lao Ministry of Energy and Mines, is confident that the project's side effects are solvable, and points out that all development projects have side–effects. Dr Phonekeo believes that the project will turn Laos into a major power exporter and become the "battery for Southeast Asia". "The Lao government has already decided to go ahead with the project because it is a good project. It will turn water into a useful resource instead of letting water flow down the river uselessly. We want to make this resource more valuable," he said. (*Radio Free Asia*, 27 February 2017)

▶▶ President Donald Trump has signed an executive order which nullifies former President Barack Obama's Clean Power Plan, which would have closed hundreds of coal–fired stations, frozen the construction of new plants and replaced them with new wind and solar farms. The Clean Power Plan aimed to curb greenhouse–gas pollution from coal–powered power plants, and President Trump's election campaign made it clear that jobs in the energy industry had higher priority over the global campaign against climate change. Barack Obama had pledged to cut US greenhouse gas emissions by 26% from their 2005 levels by 2025, and the Clean Power Plan was an essential part of this strategy. Although Mr Trump has not formally withdrawn from the Paris Agreement, which aims to keep global warming within 3.6°C and avoid catastrophic climate change, the US, the world's second–largest polluter, has signaled its non–compliance. (*New York Times*, 28 March 2017)

▶▶ Anne Hidalgo and Sadiq Khan, the mayors of Paris and London respectively, announced schemes to score new vehicles on their emissions and impact on air quality. This will enable car buyers to identify the most environmentally–friendly models and chose cars that will reduce pollution. Existing scoring schemes only cover some pollutants and require vehicles to meet standards in laboratory conditions only, when actual road emissions can be up to 15 times higher. The new "cleaner vehicle checker" will allocate each model with a score, based on all pollutants released during on–road conditions, and will more clearly and accurately detail actual emissions. The scheme aims to restore public confidence, after many motorists bought cleaner cars, only to find out that their pollution was much higher because manufacturers used "cheat devices", or there were flaws in the testing process. Worldwide, other cities, including Seoul, Madrid, Mexico City, Milan, Moscow, Oslo and Tokyo have committed to work with partner cities to develop a global scoring system which is relevant and accessible to all citizens. "For too long, some vehicle manufacturers have been able to hide behind inconsistent regulation and consumer uncertainty about the damage their cars are causing. This announcement is a wake–up call to car companies that they need to act now," said Mayor Hidalgo. (*Cities Today*, 13 April 2017)

▶▶ Global emissions of greenhouse gases have been stable for the past three years, helped by China's 4–year economic slowdown. However, China's economic growth picked up, growing at an annualised rate of 6.9% in the first quarter of 2017 – its fastest rate in 18 months. This welcome economic revival has led to increased smog levels in northern China and the southern manufacturing areas, after 3 years of improved air quality and reduced coal consumption. China's greenhouse gas emissions fell by 1% in in 2016, which combined with lower US emissions, had helped stabilize global emissions. However, official data shows that key industrial areas have suffered marked deterioration in air quality, with PM2.5 levels 32% higher compared to 2015 (PM2.5 particulates are particles with a diameter less than 2.5 μm). This data raises questions on whether China's stablising emissions are a result of policies to clean up its air quality and comply with international agreements on climate change; or simply the result of weak economic growth. Moreover, the falling demand for coal has triggered the diversification of coal into gas, which helps China meet its goals for gas usage, but without reduction in coal dependency. If the projected coal–to–gas plants are built, China's carbon emissions would increase by 1.5% each year. (*Financial Times*, 26 April 2017)

▶▶ Every year, illegal fishing removes an estimated 26 million tonnes of seafood from the world's oceans, worth an estimated US$ 26 billion. This is compounded by its linkages with human trafficking and labour exploitation, which support illegal fishing activities. Illegal fishing gravely threatens the environment, livelihood and health of the Pacific Island nations, whose ocean resources are already threatened by climate change. The problem was considered by the World Economic Forum's ASEAN conference, and

several obstacles to tackling illegal fishing were highlighted. First, the lack of prosecutions and convictions over human trafficking are no threat to the industry's value, and strong government action is the only way to combat this. Increased co–operation between countries to check boats, limit fishing permits, and revoke licenses if any breaches of the law occur is also vital. The recent Tuna Traceability Initiative is an example of how this can work in practice – organizations must co–operate to converse and manage fish stocks, including companies fully disclosing their environmental management processes and ensure that no slavery is used in the supply chain. (*Devex*, 5 May 2017)

# ▶ Food, Water and Sanitation

▶▶ In an effort to tackle obesity, France has banned restaurants from offering unlimited sugary drinks, either at a fixed price or for free. France's rate of overweight or obese adults (15.3%) is below the EU average (15.9%), but is rising, and past the age of 30, nearly 50% of French men and 41% of French women are overweight or obese. The move will affect all public eateries, from fast–food restaurants to school canteens, and targets soft drinks, including sports drinks containing added sugar or sweeteners. The WHO recommends that sugary drinks are taxed, partly due to their links with obesity and diabetes. Elsewhere, a 10% tax on soft drinks in Mexico reduced consumption by 6% in its first year, and the UK will introduce a soft drinks tax in 2018. However, a court blocked an attempt in New York to ban "super–sized" sugary drinks in 2013. (*BBC*, 27 January 2017)

▶▶ According to the South Sudan government and three UN agencies, famine has been declared in parts of South Sudan – the result of the country's protracted civil war and devastating economic crisis. According to UN officials, President Salva Kiir's government is blocking food aid to some areas. More than 100 000 people in two counties of Unity State are affected, with fears that famine will spread to an additional 1 million people, as 1–in–3 households in South Sudan face food insecurity, and nearly 75% have inadequate food supplies. Widespread hunger has been worsened by South Sudan's economic crisis, where crippling inflation makes food unaffordable for many families. Providing humanitarian aid is hampered by fighting between the government and armed groups, coupled with the affected population's inaccessibility – 70% life in the bush. However, UN official Joyce Luma highlights how much of the famine is man–made. "There is only so much that humanitarian assistance can achieve in the absence of meaningful peace and security," she says. (*Al Jazeera*, 21 February 2017)

▶▶ The spread of quinoa consumption in developed countries illustrates how increasingly people are eating unfamiliar grains, as westerners eat less wheat and more millet, sorghum, teff and quinoa, and middle–class Asians eat more wheat in place of rice; and West Africans eat 25% more rice per head than 2006, while millet consumption has fallen by the same amount. These trends show increased prosperity and expanding choice, as better farming techniques improve yields, and rapid urbanisation means fewer people growing their own grains, but have the money to try new varieties. And globalisation means that food and farming techniques cross borders, enabling more people to try new flavours and foodstuffs. This is part of a broader picture of falling hunger levels – between 1990 and 2015, the proportion of malnourished children fell from 25% to 14%, the proportion of income that poor people spend on food fell from 79% to 54%, and among under–nourished people, the average calorie shortfall fell from 170/d to 88/d by 2016. In light of these benefits of globalisation, Donald Trump's plans to erect trade barriers and possibly start a trade war give food for thought. (*Economist*, 9 March 2017)

▶▶ According to the UN's World Water Development Report, globally more than 80% of wastewater is discharged untreated into rivers and lakes, with negative consequences for health and the environment. However, according to the report's editor–in–chief, Richard Connor, wastewater is a resource which could help meet the water, energy and nutrient needs of a growing global population. Wastewater contains nutrients such as phosphorus and nitrates which could be turned into fertiliser, and treated sludge can be turned into biogas that could power wastewater treatment plants. The UN estimates that the world will need 55% more water and 70% more energy by 2050 to meet global population growth, and more people also means more wastewater. Dealing with wastewater is also a huge challenge within informal settlements in rapidly–growing cities in developing countries. He calls for governments to invest in smaller, decentralized treatment systems that are cheaper and easier to maintain, and notes that not all water needs

to be treated to drinking quality, but to a level where it can be used by industries, municipalities, agriculture or for cooling in power plants. (*Thomson Reuters Foundation*, 22 March 2017)

▶▶ More than 1–in–5 of South Africa's children suffers from stunted growth, and according to the 2016 Global Nutrition Report, South Africa ranks 70 out of 132 countries on this indicator. It performs slightly worse than several poorer African countries, including Gabon, Ghana and Senegal, and only slightly better than many others, including Somalia and Swaziland. There has been only a slight reduction in stunting among South Africa's children over the past 20 years, and the country's system of social grant payments is doing little to tackle the problem. South Africa's parliament approved a slight increase to these grants, and the Child Support Grant covers 12 million children – almost 66% of all children in South Africa. Despite this coverage, the grants are not tackling malnutrition, partly because any increases in their value have been outstripped by food price inflation, and they cover less than two–thirds of the cost of a providing a nutritionally–adequate diet. Second, the grants are often partially spent on non–food needs for the household as a whole. Third, the grants do not tackle the other causes of malnutrition in South Africa, including unsanitary water supplies leading to diarrhea or worms; and the low number of women breast–feeding their babies, which can damage a child's nutritional status from birth onwards – South Africa has one of the lowest compliance with WHO breast–feeding recommendations in the world. (*The Conversation*, 2 April 2017)

# ▶ Peace and Human Rights

▶▶ Women and girls in Afghanistan can face imprisonment of up to 5 years in the country's so–called "moral prisons", for crimes such as running away from home (even if fleeing violence), or for sex before marriage (*zina*). According to the campaigning group Human Rights Watch, these incarcerations are increasing, from 400 in 2011 to 600 in 2013. The Afghan government has consistently rejected abolishing the prosecution of women for moral crimes. Women imprisoned for moral crimes have described imprisonment without trial, or on false charges, or for *zina* despite being raped. Afghanistan also permits the use of "virginity tests" – with or without the consent of the woman or girl concerned – for those who have fled their homes or entered public spaces without male supervision. Conditions inside the prisons are harsh, with inadequate ventilation, space and sanitation. Many inmates give birth inside prison, or have their children with them during their imprisonment. After their sentences, women are transferred to secret shelters to protect them from honor killings. Afghanistan's justice system favors men, with a reported 5132 new cases of violence against women (including 241 murders) in the first half of 2016 – in almost all cases, the perpetrators were unpunished. In addition, informal courts, chaired by powerful male fundamentalists, have carried out public lashings and executions against women, and in the past the Afghan government has attempted to make stoning legal for certain violations of Sharia law, such as adultery. It has also failed to fully implement the country's 2009 Elimination of Violence Against Women law – a presidential decree which aimed to protect the rights of women and girls. (*The Diplomat*, 8 March 2017)

▶▶ According to sources in North Korea, women serving in the country's military and construction brigades are routinely abused by their supervisors, and some are pressurised into providing sexual favors and forced into sex work. North Korea's semi–military construction brigades, known as "storm troopers" will assign women to the most difficult workplaces if they reject their commanders' sexual demands. Moreover, women cleaning up after the floods in Yonsa country could not bathe at night despite being covered in mud, because border guards prevented them from approaching the Tumen River. "Although equal rights for both sexes have been guaranteed in North Korea for more than 70 years, it is hard to find another country in which women's rights are trampled this badly," an unnamed source said, calling for compulsory service in the army and construction brigades to be immediately abolished to safeguard women's rights. (*Radio Free Asia*, 10 March 2017)

▶▶ Police have used tear gas and bullets to disperse protesters who had gathered in Kinshasa, the capital of the Democratic Republic of Congo, and a number of injuries have been reported. Protests began when negotiations over the departure of President Joseph Kabila after 17 years in power collapsed – an outline peace deal was agreed in 2016 but has proved difficult to finalise. Church leaders had mediated talks between the government and opposition, but have withdrawn after both sides failed to agree on issues such

as the choice of a transitional prime minister. Mr Kabile's term ended in December 2016, and the opposition has accused the government of sabotaging efforts to offer him a peaceful exit. The main opposition party, the Union for Democracy and Social Progress, has called on citizen to take part in a peaceful march on 10 April, to "resist the dictatorship taking root." (*BBC*, 29 March 2017)

▶▶ Despite tensions over other policy areas, global health is emerging as a potential area of partnership between the USA and China. Both countries collaborated in the SARS outbreak in 2002, and Ebola in 2014, when staff at the US Center for Disease Control and Prevention (CDC) worked with staff at Chinese laboratories. This partnership is ongoing, as China and the US's CDCs work to build an African CDC to combat infectious diseases, and is expanding into the private arena. This is illustrated by the Bill and Melinda Gates Foundation part–funding the Global Health Drug Discovery Institute in Beijing – the first foreign–funded NGO to operate in China, which will focus on early drug discovery to combat infectious diseases such as TB, malaria and HIV. This evolving role is part of China's long–term strategy of building up its pharmaceutical industry, and becoming a key player in global health, as it moves from being an aid recipient to an aid provider. During the Ebola outbreak, Chinese scientists reverse–engineered the US/Canadian drug, ZMapp, after the manufacturers exhausted their limited supplies – a key indicator of China's role in international health crises. Moreover, the potential reduction in US aid contributions under the Trump presidency (the US is currently the largest global health funder, with an estimated US$10.2 billion of aid in 2016), creates a potential void that China could be positioned to fill. (*Forbes*, 26 April 2017)

▶▶ Several years after civil war in the Central African Republic (CAR) killed thousands of people and left hundreds of thousands of people displaced, aid workers have warned that the country may be returning to conflict. In recent months, armed groups have killed at least 45 people and burned villages, and more than 100 000 people have fled their homes. The conflict is mainly between mainly Christian rebels (anti–balaka) and the mostly Muslim former Séléka rebels. Anti–balaka rebels had used the village of Bambara as a base in northern CAR; the village was then attached by former Séléka rebels, killing 25 people and burning 600 homes. The surviving villagers have no food or seeds, and lack clean water and education, as the school was also destroyed. About 20% of the CAR's population – about 400 000 people – are displaced, and according to the agency Médecins sans Frontières (MSF), civilians are being attached at levels not seen in years. Since the civil war, more than 50% of the population rely on humanitarian aid, but aid levels are only 10% of what is required. According to the UN, this lack of support further damages any chance of peace. MSF are experiencing severe difficulties in reaching distant rural areas in need. "CAR is one of the poorest countries in the world, and needs to be supported but the people are focusing on the conflict. But it takes time for people to solve it. During this time, we should be able to carry on with normal activities to give this access and it's not easy," says Abdel Kader Tlidjane of MSF. (*Voice of America*, 6 May 2017)

# ▶ Science and Technology

▶▶ Despite many tragedies in 2016, such as the bombing of hospitals in conflict zones, the increasing threat of Zika and antibiotic–resistant microbes, the re–emergence of polio in Nigeria and the revival of yellow fever, there were many inspiring developments within global health. One of these was the continuing progress in combating malaria – Africa, which has the highest mortality rates from malaria, saw a fall in deaths from 800 000 in 2000 to 400 000 in 2016. In addition, European drug regulators approached the first human vaccine against malaria – although its protection weakens over time, it is still a major breakthrough. 2016 also saw the approval of the first vaccine against dengue fever, which causes nearly 50 million infections a year and is the world's most significant and fastest–growing mosquito–borne viral disease. HIV infections and deaths have stabilized, the Americas are almost free from river blindness and other tropical diseases nearing elimination include lymphatic filariasis and guinea worm. An experimental Ebola vaccine has been produced, and although it is not yet approved an emergency stockpile of 300 000 doses has been created in the event of another outbreak. (*Project Syndicate*, 17 January 2017)

▶▶ An outbreak of yellow fever in Angola in 2016 infected more than 7000 people and caused hundreds of deaths before it was brought under control. Yellow fever is vaccine–preventable, but the outbreak highlighted that the WHO's supply of 6 million doses was inadequate – catastrophe was averted by interna-

tional co–operation, science and luck, as drought reduced the population of yellow–fever carrying mosquitoes. It shows the fragile state of the world's systems for responding to dangerous pandemics, because only a few companies manufacture yellow–fever vaccine, thanks to unstable markets and uncertain profits, and if yellow fever had spread into China by returning migrant workers, demand would have far exceeded global manufacturing capacity. The new Coalition for Epidemic Preparedness Innovations (CEPI) exists to facilitate the development of vaccines for threatening diseases, and to build capacity to respond when new diseases emerge, and is an important milestone in epidemic preparedness and prevention. However, effective pandemic preparedness depends on our ability to connect innovations from R&D to the logistical capacities to deliver supplies where they are needed. Local surveillance capacities, laboratory capacity, diagnostic tools and health information systems must also be strengthened, and emergency operations centers established to improve responses, plus training health workers in digital technologies. Strengthening every link in the chain of epidemic preparedness and response is vital to ensure that the next outbreak of disease does not wreck the same devastation as Ebola, Zika or yellow fever. (*Financial Times*, 27 January 2017)

▸▸ The ability to use drones to sample animals and people to determine which pathogens are present in an area and where they are hosted would be invaluable in understanding how diseases spread, and how to predict and pre–empt their outbreaks. Drone technology is not yet sufficiently advanced to allow this, but scientists at Microsoft Research have designed a system that captures mosquitoes and analyses their pathogen load from drawing blood from feeding off their hosts, thereby detecting blood–borne pathogens present in the host other than those transmitted by mosquitoes, eg, malaria. Ethan Jackson and Jonathan Carlson of Microsoft Research designed portable mosquito traps that lures in the insects (the traps can be fine–tuned to detect mosquitoes of certain species). The captured insects are extracted, triturated and their collective DNA analyzed and matched against a database of known sequences, potentially also identifying unknown viruses. Ultimately, it is hoped to produce traps that can be carried, deployed and collected by drones in inaccessible areas, which are home to wild animals that act as reservoirs for pathogens like Ebola that can spread to humans. (*Economist*, 23 February 2017)

▸▸ Each day, 1300 children die of diarrhea, and rotavirus causes 33% of these deaths, making it the second–largest cause of death among children and babies. Rotavirus is vaccine–preventable, but most of these children live in sub–Saharan Africa, with massive problems in keeping vaccines cold enough during transit and storage. However, a new heat–stable rotavirus vaccine, BRV–PV, has been developed and a Phase II study found that it protects against gastroenteritis in 66% of children who receive it. A trial was conducted in Niger, which has a population of 20 million people, half of whom aged under 15, and the majority living in poverty. It is also land–locked and largely desert, with little access to electricity and water, and with most people living far from health centers. BRV–PV outperformed both existing vaccines in the trial, and is being reviewed by the WHO for pre–qualification, which would make it available in low–income countries. A heat–stable vaccine offers hope for reaching more children, and the cost, at US$ 2.50/dose, is lower than both existing vaccines that require refrigeration – making a huge difference to the lives of children and their families. (*Forbes*, 23 March 2017)

▸▸ The Democratic Republic of the Congo (DRC) is moving toward using an unlicensed vaccine against an outbreak of Ebola in a remote area. The WHO has issued a "donor alert", requesting US$ 10.5 million to support the vaccine trial, including surveillance, treatment, and conventional prevention and control techniques. The DRC government submitted a formal vaccine trial protocol to an ethical review board. The vaccine was produced by Merck and stockpiled in the USA after the 2014 outbreak in West Africa. The WHO and Médecins sans Frontières (MSF) set up vaccine trial in Guinea, with an unusual "ring vaccination" design that selectively vaccinated those who were most likely to have had contact with a known case. The initial results showed 100% protection 10 days after immunisation, but the unusual trial design dissuaded Merck from pursuing it further, and the vaccine can still only be used in trial setting. Epicenter (MSF's research arm) and DRC's Ministry of Health have written a protocol for a new ring vaccination study, but without a control group because withholding the vaccine from some participants is no longer seen as ethical. However, this means that the trial cannot evaluate its efficacy. (*Science*, 24 May 2017)

NEWS

# Research for Actionable Policies: implementation science priorities to scale up non–communicable disease interventions in Kenya

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Low– to middle–income countries (LMICs) are disproportionately affected by the rise in prevalence of non–communicable diseases (NCDs). According to the World Health Organization, four groups of diseases– cardiovascular disease, cancer, respiratory disease and diabetes – comprise 82% of NCD deaths worldwide and three–quarters of the deaths related to NCD occur in LMIC [1]. In Sub–Saharan Africa, the World Bank estimates that nearly 46% of all deaths will be attributable to NCDs by 2030, and 41% of all deaths for those aged 15–59 will be due to NCDs [2].

Similar to other Sub–Saharan African countries, Kenya is experiencing an explosive growth in NCDs, especially those related to cancer and cardiovascular diseases [3]. There is therefore an urgent need to determine implementable interventions to reduce the growing burden from these and other NCDs, including respiratory diseases, injuries and mental health. Although there are many ongoing research studies and demonstration programs [4], it is not clear whether these activities address the Kenyan Government's evidence needs and priorities to support their NCD strategy [5]. To understand the current research landscape in order to guide the implementation research agenda in Kenya, RTI International, Kenya Ministry of Health, NCD Alliance Kenya, Kenya Medical Research Institute, and University of Nairobi hosted a two–day symposium on September 7–8, 2016 in Nairobi, Kenya. The symposium was entitled, "Research for Actionable Policies: Implementation Science Priorities to Scale Up Non–Communicable Disease Interventions in Kenya." The sections that follow provide an overview of the meeting including its purpose and objectives, a summary of the proceedings and recommendations to address gaps in NCD implementation science research in Kenya.

## SYMPOSIUM OBJECTIVES AND STRUCTURE

The symposium addressed three specific objectives. First, we wanted to catalog promising and innovative intervention strategies applicable to the Kenyan setting in order to account for existing programs and ongoing implementation research activities. Next, we endeavored to identify gaps in research to support implementation of cost–effective interventions and assess areas where research capacity is needed. Lastly, the symposium participants generated recommendations to create a road map for implementation science research to advance evidence–based NCD prevention and control in Kenya. The symposium attempted to address a broad range of NCDs but its main focus was on cardiovascular diseases and cancers as these two diseases pose the highest burden.

Representatives from the Kenya's Ministry of Health opened the symposium by setting the framework for the meeting and outlining the importance of implementation science. The US National Institutes of Health defines implementation science as the study of methods to promote the integration of research findings and evidence into health care policy and practice. The key challenge posed to the participants was to consider whether the current implementation science research conducted in Kenya supported the government's NCD strategy [5], and if the research did not, how could the country move toward using health research to inform policy and practice.

The two–day symposium consisted of 14 sessions [6]. During the first day, stakeholders presented on the burden of NCDs internationally, in Sub–Saharan Africa and in Eastern Africa with a focus on Kenya. They also discussed the role of research and strategic planning to combat them. Toward the end of day one, participants convened in small groups to discuss gaps in NCD implementation science research and brainstorm ideas to address the gaps. On the second day, panel members presented and discussed program implementation at the community level and through public–private partnerships. The symposium closed with a panel discussing lessons learned from the two days and summarizing specific recommendations to guide future implementation science research in Kenya. Approximately 100 individuals representing multiple disciplines from research institutes, civil society, governmental organizations, health care providers, industry and international organizations participated during each day of the symposium.

## OVERVIEW OF THE PROCEEDINGS

### Burden of NCDs – challenges and opportunities

*Risk factors*

NCDs account for 27% of all deaths in Kenya, totaling almost 100 000 people per year [7]. Additionally, NCDs contribute to over 50% of inpatient admissions and 40% of hospital deaths and therefore have a substantial impact on health care budgets [7]. Data from the 2015 Kenya StepWise Survey indicates that approximately 8% of the Kenyan population smoked daily, between one–fifth and one–quarter were exposed to second hand smoke, 17% of men and 35% of women were overweight or obese and nearly one–quarter of the population had high blood pressure; all of these risk factors and conditions are contributing

risk factors to NCDs [8]. These data support the urgent need to have implementable interventions to reduce the projected high burden of NCDs in Kenya. In subsequent presentations, the NCD leaders from the Tanzanian and Ugandan Ministries of Health and other researchers acknowledged that NCD trends in additional East African countries were overall similar to those reported for Kenya. Further, the symposium participants concluded that the challenges of implementing health care interventions along the continuum of care had many similarities across these countries, although interventions would need to be tailored to ensure optimal integration with the existing health care system and infrastructure in each country.

### Current initiatives to address policy gaps

In 2015, Kenya launched the National Strategy for the Prevention and Control of NCDs (2015–2020) to reduce NCD mortality by 25 percent by 2025 in accordance with World Health Organization's (WHO) recommendations [5]. In addition, Kenya has also developed a National Diabetes Strategy (2010–2015) and a National Cancer Control Strategy (2011–2016) [9,10] which are intended to raise patient awareness and spur initiatives to improve management infrastructure. Furthermore, to address key risk factors for NCDs, Kenya has developed policies and regulations to address tobacco use and excessive alcohol consumption [11]. The Tobacco Control Act of 2007 is the principal law governing tobacco use in Kenya. This comprehensive law defines key terms and covers topics including restrictions on public smoking; tobacco advertising, promotion and sponsorship; and packaging and labeling of tobacco products. The Tobacco Control Regulations of 2014 further regulates selected provisions under the Tobacco Control Act including public smoking restrictions, tobacco product and tobacco industry disclosures, which came into effect in September 2016. Currently, there is a 49% tax on the sale price of tobacco products. In 2010, the Alcoholics Drinks Act was enacted by the Kenyan parliament. It has not yet been fully implemented nationwide as devolution, which was adopted in 2013, shifted decisions about whether to adopt and implement the law to Kenya's 47 county governments.

Overall, Kenya has made efforts to generate policies through legislation and increase knowledge through research on tobacco and alcohol control [12-14]. Clearly more needs to be done but there are other areas related to diet, specifically salt and sugar consumption, which currently have no legislation nor large–scale research initiatives. High levels of obesity, especially among women, and hypertension are the main risk conditions for NCDs in Kenya and therefore addressing the underlying risk factors could have a substantial impact on reducing the burden from NCDs. Salt reduction is one of the most cost–effective interventions and implementing public awareness programs using mass media on diet and physical activity is classified as a 'best buy' (or best practice) [15,16]. Research is required to identify optimal approaches that should be adopted in the Kenyan context to ensure policies are successful when implemented.

Evidence from other countries points out that successful implementation of targeted policies can lead to reduction in harmful risk factors and risk conditions [15,16]. An overview presentation from the US Centers for Disease Control and Prevention provided several examples on policy approaches to successfully address NCDs that have been applied in the United States [17,18]. These include defining national targets, such as the decades–long Healthy People initiatives, promoting multisector NCD action plans, implementing policies to address NCD risk factors and ensuring appropriate treatment when required. High impact successful initiatives have included national, state and local level policies and legislations on tobacco control, enforcements of alcohol levels to reduce road traffic accidents and initiatives to reduce sodium content in the food supply.

### Economic burden and finances

Given that NCDs are debilitating and long–lasting, they are often expensive to treat. And, as NCDs continue to affect younger populations, future productivity is imperiled. According to survey findings from Kenya, NCDs are associated with a 33.2% reduction in household income [19]. Further, in comparison with households with other chronic conditions, those with NCDs had 26.1% lower average income. Additionally, there was an inverse relationship between education and the presence of NCDs, which highlights the potential for NCDs to increase the disparities already experienced by those who are less affluent.

Only a small percentage of Kenyans have health insurance and participants offered a number of suggestions to reduce the economic burden from NCDs [20]. The National Hospital Insurance Fund (NHIF) is one possibility to assist Kenyans diagnosed with NCDs. The program collects a percentage of employees'

salary and places it into a risk pool, and participants can select various benefit packages, which include inpatient and other comprehensive selections. The government of Kenya has designated the NHIF as the driver of its approach to universal health coverage and anticipates that increasing percentages of the population will be covered under various schemes over time. Because of the relationship between education and NCDs, symposium participants also suggested that public education be improved with an increase in country–wide NCD awareness campaigns and affordable preventive health care services.

## Evidence–based strategic planning to address NCDs in Kenya

### Model–based prioritization of interventions

Researchers from Kenya's Ministry of Health and RTI International spoke to the importance of strategic planning when addressing NCDs in Kenya. First, it was necessary for the country to assess the burden of NCDs and consider the consequences of inaction. Second, the country should assess the effectiveness of primary prevention (eg, immunizations, education) and secondary prevention (eg, screening and treatment, wellness care). Third, Kenya needs to examine the cost of implementation and determine the optimal interventions to target in the short–term, medium–term and long–term timeframes. This systematic approach will also identify the gaps in the research and data sources that need to be addressed to inform future strategic planning.

RTI scientists described qualitative and quantitative tools used to inform strategic planning, including economic modeling to simulate the impact of interventions. For example, population–attributable risk models developed by RTI researchers indicated that if tobacco were no longer a factor in individuals' behaviors (ie, if people no longer smoked), deaths attributed to cardiovascular disease (CVD) and cancer would be reduced by 9% by 2030 (compared to not doing anything); if high blood pressure was no longer a risk factor, deaths attributed to CVD would be reduced by 33% by 2030 (compared to not doing anything) [21].

Additionally, in operationalizing Kenya's NCD Strategic Plan, RTI researchers reiterated the importance of considering the cost of implementing interventions alongside the projected benefits to ensure interventions are selected to achieve maximum impact [22]. The preliminary research presented indicated that women's health can be improved by reducing obesity through diet and physical activity interventions; taxes applied to tobacco and alcohol will have a greater impact on the health of men than women because of the existing patterns of smoking; and management of hypertension is essential but potentially expensive to provide on the scale required, so primary prevention should be intensively pursued.

### Data needs for planning and evaluating NCD interventions

Several presenters focused on the benefits and challenges of collecting data to monitor NCDs. Benefits included understanding NCD patterns, conducting research reflective of the data, and supporting health departments in guiding and planning disease prevention and control programs. Currently, there is limited data on NCDs to monitor and track the impact of interventions, but new data initiatives are in various stages of planning and implementation. Kenya Medical Research Institute (KEMRI) staff presented plans to expand cancer registration in Kenya to create a National Cancer Registry and a pilot study is under way to evaluate opportunities to create a stroke registry [23]. However, several challenges remain, including lack of staff at public health institutions to ensure high quality data collection at the point of service delivery, lack of continuity of funding and reliance on manual data collection and reporting [24]. The Academic Model Providing Access to Healthcare (AMPATH) has developed an electronic health information system that has been successfully implemented in Western Kenya and this approach could provide important lessons for other institutions to adopt comprehensive electronic health information technology systems [25,26].

### National– vs county–level planning

Several presenters discussed experiences in NCD planning at both the national and county level. Presenters noted the necessity for Kenya to improve its health infrastructure due to the loss of health tourism dollars to India, South Africa and the United States. They argued that maintaining these resources within Kenya will allow for investment in additional health care facilities. Although Kenya does have two public hospitals to which patients from Tanzania and Uganda travel to, these hospitals cannot meet overall de-

mand and there is a need to offer competitive pricing. Tertiary level hospitals can only be established in specific locations and therefore coordination between the national and county level governments is critical to provide NCD services across the continuum of care.

A Nairobi City Country representative described the establishment of an NCD Unit in the County Health Office in response to a key objective in the County's Health Sector Strategic and Investment Plan 2013–2018. The goals of the unit include improving awareness of all NCD risk factors, strengthening screening programs and treatment for all NCDs, and developing specialized clinics with sustainable services. As a result of the unit, to date, there has been improvements in NCD service delivery but there have been challenges as well, including limited funding, poor data collection and the need to address multiple risk factors, such as environmental pollution.

## NCD clinical– and community–level implementation

### Integration of service delivery

Several models of integrating service delivery were presented. The program at AMPATH provides integrated services including breast and cervical cancer screening. The cervical cancer screening program is well established while the breast cancer screening initiative using clinical breast exam is relatively new. A recent study found that those with prior knowledge of breast cancer risk factors are more likely to participate in screening [27]. A key feature at AMPATH is the focus on increasing linkages with patients and retaining individuals so they stay engaged and receive continual services. There are ongoing plans to track patients using common electronic medical records (EMR) and universal identification across health centers to monitor success of integrated delivery and retention.



Photo: 2016 Symposium on Non–Communicable Diseases (front page of the conference program).

Representatives from MSF Belgium described a low–cost approach to integrated NCD care using simplified treatment and referral guidelines and a one–stop clinic location for all basic services. The patient–focused approach is supported through task shifting to allow NCD patients to be seen on all clinic days and 'Adherence Management Clubs' have been established where HIV and NCD patients meet in groups to facilitate compliance with medications. NCDs are chronic diseases by nature and thus pose ongoing challenges related to patient retention and long–term disease management.

Additionally, the community–based hypertension management under AstraZeneca's Healthy Heart Africa program aims to increase capacity through training of health care workers and improvement of the medication supply chain. Further discussions were also focused on leveraging the HIV platform to offer NCD services. AstraZeneca and the United States President's Emergency Plan for AIDS Relief (PEPFAR) have recently announced a pilot initiative in Kenya which will provide an opportunity to use hypertension as an entry point to provide HIV services to a key population of younger working age males (25–50 years) and, alternatively, hypertension services to a large cohort of individuals through the HIV/AIDS infrastructure developed by PEPFAR. Integration of health services is not without its challenges and a recent study in Kenya which found resistance among health care workers to incorporate NCDs into HIV programs due to the perceived substantial increased workload. Similar findings related to workforce related barriers to integration have also been reported in Uganda and Tanzania [28,29] and

therefore these challenges to integrated service delivery need to be a focus of ongoing implementation research.

### Infrastructure and capacity building

A multidisciplinary team of researchers presented on the need to increase staff capacity and their ability to provide all services related to cancer screening programs. Statistics presented showed that Kenya is understaffed in numerous key provider categories including oncologists, radiation therapists and oncology nurses [30]. Participants stressed the need for better infrastructure in order to increase access to diagnostic and treatment services, which are the cornerstone of any successful screening program. A critical need identified was the improvement of laboratory capacity in Kenya which was described as one of the weakest links in the current health care system. A World Bank–supported demonstration project is establishing a network of laboratories to increase access to diagnostic services for chronic diseases and NCDs. Other key areas for improvement are palliative services and hospice care, which are both inadequate to meet the current patient needs.

### Patient awareness and barriers to cancer care

Researchers in many of the sessions noted that not all Kenyans were familiar with NCDs, and even when aware, very few have been screened for NCDs. For example, results from an analysis of the 2014 Kenya Demographics and Health Survey indicated that 76% had heard of cervical cancer, while only 14% of women have been screened, and only 65% of men had heard of prostate cancer, with only 3% having been screened [20]. One of the presenters provided a framework on how to utilize health communication science to change patient behavior for NCD prevention and control, which included educating patients about how their behavior contributes to risk factors and motivating them to be screened. A recent patient survey at Kenyatta Hospital showed that almost a third of the patients had missed or delayed treatment mainly due to financial reasons, problems with getting transportation for treatment, and lack of accommodations once in Nairobi. Increasing patient awareness is important but there are additional barriers that need to be addressed to ensure optimal delivery of services along the continuum of care.

### Public–private partnerships

Government funding of screening, diagnosis and treatment programs can be enhanced with partnerships with private entities to fill gaps in health care service delivery. A panel from the pharmaceutical and diagnostic industry spoke to their companies' programs and partnerships in Africa and in Kenya specifically. Examples of activities partners conducted included training of health care staff and providers about diagnosing and treating NCDs and simplifying treatment protocols for adoption. Many of the companies were committed to increasing access to prescription drugs for patients and offered treatments at reduced or affordable prices. Companies also worked with local civil society to raise awareness of NCDs and improve skills in outreach, advocacy and fundraising. Novo Nordisk also presented an innovative approach through their Base of Pyramid project to collect and analyze data for evaluation and program improvement. Coordination of activities between the private and public sectors to ensure synergies and to reduce duplication was indicated as key aspect in discussion sessions.

## SUMMARY OF KEY RESEARCH RECOMMENDATIONS

Several critical research gaps were identified during group discussion, panel presentations and participant dialogue. The research roadmap for Kenya should include the following recommendations.

1. Evaluate optimal approaches to implement policies for primary and secondary prevention tailored to the Kenyan setting:

   • There is lack of systematic knowledge on dietary patterns and individual food purchase decisions. Policies to reduce salt consumption, which has shown to reduce high blood pressure and is a WHO 'best buy' intervention, should be implemented in Kenya after research on optimal implementation strategies is conducted. Additionally, obesity is a substantial risk factor for NCDs, especially among women, and interventions to reduce sugar consumption should be systematically evaluated.

   • Interlinkages between infections and NCDs, especially cancers, is well established and adequate research into scale up of vaccination programs to reduce targeted infections is required (especially Human Papillomavirus vaccine to substantially decrease the incidence of cervical cancer).

- It is also important to assess and understand the life course perspective as many of the risk factors for NCDs can be present at birth or acquired during early childhood (such as stunting which increases risks of nutrition–related chronic diseases including diabetes, hypertension, and obesity in the future).
- Given resource constraints, it is essential to understand which cost–effective interventions are most affordable in the Kenyan context to operationalize national NCD strategic plans.

2. Generate evidence–based health communication messaging for all key stakeholders and strengthen community participation:

- There is a lack of understanding of the patients' perspective and their health seeking behavior. A systematic evaluation of the social determinants of the use of preventive services is required.
- Research is needed to determine the best approaches to communicate risk factors to patients and communities. Providers need to be engaged as well given the vital role of patient–provider communication in increasing use of NCD preventive services.
- Additionally, improved approaches to communicate with policy makers is necessary to appropriately and successfully advocate for NCDs.

3. Assess capacity to deliver NCD services along the continuum of care:

- A systematic evaluation of infrastructure investments that are required to provide optimal oncology diagnostic and treatment services should be initiated. Screening programs for breast and cervical cancer cannot be scaled up without adequate provision of services along the continuum of care for appropriate triage for diagnosis and treatment.
- Provider training needs should be evaluated from the primary level to the specialty care setting. Overall, health services delivery is still geared toward addressing communicable diseases and there needs to be a shift to dual care for communicable and non–communicable diseases.
- Better understanding of task shifting and task sharing is needed to ensure NCD program implementation leads to successful scaling up of services. Integration with other successful programs, such as maternal and child health services, should be evaluated to assess efficiency in NCD service delivery.

4. Ensure the NCD planning process is evidence–based and data–driven through targeted data collection efforts:

- Estimates of regional data are not accurate or nonexistent; this information is needed to evaluate the extent to which NCD policies and interventions are generalizable across regions in Kenya.
- Opportunities need to be explored that piggyback NCD–related data elements onto existing data collection mechanisms and encourage standardized data collection at the county level.
- Support should be provided to ensure sustainability of the newly–launched National Cancer Registry and planned establishment of the stroke registry.

5. Investigate innovative approaches to finance NCD services along the continuum of care:

- The National Health Insurance Fund is evaluating coverage for cancer screening; stakeholder engagement is needed to ensure that the preventive package of coverage is comprehensive and appropriate for the Kenyan setting.
- The role of private insurance and other risk–based pooling of resources needs to be evaluated.
- Cost versus quality of coverage in the public versus private sector should be evaluated to provide health consumers with more transparent information for decision making and facility selection.

Additional recommendations were also shared on how to address the research gaps identified. The steps include:

1) Advocating for a systematic process to develop research capacity across Kenyan institutions so researchers can contribute towards addressing the identified gaps. Initiatives could include fellowships, hands–on mentoring and other training programs.

2) Leveraging existing data sources from national and local surveys and studies to get a deeper understanding of NCD risk factors and the underlying social determinants.

3) Engaging in public–private partnerships to enhance resource sharing and address common goals of increasing awareness of NCD risk factors and availability of screening, diagnosis and treatment services.

4) Collaborating to seek strategic funding for new research studies that avoid replication to ensure efficient use of limited resources.

5) Enabling deeper regional cooperation across East African countries to allow for the sharing of lessons learned, as much of the underlying patient and health system factors are similar.

## CONCLUSIONS

The NCD–related research recommendations proposed in this report will require resources to implement, but the cost of inaction is extremely high [31]. Partnerships and multilevel coordination are essential to ensure available funding is maximized and duplication is avoided. The recommendations from this symposium can serve as a road map to guide the future research investments that have to be made to support the planning and implementation of policies and interventions that are likely to yield maximum benefits to Kenyan society. Implementation cannot wait until all the evidence is gathered, as the needs are immediate and pose a high burden to individuals, communities and the nation as a whole. Targeted pilot programs can serve as a vehicle to test strategies on a limited scale and lessons learned can then guide widespread implementation. The county–level organizations and the national government will need to coordinate implementation activities to ensure that an optimal learning environment is created where evidence generated in one county can be disseminated to improve the health of all Kenyans.

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# A new paradigm on health care accountability to improve the quality of the system: four parameters to achieve individual and collective accountability

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Healthcare systems the world over are facing significant financial pressures and growing demands for services. Many nations have therefore set common goal of improving the population's health, the quality of the outcomes, and the containment of costs [1].

A recent perspective considers health care systems as "high reliability organizations" (HROs), which are complex systems operating in a *high–stress environment* without losing sight of the objective to provide high quality results while still focusing on the assessment and management of risks [2].

So, the growing demand among patients for increasingly high quality treatments, the obligation to reduce adverse events in health care, the need for transparency in health care systems, and the current economic situation compound the difficulties in improving health care delivery. The debate on these issues now transcends national borders and single organisational, political and jurisprudential systems. Also, the problem of escalation of litigation in health care is applicable to all physicians regardless of age, geographical origin, and specialisation and it should be solved.

Therefore, these changes in the health care systems' priorities have set the ground for an interdisciplinary approach necessary to assess the activities of health care professionals and, in general, of health care systems.

> The current healthcare systems' priorities set the ground for an interdisciplinary approach to assess the activities of healthcare professionals and of healthcare systems themselves.

## TIME IS RIPE

Increasingly, the concept of health care professional responsibility concentrates only on medical malpractice. However, health care accountability does not depend on the hypothesis of a patient's damage claim and should instead reflect all

> Development and combination of professional competence, information accessibility, awareness, and gratification would allow better achievement of the target of individual and collective accountability.

conditions necessary for the daily delivery of high quality health care services to the system users, which constitute rational use of the economic resources.

We believe medico–legal activity should not "merely" contribute to the evaluation of other physicians' conduct within medical malpractice, but – as other disciplines do – it may provide further reflection to stimulate the comparison between different health care professionals and to provide a valuable support to the activities of clinical risk management.

With this background, we therefore believe that the time is ripe to offer a new technical paradigm for professional accountability, valid to lead the assessment (*ex post*) of the physicians' conduct within the medical malpractice toward applications (*ex ante*) useful to improve the health care professionals' approach to the system.

This paradigm is based on four distinct pillars, interlinked and interdependent.

## PROFESSIONAL COMPETENCE AND INFORMATION ACCESSIBILITY

The first parameter is *competence*, defined by Epstein and Hundert as "the habitual and judicious use of communication, knowledge, technical skills, clinical reasoning, emotions, values and reflection in daily practice for the benefit of the individual and community being served" [3]. This is necessarily a progressive acquisition involving some selective stages formed not only by theoretical knowledge, know–how and self–management skills, but also by the ability to teach and pass on. To make this concept really useful, the physician should be able to document both the competence acquired and the concise quality level of his performance, since the health care system's users require a level of performance aimed at excellence. This, on the other hand, could exclude from the system those physicians whose performances fall below the expectations required [4]. However, there is still intense debate about how best to assess and measure the competence and performance of health care professionals. Likewise, health care facilities should also be able to document the level of their performance.

This aspect draws upon the *information accessibility* parameter because, now that the doctor–patient relationship no longer focuses on a paternalistic approach but rather on a "patient–centred" one, the patient's information health needs must be satisfied. Information accessibility should cover the competence and the performance quality of the individual physician and the health care structure. In the former case, emphasis is placed on the curriculum, the individual and team membership performance statistics, the prevailing working activity areas (particularly in the case of super–specialised physicians), any contributions to national and international clinical and scientific progress, and multidimensional feedback data (not only technical but also relational) concerning patients already treated. Whereas information accessibility within the health care facility requires the actual availability of clinical services, the ordinary staffing and diagnostic–therapeutic equipment, the waiting times' average values to access the services, the general and sectoral performance statistics, the overall and sectoral accident rate statistics, any scientific and academic collaborations, and multidimensional feedback data related to patients already treated and transited users. Sharing such information with service users could furthermore encourage a "healthy" competition amongst those providing the treatment (physicians or health care facilities) and this, in turn, could stimulate the continuous quality improvement of the services provided.

## AWARENESS AND GRATIFICATION

Another parameter to be taken into account is the *awareness*, intended as the consciousness every physician should have about the significance and the implications of each medical act, not only with a view to patient health protection, but also toward the health care facility where the physician operates, any insurance company, and the entire health care system. This aspect also includes the judicious use of available instrumentation and equipment so as to achieve the maximum performance not only economically, but also in terms of management and system optimization. The awareness of each medical act's implications could also help reduce the phenomenon of defensive medicine [5].

Lastly, the final assumption of the paradigm presented here is the health care professional's *gratification* that, though it may seem a matter of little interest, is actually a crucial requirement to maintain motivat-

> The individual physician and the health-care systems have to respond to the patient's and society's expectations and the healthcare systems have to lead their professionals.

ed professional behaviour. Generally until a few years ago physicians were satisfied with their career path though some dissatisfaction was derived from salary, the time spent at work, the administrative–bureaucratic aspects of daily practice, and the reduction of professional autonomy [6].

At this stage, leaving the economic aspect specifically aside, the desirable physician's gratification should include the explicit recognition of the objective professional value of the individual doctor within the hospital or the system where he/she operates and also the guarantee of a merit–based tasks' hierarchy (thus recalling the *competence* acquiring process): this would result in the physician's perception of the trust patients and the entire health care system are placing in his/her work, and would lead to a higher satisfaction of the professional himself. The climate of mistrust directed towards the medical profession also implies that the physicians' gratification should be subject to a media re–accreditation of the entire profession.

## FOUR PARAMETERS TO ACHIEVE ACCOUNTABILITY

The development of each of the four proposed parameters (*competence, information accessibility, awareness and gratification*) (**Figure 1**) and their combination would allow better achievement to the coveted target of *accountability* within health care, as outlined decades ago [7,8].

Accountability was originally established as an individual professional's domain but, alongside the evolution towards a complex health care system, it has necessarily extended to a collective and rather systematic level [9]. The knowledge that, currently, the system complexity determines the errors to a much greater extent than the individual professional's behaviour, has led to a progressive re–evaluation of the concepts of responsibility and accountability. This, however, still requires a cultural change so as to ensure that the whole society comprehends that health care safety depends not only on the individual physician but also on the system and that, in case of a system failure, the individual professional is not solely responsible.

Accountability has evolved from an individual to a collective dimension, namely a concept in which all providers, in concert with health care institutions, work collaboratively to share responsibility for transparency, error prevention and 'making the patient whole', as defined by Bell et al. [10]. In other words, accountability is the synthesis between credibility and reliability, both of the individual professional, and the institutions and the health care system. On the one hand the individual physician acquires the tools to adequately respond to the patient's expectations (horizontal accountability) and to the obligations to society, which inevitably result from the position of a health care system within the society (thus distinguishing a vertical accountability). On the other hand, the health care system acquires the tools for proper management control of its professionals, with the possibility to monitor physicians' placement in certain positions and for the appropriate time, according to their competence and level of performance.

In conclusion, we believe that the physician's "patient–centred" orientation also involves the paradigm of the health care accountability approach previously outlined, which is consistent with the current complexity of health care systems and society's demands.



**Figure 1.** Four parameters to achieve health care accountability.
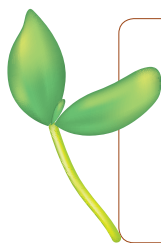
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# Does SDG 3 have an adequate theory of change for improving health systems performance?

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Given the importance of Sustainable Development Goal 3 (SDG 3) setting national agendas and policies to improve public health, this article examines whether SDG 3 and its associated indicators have an adequate theory of change for improving health systems performance. To do so, this article maps all SDG 3 indicators to a prominent health systems framework. The analysis reveals that SDG 3 tracks four input indicators, 15 output / outcome indicators, and 18 impact indicators. Unlike the Millennium Development Goals (MDGs), SDG 3 tracks population health across a wide array of disease areas. However, SDG 3 has several limitations in its approach to improving health systems performance. It does not track primary health care inputs, financial risk protection, or user satisfaction with the health system, and it does not provide a comprehensive approach to prevent, diagnose, treat, and manage any disease. Future directions for research include conducting a similar mapping for other SDGs and documenting early country experiences implementing SDG 3 given these challenges.

## INTRODUCTION

Sustainable Development Goal (SDG) 3 aims to "ensure healthy lives and promote well–being for all at all ages" [1]. Unlike the Millennium Development Goals (MDGs), SDG 3 takes a comprehensive view of health and well–being by expanding its focus beyond a core set of diseases. Given the global prominence of the SDGs for driving the development agenda, it is important to consider whether SDG 3 and the indicators it tracks are well–designed to achieve this intended goal.

In order to examine whether SDG 3 can actually help achieve this goal, this article considers whether it has an adequate theory of change (ToC) for improving health systems performance. Such an analysis rests on two core assumptions: 1) in order to achieve the SDG 3 goal, one must improve health systems performance, and 2) in order to achieve this goal, the approach must have a strong underlying ToC. Each assumption is considered below.

Since the launch of the MDGs, experience has shown that without improvements in health systems performance, progress on the MDGS was both limited and potentially un-

> SDG 3 includes indicators on a broad range of disease areas, but has several limitations for guiding policy formation, policy coherence, and program implementation to improve health systems performance at the national level.

> In particular, SDG 3 does not track primary health care input or impacts related to financial risk protection and user satisfaction with the health system, and it does not provide a comprehensive approach to prevent, diagnose, treat, and manage any disease.

sustainable [2]. Bottlenecks in the health system limited nations' ability to achieve progress on combatting specific diseases. In addition, theoretical and empirical work has argued that providing services which are not only clinically effective but also affordable and acceptable has intrinsic and instrumental value. Recognizing the importance of overall health systems performance, numerous organizations including WHO, the World Bank, Global Fund, and GAVI have focused on health systems strengthening (HSS) as an important component of public health programming. Therefore, since SDG 3 aims to improve both health and well–being for all populations in a sustainable way, achieving this goal will likely require broad improvements in health systems performance.

With regards to the second assumption, theories of change (ToC) are standard practice in public health and development [3,4]. They help guide priority–setting, decision–making, monitoring and evaluation, budgeting, and resource allocation, among other activities. A strong ToC can ensure that all stakeholders work toward the same goal(s). The SDGs aim to improve both the coherence of development policies and their implementation at the national level, and the United Nations has offered formal guidance on ways that nations can integrate and tailor the SDGs into their national policies [5]. This guidance explicitly advocates for horizontal policy coherence (ie, coherence across different programs and sectors), vertical policy coherence (ie, coherence between different stakeholders), and linking national policies based on the SDGs to budgets [6]. Given that the SDGs aim to improve policy coherence and drive implementation at the national level, it is instructive to consider whether they have internal coherence and a strong underlying logic themselves. The ToC approach provides a useful approach to explore this question. If the inputs and outputs tracked under SDG 3 have clear linkages to improving its impact indicators, then working toward SDG 3 will allow countries to pursue a comprehensive program for improving health systems performance. On the other hand, if the inputs and outputs tracked do not link to each other or do not have logical connections to impact indicators, then aiming to improve all indicators under SDG 3 could lead to a haphazard and uncoordinated set of public health programs.

## ANALYTIC APPROACH

To address this question, this analysis maps all indicators for SDG 3 as inputs, outputs/outcomes, or impacts, using the formal definition of each [7]:

- **Inputs:** "The human financial, and community resources a program has available toward [implementing a program]"
- **Outputs:** "Direct products of program activities"
- **Outcomes:** "Specific changes in…behavior, knowledge, skills, status, and level of functioning"
- **Impacts:** "The fundamental intended or unintended change occurring in organizations, communities, or systems"

All indicators are drawn from the official list available from the UN Statistics Division and associated metadata [1]. The 16 tracer indicators proposed by the Inter–agency and Expert Group (IAEG) on SDGs for indicator 3.8.1 (coverage of essential health services) were also included for analysis [8]. This analysis refers to these indicators as UHC tracer indicators.

Health systems theory formally defines the three intended impacts of a health system as population health status, financial risk protection, and user satisfaction with the system [9–11]. Working backward from this definition, outputs/outcomes should refer to the results of activities or changes in the population which can ultimately affect at least one of these three impacts, and inputs should refer to any resources in the system directed toward changing outputs, outcomes, or impacts.

In order to map SDG 3 indicators, this analysis uses a health systems framework which has a structure very similar to that of a stan-

> These missing components are critical for improving health systems performance, and policymakers and practitioners should consider how to incorporate them into efforts to achieve SDG 3 at the national level.

dard ToC [9]. This framework clearly maps to inputs, outputs/outcomes, and impacts, and it further breaks down each of these three areas into relevant sub–categories (see **Figure 1**). Of course, many other frameworks for health systems exist, such as the WHO Building Blocks and the Flagship Framework, and one could also conduct this mapping exercise using those frameworks. However, these two frameworks do not fit as closely with a standard ToC; the Building Blocks framework does not necessarily explain how different building blocks relate to each other, and the Flagship Framework does not explicitly consider inputs to the health system [12].

## RESULTS OF MAPPING SDG INDICATORS TO A HEALTH SYSTEMS THEORY OF CHANGE

This section summarizes the key results of mapping SDG 3 indicators to a ToC. Of the 16 UHC tracer indicators, the analysis excluded five that were duplicative with SDG tracer indicators (excluded UHC tracer indicators, and the SDG indicators that they duplicated: family planning coverage [3.7.1], Tobacco, non–use [3.a.1], Health worker density [3.c.1], Access to essential medicines [3.b.1], and Health security: IHR compliance [3.d.1]). See **Figure 1** for a schematic of the full results of this mapping exercise.

## INPUTS (AND MEANS OF IMPLEMENTATION TARGETS)

SDG targets are divided into Means of Implementation (MoI) targets and other targets [13]. MoI targets are meant to summarize the resources needed to achieve all other targets. SDG 3 has five MoI targets: A) prevalence of tobacco use, B.1) proportion of the population with access to affordable medicines and vaccines, B.2) total net ODA to medical research and basic health sectors, C) health worker density and distribution, and D) IHR capacity and emergency health preparedness. Three of these indicators (total net ODA, health worker density and distribution, and IHR capacity) serve as inputs to the health system, whereas the other two are outputs/outcomes. The analysis also classifies one UHC tracer indicator, basic hospital access, as a health systems input.
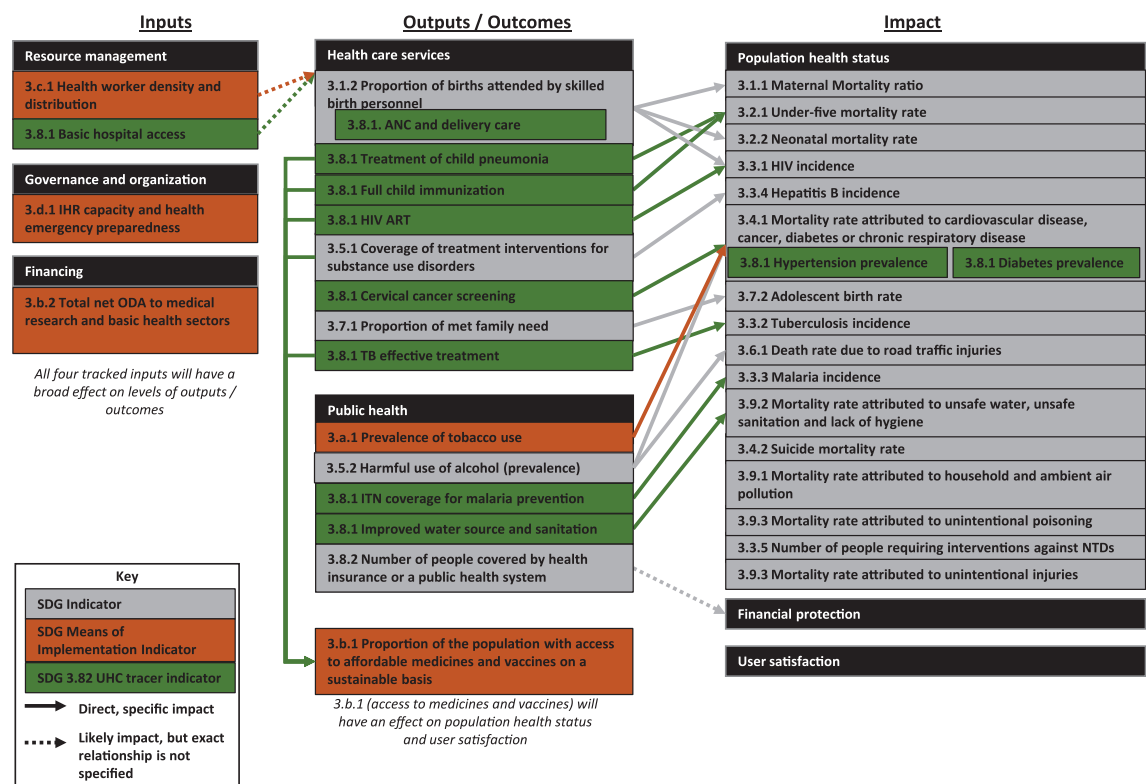


**Figure 1.** Mapping of SDG 3 indicators to a health systems framework.

Photo: The Queen 'Mamohato Memorial Hospital in Lesotho. Experience with this hospital highlighted problems of investing in hospital care without a strong primary health care system. Photo from the collection of Patrick Smith, used with permission. More at: A dangerous diversion: Will the IFC's flagship health PPP bankrupt Lesotho's Ministry of Health? OXFAM Briefing Note, 7 April 2014.

The four indicators classified as inputs fall across the categories of financing, resource management, and governance and organization. With regards to financing, Indicator B.2, total ODA for health, can have an impact on health systems outputs, but there is no clear linkage between this indicator and any specific outputs or impacts tracked by SDG 3. It is not even clear what improvement on this indicator would look like. While an increase in ODA may signify increasing expenditure on health, it does not take into account government and out–of–pocket spending on health, and it may also cause or exacerbate issues with donor dependency in low– and middle–income countries (LMICs). Further, given the variation in efficiency of health spending across countries, an increase in total ODA may not necessarily represent any changes to health systems outputs.

The two resource management indicators, total health workforce and basic hospital access, will impact the availability of health care services and associated outputs. Indicator C, total health workforce, currently measures total physicians and nurses/midwives per capita and will likely expand to include dentists, pharmacists, and possibly other health personnel [14]. The one governance and organization indicator, International Health Regulation (IHR) compliance, focuses on key competencies designed to "prevent, protect against, control and provide a public health response to the international spread of disease" [15].

The fact that two MoI indicators represent outcomes, rather than inputs into the system, suggests that measuring them will not necessarily help countries identify the root causes of problems in the health system or ways to address these issues. Indicator A, prevalence of tobacco use, is meant to measure implementation of the WHO Framework Convention on Tobacco Control, but is actually an intended outcome of this regulation, not a measurement of implementation itself. As of the end of 2016, the UN had not released a final definition of metadata for Indicator B.1 (proportion of the population with access to medicines and vaccines). However, the wording of this indicator suggests that it does not actually capture an input, such as the (per–capita) number of medicines in the country or existence of a national essential medicines list, but rather what percentage of the population gets access to these medicines. Therefore, poor performance on this indicator will not necessarily indicate a shortage of medicines, since populations might lack access to medicines for other reasons (eg, physical distance to a health center, poor supply chain management). Further, four of the 16 UHC tracer indicators monitor the coverage for medicines and vaccines, and may therefore duplicate Indicator B.1.

Many of the outputs / outcomes and impact indicators discussed below have no MoI indicators which directly precede them or influence their progress. There are no input indicators which measure access to primary health care, community–based health services, or health education.

## OUTPUTS/OUTCOMES

Five SDG indicators and eight UHC tracer indicators classify as health systems outputs or outcomes (in addition to the two MoI indicators mentioned earlier). There is at least one indicator that tracks an output related to each Millennium Development Goal (MDG) priority disease (HIV, malaria, maternal health, newborn / child health), as well as TB, substance use disorders, cervical cancer, family planning, tobacco use, alcohol use, and water/sanitation. These indicators are split across health care services and public health. All disease–related outputs link to at least one health systems impact indicator, suggesting that there is a clear and logical linkage between improvements on health systems outputs and health systems impacts.

Indicator 3.8.2, the number of people covered by health insurance, does not link to any impact indicator tracking financing risk protection (such as the percent of the population experiencing catastrophic or impoverishing health expenditures).

The MoI indicator tracking proportion of population with access to medicines and vaccines (B.1) will of course change impact indicators, but it is impossible to assess how it will do so until the UN releases the tracer medicines which will make up this indicator.

## IMPACTS

All impact indicators measure population health status across a wide variety of disease areas. Some measure disease transmission rates (eg, HIV incidence, TB incidence), whereas many others measure mortality rates. There are no indicators to track financial risk protection or user satisfaction.

Although every output indicator links to an impact indicator, not every impact indicator has a preceding output indicator. Indeed, of 18 impact indicators, five do not have a preceding output indicator (mortality due to suicide, air pollution, unintentional poisoning, neglected tropical diseases, and unintentional injuries). This suggests that the SDGs do not give clear guidance on how to address one–third of the impacts targeted. Of the 12 impact indicators which do have a preceding output, 11 have a preceding output indicator from either health care services or public health, but not from both. The one impact indicator which has preceding outputs from both health care services and public health is 3.4.1 (mortality from select NCDs), and the preceding outputs (cervical cancer screening, prevalence of tobacco use, and harmful use of alcohol) actually address very different diseases.

## SELECT LIMITATIONS OF SDG 3 AND POTENTIAL IMPLICATIONS

The results of this mapping exercise have important implications for public health programming and policies. Unlike the MDGs, SDG 3 clearly takes a comprehensive view of the potential epidemiological challenges that a country may face. However, SDG 3 fails to take a holistic view of the health system, its goals, and the resources /activities needed to achieve these goals. In particular, SDG 3 has three limitations for guiding policy and practice to improve health systems performance. See **Table 1** for a summary of the limitations of SDG 3 and potential implications.

1 **Few indicators track the status of the primary health care (PHC) system.** A strong PHC system can serve as the basis for achieving universal health coverage and a stronger health system overall [16]. Given that PHC can address 90% of health care demands, and many "good buys" for combatting diseases can be integrated into PHC systems, prioritizing hospital access over PHC access can lead to inefficiency and misallocation of resources in the health system [10,17]. However, SDG 3 places very little focus on PHC. The two indicators for resource management – health worker density and hospital access – neglect key health systems inputs at the PHC and community levels, such as access to a PHC clinic, the availability of essential medicines at these clinics, health education, and the ratio of lay health workers such as community health workers per population. Given the importance of PHC for improving population health and creating the foundation for a strong health system, policymakers and practitioners should consider how to integrate a PHC approach into achieving SDG 3.

2 **There is no comprehensive approach to prevent, diagnose, manage, and treat any disease.** As mentioned earlier, an impact indicator for a specific disease links to a preceding output indicator either from health care services or public health, but never both. This structure suggests that, while SDG 3 identifies targeted interventions that can address many of its priority diseases, it does not promote a comprehensive approach to preventing, diagnosing, treating, and managing any given

**Table 1.** Select limitations of SDG 3 identified by this analysis and potential implications

| Limitations of SDG 3 | Potential implications for policy and practice |
| --- | --- |
| SDG 3 does not systematically track indicators related to primary health care, which can serve as the foundation for a strong health system. | Policymakers and practitioners should consider how to integrate a PHC–based approach which can effectively and efficiently improve health systems performance into the SDG indicators in their specific contexts. |
| SDG 3 does not provide guidance on how to systematically prevent, diagnose, treat, or manage and given disease. | Policymakers and practitioners should formulate and implement holistic approaches to addressing the highest burden diseases in their specific context, while specifically considering how to integrate these efforts into the health system, including PHC–based approaches. |
| SDG 3 does not track impacts related to financial risk protection or user satisfaction with the health system. | Policymakers and practitioners should include indicators on financial risk protection and user satisfaction in their monitoring and evaluation of the health system and design health systems components, such as insurance schemes and essential medicines packages, with these in mind. |

disease. The output indicators also do not track certain key health behaviors which can impact population health through disease prevention, such as condom usage and physical exercise. (SDG 3 also does not include any indicators on nutrition, but SDG 2 covers these.) Further, of the five impact indicators which have no preceding outputs, many can be addressed through environmental health or other programs. Policymakers and practitioners should recognize that the disease–specific guidance in SDG 3 is only very summary, and that an internal ToC is likely needed for improving population health for each disease. Following from the point about PHC, policy and practice should also consider how integrated prevention, diagnosis, treatment, and management can occur at the PHC level.

3 **The indicators do not track impacts related to financial risk protection or user satisfaction with health services.** As already discussed, ignoring these indicators has significant implications for the functioning of country's health system. Failing to protect individuals against financial risk from health expenditures can negatively impact people's access to care as well as the non–health aspects of their lives [18]. Similarly, a patient's satisfaction with services and the overall responsiveness of the health system to the patient's needs can impact patient well–being and future interactions with the health system [19]. Policymakers and practitioners should take into account the effect that providing services to improve population health will have on patient's financial status and satisfaction with the health system, as well as the linkages between these impacts and population health.

Overall, this lack of a systems–wide approach for improving public health could lead to significant challenges for countries aiming to implement SDG 3. In particular, it could limit the overall improvements to health systems performance because it could promote an uncoordinated approach to improving health, especially without a focus on PHC.

## LIMITATIONS OF THIS APPROACH

This analytic approach has several limitations. As mentioned earlier, many health systems frameworks exist, and this mapping exercise could use other frameworks which might lead to different conclusions. In addition, as with any ToC, this approach presents a highly linear way to understand SDG 3 and its underlying logic. Of course, as the field of systems thinking has revealed, changes to complex systems can have unpredictable and multi–directional results, and this analytic approach does not reflect that complexity [20]. This approach does not map the linkages between impact indicators (eg, a change in HIV incidence could affect other impact indicators such as TB incidence and under–five mortality). Nonetheless, clearly laying out the first–order linkages between different SDG 3 indicators at least gives a working model for understanding if this model provides a logical and robust approach to improving public health more broadly.

## CONCLUSION AND FUTURE DIRECTIONS

This article likely represents the first attempt to map SDG 3 indicators to a ToC for improving health systems performance. This mapping highlights several challenges with the structure of SDG 3, namely the lack of a holistic approach to improving health systems performance. Given the novelty of the SDGs, it is still too early to evaluate the impact of this potential shortcoming. However, these findings point to two key next steps for future investigation. First, researchers can systematically map the indicators for the other SDGs in a similar way and link the ToCs from different SDGs to each other. Doing so will help identify similar challenges for other SDGs, as well as potential linkages between the SDGs. Second, researchers, practitioners, and policymakers should document early experiences trying to implement SDG 3 to determine whether countries recognize these implicit limitations and, if so, how they are responding to them.
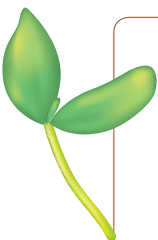
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# Lessons from Brazil: on the difficulties of building a universal health care system

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> A number of developing countries that are often referred to as emerging economies have turned their attention to addressing their public health issues in more comprehensive and systematic ways.

A number of developing countries that are often referred to as emerging economies have turned their attention to addressing their public health issues in more comprehensive and systematic ways. One of the most notable recent additions to the ranks of these countries is India, where consultations about building a universal health care system have been going on since 2015. While the trajectory of this particular initiative and similar ones elsewhere is yet to be determined, the aim of this piece is to draw some lessons from an emerging economy that, for contingent historical and political reasons, started building a universal public health care system earlier: Brazil. The key argument offered from the Brazilian experience is that building a robust public health care system based on the principles of universality and equity is a challenge of a political economy nature and one that ought to be met at multiple levels simultaneously.

The Indian National Health Policy draft published in 2015 recommended the creation of a universal health care system in India based on equity and universality [1], a progressive move that should be unanimously applauded especially in light of the relatively poor state of health in the country. The challenges of building a public health care system have been enormous wherever this project has been attempted, as any historical overview of the more successful public health care systems would confirm. These challenges are obviously time– and place–specific, as those drafting the Indian National Health Policy seem to be well aware of. One interesting element of this initiative is the relatively delayed response of the Indian state to fulfilling the right to health that, although not explicitly listed as a fundamental right in the Indian Constitution, has been consistently interpreted by the judiciary as central to the right to life guaranteed under Article 21. Another interesting element of this public health initiative relates to its appeal to universality and equality at a time these principles have come under increased pressures – not only of a financial nature – in many existing and well–established public health care systems (eg, in Europe). Both these characteristics – the relatively late emergence of efforts to build a public health care system and doing so upon principles of universality and equity currently under threat everywhere – will no doubt generate daunting challenges to Indian policymakers. It would be futile, of course, to engage in speculation regarding the fate of this policy initiative at this point in time. What would be more productive – and this is the route this article offers – is to attempt to draw lessons from other countries that, like India, also started building their public health care systems relatively late and, like India, face enormous challenges relating to disease burden, inequality in access and quality of health care and a large socially– and eco-

> The aim of this viewpoint is to draw some lessons from an emerging economy that, for contingent historical and political reasons, started building a universal public healthcare system earlier – Brazil.

nomically–excluded part of the population coexisting with a relatively strong and growing private health care industry. One such case is Brazil.

From the early 1920 until the new Constitution of 1988, the Brazilian state had presided over a health care system characterized by a deeply discriminatory principle that restricted medical coverage, and other social rights, to those in the formal job market, excluding agricultural workers, the unemployed and the informal sector workers, in short, the majority of the population [2]. Even during 1950–1980, when Brazil's economy was growing at an average of nearly 7% per annum, compared to the 5% global annual average and nearly double that of India, the focus of Brazil's "conservative–informal" welfare regime remained on those groups with the strongest potential to organize politically – ie, the formally employed – while the excluded majority relied on a mixture of familial, philanthropic and meager public care if and when these existed. Healthcare services to the formally employed were based on a dual, private–public financing system and were provided mostly through the private health care sector that started to expand considerably after the military regime came in power in the mid–1960s.

The new Brazilian Constitution of 1988 achieved more than the political inclusion of what had been an excluded majority for the first time in Brazil's history. The crowning victory of various social movements that had insisted on the simultaneous and universal recognition of political and *social* rights, the Constitution laid out the foundations of a welfare state in Brazil. Setting out the blueprints for a welfare state based on universal social rights was no doubt a tremendous achievement, not only on account of other social right systems in the region maintaining their stratified and exclusionary nature, but also on account of the fact that it emerged at a time when the European welfare system was coming increasingly under pressures of various kinds. Having been one of the most organized social movements that led to the overthrow of the military regime and to the new Constitution, the *movimento sanitário* (health care movement) achieved perhaps the most radical institutional rupture in Brazil's social policy design: universal and equitable health care for all (Art. 196). For the first time, the Brazilian state was called upon to guarantee free and universal health care for nearly 200 million Brazilians through the Unified Health System (*Sistema Único de Saúde*, SUS).

A cursory glance at Brazil's improving health indicators suggests that the SUS has had a number of notable and important achievements. The most important are in primary/basic health care, prenatal care, vaccination and the free–for–all National AIDS Program, referred worldwide as the "Brazilian AIDS model". Given the enormity of the SUS, it is not surprising perhaps that it should still suffer from a number of persistent problems, such as gaps in coverage, regional disparities and barriers to accessing specialist and high–complexity care. However, the main challenges to universal health care in Brazil – and indeed elsewhere – are not of an organizational, but primarily of a political economy nature. More specifically, three of the key challenges facing the universal health care system in Brazil are its persistent underfunding, the de–universalization of the right to health and weak pharmaceutical productive capacities needed to sustain it, considered in turn below.

The trajectory of the Brazilian universal health care system has been determined in part by its emergence at a time when the transformation of the Brazilian state along neoliberal lines made its success a particularly challenging task. It is difficult to overlook the fact that whereas health care provisions had been partial and exclusionary during Brazil's period of fast economic growth, they became constitutionally universal when Brazil's economic fortunes plunged and its earlier economic successes started to unravel. It is now generally accepted that the period following the debt crisis of the early 1980s up until the 1990s was a "lost decade" for Brazil. Most economic and social indicators deteriorated. For instance, during 1980–1999 GDP grew at around 2.5% per annum – nearly half that of India during this period – and the income of the richest 10% divided by the income of the poorest 10% of the population increased from a factor of 22 in 1960, to 80 in 1989, making Brazil the second most unequal country in the world [3]. The most notable success of the earlier period, the industrial base, became undone as de–industrialization, de–nationalization and deterioration of technological intensity took hold: the share of industry fell as low as 27% of the GDP in the late 1990s, from a high 44% in 1980, and the share of high–tech manufactures represented only 7.9% of Brazil's total merchandise exports in 2004 compared to 30.5% for China and a 29% world average [4].

> The key argument offered from the Brazilian experience is that building a robust public healthcare system based on the principles of universality and equity is a challenge of a political economy nature and one that ought to be met at multiple levels simultaneously.

Although these developments characterized to a lesser or greater degree most countries in the region, the peculiar way in which they unfolded in Brazil had much to do with the manner in which neoliberal reforms were implemented, especially during the 1990s. What is most relevant to the discussion here is the commitment to neoliberal macroeconomic orthodoxy: the triad of high primary budget surpluses, an inflation–targeting regime and a floating exchange rate with relatively free capital mobility. Despite the shift from neoliberalism to what is often referred to as the neo–developmentalism with the coming in power of the PT (*Partido dos Trabalhadores* – Workers Party) in 2003, this commitment has remained intact. In turn, this continued commitment to neoliberal macroeconomic prescriptions perpetuated a "deadly triad" of overvalued exchange rates, high interest rates and relatively low levels of public and private investment, shifting the level of accumulation toward financialization and commodity extraction/production. In practice, this orientation has resulted in a massive transfer of resources to the financial sector, at the expense of both productive sectors and of social policy. As a result, all three challenges mentioned above – underfunding, the de–universalization of the right to health and weak pharmaceutical productive capacities in health care – have also been perpetuated, raising serious questions about the sustainability of the Brazilian universal health care system in practice.

Underfunding became a problem as soon as the ink on the new Constitution dried. Aiming to bring the social *on par* with the economic, the funding of the universal social security system in Brazil – consisting of social insurance (pensions), health care and social assistance – was to be separate from the fiscal budget. Nonetheless, despite the constitutional principle of integrality of the social security system, in practice, the three areas were separated and, besides, debt repayment took precedence overall. Having already been significantly reduced between 1989–1992, health care funding suffered two additional blows in the early 1990s. First, the main social contribution, payroll taxes, were earmarked for social insurance payments (pensions), thus reducing the funds available for health care. Second, a new Emergency Social Fund was established which, despite its name, allowed the government to direct up to 20% of taxes/contributions toward debt repayment, further reducing funding available for health care. In light of chronic funding shortages in the health care sector, a new tax (CPMF) levied exclusively for this purpose on financial transactions was introduced in 1996, but only about one–third of it was actually used for this purpose, the rest being channeled toward debt repayment and, later, to other social assistance programs [5].

Although GDP grew at an average annual rate of 4.5% during the 2004–2010 (neo–developmentalist) period, the issue of underfunding of the health care sector was not resolved. Federal social spending increased from 12.6% to 15.8% of the GDP between 2000 and 2009, but nearly half of it was claimed by social insurance (pensions), as had happened during the 1990s [6]. Likewise, the 30% share of Social Security Budget committed to health care was never respected and the 'de–earmarking' mechanism regularly channeling funds from it to debt repayment continued. Besides, the 1996 financial transaction tax collected specifically to fund health care, although never exclusively used for this purpose, was completely dissolved in 2007 and no new taxes or financial instruments have been put in place to address the chronic shortfall in the sector. The result has been that *federal* spending on health care remained practically unchanged from 1995 onwards at around 1.8% of the GDP, and the total public health care expenditure rose only from 3.2% in 2003 to 3.9% of GDP in 2012 [7]. This is higher than the 1.14% equivalent share in India in 2012, but still constitutes less than half the 8.3% average in countries with a similar commitment to universal health care.

That the financial base of the Brazilian health care system is incompatible with the constitutional commitment to universality is also visible in the low share of *public* health care expenditure which continued to be below 50% of the total health care expenditure during 1990s and 2000s, compared to a minimum of 70% for other universal health systems. This has resulted in a situation where less than 30% of Brazilians who continue to use private health insurance and facilities constitute more than 50% of the total health care expenditure in Brazil. In India, the private sector today provides nearly 80% of outpatient care and about 60% of inpatient care [8], but presumably many in need of health care do not appear as patients of any kind in government's statistics. What the Brazilian figures suggest is that the legacies of the

previous discriminatory health care system are still in operation and the constitutional principle of universality is yet to be realized in practice. This is in fact a wider problem that relates to the de–universalization of the social rights in general. Indeed, although social spending grew during the 1990s, it remained woefully inadequate to support the universal social security rights guaranteed by the Constitution. Social policy during this period was one of 'inclusive liberalism' whereby various conditional cash transfer programs targeting the poorest sabotaged the achievement of universal social rights guaranteed by the Constitution, including that of health. It is true that the neo–developmental state achieved some remarkable successes in social policy, the most important of which have been the reduction of wage inequality, the rise of the (real) minimum wage and the rise of income of the poorest, especially via targeted social programs such as *Bolsa Família*. Although poverty levels fell and the Gini coefficient was reduced for the first time in decades, income inequality remained high: in 2007, the income shares of the poorest and richest 10% were 0.9% and 44%, respectively [9]. More importantly, the tendency of social spending to reinforce in some respects the de–universalization of social rights that was put in train during the previous decade was not reversed. On the contrary, the strong expansion of *private* social services and the continued preference for conditional cash transfers targeting the poorest continued to compromise the constitutional universality of social rights.

The challenges of underfunding and de–universalization of the right to health in practice stem in large part from the contradictions between a neoliberal monetary policy and a neo–developmentalist social policy. One way in which these contradictions manifest themselves can be grasped by the following figures: around 8.1% of the GDP was handed out to domestic and foreign creditors as debt repayments in 2005, compared to a modest 3.3% of the GDP on public health care expenditure, and a dismal 0.3% of GDP toward the flagship *Bolsa Família* program [7]. It must be added that contradictions exist not only between macroeconomic and social policies, but industrial policies, too. No substantial industrial policy measures were taken during the 1990s in Brazil. As mentioned earlier, this period was characterized by de–industrialization, de–nationalization and falling technological intensity. This broader context had negative consequences for the national health–pharmaceutical sector. Instead of thriving at the time the SUS was being rolled out, the domestic health–pharmaceutical system that had been weak and dominated by imports and foreign pharmaceutical companies earlier on, became even weaker during this period so that only one among the top 20 pharmaceutical companies in Brazil in the mid–1990s was nationally–owned [10]. One outcome of such weak national productive capacities was the rapidly increasing trade deficit of the health care sector, growing from US$2.4 billion in 2003 to just over US$ 10 billion in 2012, half of which was accounted for by the deficit in the pharmaceutical sector alone [7].

The fortunes of the national pharmaceutical sector took a favorable turn with the introduction of the generics category in the market following the creation of a new agency in 1999 (ANVISA) and, after the rise of the neo–developmental state in 2003, with the health–pharmaceutical sector singled out as one of four strategic sectors in its first industrial policy. Following the focus of industrial policies on the sector, considerable funds have been channeled toward the health–pharmaceutical sector, primarily via the BNDES Profarma Program, largely on enhancing productive capacities, but innovation, too. As a result of these and other measures, the share of generics markets in Brazil grew to 17% of the total market in 2008, of which 88% was controlled by Brazilian firms [10]. Although it is too early to evaluate the outcome of these recent efforts, it must be noted that the lack of rules aimed at controlling foreign ownership has contributed to a new wave of acquisitions has already seen some of the emerging/successful domestic companies bought by foreign pharmaceutical companies, a development that does not bode well for the success of Brazil's universal health care system. 48 transnational pharmaceutical companies still account for around 80% of the total market (by revenues), followed at a long distance by public laboratories and private Brazilian companies, contributing to a growing sectoral trade deficit.



Photo: Unidade Sanitária Rural de Pendanga, Ibiraçu (Brazil) – a rural health clinic in Brazil. Via Wikimedia Commons Creative Commons Attribution–Share Alike 3.0 Unported.

The challenges facing Indian policymakers in their efforts to build a national health care system will no doubt be many and finding ways to meet them can only partially be helped by observing the trajectory of similar efforts elsewhere. At the very least, this brief discussion indicates that unless social, macroeconomic and industrial policies are co–articulated and directed toward serving the needs of the society as a whole, a universal health care system in a country with high income concentration like India and Brazil risks becoming an inferior subsystem that attends predominantly but inadequately to the poorer segments of society. Political will and persistence is crucial; in the case of Brazil, for instance, the recent removal of the PT–led government and its replacement by a neoliberal–minded one may weaken the fragile foundations of Brazil's universal health care system. The key challenges to building and maintaining a successful universal health care system have always been and remain of a political economy nature.
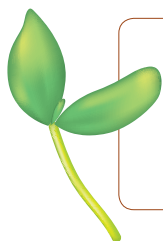
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# Stopping female feticide in India: the failure and unintended consequence of ultrasound restriction

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Female feticide is an alarmingly common practice in India, as evidenced by the most recent Indian national census in 2011 indicating only 914 females for every 1000 males in the zero to six years age range [1]. The root cause of female feticide, a form of structural violence against women, is multifaceted and complex. As the Indian Ministry of Health and Family Welfare states in its 2006 annual report, "the social, cultural and religious fibre of India is predominantly patriarchal, comprehensively contributing to the secondary status of women" [2]. The high rates of female feticide reflect this secondary status. A lower earning capacity, the patrilineal social structure dictating inheritance, and the widespread practice of dowry contribute to the diminished position of women [2]. Improvement in the socioeconomic conditions in India has done little to raise the status of women. Recent evidence reveals that sex selection remains common among the affluent and educated in India [3].

In an attempt to curb female feticide, the Indian Government enacted the Pre–Natal Diagnostic Techniques (PNDT) Act of 1994, which prohibits sex selection and regulates prenatal diagnostic techniques to prevent their misuse. To this end, the government established a bureaucracy controlling the sale and regulating the use of ultrasound machines, a key diagnostic modality used to facilitate sex–selective abortions. Following the initial implementation of the PNDT Act, a further decline in the 2001 Indian national census sex ratio prompted the passage of an amendment, the Pre–Conception and Pre–Natal Diagnostic Techniques (PCPNDT) Act of 2003, which addressed pre–conception sex determination and strengthened enforcement of the PNDT Act.

The continual decline in the sex ratio with each national census since the inception of the PNDT Act calls into question its effectiveness. Census data shows that the sex ratio declined from 945 females for every 1000 males in the zero to six years of age range in 1991 to 927 females for every 1000 males in 2001 to 914 females for every 1000 males in 2011 [1,2]. A well–intentioned legal tool based on the principle of deterrence, the PCPNDT Act also suffers from weak implementation [4]. In its 2010 review of the PCPNDT Act, the Public Health Foundation of India acknowledges, "Data till 2006 reveal that as many as 22 of the 35 states in India had not reported a single violation of the Act since it came into force" [4].

It is difficult to ascertain whether the failure of the Act to substantially reduce female feticide is due to ineffectiveness or improper implementation. However, the unintended consequence of the PCPNDT Act is clear. To prevent misuse, the Act created a system wherein all individuals and

> Female feticide is a common practice in India, and the Indian government's attempt to discourage female feticide, via the Pre-Conception and Pre-Natal Diagnostic Techniques Act, has the unintended consequence of restricting the medical community's access to ultrasound.

Photo: Photo from the personal collection of Gunisha Kaur, used with permission.

institutions must register under the Act to legally purchase an ultrasound, regardless of whether the intended use involves pre-natal diagnostics. Furthermore, all ultrasound practitioners, whether those using ultrasound for echocardiography or those using ultrasound for placement of central vascular access, are mandated to register with the Act. The system has resulted in onerous, time–consuming registration paperwork that discourages medical professionals outside of radiology from using ultrasound. By creating these bureaucratic barriers to ultrasound use unrelated to prenatal diagnostics, the Act restricts the medical practice of a broad range of physicians.

Affecting specialties as diverse as trauma, cardiology, and anesthesiology, advances in ultrasound have transformed the practice of medicine in the years since the PNDT Act was first passed. For example, in 1994, the year the PNDT Act was enacted, anesthesiologists rarely used ultrasound. Today, it is a staple of daily anesthesiology practice as a procedural and diagnostic tool, and it is the standard of care for peripheral nerve blocks and central vascular access. Beyond the operating theatres, ultrasound is commonplace in both operating theaters and intensive care units in the form of lung ultrasonography, transthoracic echocardiography, and transesophageal echocardiography.

To determine awareness of the PCPNDT Act and to gauge the accessibility of ultrasound, an anonymous survey was performed in the anesthesiology departments of hospitals in the State of Punjab, which has one of the highest rates of female feticide in the country [1]. The survey, sponsored by the Department of Anesthesiology at Weill Cornell Medical College as part of its Global Health Initiative, was conducted in person during February and March of 2016 at eight Punjabi tertiary care hospitals associated with medical colleges, both private and government–run. Anonymity was necessary to protect participants from potential legal ramifications of ultrasound use that was not compliant with PCPNDT regulations. At each hospital, a five–question survey was administered to a senior member of the anesthesiology department. The five questions addressed the following: awareness of the PCPNDT Act, number of anesthesiologists in the department with PCPNDT Act certification to use an ultrasound, number of PCPNDT registered ultrasounds available for use in the operating theaters, number of PCPNDT registered ultrasounds available for use in the intensive care unit, and incorporation of ultrasound in the medical school curriculum.

All eight anesthesiologists were aware of the existence and the purpose of the PCPNDT Act. Yet, none were able to articulate the Act's specific regulations pertaining to their practice. Only two of the eight anesthesiology departments had PCPNDT certification for anesthesiologists in the department to use an ultrasound. These two departments had ultrasound available in both the operating theaters and the intensive care units. However, one department without PCPNDT certification for its anesthesiologists had ultrasound available in the operating theaters. The department without proper registration did not appear to fully grasp the potential legal consequences of this breach of the PCPNDT Act. None of the anesthesiologists were involved in teaching ultrasound to medical students.

It is striking that the vast majority of anesthesiologists in these tertiary care centers did not have access to an ultrasound and that one third of those that did have access to ultrasound were non–compliant with PCPNDT regulations. All of the anesthesiologists surveyed expressed frustration at this inaccessibility, echoing the sentiment that care could be improved if this important tool was more widely available. One anesthesiologist cited a delay of nearly two years to obtain an ultrasound due to the PCPNDT registration process. How can the Indian anesthesiology community, or other medical disciplines that rely heavily on ultrasound, uphold the standard of care when access to this critical imaging modality is limited? Given that the census data has not shown a signif-

*This restriction prevents Indian physicians from accessing a valuable imaging modality, and it has not translated into the social change intended by the Pre-Conception and Pre-Natal Diagnostic Techniques Act.*

icant decrease in female feticide since the inception of the Act in 1994, it is difficult to justify the sacrifice in patient care.

The PCPNDT Act oversimplifies a complex problem by placing the moral and legal onus on physicians instead of on patients committing female feticide and the families supporting them. As the former Indian Health Minister Harsh Vardhan aptly stated in October 2014: "It is clear that the focus on the providers of sex selection services has not worked through 20 years. We need to go into the root cause and build up a social movement" [5]. The "Save the girl child, educate the girl child" campaign and free government education for girls in Punjab are steps in the right direction. However, given the concentration of sex imbalance among the highly educated, it follows that a nuanced, multidimensional approach extending beyond educational opportunities is required to achieve social parity for women.

Indian society as a whole shares the collective responsibility for female feticide. Yet, Indian physicians are in a unique and powerful position. They have the capability to disrupt the structural violence against women by refusing to participate in female feticide, a clear breach of medical ethics, as defined by the principles of beneficence and nonmaleficence. Despite its shortcomings, the PCPNDT Act is a well-intentioned piece of social legislation that strengthens the practice of medical ethics by providing a legal incentive for Indian physicians to uphold their obligations [4]. While the PCPNDT Act succeeds in acknowledging and drawing attention to a grave societal problem, its failure to significantly curb female feticide and its unintended consequence cannot be overlooked. The burdensome restrictions on ultrasound, which prevent Indian physicians from accessing a valuable imaging modality, have not translated into the social change intended by the PCPNDT Act. Ultimately, ending female feticide will require a solution as multifaceted and complex as the underlying root causes.
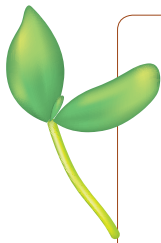
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# Zika: information in the nick of time

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The association of Zika virus with microcephaly and other neurologic issues has led to widespread concern throughout the world. These concerns have led local and national government health agencies to take a variety of measures to inform the public, and to prevent the spread of the virus. In Florida, for example, there was widespread spraying in a Miami neighborhood where 16 cases of autochthonous transmission had been found, and an urgent travel alert issued quickly [1]. Newspapers rapidly began urging people, especially pregnant women, to take specific precautions. They offered suggestions that included chemical clothing treatment, wearing long sleeves and pants, and even staying indoors as much as possible [2]. In February 2016, CBS reported that mosquito repellent sales in the United States had already increased by 11.9% from 2015 [3].

Some of the success of government efforts lies in the perceived threat of the virus. In Puerto Rico, despite a widespread information campaign, there was clearly resistance to mosquito control efforts, and the incidence of cases increased steadily [4]. To be most effective, public health campaigns must provide information to the people and help them understand the threat of the disease, in language and format that are accessible to that population. To further understand the "knowledge gap," we conducted an informal survey of knowledge of Zika and the potential consequences in an endemic area of rural Guatemala.

For two weeks in May and June of 2016, a group of medical students and physicians from the University of Wisconsin School of Medicine and Public health worked in ten different rural villages outside of San Lucas Tolimán, Guatemala, as part of an annual collaborative outreach project. The primary intent for this program is to provide basic medical care to populations with poor health care access, as well as basic preventive health education, but the clinics also provided an opportunity to assess baseline knowledge about Zika in local populations. At their clinic intake, each pa-



Photo: How children are learners and potential teachers (from Jessica Walker's personal collection)

tient was queried regarding what they knew about mosquito–borne illnesses. If they did not mention Zika, they were asked if they had heard of the disease. Finally, patients were asked what they do to protect themselves and their families from mosquitos.

A total of 116 patients were surveyed. 46% of people had heard of Zika, 39% of people had heard of Chikungunya, 40% of Dengue, and 25% had no knowledge of any mosquito–borne illnesses. The results were not uniform across villages, but patients generally had little knowledge about the symptoms and consequences of Zika. For example, some surmised that Zika caused nosebleeds, while this would more likely be a symptom associated with severe dengue infection. In one village, nearly all patients reported that they burn garbage to get rid of mosquitos, a practice that may not be useful and certainly could have other detrimental health effects. Patients seemed much better informed about diseases that had recently plagued their villages, such as chikungunya, which reached epidemic proportions in 2015 [5].

So why did this rural population have such little knowledge about the current threat of Zika? One answer may lie in the more detailed knowledge of chikungunya and dengue, diseases that have affected, and still do affect, these communities. It stands to reason that patients' ability to better describe these diseases may be from having experienced them already, as these diseases have circulated in the area for many years. However, if we make that assumption, it raises another troubling issue; the percentage of patients who were able to identify these endemic diseases was still less than 50%. This figure suggests that, even in areas affected by dengue and chikungunya, education about recognition and prevention has been suboptimal. When considering a disease as dangerous as dengue, which is estimated to hospitalize 500 000 people each year and kill at least 12 500, the knowledge gap surrounding mosquito–borne illness must be addressed [6].

So what can be done in resource–limited areas to improve knowledge and limit mosquito–borne disease? At the level of public infrastructure, the government in Guatemala and organizations such as the Red Cross are increasing spraying efforts and distributing insect repellent in order to limit mosquito bites in response to Zika [7,8]. On the public information side, our survey yielded some positives, as some patients did have accurate information about the threat of Zika. Their sources of information were community health promoters and primary schools, where children educated about the virus brought information home to their families. These sources of information are readily accessible vehicles for public health education efforts. Perhaps using Zika as a newly emerging threat could offer a new opportunity to share the importance of all vector–borne infections, open new avenues of communication, and foster the development for more comprehensive education on all severe mosquito–borne illnesses. If we start by educating children and community health promoters, the information may be disseminated more quickly within the community.

The public's captivation with Zika is likely to wane over time, but the reality is that other diseases such as yellow fever, malaria, dengue and chikungunya are endemic in many regions, and control remains elusive. The successful dissemination of information in areas where technology may be limited is imperative, to help limit the impact of the mosquito epidemic in Latin America and other resource limited settings. It is not enough to provide mosquito repellent and bed nets, or to spray insecticide, if the people do not understand the importance of these interventions. Many communities remain afflicted by these illnesses because they are unaware of the mechanisms of transmission or effective personal protection interventions.

Coordinated efforts to educate, support, and follow up with these communities is needed, in order to ensure that there is genuine understanding, as well as a sense of empowerment against these diseases. Word of mouth travels rapidly in countries with little access to technology, and as evidenced by our experience, schools can be used as a valuable educational and informational resource. Every opportunity must be found to utilize public health and educational activities, in coordination with governmental and private sector interventions.

As it stands now, there is no cure for most of these diseases, but there is prevention. And in the future, there may be more an array of vaccines to offer for many of these conditions, but acceptance will partially depend on understanding of the importance of these diseases. We must seize the opportunity that Zika has provided and re–start the conversation in these areas. Vector–borne diseases do not have to be considered inevitable.
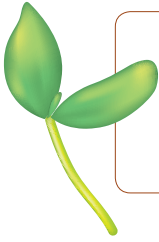
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# Men's health: time for a new approach to policy and practice?

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The United Nation's (UN) Sustainable Development Goal 3 on health and well–being contains important commitments to reducing by one third premature mortality from non–communicable diseases (NCDs), promoting mental health and well–being, strengthening the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol, and halving the number of global deaths and injuries from road traffic accidents. The Goal also aims to ensure universal access to sexual and reproductive health–care services, including for family planning, information and education, and to improve the implementation of the World Health Organization (WHO) Framework Convention on Tobacco Control.

All these commitments, if successfully implemented, would be particularly beneficial to the health of men and boys across the world; equally, they cannot be optimally realized without an approach that takes account of the specific health needs, social contexts and the related health practices of men and boys, and perceives addressing this area as a pathway to better well–being and equality for all. At present, such an approach is not reflected in policy and practice.

## MALE MORTALITY

WHO data shows that, globally in 2012, 52% of all deaths from NCDs were male. Males were more likely than females to die prematurely (under 70 years) from NCDs in almost every country (females were more likely to die prematurely from NCDs in just four countries). The proportion of premature NCD deaths in males was twice or more that in females in 11 countries, including Russia where 52% of male NCD deaths were premature compared to 24% of female NCD deaths.

The major risk factors for NCDs include unhealthy diets, tobacco use and the harmful use of alcohol. Men do worse than women in respect of all of these. Data from the Global Burden of Disease Study 2010 shows

> Globally, men's health outcomes are poor: male life expectancy at birth, at 68 years, lags five years behind female life expectancy and the global "gap" is predicted to increase. By 2030, male life expectancy could be seven years shorter than female life expectancy. Men take significant risks with their health (e.g. alcohol, tobacco, diet) and under-use primary healthcare services. Men's health has not been systematically addressed in most countries or globally.

that, in that year, 55% of deaths from dietary risk factors were male as were 72% of deaths from tobacco smoking and 65% of deaths from alcohol. More males than females also died from environmental factors (unimproved water and sanitation, air pollution) and also drug use. There was a particularly large sex difference for deaths caused by occupational risks: 88% of deaths from this cause were male in 2010.

Males accounted for 82% of all homicide victims in 2012 and have estimated rates of homicide that are more than four times those of females (10.8 and 2.5, respectively, per 100 000), according to WHO data. Males were also almost twice as likely to die by suicide as women. In high–income countries, men were three times more likely to die by suicide.

Life expectancy data also highlights the health burden borne by men. Globally, male life expectancy at birth, at 68 years, lags five years behind female life expectancy and the global "gap" is predicted to increase over the next 15 years: by 2030, male life expectancy could well be seven years shorter than female life expectancy [1]. There is not a single country where male life expectancy exceeds female and there are currently 27 countries in the world with male life expectancy below 60.

## USE OF HEALTH SERVICES

The under–utilization of primary care services by men has also been identified as a problem in many countries. In Europe, infrequent use of, and late presentation to, such services has been associated with men experiencing higher levels of potentially preventable health conditions and having reduced treatment options [2]. This is particularly the case for mental health problems. Studies in sub–Saharan Africa have reported similar findings about men's use of HIV services and also found that men are proportionally less likely to test for HIV and begin treatment regimes and more likely to die while on treatment [3–5]. Within the context of family planning, there has been little shift globally in men's use of contraception over the last 20 years, with the burden of responsibility remaining firmly with women [6].

There are also significant structural barriers that inhibit men's ability to self–care and to access services effectively. Many primary care services are available only at times when men are at work, for example [7]. It has been suggested that the feminine ambience of services also deters men who in any case view health as a predominantly female domain. Health awareness campaigns have often failed to engage men and have, deliberately or inadvertently, been aimed primarily at women [8].

## HEALTH LITERACY

Men tend to be less knowledgeable than women about specific diseases, risk factors and health in general. A recent study of weight, diet, physical activity and nutritional knowledge among university students in the USA found that men were more likely to be overweight or obese, more likely to consume red meat, fast food, sugar–sweetened beverages, wine and beer, and less likely to be knowledgeable about nutrition [9]. Other research has found that men are less likely to recognize that they are overweight and are less well–informed about the common symptoms of cancer.

## RISK–TAKING AND MASCULINITY

Men's risk–taking behaviors and their under–use of health services are in large part linked to male role norms. These norms vary according to social and cultural contexts but also appear consistent across many countries in terms of health behaviors. In rural India, for example men's use of tobacco is closely linked to their perception that a "real man" should be daring, courageous and confident and able to demonstrate his manliness by smoking [10]. A study of men in Russia suggested that heavy drinking of strong spirits "elevates or maintains a man's status in working–class social groups by facilitating access to power associated with the hegemonic ideal of the real working man" [11]. Evidence shows that promoting positive models of manhood, such as caring and involved fatherhood, while concurrently addressing structural barriers, can improve men's help and health–seeking behavior [12].

## TAKING ACCOUNT OF SEX AND GENDER

We do not argue that tackling men's health is more important than addressing women's health; in reality, there is not a binary choice to be made nor is this a zero sum game. In specific areas of health, women's

outcomes are worse than men's. Moreover, in many countries, women are denied equal access to health services, and gender power dynamics mean they often lack autonomy in health–related decision–making. Women's health problems are inextricably linked to many social, economic, legal, political and cultural forms of discrimination. It is therefore right that women should be regarded as a priority for action by global and national health organisations. As the data highlighted above shows, however, men also face a wide range of serious health problems which require a complementary approach.

The need to take account of sex and gender in relation to the health of both men and women is well–established in the literature. It is now a quarter of a century since England's Chief Medical Officer included a path–breaking chapter on men's health in his annual report on the state of the nation's public health and emphasized the importance of paying greater attention to sex differences in disease susceptibility "to the benefit of men and women alike." More recently, in a report on the social determinants of health for WHO Europe, Michael Marmot recommended that strategies should "respond to the different ways health and prevention and treatment services are experienced by men [and] women" and policies and interventions should be "responsive to gender" [13]. The head of WHO's gender, equity and human rights group has also written about the importance of "capturing the different experiences of men and women" [14].

These insights have not yet been translated into action at the strategic level, however. An analysis of the policies and programmes of 11 major global health institutions, including WHO, found that they did not address the health needs of men [15]. The UN's Global Strategy for Women's, Children's and Adolescents' Health (2016–30) overlooks boys and world leaders at the 2016 G7 Ise–Shima Summit in Japan made important commitments to improving women's health but did not mention men, or how they could be engaged to support improvements in women's health. The flagship global strategy for increasing contraceptive uptake by an additional 120 million users, Family Planning 2020, includes only women as users and not men. Global health NGOs have shown insufficient interest in men as a specific group. Only four countries – Australia, Brazil, Iran and Ireland – have developed national men's health policies. In most other countries, men's health is not recognized as an issue of concern by governments or health providers.

> Sustainable Development Goal 3 on health and well—being, which includes a commitment to reducing by one third premature mortality from non–communicable diseases, cannot be optimally realised without an approach that takes account of the specific health needs, social contexts and the related health practices of men and boys. Improving men's health would also benefit women's health and reduce health system costs.

## THE BENEFITS OF IMPROVED MEN'S HEALTH

As stated in the WHO Constitution, "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being" [16]. Increasing men's ability to lead healthy and fulfilling lives is an ethical imperative. Improving men's health would not benefit just men, however. Improved sexual and reproductive health for men would have immediate and obvious benefits for women as well as men themselves. Lower male premature mortality and morbidity rates would reduce the burden on women and families who depend on men's incomes. Improved mental health and lower levels of alcohol consumption would help to reduce male violence toward partners and others.

Healthier men would reduce the economic costs of lost productivity and health treatments. Men's premature mortality and morbidity has been estimated to cost the United States economy approximately US$ 479 billion annually [17] while the economic burden associated with smoking, excess weight, alcohol and physical inactivity in Canadian men is believed to be about CA$ 37 billion a year (US$ 28 billion). Retirement ages are rising internationally so it is increasingly important to enable men to remain economically active for longer.

## WHAT WORKS WITH MEN

There is a growing evidence base from around the world showing that well designed health interventions aimed at men can improve outcomes for themselves and others and transform harmful gender norms.

The Football Fans in Training program in Scotland, now extended into other European countries as Eu-roFIT, shows that professional sport can be an effective medium for engaging men in lifestyle improvement programmes [18]. A study of the core elements that make for successful work with boys and men on mental health promotion, early intervention and stigma reduction found that the settings within which interventions take place need to be "male friendly" and culturally sensitive to the specific requirements of different groups of men and boys [19]. Interventions that aim to reshape male gender roles in ways that lead to more equitable relationships between women and men can reduce sexually transmitted infections and prevent intimate partner violence [20]. Easier–to–access primary care services could also reduce some of the barriers to service use experienced by men.

## NEXT STEPS

For progress to be made, we believe that global health organizations and national governments should, as part of a comprehensive approach to gender and health, address the health and well–being needs of men and boys in all relevant policies (eg, on obesity, cardiovascular disease and cancer) and through the introduction of specific men's health policies. Educational programmes in schools and male–targeted health information can be used to encourage and support boys and men to take better care of their own health. Health practitioners must inform themselves about the psychosocial aspects of men's health, as well as male–specific clinical issues, and medical training programmes should cover gender and other social determinants of health. Workplaces have a key role, in terms of not only reducing exposure to hazards but also providing a setting for health promotion.

It is essential for work with men to focus on those groups with the worst health, such as economically disadvantaged men, gay and bisexual men, men who are homeless, migrants or offenders, and men from specific racial and ethnic groups. It is important to recognize that most men want to enjoy good health and well–being and that their strengths and the "positive" aspects of masculinity (for example, a desire to provide for and protect one's family) can be harnessed to help them achieve better outcomes. But in order to improve men's health successfully, there must be a commensurate policy and programming response. Further research is also needed into how to influence men's health behaviors and improve their use of primary care services.

One thing is clear: the Sustainable Development Goals and better health for all cannot be achieved if the many challenges currently facing men are left hiding in plain sight.



Photo: Courtesy of the Institute for Reproductive Health, Georgetown University, USA
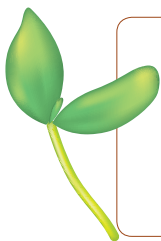
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# Surveillance of antimicrobial consumption: methodological review for systems development in Thailand

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The increased trend of antimicrobial resistance has become a global threat to human security, causing serious negative impacts on human, animal and environment. Inappropriate uses of antimicrobial are main drivers of the emergence of resistant bacteria [1].Combating AMR requires in–country multi–sectoral actions and global collective efforts using "One Health" approach.

The Thai National Strategic Plan on AMR (2017–2021) was developed through a full engagement of stakeholders and National Health Assembly processes [2]. The Thailand Cabinet endorsed it in August 2016. Two out of the five targets are 20% and 30% reduction in antimicrobial consumption in human and animal by 2021, respectively (see **Box 1**).

To optimize use of antimicrobial agents in human and animal, as recommended by the WHO Global Action Plan [3], countries need to develop a sustainable system which monitors their consumption and disseminate the information for policy decision. For example, France had a high human antibiotic use in the EU, and implemented a national campaign which resulted in a significant reduction in consumption [4]. This paper reviews international approaches on surveillance of antimicrobial consumption in human and animal, analyzes antimicrobial sales reporting systems and assesses how the surveillance system can be developed and sustained in Thailand.

**Box 1** Goals of the National Strategic Plan for AMR

By 2021:

1. 50% reduction in AMR morbidity
2. 20% reduction in antimicrobial consumption in humans
3. 30% reduction in antimicrobial consumption in animals
4. 20% increase of public knowledge on AMR and awareness of appropriate use of antimicrobials
5. Capacity of the national AMR management system is improved to level 4 (measured by the 2016 WHO's Joint External Evaluation for International Health Regulation 2005)

Reviews of international experiences in particular ESAC and ESVAC found useful and applicable to developing countries, although there is a need to establish or strengthen sales data systems. System analysis of legal framework and reporting systems that captures antimicrobials sales data contributes to the design of Surveillance of Antimicrobial Consumption.

# ANTIMICROBIAL CONSUMPTION IN HUMAN AND ANIMAL: REVIEW OF INTERNATIONAL APPROACHES

## Human consumption

Since 2011, European countries have been developing a surveillance system for human. The European Surveillance of Antimicrobial Consumption Network (ESAC–Net) [5], covers 30 European Union and European Economic Area (EU/EEA) countries. It provides cross–country analysis and information is fed back to member countries to inform policy, as well as making publicly assessable information through the interactive database.

Data sources are either national sales of antimicrobials or reimbursement data available from health insurance systems. These data disaggregate consumption by community (ambulatory care) and hospital care (**Table 1**).

The surveillance system may cover hospital or community levels [6]. Monitoring consumption in hospital settings is useful for impact assessment of AMR leading to attribution of morbidity and mortality on health care cost and for micro–policy decision on rational use. Monitoring consumption in community is more complex than a hospital setting, where national sales data to communities are used for estima-

**Table 1.** Two data sources used by ESAC–Net and ESVAC: reimbursement vs sales data

| Country | Reimbursement data | | | Antimicrobial sales data | | | Animal uses |
|---|---|---|---|---|---|---|---|
| | Human, community uses | Human, hospital uses | Human, combined community and hospital uses | Human, community uses | Human, hospital uses | Human, combined community and hospital uses | |
| Austria | X | | | | | | X |
| Belgium | X | X | | | | | X |
| Bulgaria | | | | X | X | | X |
| Croatia* | X | X | | | | | |
| Cyprus | | | X | | | | X |
| Czech Republic | X | | | | | | X |
| Denmark | | | | X | X | | X |
| Estonia | | | | X | X | | X |
| Finland | | | | X | X | | X |
| France | | | | X | X | | X |
| Germany | X | | | | | | X |
| Greece* | | | | X | X | | |
| Hungary | X | | | | | | X |
| Iceland | | | | | | X | X |
| Ireland | | X | | X | X | | X |
| Italy | | X | | X | | | X |
| Latvia | | | | X | X | | X |
| Lithuania | | | | X | X | | X |
| Luxembourg | X | | | | | | X |
| Malta* | | | | X | X | | |
| Netherlands | | | | X | X | | X |
| Norway | X | X | | X | X | | X |
| Poland | | | | X | | | X |
| Portugal | X | X | | X | | | X |
| Romania* | | | X | | | | |
| Slovakia | | | | X | X | | X |
| Slovenia | X | X | | X | X | | X |
| Spain | X | | | | | | X |
| Sweden | | | | X | X | | X |
| United Kingdom | X | | | | | | X |

*No data in animals.

Producing meaningful and user–friendly information on magnitude and profile of antimicrobial consumption and effective dissemination contribute to public and policy maker awareness, effective interventions and support sustaining Surveillance of Antimicrobial Consumption.

tion. A majority of developing countries do not compile national sales data to communities. Alternative ways of capturing antimicrobial use are surveys of pharmacies, sentinel in specific sites or prospective household survey.

### Animal consumption

The European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project was established in 2009 [7]. It reports antimicrobial consumption in animal by collecting sales data of veterinary antimicrobials in 26 countries, which covers 95% of total food–producing animal populations.

The data sources came from wholesalers (17 countries), marketing–authorization holders (4 countries), both wholesalers and marketing–authorization holders (2 countries). Some countries provide feed mill data (**Table 1**) [7]. In all countries, it is mandatory by Law for pharmaceutical operators to report their sales data to the national authority, except in France, Hungary, Netherlands and Spain.

### Analysis of data sources: reimbursement vs sales data

As seen in **Table 1**, antimicrobial sales data for human use is the main source in a majority of the 30 EU/EEA countries. These data are able to be disaggregated by community and hospital uses; while all countries are reliant on sales data for antimicrobial agents used in animals. Most European countries had achieved universal health coverage; still there are limitations in capturing antimicrobial consumption from reimbursement databases. In developing countries with limited population coverage by insurance schemes, more limitation of reimbursement data for estimate of antimicrobial consumption is expected.

This indicates that development of the surveillance system requires strengthening of antimicrobial sales data for both humans and animals. Reviews found that approaches used by EU/EAA countries can be applied to developing countries given there is a good antimicrobial sales data systems in both sectors.

## UNDERSTANDING THE LANDSCAPE OF DRUG AUTHORIZATION IN THAILAND

### Legal frameworks and actors

Two laws govern the distribution of antimicrobials for human and animals: the 1967 Drug Act responsible by Thai Food and Drug Authority (Thai–FDA); and the 2015 Animal Feed Quality Control Act, responsible by Department of Livestock Development. It is noted that a majority of antimicrobials used in livestock are consumed through medicated feeds, and much less on finished products mostly applied to pets.

Key actors are importers, local manufacturers and pharmacies which are authorized to sell antimicrobials by Thai–FDA. Antimicrobials can be used upon prescription, but in practice the requests from customers and farmers could influence dispensing in private pharmacies. A major loop–hole in enforcing the Drug Act is the lack of effective measures and monitoring systems for antibiotic distribution especially active pharmaceutical ingredients (API).

### Reporting sales data by operators

There are two mandatory sales reporting systems by the importers and manufacturers. First is the four–monthly report of sales and distribution of potentially abused medicines by consumers, such as steroids, tramadol and dextromethorphan. This system is designed for tight control of distribution of these medicines to prevent drug abuse. Second an annual report of production and importation of all pharmaceutical products where historically Thai–FDA did not request to provide distribution details.

To facilitate development of surveillance system, the existing two reports needs to revise in order to track the distribution of antimicrobials from productions/importation to users. However, the Thai–FDA has to issue regulations to add highly potentially antibiotics to the four–monthly report. Moreover, a greater re-

liance on the annual report on production and importation with volumes and values of product and it requires them to report data on distribution channel. There is a gap which is the lack of reporting on the production of medicated feeds. **Figure 1** presents the distribution channels.

With reference to reviewed information from ESAC and ESVAC, the planned Thailand systems where data sources on total sales for human are the combine of community and hospital levels and sales data for animal happens to be similar to Iceland (**Table 1**) where antimicrobials sales data are available on combined community and hospital care in humans; and totals are available for animal use. The breakdown by community and hospital use will be discussed further in the subsequent section.

Key parameters in the electronic reporting will include: the operator's unique ID; pharmaceutical product unique ID with reference to the License ID assigned by Thai–FDA; Anatomical Therapeutic Chemical (ATC) classification); quantity and value including package size; doses; and forms. The objectives are to estimate human consumption as measured by Defined Daily Dose (DDD) and animal consumption as measured by milligram of antibiotic.

## DEVELOPMENT OF SURVEILLANCE OF ANTIMICROBIAL CONSUMPTION: METHODOLOGICAL APPROACHES FOR THAILAND

Currently, there is no system to monitor consumption of antimicrobial in Thailand. The Thai Surveillance of Antimicrobial Consumption (Thai SAC) is developed to fill the gap, which provides a 2017 baseline consumption and a long term monitoring process. In 2017, grants from USAID, WHO and FAO had been approved for research and development of the Thai surveillance system. Research team comprises of Thai–FDA, Department of Livestock Development, universities and International Health Policy Program of the Ministry of Public Health. Systems analysis was conducted to understand the distributional channel, legal framework and sales reporting systems; all forms the basis of the surveillance system development.

All medicines in the Thai–FDA registration database are assigned with ATC classification code for human drugs and ATCvet for veterinary medicinal products. The scope of surveillance system will cover antimicrobials at least for systemic use, J01 in human and QJ01 in animal.

The design of Thai Surveillance of Antimicrobial Consumption is based on national sales data, which is a mandatory report by importers and manufacturers to the Thai–FDA; as use data by clinical conditions, age and gender are not readily available.

The antimicrobial sales data will be verified for their adequacy, accuracy and completeness before analysis. In human, antimicrobial consumption is measured by DDD per 1000 inhabitants–day [8]. The consumption of antimicrobials in animal is measured by milligrams of API per population correction unit
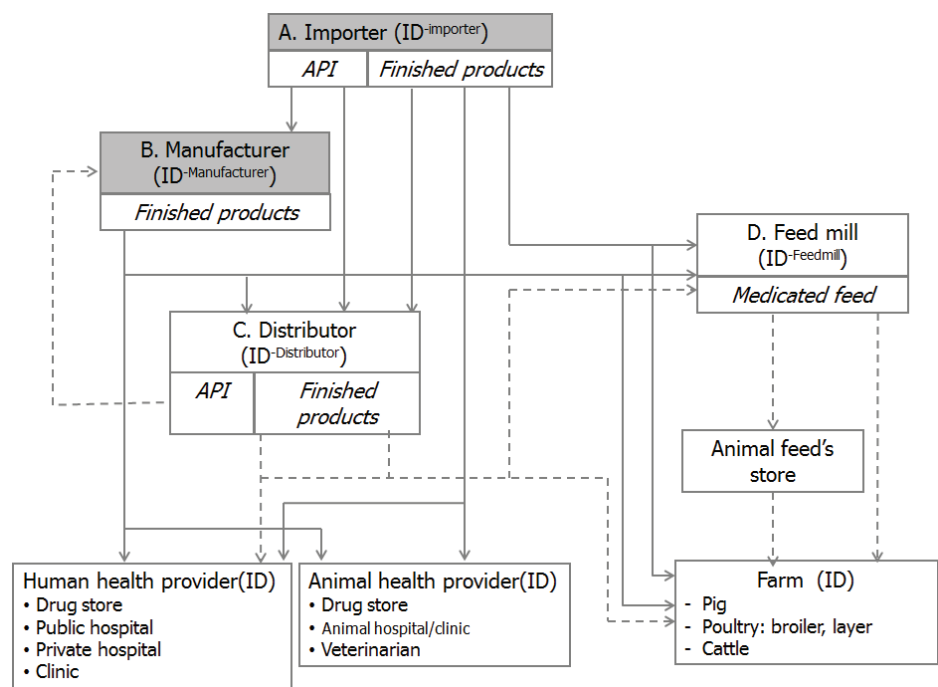


**Figure 1.** Distributional channels by antimicrobial agents. This study covers solid line which includes antibiotic sales data from importers and manufactures. The dotted line distributions are outside the scope of this study.

Photo: from the International Health Policy Program, Ministry of Public Health, Thailand, taken by Phanit Phacharaphimansakul (used with permission)

(PCU). The PCU is the estimated weight for each animal species at treatment of livestock and of slaughtered animals at import and export for fattening and slaughter [7]. As there is no PCU in Thailand, we will use PCU following the ESVAC to facilitate international comparison.

## CHALLENGES AND SOLUTIONS

A few challenges are identified for improvement of methodological approaches. Development of Surveillance of Antimicrobial Consumption relies on two sets of parameters: the numerators are total antimicrobial sales for human and animal consumption; the denominators are the total human and animal population.

### The numerators

The completeness and accuracy of reporting by operators, though mandatory, is an initial challenge. However, electronic submission with reference to the unique identification number of each ATC code would facilitate accuracy of reporting.

There are total 774 importers and 184 manufactures; for which representative samples of operators selected for on–site verification. This will gradually improve the quality of reports. Command and control, though a mandatory requirement by Thai–FDA, may not work well. Rather, effective communication between Thai–FDA and the operators and social recognition of their contributions to surveillance data are essential for adherence to quality report.

We assume that the total antimicrobial production and importation (though certain unknown size of reported illegal importation and production) minus total exports is the total consumption in both sectors. Although there is variation in annual stock, in an efficient pharmaceutical market, the stock level should be constant.

The annual report by operators does not disaggregate by community, hospital and animal species. For human antimicrobials, we plan to disaggregate by using national insurance reimbursement data set or surveys of organisations. Antimicrobial consumption by key species of food animals is important for specific policy intervention, efforts are planned to disaggregate data by special surveys, including the estimate of total consumption in the aquaculture.

The off–label use of human antibiotics in pets and plants in particular citrus trees for the treatment of Greening Diseases [9] is commonly observed in Thailand; efforts are under way to investigate sources and magnitude of antibiotic use in pets and plants with supports from FAO by this research program.

### The denominators

The Department of Livestock Development has yet to strengthen the data systems for accurate statistics on the total number of livestock by species. Not all livestock are raised through commercial standard farming systems, estimate size of local backyard farming contributes to accurate consumption per PCU. Estimate total national number of pets, most common are dogs and cats, and total PCU in aquaculture are the future research agenda.

### The sustainability of the surveillance system

Sustainability of the surveillance system not only depends on the mandatory reporting system, other enabling factors are for example effective communication with the operators, user friendly electronic submission, systems which facilitate e–submission and safeguard confidentiality of sales data.

Relevant authorities had fully involved in the surveillance system design and development; this ensures long term sustainability in particular the IT systems. Policy decision based on evidences and publicly accessible report foster political support for a sustainable Thai Surveillance of Antimicrobial Consumption.

## CONCLUSION

In responses to AMR, the Thai national surveillance system is critical for monitoring total consumption for which effective policies can be introduced to curb down excessive consumption. The current design disaggregates human consumption by level of care such as hospital and pharmacies; however point prevalence surveys are needed to estimate consumption by clinical conditions, age and gender. The current design does not differentiate consumption by animal species; further monitoring of veterinary prescription support consumption by animal species.

Reviews of international experiences and the analysis of how to design a Thai Surveillance of Antimicrobial Consumption are useful to developing countries to apply to suit the national data systems. The Political Declaration of the High–Level Meeting of the UNGA on AMR in September 2016 which calls for "Improve surveillance and monitoring of AMR and the use of antimicrobials to inform policies" [10] puts pressure on countries to develop surveillance system and ensure its use for policy decision.

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# Empowering people for sustainable development: the Ottawa Charter and beyond

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In November 1986, 212 participants from 38 countries convened in Ottawa, Canada, at the first International Conference on Health Promotion organized by the World Health Organization (WHO), Health and Welfare Canada, and the Canadian Public Health Association. Although not representative of the entire globe, these participants adopted the *Ottawa Charter* on health promotion as "*the process of enabling people to increase control over, and to improve, their health*". The five action areas identified were to: build healthy public policy; create supportive environments; strengthen community action; develop personal skills; and re-orient health care services, toward prevention of illness and promotion of health [1–3]. The *Charter* laid the foundation for subsequent efforts in advancing global health over the next 30 years, including development of the Millennium Development Goals (MDGs). The MDGs have given way to a more robust and comprehensive agenda, the Sustainable Development Goals (SDGs) [4], underpinned by the principles of reducing inequities and universal health coverage (UHC). Thus the vision of the *Charter* is foundational to progress in health care over the last 30 years. Here, we review the progress made and discuss the unfinished agenda of the *Charter* as well as opportunities to accelerate its objectives in the context of UHC and the SDGs, through collaborations of international and local health organizations.

The notion of UHC was articulated earlier in September 1978 when the *Alma Ata Declaration* on primary health care was adopted at a joint conference of the WHO and United Nations Children's Emergency Fund (UNICEF) [5]. This declaration emphasized the importance of 'health for all', a message strengthened through the *Charter* and in the WHO strategy to ensure '*Health for All by 2000*'. In this regard, the *Alma Ata Declaration* and the *Charter* were seminal documents that shaped the global health agenda. The *Charter* urged nations to advocate, enable, and mediate, in order to achieve progress in the five action areas [3]. While the ambitious agenda of the *Charter* and *Health for All* were not fully realized, this heralded the era of the MDGs that guided the global health agenda from 2000–2015, and yielded substantial but uneven gains. The MDGs have been replaced by the SDGs, which comprise of 169 targets, and were adopted in September 2015 by 193 nations [6]. The Ottawa Charter notes that "*peace, shelter, education,*

> While a global agenda is required to highlight our shared challenges, nations will have to articulate their individual developmental agenda based on their local needs and priorities.

> Empowering people and communities is challenging, but without this, we are unlikely to make substantial progress. In fact, any strategy that fails to focus on and include people, will not succeed.

food, income, a stable eco–system, sustainable resources, social justice, and equity" are fundamental resources for health [3], and the SDGs address these domains. Countries have achieved different levels of success in these domains, and rather than prioritize the relative importance of domains for a particular country, we propose that countries acknowledge the interdependence of these different domains and that health cannot be improved in isolation of these domains. While the ambitious SDG agenda reflects the complexity and intersectoral relations required to achieve optimal health, it has also established broad, incompletely defined targets that are difficult to quantify, measure, implement, and evaluate. In addition, achieving UHC to ensure people have access to affordable, high–quality health care is a core element and enabler of success of the SDGs. However, achieving UHC and thus the SDGs will remain beyond the reach of many nations that are struggling with geopolitical and economic instability. Given the known "inverse equity hypothesis" of inequities worsening as new interventions are introduced [7], the implementation of UHC and new interventions for SDG3 must be undertaken with a specific focus on reaching all and reducing inequities.

Empowering of individuals and communities to advocate for and improve access to health care is central to success of the *Charter* and all subsequent global health frameworks. However, empowerment of the disadvantaged is difficult and three decades after the adoption of the *Charter*, a key unanswered question is *how best to empower people.* Empowering and enabling people to take charge of and improve their health are weighty undertakings. Within the health care framework, it requires health literacy and access to health information; access to affordable health services and medicines; and, a resilient patient–centered health care system. More importantly, health care cannot be realized without exploring the impact of non–health sectors including geopolitical, economic, and financial stability; policies on manufacturing and pricing of medicines; and political will to implement and evaluate change. In many parts of the world achieving equity in health outcomes based on socioeconomic gradients, gender or geography requires policies and empowered communities to exercise their political capital in achieving these goals. In addition, global armed conflicts result in reduced access to health services, forced migration, social breakdown, and heightened stress, all of which have negative consequences on health [8]. The Rio 20+ summit aimed to advance sustainable development, and highlighted the impact of environmental changes (for example: climate change, loss of biodiversity, using indoor cooking fuels) on health [9]. It is becoming more apparent that environmental pollutants can have a significant impact on overall health [10,11].

*How do we empower people?* As outlined in the *Charter* and emphasized by the SDGs, the current focus is on enabling people to take control of their health. To achieve this, interventions at the community and individual levels are required. Mass public health campaigns can educate communities on behaviors including use of alcohol, tobacco, and safer–sex practices [12]. The value of community engagement and support groups has been well documented through a range of large scale evaluations in maternal and newborn health [13]. At the individual level, people should have access to affordable, high–quality health care, which is at the core of achieving UHC. However, access is problematic and is likely to assume crisis proportions as the WHO projects a shortage of 12.9 million health workers over the next two decades [14]. Moreover, low and middle–income countries (LMICs) will be severely affected by the ongoing migration of their workforce to high–income countries (HIC). In addition, the unaffordability of essential medicines threatens to increase the global burden of cardiovascular, respiratory, and other chronic, non–communicable illnesses. Finally, all nations will require evaluation of local and regional health outcomes to identify additional gaps, develop interventions, and monitor impact on health outcomes. Without clarity on *who*, *how*, and *how often* health outcomes should be monitored, and without effective monitoring systems in place, nations will be unable to improve outcomes and achieve many of the 169 targets of the SDG. Therefore, successful empowerment of people will rely on an educated population that is aware of these ground realities and can advocate for change. The Treatment Action Campaign (TAC), formed in 1998, has advocated for improved HIV care in South Africa has focused on empowering people by improving health education, increasing access to essential medicines, taking on government policy, and effecting social change [15]. The successes and challenges experienced by the TAC can help other global organizations in their efforts to empower people.

*Where do we go from here?* Thirty years after the *Charter*, we are still working toward the unfinished agenda of empowering people, and there remain several challenges. A study of semi–structured interviews with 22 health leaders from LMICs and HICs identified challenges associated with empowering people:

Photo: Women beggar, by Tomas Castelazo, own work, CC BY-SA 3.0

first, the term 'empowerment' may be considering 'soft' or 'opaque' and does not easily translate into action; second, empowering people shifts the power dynamic from governments to citizens, and may not be viewed positively in all countries; and, people in many countries have been disenfranchised, and instilling confidence and hope remains challenging [16]. To achieve any of the aspirational SDGs, we will require a holistic effort from HICs to assist LMICs monitor their health systems and reach their health targets. Many countries are moving toward a more nationalistic agenda, and international efforts (particularly, to help LMICs) are likely going to decline. The Ebola crisis largely affected LMICs, and yet, it was argued that HICs are obligated to contribute to humanitarian assistance and global justice [7]. However, non–communicable diseases will require a longer–term commitment, and LMICs will rely on HICs for guidance and financial assistance in improving health. We will also require a concerted approach to reduce the cost of medicines and increase access to affordable health care. In many instances, lack of political support has been a major obstacle to implementing the health agenda. These cannot be achieved in the absence of reducing road injuries, improving fuel sources to reduce air pollution, reducing wars and conflict, improving political and environmental stability, managing population growth, and ultimately, sharing experiences with other nations that may be at a different point on the trajectory toward achieving UHC and the SDGs. All of these facets are important, and nations will have to articulate their individual developmental agenda based on their local needs and priorities. The SDGs should serve as a guide and framework for ongoing improvement and robust implementation research to guide policy. An immediate priority therefore is to develop an agenda for implementation that engages and empowers people.
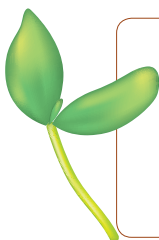
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# Reducing maternal mortality in sub–Saharan Africa: the role of ethical consumerism

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Between 1990 and 2015, the maternal mortality ratio for sub–Saharan Africa as a whole fell by roughly 45 percent [1]. Unfortunately, this decline has not been uniformly distributed across the region. A number of countries have shown little or no progress and continue to experience mortality rates that rank among the highest in the world. In countries such as Angola, Liberia, Sierra Leone, Chad, Somalia and the Democratic Republic of Congo (DRC) a significant impediment to progress has been the decimation of health infrastructure by protracted regional and civil armed conflicts. During times of conflict, there is also increasing evidence of violence being directed specifically against pregnant women [2]. The 1990s saw the emergence of warfare in Africa as a means of accumulating wealth and power [3]. In–depth analyses by the United Nations and others have identified competition among various groups for the illegal expropriation and sale of the region's vast natural resources, as both an underlying cause of conflict and also as a catalyst for ongoing conflict [4]. It has been estimated that Maternal Mortality rates are at least 30% higher in sub–Saharan African countries that have experienced recent conflict than in those which are conflict free [5]. Addressing the underlying issues relating to the protracted cycles of conflict is therefore an essential precursor to developing an environment in which interventions to address maternal mortality, or indeed any other health issue, can be implemented.

> In order to accelerate progress in the reduction of global maternal mortality, it is important that attention is given to broader development principles such as human rights, conflict resolution and poverty reduction.

The majority of the natural resources illegally expropriated in sub–Saharan conflict areas are eventually consumed in high–income nations, such as the UK. In a number of regions, this has inadvertently provided financial capital to various armed groups [4]. For example, chronic low–level warfare and societal instability in Chad is thought to be strongly related to competition for control of the country's oil reserves. In Sierra Leone, the revenue which was used to fund the civil conflict which destroyed much of the country's health infrastructure is thought to have come from illegally traded diamonds [3]. This state of affairs raises significant moral and ethical concerns for consumers in high–income countries about the circumstances surrounding the production of their consumer goods. It also highlights the collective influence that can potentially be wielded by consumers to effect change through alterations in their purchasing habits. By engaging in so called 'ethical consumerism' and refusing to purchase goods whose production may have involved illegal resource expropriation, collective consumer action has the power to significantly reduce the resources available to armed groups and other perpetrators of serious human rights abuse [4].

## ETHICAL CONSUMERISM

Ethical consumerism involves the alteration of purchasing patterns to promote a certain set of moral values. Commonly, this involves boycotting products considered to be unethical and favoring the purchase of products which minimise harm to humans, animals or the environment. For example, ethical consumer movements such as the "Fair Trade Foundation" have presented consumers with an alternative range of food and clothing products whose sale results in a larger proportion of the purchasing price being allocated to producers in developing countries. This approach has been successful in utilizing market forces to improve trading standards, stimulate economic development and accelerate progress toward a number of Millennium Development Goal (MDG) targets. In terms of maternal health, quantitative impact data relating to Fair Trade interventions, has shown them to be beneficial both via the collateral effects of poverty reduction and through specific programs which have allowed women to earn a living wage and to reinvest some of their earnings in the development of health care infrastructure [6].

The principle of consumers and indeed nations having the right to base their purchasing patterns on ethical considerations is enshrined within international trade law [7,8]. A growing body of evidence demonstrates that the loss of revenue that results from ethically motivated collective consumer action, can act as a potent stimulant for behavior change among exploitative producers and intermediary companies [9]. The ability of consumers to make informed ethical choices is however confounded by the highly complex and convoluted nature of international trade relationships. The manufacturing, processing and distribution of many products frequently involve tangled chains of multiple, international, participants. Any participant can behave in ways that may be considered unethical, not only by the end–consumer, but also by the other participants in the trade chain. Providing complete transparency for consumers about the actions of all participants within a trade chain is therefore difficult, but not impossible. The illegal expropriation of natural resources in sub–Saharan Africa, most notably the DRC provides an illustrative case in point.

## MATERNAL MORTALITY AND CONFLICT MINERALS IN THE DEMOCRATIC REPUBLIC OF CONGO

The civil conflict in the Democratic Republic of Congo is estimated to have claimed upwards of 4 million lives since 1998 [10] and has been fuelled to a large extent by competition for the country's natural resources. The mineral resources in the DRC have been estimated to have a value of 15 Trillion pounds – more than the combined GDP of Europe and the United States [11]. In spite of this vast potential wealth, in 2013 the DRC was placed 186th out of 187 countries in the UN Human Development Index, which ranks nations based on a composite statistic of life expectancy, education and indices of income inequality [12]. At the height of the civil conflict, estimates suggested the maternal mortality ratio in the DRC was upwards of 1100 per 100 000 [1]. The eastern DRC also suffers from the highest rates of sexual violence anywhere in the world with rape frequently being employed as a weapon of war. One study reported an incidence of 48 rapes occurring every hour in the eastern DRC [13]. At the height of the civil war between 1998 and 2003, an estimated 98% of the mining industry in DRC was driven by enforced labor under the control of various militia groups. The main objects of expropriation were gold and minerals such as Casserite (tin ore), Wolframite (tungsten ore) and Coltan (tantalum ore) which are essential for the manufacture of consumer electronics such as mobile phones. Investigations undertaken by an Expert Panel at the request of the UN Secretary General identified that these minerals are distributed globally to be used in manufacturing processes via multiple intermediary companies, several of which are UK–based [4]. Eventually, the minerals end up in the hands of consumers who through the purchase of phones, laptops and various other electronics, inadvertently helped to fund and perpetuate a conflict which has been described as "the world's deadliest humanitarian crisis" [8].

> In order to accelerate progress in the reduction of global maternal mortality, it is important that attention is given to broader development principles such as human rights, conflict resolution and poverty reduction.

Photo: Child labor: artisan mining in Kailo, DR Congo. By Julien Harneis (Flickr: Mining in Kailo) [CC BY–SA 2.0 (http://creativecommons.org/licenses/by–sa/2.0)], via Wikimedia Commons.

In 2011, the United States senate passed a landmark reform on trade transparency in the form of the "Dodd–Frank Wall Street Reform and Consumer Protection Act". As a result of campaigning from numerous lobby groups, Section 1502 of the act stipulates that companies operating in the US whose products contain Cassiserite, Wolframite and Coltan must submit to the Federal Securities and Exchange Commission, whether their minerals have been sourced in the DRC or surrounding countries. Companies who report that they do source their minerals from these regions must detail the measures that they have taken to ensure that they have not been obtained from armed groups that have been involved in massacres and other atrocities. The legislation is a demonstration of the power of collective consumer activism and lobbying, to effect legislative change at the highest level. The transparency that the act affords also provides consumers with the information required to make informed choices about their purchases. In 2014, the anti–genocide campaign group "The Enough Project" reported that most of the mineral mines in Congo were no longer under the control of militia groups. This transition has been lauded as a triumph of consumer activism with the changes being attributed to the Dodd–Frank Act and the ensuing efforts of electronics manufacturers to examine and reform their supply chains [9]. As a result of the marked reduction in the availability of financial capital to fuel ongoing conflict, increasing amounts resources are being diverted toward health care and other areas of societal development. With regards to maternal health, there is a renewed focus on the provision of skilled birth attendance, emergency obstetric care and improving access to contraception [14]. In 2015, the maternal mortality ratio in DRC was estimated to be around 693 per 100 000 [1]. This figure still represents one of the highest maternal mortality ratios in the world and is subject to a degree of uncertainty due to the challenges of accurately measuring mortality in regions without formal civil registration systems. Nevertheless, the data are highly suggestive of a marked reduction in maternal mortality since the end of the civil conflict.

## CONCLUSION

A maternal death, no matter where in the world it occurs, will be embedded in a complex network of biological, cultural, political and socio–economic causal factors. Sadly, vital branches of the networks that contribute to so many maternal deaths in sub–Saharan Africa extend across countries and continents to involve consumers from all over the globe. The World Health Organization has highlighted that a significant drawback of MDG 5 was the insufficient attention that it paid to broader development principles such as human rights and poverty reduction [15]. Ethical consumerism provides a means by which individuals and advocacy groups concerned with maternal mortality can actively engage with these issues. This approach, employed in conjunction with sanctions and international legal prosecutions has also been endorsed by the UN as a powerful means by which the international community can contribute toward creating an environment of sustainable, basic security in sub–Saharan Africa where improved health infrastructure can continue to develop and save mothers lives [4]. The need for our collective action becomes all the more apparent if we consider that in spite of the progress of the last quarter century, sub–Saharan Africa still has more than 160 000 maternal deaths every year, which is now more than half of the entire global burden [1].

A number of organisations collate data about company and country trade practices and present the information in the form of "ethical shopping guides" to help consumers make informed choices. These organisations include "The Ethical Consumer Organisation", "The Ethical Company Organisation" and the

"Fair Trade Foundation". Other groups such as Raise Hope for Congo, The Enough Campaign and Fairphone deal directly with issues relating to conflict minerals in the DRC. The websites of any of these organisations are an ideal starting point for anyone wishing to engage with ethical consumerism.
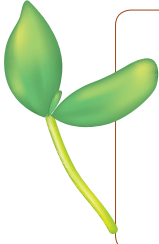
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VIEWPOINTS

# Economics in "Global Health 2035": a sensitivity analysis of the value of a life year estimates

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**Background** In "Global health 2035: a world converging within a generation," *The Lancet* Commission on Investing in Health (CIH) adds the value of increased life expectancy to the value of growth in gross domestic product (GDP) when assessing national well–being. To value changes in life expectancy, the CIH relies on several strong assumptions to bridge gaps in the empirical research. It finds that the value of a life year (VLY) averages 2.3 times GDP per capita for low- and middle–income countries (LMICs) assuming the changes in life expectancy they experienced from 2000 to 2011 are permanent.

**Methods** The CIH VLY estimate is based on a specific shift in population life expectancy and includes a 50 percent reduction for children ages 0 through 4. We investigate the sensitivity of this estimate to the underlying assumptions, including the effects of income, age, and life expectancy, and the sequencing of the calculations.

**Findings** We find that reasonable alternative assumptions regarding the effects of income, age, and life expectancy may reduce the VLY estimates to 0.2 to 2.1 times GDP per capita for LMICs. Removing the reduction for young children increases the VLY, while reversing the sequencing of the calculations reduces the VLY.

**Conclusion** Because the VLY is sensitive to the underlying assumptions, analysts interested in applying this approach elsewhere must tailor the estimates to the impacts of the intervention and the characteristics of the affected population. Analysts should test the sensitivity of their conclusions to reasonable alternative assumptions. More work is needed to investigate options for improving the approach.

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In its 2013 report, "Global health 2035: a world converging within a generation," *The Lancet* Commission on Investing in Health (CIH) recommended the use of a "full income" approach to incorporate the benefits of health improvements into national accounts [1]. Under this approach, the value of changes in life expectancy are added to the value of changes in gross domestic product (GDP) to capture the effects of health improvements at the population level.

To support this approach, prominent members of the Commission, including economists Dean Jamison, Lawrence Summers, and Kenneth Arrow, developed an innovative method for estimating the value of an increase in

population life expectancy and translating the results into an average value of a life year (VLY) [1]. They adjust a US estimate of the value of mortality risk reduction, assuming this value is proportional to GDP per capita and to remaining life expectancy. In their main result, they decrease the value for children aged 0 through 4 by 50 percent, then divide the total by the life expectancy gain to estimate VLY. This VLY is 2.3 times 2000 GDP per capita for life expectancy gains experienced by low– and middle–income countries (LMICs) from 2000 to 2011, assuming the gain is permanent, or 3.0 times GDP per capita without the reduction for young children. The CIH also reports the value of life expectancy gains for other country groups and time periods using the same approach, and applies the results to estimate the benefits of the interventions it recommends.

This VLY is within the range of the illustrative estimates of 1.0 to 3.0 times GDP per capita referenced by the 2001 Commission on Macroeconomics in Health (CMH), currently used as cost–effectiveness thresholds in the World Health Organization's Choosing Interventions that are Cost–Effective program and elsewhere [2,3]. The CMH multipliers were intended as rough estimates of the value an average individual might place on an incremental change in life expectancy [4]. In contrast, the CIH multiplier is based on a specific historical gain.

The CIH faced many challenges in developing its approach. We examine the sensitivity of the 2.3 times GDP per capita estimate highlighted in its main report to changes in the parameter values [1]. Our goal is to investigate the effects of plausible alternative assumptions and to provide insights into the uncertainties in the results as well as the issues that arise in tailoring the approach for application elsewhere.

## General framework

Conceptually, the CIH approach is intended to reflect the value that members of a population place on specific changes in their own life expectancies. In this context, money is not of interest per se: it measures the extent to which individuals are willing to trade consumption of other goods and services for a life expectancy increase. Because these preferences are likely to vary across individuals and societies, ideally such analyses would rely on estimates from the affected population. However, due to gaps and inconsistencies in the empirical research, these values must be extrapolated from studies of other populations that differ in significant respects.

The CIH starts with an estimate of the value per statistical life (VSL), which represents a population average of individuals' marginal rates of substitution between money and mortality risk in a defined time period [5]. Conventionally, VSL is estimated by dividing empirical estimates of individual willingness to pay for a small change in one's own risk by the risk change.

The associated value per statistical life year (VSLY) could be estimated directly by researching the values individuals place on an increase in life expectancy, but few empirical studies exist. Instead, VSLY is usually estimated as a constant, by dividing average VSL by the remaining (discounted) life expectancy for the average individual [6,7]. Valuing current mortality risk as the product of a constant VSLY and remaining life expectancy yields values that decrease with age.

The CIH also derives a value per life year from a VSL estimate, but uses a different approach, as described in detail in the Methods section. The result is the average value of a specified population increase in life expectancy. Analysts who are interested in applying the CIH approach would need to follow the same steps to calculate the VLY associated with a particular policy. We follow the CIH practice and use the term "VLY" to distinguish their population–based quantity from the conventional VSLY.

Monetary values for improved survival are expected to vary with characteristics of the affected population and the mortality risks. The effects of many characteristics are not well–understood; there are significant inconsistencies and gaps in the available research even for high–income countries [8,9]. In its analysis, the CIH focuses on the variation associated with income and age–specific life expectancy.

Most VSL studies address high–income countries [10–12]. Research on the relationship between income and VSL generally confirms that VSL increases with income, as anticipated. However, the proportional change in VSL in response to a proportional change in income (ie, its income elasticity) is uncertain. While theory and empirical studies generally support elasticities greater than one, some studies report elasticities as high as two or three while others report values less than one [13]. Income elasticity is of particular importance when extrapolating from very high to very low income countries because the range of potential elasticities may affect the resulting VSL by orders of magnitude. Theoretical models suggest VSL will exceed the present value of future income or consumption because VSL reflects non–monetary benefits

of living in addition to the monetary value of consumption and future earnings. Thus the income–adjusted VSL should not fall below the present value of income or consumption [13].

The theoretical and empirical evidence on the relationship between VSL and age or life expectancy is inconsistent, and generally does not support the hypothesis that VSL is proportional to (discounted) life expectancy nor the application of a constant VSLY [14,15]. Some studies find an inverse–U relationship between VSL and age for working–age adults, consistent with the prediction of life–cycle models [16–18]. Other studies, which include adults older than working age, find that values may decrease or remain constant with age [19,20].

Much of the research in higher–income countries suggests that adults value reducing risks to children more than to themselves [21–23]. The CIH posits, however, that particularly for countries with relatively low life expectancies, where much of the life expectancy gain results from decreased infant and child mortality, "[i]t is plausible that many societies and individuals will value reducing death rates at very young ages less than reducing death rates among, say, 25 year olds." [1]. The CIH notes that empirical evidence supporting such lower values is "limited."

## METHODS

The CIH faced two major challenges. First, most empirical estimates of the value of mortality risk reductions focus on high–income countries, while the CIH was interested in values for LMICs. Second, the available values are for a reduction in current mortality risk, while the CIH was interested in the value of life extension.

The CIH approach to the first challenge is relatively straightforward. They begin by dividing a VSL estimate by 10 000 to yield the value of a standardized mortality unit (VSMU) in 2011 dollars. They use "SMU" to refer to a 1 in 10 000 risk reduction for the current year and "VSMU" to refer to individual willingness to pay for this risk change. They use this terminology in part because the VSL concept is widely misunderstood [24]. It is not the value of saving a life with certainty; rather the VSL is derived from the value that an individual places on small changes in his or her own mortality risk, such as a 1–in–10 000 reduction.

The CIH states that it is reasonable to assume that the US VSMU was 1.8 percent of US GDP per capita in the year 2000, and that this ratio is constant across time and populations. In other words, they assume an income elasticity of 1.0: a one percent change in GDP per capita is associated with a one percent change in VSL and VSMU. For LMICs, the CIH uses the average of 2000 and 2011 GDP per capita, estimated as US$ 2718 and US$ 4201, respectively.

The CIH approach to the second challenge is more complex, and differs from the approaches commonly used. To estimate the value of a change in population life expectancy, they associate that change with a set of age–specific changes in current mortality risk valued using a set of age–specific VSMUs. To derive these VSMUs, the CIH requires data on population survival rates for each year of age, which are not available for most LMICs. They instead rely on Japanese life tables which reflect a similar change in average life expectancy at birth as found in the LMICs over the period of concern, noting that Japan provides "good historical data." More specifically, they estimate that life expectancy at birth across all LMICs in 2000 and 2011 was 65 and 68 years, respectively. They find that Japanese life tables for 1955 and 1961 reflect a similar life expectancy at birth. CIH then uses the corresponding Japanese age–specific mortality rates to calculate changes in age–specific mortality risk for LMICs.

In its calculations, the CIH uses age groups (generally 10–year increments, although 5–year increments are used for ages 0 through 9 and a single category is used for age 80 and higher), applying values for the midpoint of each age group from the life tables. They assume that the US VSMU reflects the value for an individual aged 35, who has 45 years of remaining life expectancy, and anchor the income–adjusted values for other countries at age 35. This anchor VSMU is then adjusted for other ages in proportion to remaining life expectancy, estimated using the 1958 (midpoint of 1955 and 1961) life table for Japan.

CIH calculates the present value of the change in life expectancy by summing, over all age groups, the product of the age–specific VSMU, the age–specific risk change, and the fraction of the LMIC population in that age group in 2005 (midpoint of 2000 and 2011). Assuming the increase in life expectancy is permanent (ie, the mortality risk reduction is sustained across all future generations), CIH calculates the present value of an infinite stream of annual values using a 3 percent annual discount rate. Dividing by

the increase in life expectancy yields the VLY. The CIH does not account for the age distribution shift that results from the change in mortality rates.

Prior to calculating the VLY, the CIH reduces the VSMUs for children aged 0 through 4 by 50 percent, to reflect the hypothesis that the affected populations place a lower value on these risk reductions than on those that occur at older ages. Elsewhere in its analysis, CIH tests the effects of eliminating this adjustment, of excluding children under 10, and of excluding adults older than 70.

In our calculations, we rely on data from spreadsheets provided by CIH staff, which include more detail but occasionally differ from the description in their report [2]. (It appears that the CIH intended to subtract health expenditures from the GDP per capita estimates, but does not do so consistently. However, this inconsistency has little effect the resulting VLY.) Like the CIH, we use income as a shorthand for GDP per capita, discount future values at 3 percent per year, calculate the value of risk reductions using their estimates of the average of 2000 and 2011 GDP per capita, and calculate the VLY multiplier based on their estimate of 2000 GDP per capita. CIH references the World Bank's 2013 World Development Indicators report as the source of the country classification used to define LMICs and the GDP estimates [25].

We explore the key assumptions listed in **Table 1**, basing our sensitivity analysis on plausible alternatives described in more detail below. Of these assumptions, we expect that the range of income elasticities will have the largest effect. The appropriate elasticity is highly uncertain, and small changes in the elasticity can alter the results by orders of magnitude.

## SENSITIVITY ANALYSIS RESULTS

We change each assumption individually then examine their joint effect. In addition, we test the effect of re–ordering the steps, calculating the VLY for the US then adjusting for income. We do not test the effects of altering the assumption that changes in value are proportional to changes in life expectancy, although this assumption is inconsistent with much of the VSL research summarized above.

### Assumption 1: VSMU

In a recent criteria–driven literature review, the authors report a central US VSL estimate of US$ 9 million, expressed in 2013 dollars at 2013 income levels [8]. Dividing by 10 000 yields a VSMU of US$ 900; 1.7 percent of 2013 US GDP per capita in 2013 dollars. This small reduction decreases the LMIC VLY from 2.3 to 2.1 GDP per capita.

### Assumption 2: income elasticity

We apply income elasticities of 1.5 and 2.0 to illustrate the effects of larger elasticities using an equation based on the average of 2000 and 2011 US GDP per capita (US$ 44 781 and US$ 48 112, respectively) from the CIH spreadsheets [13].

$$VSMU_{LMICs} = VSMU_{US} \times (GDP \text{ per capita}_{LMICs}/GDP \text{ per capita}_{US})^{Income\ Elasticity}$$

Because changing the elasticity has an exponential effect, the range of elasticities found in the literature significantly affects the estimates. Increasing income elasticity to 1.5 and 2.0 decreases the LMIC VLY to 0.6 and 0.2 GDP per capita, respectively, violating the expectation that individuals will value an increase in life expectancy by an amount that exceeds what they would earn over the same time period.

**Table 1.** Assumptions explored in sensitivity analysis

| CIH Main Case | Sensitivity Analysis |
|---|---|
| 1. Assume VSMU is 1.8 percent of GDP per capita. | 1. Assume VSMU is 1.7 percent of GDP per capita. |
| 2. Assume an income elasticity of 1.0. | 2(a,b). Assume an income elasticity of 1.5 or 2.0. |
| 3(a). Convert increases in life expectancy to changes in age–specific mortality rates using Japanese life tables. | 3(a). Replace Japanese life tables with Bulgarian life tables. |
| 3(b). Adjust the VSMU for age by the ratio of the remaining life expectancy at each age and at the anchor age of 35, which is the age at which US life expectancy is 45 years. | 3(b). Replace the anchor age of 35 with the age at which remaining Bulgarian life expectancy is 45 years (age 25). |

CIH – Commission on Investing in Health, VSMU – value of a standardized mortality unit, GDP – gross domestic product

## Assumption 3: life tables and anchor age

We replace the Japanese life tables with life tables from a LMIC that yields a similar change in life expectancy but with a different pattern of age–specific mortality. We selected the Bulgarian life tables from 1955 and 1958 as an illustrative example because they are from the same data source as the Japanese life tables; this source includes life tables for only one other LMIC (Ukraine) [26]. We also consider the effect of changing the anchor age from 35 years to the age at which remaining life expectancy is 45 years (as assumed by the CIH for the US). For Bulgaria, this is age 25 using the midpoint (1956 or 1957) life table. Changing the life tables while keeping the anchor age at 35 reduces the GDP per capita multiplier to 1.7. Moving the anchor to age 25 leads to a further decline to 1.4.

This analysis suggests that the VLY is sensitive to the age distribution of the survival gains. Improvements in Bulgarian survival rates between 1955 and 1958 were more concentrated in younger age groups than in Japan. We illustrate the distribution in Figure 1, which calculates the change in age–specific SMUs using each set of life tables and weights the results by the LMIC population within each age group.

## Combined effect

We combine a VSMU of 1.7 percent of GDP per capita, an income elasticity of 1.5, and Bulgarian life tables anchored at 25 years of age, and find the VLY decreases to 0.4 times GDP per capita.

Repeating each analysis without the reduction for ages 0 through 4 used in the original CIH estimates increases the estimates in each case, as expected. **Table 2** summarizes these results.

## Alternative sequencing

The CIH adjusts the VSMU for income then calculates the VLY. We reverse the order, calculating VLY for the US (using US life tables from the same data source [26]) for the same period (2000 and 2011), then adjusting for income based on the average of the LMIC 2000 and 2011 values. Without reducing the values for young children, we find that the VLYs for LMICs range from 0.1 to 2.0 GDP per capita, depending on the income elasticity (**Table 3**).

As in some of our earlier calculations, the resulting VLY is less than GDP per capita for LMICs when income elasticities of 1.5 and 2.0 are applied, contrary to theoretical expectations. Thus we explore the effect of using GDP per capita as a lower bound. To be consistent with the CIH approach, we set the lower bound at the average of 2000 and 2011 GDP per capita, and express the VLY as a multiplier of 2000 GDP per capita. We find the multiplier becomes 1.3 to 2.0, depending on the income elasticity. Using the average of 2000 and 2011 GDP per capita as the base would decrease the multiplier.
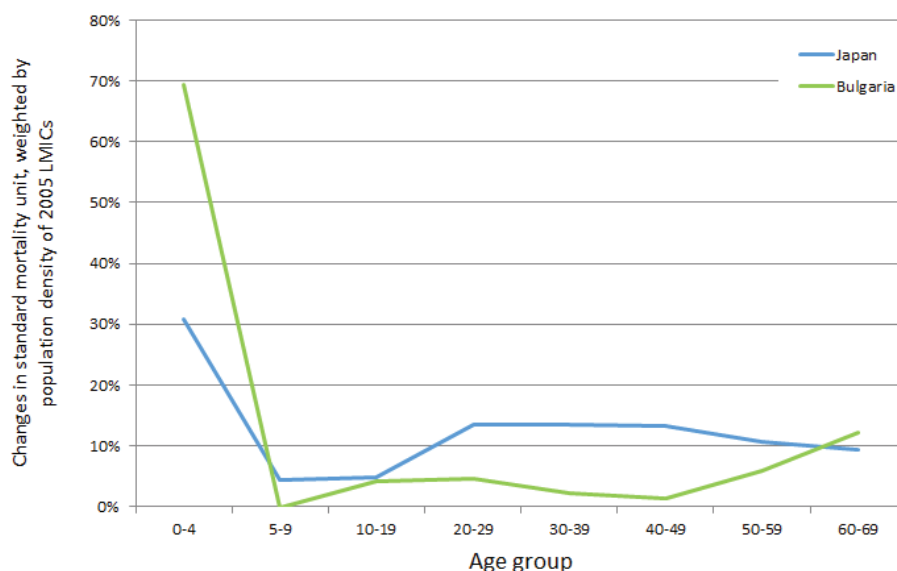


**Figure 1.** Distribution of the changes in the standard mortality unit by age group in Japan (between 1955 and 1961) and Bulgaria (between 1955 and 1958), weighted by the population density of low– and middle–income countries (LMICs) in 2005.

**Table 2.** Results with alternative assumptions

| SENSITIVITY ANALYSIS | LMIC VLY AS MULTIPLIER OF GDP PER CAPITA | |
|---|---|---|
| | With 50% reduction for ages 0 through 4 | Without reduction for ages 0 through 4 |
| Original CIH estimate | 2.3 | 3.0 |
| (1) VSMU = 1.7% of GDP per capita | 2.1 | 2.8 |
| (2a) Income elasticity = 1.5 | 0.6 | 0.8 |
| (2b) Income elasticity = 2.0 | 0.2 | 0.2 |
| (3a) Bulgarian life table, anchoring at age 35 | 1.7 | 2.9 |
| (3b) Bulgarian life table, anchoring at age 25 | 1.4 | 2.4 |
| Combination: VSMU = 1.7% GDP per capita, income elasticity = 1.5, Bulgarian life table anchoring at age 25 | 0.4 | 0.6 |

LMIC – low– and middle–income country, VLY – value of a life year, CIH – Commission on Investing in Health, VSMU – value of a standardized mortality unit, GDP – gross domestic product

## DISCUSSION

The CIH methodology is fundamentally different from the traditional VSLY approach. Rather than deriving a VSLY from a VSL estimate then applying it to predicted life expectancy gains, the CIH estimates the value of age–specific changes in risks, weights by the population age distribution, then divides by the population life expectancy gain (assuming it is permanent) to calculate the average VLY.

For example, using the CIH methodology, the VLY for the change in US life expectancy from 2000 to 2011 is roughly US$ 68 000. Using the conventional approach to calculate a VSLY from a VSL yields a much larger value. The CIH assumptions yield a US VSL of US$ 7.5 million (180 times the average of 2000 and 2011 US GDP per capita). Dividing by an average remaining life expectancy of 45 years yields a VSLY of US$ 170 000, or US$ 300 000 if future years are discounted using the CIH rate of 3 percent annually. Thus the choice of approach may significantly affect the analytic conclusions, but without more empirical research it is difficult to determine which approach is most appropriate. Both have significant limitations and illustrate the enormous challenges that analysts face, given the inconsistencies and gaps in the research literature and the many ways in which they can be addressed.

The CIH approach is designed to compare the value of the historical life expectancy gains over time, across countries and regions, or across interventions. The resulting VLY estimate is an analytic *output*; it is not a value intended to be used as an *input* to value life expectancy gains in other settings. The estimates underlying the average VLY vary by country and age group, and reflect survival gains over a particular time period. Thus the 2.3 times GDP per capita value should not be directly applied in other settings.

Instead, analysts interested in applying the CIH approach would need to follow the same steps in their calculations. We find that the CIH estimate of the average VLY is very sensitive to the underlying assumptions, ranging from 0.2 to 3.0 times GDP per capita. Thus analysts should examine the inputs and assumptions and adapt them to their setting. Note, however, that multipliers less than 1.0 times GDP per capita (for the same year) seem implausible, given that we expect the VLY (as well as the VSLY) to exceed annual income. Thus GDP per capita should be used as a lower bound. Our results also suggest that analysts should explicitly address uncertainties in these values and discuss the implications for decision-making.

More specifically, as illustrated in our sensitivity analysis, the value of changes in life expectancy in LMICs is highly sensitive to the income elasticity used. However, our reviews of the literature suggest that more

**Table 3.** Results with alternative sequencing

| SENSITIVITY ANALYSIS STARTING WITH A US VLY | LMIC VLY AS MULTIPLIER OF GDP PER CAPITA, WITHOUT REDUCTION FOR AGES 0 THROUGH 4 | |
|---|---|---|
| | Without income floor | With income floor |
| (a) Income elasticity = 1.0 | 2.0 | 2.0 |
| (b) Income elasticity = 1.5 | 0.5 | 1.3 |
| (c) Income elasticity = 2.0 | 0.1 | 1.3 |

LMIC – low– and middle–income country, VLY – value of a life year, VSMU – value of a standardized mortality unit, GDP – gross domestic product

work is needed to determine the appropriate elasticity [13]. In the interim, analysts should test the sensitivity of their conclusions to a reasonable range of elasticities. In some cases, they are likely to find that an intervention is cost–beneficial, or is not cost–beneficial, regardless of the elasticity estimate; in other cases, the conclusions may be more uncertain. Highlighting such findings will aid decision–makers and other stakeholders in understanding the degree to which they should have confidence in the results.

The relationship of the VLY or VSLY to age or life expectancy is more complex and more difficult to resolve, raising both empirical issues (whether individuals' willingness to pay for their own risk reductions varies by age) and normative issues (how society should value risk reductions depending on the age of those affected). As discussed earlier, the available VSL research is not conclusive, but suggests that adults in high–income countries may place higher values on risk reductions that accrue to children, that adult values for their own risk reductions over their working years may follow an inverse–U pattern, and that the values held by older adults may remain constant or decrease with age. It is unclear whether similar patterns are likely to hold in LMICs, given cultural and other differences.

Both the CIH VLY approach and the standard VSLY approach simplify this age relationship. In its main results, the CIH down–weights the values for young children, but otherwise both the VLY and the VSLY approach lead to total values that decrease with age. More work is needed to examine the empirical and normative concerns that underlie these age adjustments. In the interim, analysts should be clear about both the rationale for their approach and the extent to which it is supported by available research, and discuss the implications of related uncertainties.

Our sensitivity analysis is not intended to be a comprehensive assessment of the effects of the CIH assumptions, nor do we intend to endorse or propose any particular approach. The limited and inconsistent empirical research means that there are numerous ways in with these values can be estimated. More studies are needed to estimate key inputs such as the appropriate VSL and the relationship between VSL, age, life expectancy, and income.

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**PAPERS**

PAPERS

# Contribution of community health workers to improving access to timely and appropriate case management of childhood fever in Mozambique

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**Background** Large scale evaluations in several settings have demonstrated that lay community health workers can be trained to provide quality case management of childhood illnesses. In 2010, Mozambique introduced the integrated community case management (iCCM) strategy to reach children in remote areas with care provided through *Agentes Polivalentes Elementares* (APEs). We assessed the contribution of the program to improved care–seeking and appropriate treatment of childhood febrile illness in Nampula Province.

**Methods** We used a post–test quasi–experimental design with three intervention and one comparison districts to compare access and appropriateness of care for sick children in Nampula province. We carried out a household survey in the study districts to measure levels of care–seeking and treatment of childhood fever after approximately two years of full implementation of the iCCM program in the intervention districts. We also assessed consistency of care with standard case management protocols comparing children receiving care from (APEs) to those receiving care from first–level health facilities.

**Results** A total of 773 children 6–59 months with fever in the last two weeks were included in the study. In iCCM served areas, APEs were the predominant source of care and treatment; 87.1% (95% confidence interval CI 80.8–93.4) of children 6–59 months with fever who sought care were taken first to an APE and APEs accounted for 86.2% (95% CI 79.7–92.7) of all first–line antimalarial treatments. Public health facilities were the leading source of care in comparison areas, providing care to 86.1% (95% CI 79.0–93.3) of children with fever taken for care outside the home. Timeliness of treatment was significantly better in intervention areas, where 63.9% (95% CI 54.4–73.3) of children received treatment within 24 hours of symptom onset compared to 37.5% (95% CI 31.1–43.9) in comparison areas. Children taken first to an APE were more likely to receive a rapid diagnostic test (RDT) (68.1%; 95% CI 57.2–79.0) and to have their respiratory rate assessed (60.0%; 95% CI 45.4–74.6) compared to children taken to health facilities (41.4%; 95% CI 33.7–49.2 and 19.4%; 95% CI 8.4–30.5, respectively). Overall, 61.3% (95% CI 51.5–71.0) of children with fever receiving care from APEs received the correct drug within 24 hours and for the correct duration compared to 26.0% (95% CI 18.2–33.9) of those receiving care from health facilities.

**Conclusion** iCCM contributed to improved timely and appropriate treatment for fever for children living far from facilities. Trained, supplied and supervised APEs provided care consistent with iCCM protocols and performed significantly better than first level facilities on most measures of adherence to case management protocols. These findings reinforce the need for comprehensive efforts to strengthen the health system in Mozambique to enable reliable support for quality case management of childhood illness at both health facility and community levels.

An estimated 5.9 million children die each year before reaching their fifth birthday; about half of these deaths are caused by infectious diseases [1]. Among children aged 1 to 59 months, pneumonia, diarrhea, and malaria remain leading causes of death, responsible for 1.8 million child deaths annually [2]. Integrated community case management (iCCM) seeks to reduce the mortality burden among children under five by improving access to equitable, life–saving interventions that address the leading causes of death such as pneumonia, malaria and diarrhea [3]. It relies on short–term training (generally one week), equipping and supervision of lay community workers to provide care for uncomplicated cases of pneumonia, malaria and diarrhea and referral for complicated cases among children age 2–59 months. In 2012, the World Health Organization (WHO) and United Nations Children's Fund issued a joint statement on the role of iCCM in reducing under–five mortality through community–based care for malaria, diarrhea, and pneumonia [3]. The joint statement urged governments adopting iCCM to support programs with adequate training, a strong supply chain, and ongoing monitoring of activities, all built upon existing infrastructure and systems [3]. As of 2014, iCCM for malaria, diarrhea and pneumonia was being implemented in 28 countries in sub–Saharan Africa, including Mozambique [4].

Mozambique is one of just 12 low–income countries to achieve its Millennium Development Goal (MDG) of reducing child mortality by two–thirds or more between 1990 and 2015 [1]. In 1990, Mozambique's under–five mortality rate was estimated to be 240 per 1000 live–births and by 2015 this had dropped to an estimated 79 per 1000 live–births [1]. Malaria is the leading cause of death among children aged 1–59 months followed by pneumonia, HIV, and diarrhea [5]. Mozambique formally introduced iCCM into the national health system in 2010, through a national program of community health workers (CHWs) referred to as *Agentes Polivalentes Elementares* (APEs) who provide iCCM services to communities located 8–25km from the nearest health facility [6,7].

Although there is global evidence that CHWs are capable of providing quality iCCM services [8–10], there are some concerns within Mozambique regarding the ability of APEs to provide quality care and the extent to which iCCM will contribute to improved treatment coverage [11,12]. Despite endorsing iCCM nationally, the Ministry of Health (MOH) in Mozambique emphasizes the health promotion activities of the APEs, recommending that APEs spend 80% of their time conducting home visits and community meetings and just 20% of their time for curative activities including iCCM [12]. While large scale evaluations from other settings have shown that CHWs implementing iCCM within existing government systems can provide quality care and contribute to increases in treatment coverage [13–15], there is limited evidence from the iCCM program in Mozambique regarding the performance of APEs implementing iCCM that can help inform national implementation and financing decisions [12].

Save the Children (SC), with funding from the Canadian International Development Agency (now called Global Affairs Canada) provided support to the Mozambican MOH for implementing iCCM from 2009 to 2013, with a focus on malaria (fever) management, the leading cause of child deaths. We present the findings of a quasi–experimental evaluation of the APE iCCM program that compares levels of care–seeking and timely and appropriate treatment coverage for fever in an intervention area with a well–supported iCCM program to levels in a comparison area where the APE iCCM program had yet to be implemented. We also compare consistency of care provided by APEs and first level health facilities with established cases management protocols.

## Program description

### Mozambique's revitalized APE program

In Mozambique, community–based health services are provided through the APEs. The APE cadre was established in 1978, but services were disrupted due to the protracted civil war, which ended in 1992 [6]. In 2010, the MOH set out to revitalize its community health worker program, aiming to train and deploy 5000 APEs across Mozambique's ten provinces – with an initial target of 25 APEs per district [6,7]. Prior to 2010, APEs were implementing community case management for some illnesses including malaria and diarrhea, but support for implementation was confined to small areas with partner support and there was no standardized training package endorsed under national MOH policies. Under the revitalized program, APEs located 8 to 25 km from the nearest health facility are designated for training in the revised national package and are meant to serve a target catchment population of 500–2000 individuals [6,7]. The national APE program is managed by the Department of Health Promotion, which coordinates technical oversight, program financing, monitoring and evaluation, and liaises with other departments in the MOH, donors and implementing partners [6]. While officially considered volunteers, the APEs re-

ceive a monthly stipend of 1200 meticais (equivalent to approximately US$ 40 at the time of the study) set by the Ministry of Health, with implementing partners being responsible to cover the stipend in the areas they support iCCM implementation [6].

Under the revitalized program, APEs receive 18 weeks of training organized into four blocks; iCCM is covered for one week during the third block [6]. APEs are trained in the assessment, classification, and treatment of common childhood illnesses, including fever, diarrhea, and suspected pneumonia, based on WHO's standard protocol for management of childhood illness by CHWs and MOH protocols. In addition to providing case management to children under–five, APEs treat other non–ICCM conditions including conjunctivitis and scabies, identify and refer children with moderate to severe acute malnutrition, and conduct home visits and community health promotion talks to relay health promotion and disease prevention messages. The APEs also deliver first aid and provide treatment for malaria and diarrhea to community members older than five years of age.

## Case management of childhood illness in Mozambique

Under the iCCM protocol, APEs assess children 2–59 months for general danger signs as a first step [16]. If general danger signs are present, APEs refer patients to government–run first level health facilities referred to as *Unidade Sanitária*. Children presenting with fever or a history of fever are tested for malaria with a rapid diagnostic test. Children between 6–59 months with a positive RDT for malaria receive artemether–lumefantrine (AL) and paracetamol from the APE. A child with a negative test is given paracetamol, and referred to the first level health facility. Children 2–59 months with cough/difficult breathing are assessed for fast breathing by counting breathes for one minute using a digital timer. A child with respiratory rate above the WHO age–specific cut–off point is classified as fast–breathing pneumonia and treated with amoxicillin dispersible tablets. Children aged 2–59 months presenting with diarrhea are treated with recommended doses of ORS and zinc.

At first level health facilities, providers follow a similar algorithm based on WHO's Integrated Management of Childhood Illness (IMCI) protocol. According to the protocol, all children presenting with fever should be tested for malaria with an RDT and if positive, given the first–line antimalarial (AL). Fever is treated with either paracetamol in suspension or tablets. Those presenting with cough/difficult breathing should be assessed by counting breaths for one minute using a timer (or if not available a watch or mobile phone). Under MOH protocols, those with fast–breathing pneumonia receive amoxicillin or cotrimoxazole in suspension (MOH protocol was amended in early 2011 to include amoxicillin as first line treatment). Children with diarrhea should receive ORS and zinc. First level health facilities typically provide IMCI services 5 days per week (Monday to Friday) from 7:00am to 3:00pm. However, health staff live on the facility grounds so in theory, they can attend to severely ill children or those with danger signs at any time. The first level facilities are usually staffed with a medical technician (Técnico de Medicina), or/and a general nurse or MCH nurse. Both nurses and medical technicians receive 30 months training. Medicines and supplies for treatment of child illness (RDTs, AL, amoxicillin or cotrimoxazole syrup, paracetamol pills or syrup, ORS and zinc) are meant to be provided to facilities monthly through provincial and district medical stores.

## The iCCM program supported by Save the Children

Save the Children provided support for iCCM implementation, with a focus on fever management, in 10 districts in Nampula province and five districts in Gaza province from 2009 to 2013. APEs satisfied national eligibility criteria including the ability to read and write in Portuguese and complete basic arithmetic. In 2010, SC trained and equipped 319 APEs across the 15 districts to deliver iCCM services. These APEs were trained before the MOH had finalized the curriculum and manuals for the revitalized APE program, a task which was completed in October 2011. Thus, the first group of APEs trained by SC received six days of iCCM training based on training modules developed by SC together with the MOH. The training included a mix of classroom exercises and clinical practical sessions to provide the necessary knowledge and skills related to iCCM. Later, this iCCM module was adapted and incorporated into the larger, national APE curriculum and training package. The APEs received a week long refresher training in March 2012.

Training activities were implemented using a cascade model, in which SC and MOH master trainers trained health facility staff and SC–employed district coordinators, who in turn trained the APEs At the end of the training, APEs were administered a clinical competency assessment and APEs who passed were award-

ed certificates upon completion of the training and provided a kit of essential drugs and supplies. The APEs kept the kit at the health post, which served as iCCM delivery site as well. The kit included: medicines specified by the national iCCM protocol including AL, amoxicillin, ORS, and zinc; respiratory timers; job aids; and a treatment register. The APEs received stipend support from Save the Children and MOH (via external funding from other donors).

During the project implementation period, SC provided technical support including development and adaptation of tools, training, monitoring, and supervision. Save the Children trained MOH staff at district and health facility levels in supervision and supply chain support. APEs were supervised monthly within their communities by district and facility based MOH staff trained on iCCM protocols, monitoring and supervision. SC placed staff at district level to support and mentor the MOH staff to supervise and monitor APEs. AL, amoxicillin, and malaria RDTs were procured by SC through local suppliers approved by the MoH. The medicines procured by SC were supplemented with medicines (ORS, AL) from the MOH system. Additionally, SC transported these medicines and supplies from the provincial capital to the districts and, in some cases, to the APEs' reference health facility. Medicines were procured and distributed to the APEs based on number of cases treated reported by APEs.

## METHODS

### Study setting

Nampula province is located in the north of Mozambique and, as of 2013, had an estimated population of more than 4.7 million. Nampula province was chosen for the endline study given that more than 90% of under–five children targeted through SC support were located within the province. We conducted a household survey in areas with iCCM services in three intervention districts (Angoche, Erati and Monapo) that had received SC support and one comparison district, Mossuril, where the APE revitalization and iCCM program had yet to be rolled out (**Figure 1**).

Angoche, Erati and Monapo were selected for the evaluation as they were the first districts in Nampula to receive iCCM training and had initiated full implementation by late 2010. The three districts had a total population of 837 245 and were served by 41 government health facilities. The districts had a high
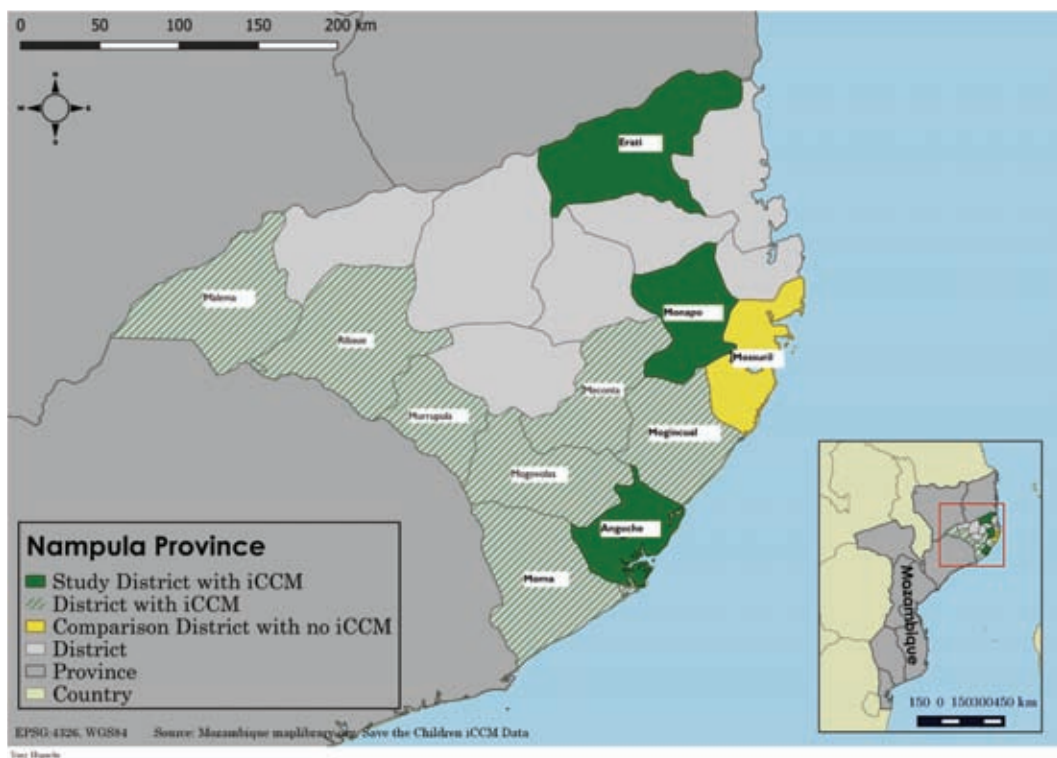


**Figure 1.** iCCM (integrated community case management) implementation supported by Save the Children and evaluation areas, Nampula province, Mozambique.

number of iCCM–trained APEs; a total of 157 APEs were trained and deployed in iCCM across these three districts, serving an estimated population of 329 752 (an average of 2213 per APE) and 61 158 children under five. Mossuril, the comparison district, was selected for the evaluation as it was geographically proximate to the intervention areas (located adjacent to Monapo district) and had a similar health service profile, with a total population of 119 223 with 10 government health facilities.

## Study design and sampling

A cross–sectional household survey was conducted in Nampula province in November 2012 after approximately two years of program implementation. The sample size of 600 households from the three intervention districts and 600 households from the comparison district was powered to detect a 20% difference in fever (presumptive malaria) treatment between intervention and comparison areas, assuming a fever prevalence of 27% and baseline treatment of 42%. Households with children aged 2–59 months were selected using a two–stage sampling procedure. In intervention districts, 30 APE catchment areas were selected with equal probability (ten per district) and in the comparison areas 30 census enumeration areas that were at least 8 km from nearest health facility (and therefore eligible for implementation of iCCM program) were sampled proportional–to–size from a listing of all eligible enumeration areas. A mapping team sketched basic maps of each selected survey cluster prior to the start of fieldwork. The maps identified boundaries of each cluster, landmarks, and buildings to allow data collection teams to locate selected households. The catchment area population of the APEs ranged from a population of 500 to 2000, located 8–25km from the nearest health facility (a small number were beyond 25km). Any APE catchment area exceeding 300 households was broken down into smaller units of 150–200 households and the unit containing the APE health post was selected for the household listing. Within each selected cluster, all households were listed and households with children 2–59 months were identified by asking the household head whether any children in that age range were resident; from those listings, 20 households with at least one child aged 2–59 months were selected using systematic random sampling. Within each selected household, one mother or caregiver was randomly selected to be interviewed regarding recent child illness and care–seeking behaviors.

## Data collection and management

The questionnaire was modeled after the UNICEF Multiple Indicator Cluster Survey (MICS) questionnaire (version 4) and included three modules: household, caregiver, and children under–five [17]. The questionnaire was translated into Portuguese and back–translated independently into English to check the accuracy of the Portuguese translation. Data collectors were provided with pictures of common medicines to serve as an aid for respondents to answer questions on medicines received during illness episodes. Trained study staff administered the questionnaire to the caregiver in each household selected for inclusion in the survey. The questionnaire was administered in Portuguese, or orally translated by the interviewer to Macua or Coti, the local languages of survey areas in Nampula province. Interviewers were taught how to correctly translate the survey questions to Macua or Coti during the training.

Data collection was led by the National Institute of Statistics (Instituto Nacional de Estatisticas (INE) in Portuguese) with technical support from SC. Data collectors with prior experience of conducting national household surveys were recruited and trained for six days, including one day of field practice. Data collection was completed in October and November 2012 by four teams of five members each, including a team leader trained to supervise the data collectors, review completed questionnaires, and perform the household sampling. Two field coordinators from INE and two from SC monitored data collection to ensure quality control of data. Data were entered into CSPro by a team of four data entry clerks and double data entry was used to ensure quality; any data discrepancies were reconciled prior to analysis.

## Data analysis

The data were analyzed in Stata IC 11.1 (STATA Corp LLP, College Station, Texas, USA). Data analysis involved calculating frequencies and cross tabulations of care seeking, coverage and consistency of care indicators (**Box 1**). We generated 95% confidence intervals (CI) for each, adjusted for clustering.

### Indicators of care–seeking and treatment coverage

We applied a standard set of metrics captured in household surveys to compare levels of care–seeking and treatment coverage in intervention and comparison areas (**Box 1**). All results focus on assessment and treatment of children aged 6–59 months as indicated by the national iCCM protocol with the excep-

**Box 1.** Indicators of care–seeking, coverage, and consistency of care

**Care–seeking and treatment coverage: intervention vs comparison areas**
- Care–seeking: Proportion of children 6–59 months with fever in the last two weeks taken to an appropriate provider (formal public or private providers).
- Treatment coverage: Proportion of children 6–59 months with fever in the last two weeks who received AL.
- Timely and appropriate treatment coverage: Proportion of children 6–59 months with fever in the last two weeks who received AL within 24 hours of onset of symptoms.

**Consistency of reported care with standard case management protocols: APEs vs first–line health facilities as first place of care**

*Appropriate assessment:*
- Respiratory rate assessment for cough or difficult breathing: proportion of children aged 2–59 months with cough and fast/difficult breathing whose respiratory rate was assessed.
- RDT for fever: Proportion of children aged 6–59 months presenting with fever who were administered an RDT

*Communication of results:*
- RDT result communication: Proportion of children 6–59 months presenting with fever who were administered an RDT and whose caregiver were told the results of the test.

**Appropriate treatment of fever:**
- Correct medication: proportion of children 6–59 months with fever who received AL.
- Rationale use of antibiotics: proportion of children 6–59 months with fever only who did not receive antibiotics.
- Timely treatment: proportion of children 6–59 months with fever receiving AL who initiated treatment within 24 hours of onset of symptoms.
- Correct duration: proportion of children 6–59 months with fever receiving AL who took AL for the recommended for 3 days.
- Overall appropriate treatment: proportion of children 6–59 months with fever who initiated AL treatment within 24 hours and took medication for three days.

**Provision of first dose and follow-up of children with fever treated by an APE:**
- First dose: proportion of children 6–59 months who received AL from APE who took first dose in presence of APE.
- Follow–up: proportion of children 6–59 months who received AL from APE who returned for follow–up.

tion of assessment of cough/difficult breathing, which is assessed for children aged 2–59 months. We report results for care–seeking and treatment coverage for fever, which was the focus of project, particularly in terms of supply chain support. We compare areas with iCCM to areas without iCCM.

*Indicators for consistency of reported care with case management protocol*

Using report from mothers or caregivers of children under–five during the household interviews, we assessed indicators of consistency of care defined based on standard case management protocols for children presenting with fever or cough/difficulty breathing in the last two weeks who were managed by APEs and by first level facilities (Box 1). Additionally, for children presenting with fever, we measured communication of RDT results and treatment to the caregiver. Under the iCCM protocol, APEs were trained to administer the first dose of treatment and to encourage caregivers to return for follow–up when children have a positive RDT. We assessed consistency with these aspects of the protocol for children treated for fever by an APE with the indicators measuring first dose and follow–up.

This is a comparison based on first source of care. Our analysis was restricted to all children with reported fever and/or cough/difficulty breathing in the two weeks prior to the household survey for which the caregiver sought care first from either an APE or first–line government health facility. Sick children (n=13) taken first to private clinics, pharmacies, drug shops, informal care providers, or public sector hospitals were excluded from the analysis to allow direct comparison of first level facilities with APEs and sick children who were taken for subsequent care after visiting an APE of first–line government facility (n=25) were excluded as it would not be possible to differentiate clearly what care was provided by what provider.

## Ethical considerations

Ethical clearance was obtained for the survey from the Ministry of Health Bioethics Committee in Mozambique. Informed oral consent was obtained from every respondent and documented by interviewers on the survey tools.

## RESULTS

Among the 1200 households surveyed with at least one child aged 2–59 months, information was collected for 1531 (753 intervention and 778 comparison) among 1534 eligible children. Characteristics of house-

**Table 1.** Characteristics of intervention and comparison areas within Nampula province, Mozambique

| Household characteristics | Intervention area | Comparison area | P–value |
|---|---|---|---|
| | N = 600 | N = 600 | |
| **Male head of household** | 83.3% | 85.7% | 0.3549 |
| **Household size:** | | | 0.5136 |
| 1–5 members | 63.0% | 61.2% | |
| 6 or more members | 37.0% | 38.8% | |
| **Marital status of caregiver:** | | | 0.0112 |
| Married | 88.2% | 80.9% | |
| Single/separated/widowed | 11.2% | 19.1% | |
| **Education of caregiver:** | | | 0.0257 |
| None | 50.3% | 59.3% | |
| Primary | 45.0% | 34.8% | |
| Middle or higher | 4.7% | 5.8% | |

holds are presented in **Table 1**. The intervention and comparison districts had similar household characteristics (**Table 1**). The majority of households in both study areas had a male head of household and fewer than six members. The intervention and comparison areas did differ significantly in caregiver marital and education status with the caregiver being more likely to be married, and educated in the intervention area.

## Contribution of iCCM to care–seeking and treatment coverage

A total of 773 children 6–59 months (346 intervention and 427 comparison) were reported to have fever in the two weeks before the survey. Levels of appropriate care–seeking from formal public or private providers for fever were significantly higher in areas with iCCM compared to those without iCCM (83.5%; 95% CI 76.7–90.4 compared to 67.0%; 95% CI 58.7–75.2; P = 0.003) (**Figure 2**). In areas with iCCM, treatment with appropriate antimalarial (AL) was significantly higher than comparison areas (79.5%; 95% CI 72.0–87.0 compared to 62.3%; 95% CI 55.2–69.4; P = 0.007). Among those seeking care for fever from a formal public or private source, 87.9% (95% CI 82.6–93.2) received AL in intervention areas compared to 74.1% (95%CI 66.0–82.2) in the comparison areas. The largest differences between intervention and comparison areas were seen in the timeliness of treatment initiation. In iCCM areas where APEs were providing care in the community, 63.9% (95% CI 54.4–73.3) of children with fever initiated AL treatment within 24 hours of symptom onset whereas in comparison areas 37.5% (95% CI 31.1–43.9) of children with fever initiated AL treatment within 24 hours (P = 0.000). APEs were the predominant source of care and treatment in the intervention areas; 87.1% (95% CI 80.8–93.4) of children 6–59 months with fever who sought care were taken first to an APE, who accounted for 86.2% (95% CI 79.7–92.7) of all first–line antimalarial treatments. Public health facilities were the leading source of care in comparison areas, providing care to 86.1% (95% CI 79.0–93.3) of children 6–59 months with fever who were taken for care outside the home.

## Consistency of care from APEs and first level facilities with standard case management protocols

We assessed the consistency of reported care with standard IMCI/iCCM protocols among children presenting with fever or cough/difficulty breathing managed by an APE and by first level health facilities (**Table 2**). About two–thirds (68.1%; 95% CI 57.2–79.0) of children presenting with fever to an APE (N = 248) were tested for malaria with an RDT and 60.0% (95% CI 45.4–74.6) of children with cough/difficult breathing had their respiratory rate assessed by an APE. In contrast, less than half of children 6–59
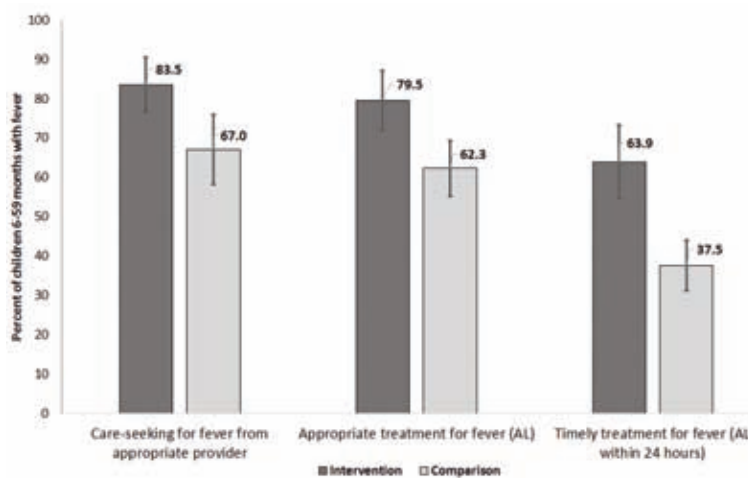


**Figure 2.** Care–seeking and treatment for fever in intervention and comparison areas, Nampula province, Mozambique

months with fever (41.4%; 95% CI 33.7–49.2%) receiving care from a first level health facility (N = 292) were administered an RDT and only 19.4% (95% CI 8.4–30.5%) of children with cough/difficulty breathing were assessed for respiratory rate. A significantly higher percentage of caregivers were counseled on the RDT results by the APE (99.4%; 95% CI 98.2–100%) compared to first level facility staff (78.4%; 95% CI 70.7–86.2%). Children receiving AL from APEs were significantly more likely to initiate antimalarial treatment within 24 hours (84.1%; 95% CI 77.6–90.7%) compared to those seeking care first and receiving AL from a health facility (56.9%; 95% CI 49.9–64.0%). Reported adherence to the recommended treatment duration of three days was also significantly higher for those receiving treatment from APEs; 77.4% (95% CI 68.3–86.4%) of children receiving AL from an APE reported taking AL for 3 days compared with 54.6% (95% CI 44.3–65.0%) of those receiving AL from a first level facility. Overall, 61.3% (95% CI 51.5–71.0%) of children with fever receiving care from APEs received the correct drug within the recommended timeframe and for the correct duration compared to 26.0% (95% CI 18.2–33.9%) of those receiving care from first level health facilities. Inappropriate treatment with antibiotics for fever only cases was low (<10%) for children treated either by APEs or health facilities (**Table 2**).

We also looked at the results for the subset of children 6–59 months with RDT+ results. Of caregivers who received the RDT results, reported malaria positivity levels were high (96.4% of those treated by APEs; 95% CI 93.8–99.1 and 93.5% of those treated by health facilities; 95% CI 88.3–98.6). Due to the higher rates of RDT testing and disclosure of results among children managed by APEs, 65.3% of children with fever cared for by APEs in the sample (162/248) were reported RDT+ compared to 29.5% of children with fever cared for by first level health facilities (86/292). Nearly all RDT+ cases received AL (97.5% of those treated by APEs and 94.2% of those treated by health facilities), but RDT+ children who received AL from APEs were significantly more likely to receive AL within 24 hours (88.0% compared to 59.3%; P = 0.000) and to take AL for the recommended 3 days (85.4% compared to 63.0%; P = 0.005). Overall, 74.1% (95% CI 64.6–83.6) of RDT+ cases managed by APEs received the correct drug within 24 hours and took for 3 days compared with 36.0% (95% CI 21.0–51.0) of RDT+ cases managed by health facilities. The number of RDT– cases was too small (6 for APEs and 6 for health facilities) to analyze.

Under Mozambique's iCCM protocol, APEs were trained to administer the first dose of treatment to the child and to counsel caregivers to return for follow–up. Of children receiving AL from an APE, caregivers

**Table 2.** Consistency with standard case management protocols by first source of care, Nampula province, Mozambique

| INDICATORS | APE | | | FIRST LEVEL HEALTH FACILITY | | | P–VALUE |
|---|---|---|---|---|---|---|---|
| | N | % | 95% CI | N | % | 95% CI | |
| **Assessment:** | | | | | | | |
| Respiratory rate assessment: Proportion of children 2–59 months with cough and fast/difficult breathing whose respiratory rate was assessed with timer | 70 | 60.0 | 45.4–74.6 | 144 | 19.4 | 8.4–30.5 | 0.0001 |
| Fever tested with RDT: Proportion of children 6–59 months with fever who were given an RDT | 248 | 68.1 | 57.2–79.0 | 292 | 41.4 | 33.7–49.2 | 0.0001 |
| **Communication of results:** | | | | | | | |
| RDT result communication: Proportion of children 6–59 months who received an RDT and whose caregiver was told the results of the test | 169 | 99.4 | 98.2–100.7 | 116 | 78.4 | 70.7–86.2 | <0.0001 |
| **Treatment:** | | | | | | | |
| Correct medication: Proportion of children 6–59 months with fever who received AL | 248 | 89.1 | 83.4–94.8 | 292 | 74.0 | 66.3–81.7 | 0.0100 |
| Rational use of antibiotics: Proportion of children 6–59 months with fever only who did not receive antibiotics | 66 | 97.0 | 92.4–101.5 | 156 | 92.9 | 87.0–98.9 | 0.2911 |
| Timely treatment: Proportion of children 6–59 months with fever receiving AL who initiated treatment within 24 hours of symptom onset | 221 | 84.1 | 77.6–90.7 | 216 | 56.9 | 49.9–64.0 | <0.0001 |
| Correct duration: Proportion of children 6–59 mo with fever receiving AL who took for 3 days | 221 | 77.4 | 68.3–86.4 | 216 | 54.6 | 44.3–65.0 | 0.0013 |
| Overall appropriate treatment: Proportion of children 6–59 months with fever who initiated AL treatment within 24 hours and took for 3 days | 248 | 61.3 | 51.5–71.0 | 292 | 26.0 | 18.2–33.9 | <0.0001 |
| **First dose and follow–up:** | | | | | | | |
| First dose: Proportion of children 6–59 months who received AL from APE who took first dose in presence of APE | 221 | 64.3 | 53.9–74.6 | – | – | | NA |
| Follow–up: Proportion of children 6–59 months who received AL from APE who returned for follow–up | 221 | 70.1 | 62.9–77.4 | – | – | | NA |

APE – Agentes Polivalentes Elementares, CI – confidence interval, AL – artemether–lumefantrine, RDT – rapid diagnostic test, NA – not applicable

reported that 64.3% (95% CI 53.9–74.6%) took the first dose in the presence of the APE and 70.1% (95% CI 62.9–77.4%) returned to the APE for follow–up. Data were not available for first dose or follow–up for children with fever managed by health facilities.

## Discussion

Our results demonstrate that trained and well–supported APEs implementing iCCM can contribute substantially to timely care and treatment of childhood illnesses in rural Mozambique. A cross–sectional household survey conducted after approximately two years of iCCM implementation showed higher levels of appropriate care–seeking in areas with iCCM services compared to similar areas without iCCM services. Critically, the provision of iCCM by community–based APEs contributed to timely treatment for fever, likely due in large part to bringing curative care closer to the home and reducing delays in seeking appropriate care. Timely treatment is especially important for children with symptoms of malaria and pneumonia, where treatment within 24 hours of symptom onset is linked to improved outcomes [18,19]. Children living in comparison areas who sought care for fever from formal public or private sources were less likely to receive treatment with AL. This could be due to medicine shortages given that the peripheral public facilities providing the majority of care in comparsion areas were reliant on the relatively weak MOH supply chain where stock–outs of essential health supplies were common during the study period [20]. Our results showed that in areas with access to iCCM, utilization of APEs as first source of care was high with APEs providing care for greater than 80% of children with fever. With more cases treated at the community level, iCCM also contributes to reduced work burden at health facilities, which are often overstretched [14,21].

Our findings provide evidence that well–supported APEs can deliver care consistent with country iCCM protocols. In study areas, the APEs provided care aligned with national guidelines and performed as well as or better than facility–based providers for measures of appropriate assessment, counselling and treatment. Children with fever taken first to APEs were significantly more likely to receive an RDT, to be counselled on the RDT results, and to receive treatment with AL than children taken to first–level facilities. Children receiving care from APEs were also more likely to have their respiratory rate assessed and inappropriate treatment with antibiotics for fever only was low, helping to allay concerns regarding the ability of CHWs to manage suspected pneumonia [22]. However, many caregivers visiting APEs for cough did not report their child's repiratory rate was assessed, indicating that the importance of conducting this assessment step should be reinforced and monitored. Our findings showed that adherence to the recommended malaria treatment duration was significantly better among those treated by APEs than by health facilities; APEs, who are selected by their communities, may be more effective than facility staff in conveying messages to caregivers regarding treatment due to a smaller case load and a closer connection to the community itself. Although based on reports from mothers or caretakers of children under–five, these findings compare well with other recent studies of CHW quality of care in Malawi and Ethiopia, which directly observed CHWs treating sick children and found that CHWs performed well compared to a gold standard clinical re–examiner in assessment, classification, and treatment of iCCM conditions [8,9].

These results were achieved within a well–supported APE program, which is critical for interpreting the findings in the context of the future of iCCM programs implemented by MOH with minimal external support. The iCCM program in Nampula was implemented with support from Save the Children, which provided technical staff and transport to conduct monthly onsite supervision of APEs. In addition to supervision, the APEs in the SC program areas were well supported with a reliable supply of materials and medications (and not reliant on MOH supply chain). Program data collected through interviews, observations and record review for the 30 APEs in the selected intervention clusters alongside the household survey indicated that the majority of APEs had the necessary supplies and medicines for iCCM provision: 90% had a functional timer; 87% had RDTs in stock; 80% had AL in stock; and 80% had first–line antibiotics available [23]. Supervision was frequent, with 80% of APEs reporting that they had been supervised in the previous month [23]. This illustrates that the positive findings reported here can only be sustained at scale with a well functioning national supply chain and other support systems in Mozambique. In 2013, SC intensive supervision and supply chain support for iCCM was phased out and management of the iCCM supply chain was handed over to the MOH, through which APEs are resupplied with a standard "kit" (push system) rather than based on reported consumption. This reduced external supply chain support, coupled with national stock–outs of AL and the use of a "kit" system, has resulted in pervasive stock–outs among APEs of critical iCCM supplies.

Our findings highlight the need for greater attention to the management of childhood illness at first level facilities and increased investment in broader health systems strengthening beyond short–term, most-

ly vertical supports [24]. Poor adherence to IMCI protocols at first level facilities has been reported in similar settings in which case management was directly observed [25,26]. In a study conducted in Ghana, just 4% of children presenting to health centers and district hospitals with cough or difficult breathing had their respiratory rate assessed and in only 1% of all cases were all 11 expected tasks performed [25]. Similar results were found in a study of children in Tanzania with acute respiratory infections in which just 5% of children with cough or difficult breathing had their respiratory rate counted at two district hospitals [26]. It was not possible to determine from our study whether lack of training, lack of supplies, poor motivation or a combination of these factors were responsible for the performance gaps at first level health facilities. Health facilities were supplied with AL through the provincial and district medical stores based on consumption reports; facility assessments conducted in Sofala province around the same time period revealed that stock–outs of AL were frequent, particularly among smaller and more rural facilities [20]. Furthermore, while RDTs were introduced in 2007 to peripheral health facilities in Mozambique, some staff may not have been well–trained or confident in their use and RDT shortages were reportedly common, due to poor consumption tracking and weak design of the supply chain system that failed to address seasonality of malaria [27]. Lack of supplies is unlikely to be the primary reason for the low levels of respiratory rate assessment, as providers could use a variety of devices for this purpose (cell phones, watches), one of which is typically on hand. The level of reported antibiotic prescription for fever only cases managed by facility providers was slightly higher than among APEs, but still relatively low and may have been underestimated; a 2011 review of patient records for febrile children in Zambia found that prescription of antibiotics for fever cases was reduced when RDT results were availabile, suggesting that greater availability of RDTs could help reduce irrational use of antibiotics [28]. The lack of adherence to case management protocols observed among facility–based providers is cause for concern given that these providers are often tasked with supervision of CHWs implementing iCCM. This finding reinforces the need to strengthen knowledge and skills of facility–based staff through routine supervision and on–the–job training, strengthen the national supply chain to ensure adequate availability of essential supplies and equipment, and address other performance–related factors [24–28].

This study is one of the first to our knowledge to use household surveys to assess aspects of consistency with iCCM/IMCI protocols. Specifically, the indicators on counting of respiratory rate, communication of RDT results, provision of first dose, and follow–up visits have not previously been measured in standard household surveys. Although these indicators have not been validated, they ask caregivers to recall noteworthy events during the examination and/or treatment course for a relatively short recall period of two weeks. A register review of activity documentation by APEs from the 30 intervention clusters found similar levels of recorded respiratory rate counting and RDT administration to that reported by caregivers during the household survey; 87% of APEs had RDT test results recorded for the five most recent cases of fever and 63% had respiratory rates documented for the five most recent cough cases [23]. We propose that these indicators be included in household surveys assessing case management for child illness and further validated, as they adequately capture provider activities and enhance the knowledge of patient–provider interaction.

Several limitations should be recognized when considering our findings. The study design was constrained by limited funding and time for evaluation and we did not have a baseline against which to measure change over time. To obtain a sufficient sample size, we only sampled households in which a child aged 2–59 months was identified during household listing. Although care was taken to identify all such households during the household listing stage, errors in age measurement or absence of any respondent in these households may have excluded some eligible households from the sample. Additionally, our sample relied on the comparison of the intervention districts to one comparison district. This sampling strategy was necessary given the rapid national roll–out of iCCM in Mozambique, but can make the results challenging to interpret as one cannot quantify or account for the potential influence of local contextual differences [29]. Although relatively small, the differences in education level between the intervention and comparison area respondents may have affected reported care–seeking practices and treatment. Consistency with case management protocols was determined based on caregiver recall, which is imperfect, and cannot be used to determine quality of care comparable to other methods such as direct observation/re–examination or record reviews [30]. Although assessing of respiratory rate is noteworthy in that it requires the health worker to use a timing device and lift the child's shirt, caregivers would not be able to tell whether the respiratory rate was calculated correctly and whether the provider made the correct classification. Similarly, for RDT use, it was not possible to determine based on caregiver report whether the RDT was administered and interpreted correctly. In addition, for fever we were unable to fully account for the differential in RDT use between APEs and the health facilities, which could also result in differences in

the treatment indicators. However, sub–analysis restricted to RDT+ cases revealed similar findings as that for all fever cases. Furthermore, we were unable to assess the quality of counseling APEs provided to the caregivers. However, high reported adherence to medication duration and high rates of return for follow–up suggest that key messages were conveyed appropriately. We excluded the small number of sick children taken first to private clinics and pharmacies, and as such cannot comment on the consistency of care provided through these other sources of care, which can be important sources particularly in more urban areas.

## CONCLUSION

This study demonstrates that well–trained and supported APEs providing iCCM significantly contributed to improved timely and appropriate treatment of fever in rural Mozambique. Demand for iCCM was strong as evidenced by high levels of utilization of APEs as first source of care in program areas. In addition, APEs provided care that was consistent with iCCM protocols and performed significantly better than first level facilities on most measures of adherence to case management protocols. These findings reinforce the need for comprehensive efforts to strengthen the health system in Mozambique to enable reliable support for quality of case management of childhood illness at both health facility and community levels.

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PAPERS

# Costs of implementing integrated community case management (iCCM) in six African countries: implications for sustainability

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**Background** Sub–Saharan Africa still reports the highest rates of under–five mortality. Low cost, high impact interventions exist, however poor access remains a challenge. Integrated community case management (iCCM) was introduced to improve access to essential services for children 2–59 months through diagnosis, treatment and referral services by community health workers for malaria, pneumonia and diarrhea. This paper presents the results of an economic analysis of iCCM implementation in regions supported by UNICEF in six countries and assesses country–level scale–up implications. The paper focuses on costs to provider (health system and donors) to inform planning and budgeting, and does not cover cost–effectiveness.

**Methods** The analysis combines annualised set–up costs and 1 year implementation costs to calculate incremental economic and financial costs per treatment from a provider perspective. Affordability is assessed by calculating the per capita financial cost of the program as a percentage of the public health expenditure per capita. Time and financial implications of a 30% increase in utilization were modeled. Country scale–up is modeled for all children under 5 in rural areas.

**Results** Utilization of iCCM services varied from 0.05 treatment/y/under–five in Ethiopia to over 1 in Niger. There were between 10 and 603 treatments/community health worker (CHW)/y. Consultation cost represented between 93% and 22% of economic costs per treatment influenced by the level of utilization. Weighted economic cost per treatment ranged from US$ 13 (2015 USD) in Ghana to US$ 2 in Malawi. CHWs spent from 1 to 9 hours a week on iCCM. A 30% increase in utilization would add up to 2 hours a week, but reduce cost per treatment (by 20% in countries with low utilization). Country scale up would amount to under US$ 0.8 per capita total population (US$ 0.06–US$0.74), between 0.5% and 2% of public health expenditure per capita but 8% in Niger.

**Conclusions** iCCM addresses unmet needs and impacts on under 5 mortality. An economic cost of under US$ 1/capita/y represents a sound investment. Utilization remains low however, and strategies must be developed as a priority to improve demand. Continued donor support is required to sustain iCCM services and strengthen its integration within national health systems.

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Although under–five mortality reduced globally from 91 deaths/1000 live births in 1990 to 43/1000 (53% reduction) in 2015, sub–Saharan Africa still has the highest under–five mortality rate, despite a 54% decline from 180/1000 in 1990 to 83/1000 in 2015 [1,2]. The major causes of these

deaths are largely preventable – neonatal disorders, diarrhea, pneumonia and malaria – for which low cost, high impact interventions and effective delivery strategies exist [1]. However, access to health facilities is poor, especially for families in rural and hard to reach areas [2].

Following the development of community health worker (CHW) programmes in the 1970s, and their decline at the end of the 80s, there is renewed interest in CHWs to improve access to services particularly in the context of task–shifting [3], with increasing evidence of their effectiveness in providing preventive and curative services [4–6]. In 2012, WHO and UNICEF issued a joint statement on integrated community case management (iCCM) as an equity–focused strategy to improve access to essential treatment services for children [7], with integrated diagnosis, treatment and referral services for malaria, suspected pneumonia and diarrhea among children aged 2–59 months (hereafter referred to as under–five) by trained and equipped CHWs. iCCM may also cover treatment of severe acute malnutrition and newborn illness [8].

Following the UNICEF endorsement, uptake of the strategy by national governments was rapid, from 7 countries in sub–Saharan Africa in 2005 to 28 by 2013, spearheaded by donor–driven initiatives providing a major share of funding [8]. Understanding the resources required to implement and scale up iCCM is critical for both governments and funders to assess value for money and affordability. This paper presents the results of an economic analysis of iCCM implementation in six sub–Saharan African countries, identifying factors which affect cost of treatment and possible areas of greater efficiency to support scale–up and affordability. This paper focuses specifically on cost to government and donors, the provider perspective. It does not cover costs to households, nor does it assess cost–effectiveness.

This analysis was part of a multi–country evaluation of the Catalytic Initiative/ Integrated Health Systems Strengthening program (CI/IHSS) in 2012–2013 [9]. These programmes were established by UNICEF with joint funding from the Department of Foreign Affairs, Trade and Development, Canada (DFATD) [10]. Ethiopia, Ghana, Malawi, Mali, Mozambique and Niger were selected for support.

CI/IHSS had a strong health systems strengthening focus (training, provision of drugs and supplies, support for supervision and development of monitoring and evaluation systems) [11]. Initially supporting mainly preventive interventions, it shifted focus to training and equipping CHWs to deliver iCCM services. This study focuses on those regions within countries supported by UNICEF, although other donors were supporting iCCM in additional regions.

## METHODS

We visited each country for approximately 10 days and interviewed Ministry of Health officials, partners, supervisors, CHWs, users and other stakeholders.

### iCCM program description

Community–based care existed in Ethiopia, Malawi and Niger focusing on mother and child and environmental issues, staffed with paid CHWs supervised by health centers staff. iCCM was added to their tasks. Ghana, Mali and Mozambique created or revitalized their CHW cadre. In Ghana iCCM is provided by volunteers while in the other countries CHWs are paid. The program was based on home visits (Ghana and Mozambique), combined with work from health posts (Ethiopia, Malawi, Mali and Niger). **Table 1** presents additional country information.

### Costs

This analyses combines a budget–holder/program (UNICEF) and health systems perspective. Health systems costs included government provider time, while program costs, included training, bicycles, kits and commodities, allowances for supervisors and review meetings and CHW stipends in Mozambique and Mali. Costing of consumables and supervision was based on clinical protocols and supervision schedules. We used actual data for number of CHWs, size of target population and number of treatments delivered.

Incremental financial and economic costs are calculated. Financial costs reflect additional expenditure incurred for the program by UNICEF. Economic costs covered all resources up to district supervision, including financial costs (although annualisation of capital is calculated differently) and opportunity costs (value of time spent on program). In Mali the stipend was fixed, independent of time spent. In Mozambique 70% of the stipend was costed reflecting the share of Malaria, Diarrhea and Pneumonia (MDP)

**Table 1.** Contextual factors

| Context | Ethiopia | Ghana | Mali | Malawi | Mozambique | Niger |
|---|---|---|---|---|---|---|
| GDP per capita 2013 in 2015 US$ | 504 | 1827 | 660 | 240 | 605 | 419 |
| Public Health Expenditure per capita 2013 in 2015 US$ | 15 | 60 | 21 | 13 | 19 | 10 |
| Under 5 mortality per 1000 live births, 2013 | 64 | 78 | 123 | 68 | 87 | 104 |
| % population living in rural areas | 81 | 47 | 62 | 84 | 68 | 82 |
| Pre–existing CHW cadre | Yes | Yes | No | Yes | Yes | Yes |
| **CHW characteristics:** | | | | | | |
| Gender | All female | 50% female | 43% female | 28% female | 30% female | 33% female |
| Educational background required | Grade 8–10 | Most illiterate | 9th grade | 12th grade | 7th grade | 12th grade |
| Duration of basic training | 1 year | 5 days | 40 days | 3 months | 4 months | 6 months |
| **Program design elements:** | | | | | | |
| Duration of iCCM training (in years) | 6 | 3 | 15 | 6 | 23 | 6 |
| Population <5 per CHW | 377 | 72 | 360 | 632 | 735 | 576 |
| Based in community or health post | Health post | Community | Health post | Health post | Community | Health post |
| Full monthly salary (US$) | 40 | Volunteer | 80 | 110 | 40 | 100 |
| Part of civil service | Yes | No | Yes | Yes | No | No, but paid by state grant |
| **Program implementation:** | | | | | | |
| iCCM trained CHWs | 27 116 | 16 812 | 1847 | 1018 | 905 | 2560 |
| CHW attrition rate | 4% | 8% | 4% | 3% | 3% | 7% |
| CHWs/Supervisor | 8 | 30 | 4 | 10 | 25 | 3 |
| Average iCCM treatments/y/CHW | 20 | 10 | 134 | 546 | 99 | 603 |
| Hours on iCCM per CHW/week | 1.2 | 1.0 | 3.1 | 7.2 | 3.0 | 8.6 |
| Treatments per capita under 5 in 2013 in CI districts | 0.05 | 0.27 | 0.27 | 0.46 | 0.14 | 1.05 |
| **Time frame:** | | | | | | |
| Design & set up | 2007–2010 | 2007–2010 | 2007–2011 | 2007–2008 | 2007–2010 | 2007–2008 |
| Implementation | 2010–2013 | 2007–2013 | 2011–2013 | 2008–2013 | 2010–2013 | 2007–2013 |
| Implementation year costed | 2012–2013 | 2012–2013 | 2012–2013 | 2012–2013 | 2012–2013 | 2012–2013 |
| Months since at scale (iCCM trained CHWs >80%) | 11 | 36 | 2 | 11 | 13 | 35 |

CI – Catalytic Initiative, CHW – community health worker, iCCM – integrated community case management

treatments among under–fives since CHWs also treat adults. For Ghana volunteers, time value was based on a basic agricultural worker's wage [12].

Budget holder costs were collected retrospectively from UNICEF country offices financial records for the CI/IHSS districts: bicycles/motorbikes, CHW kits and life span per type of equipment, training, salaries/stipend, supervisors allowances, CHW and supervisors attrition rate, malaria positivity rate and unit costs of drugs and rapid diagnostic tests (RDT). All drugs and tests were sourced from UNICEF, apart from malaria supplies in Mozambique, local cost of drugs were provided by UNICEF country offices.

Data were also obtained for the CI regions on the numbers of CHWs trained, frequency and duration of supervision visits, attrition rates, number of treatments per condition, and number of under–fives targeted, from UNICEF and CI/IHSS program documents.

## CHW time

CHW time on iCCM was calculated as follows: 1) Average visit duration was set at 30 minutes (based on a previous costing study in Malawi [13]). 2) Travel time was added when iCCM was provided at household level. 3) An additional 20% of visits was added to reflect visits without treatment (eg, Malaria negative tests) while requiring CHW time; drawing on the malaria positivity rate, the share of malaria treatments in case load, and adding a small fraction for other visits without treatment 4) CHW time on supervision or community meetings and visits to the clinic for refilling of kits. 5) The above enabled to calculate the average time per week per CHW. It was assumed that a CHW works an average of 46 weeks per year. Time on iCCM was also used in the sensitivity analysis to assess time impact and feasibility of a 30% increase in demand.

### Time line and analysis time horizon

iCCM costs are incurred in 3 overlapping phases. First is the design phase (formative research, design of the intervention, of the training and of materials). These, often substantial, one–off costs are not included because they will not be incurred again if iCCM is scaled–up. Second is the set–up phase (purchase of equipment, training) and the third is the implementation phase. Phases 2 and 3 are the focus of this study. Set–up data were collected for several years, and for 1 year for the implementation phase: the year 2012/13, the only year where iCCM was at scale in the 6 countries (**Table 1**).

### Analysis

Set–up costs were annualized, using a 3% discount rate for economic costs [14] and straight depreciation for financial costs. In the perspective of assessing cost of an on–going program, annualisation of equipment cost was based on the life span of each piece of equipment. Similarly, we annualised training costs, not as per length of intervention, but of the likely life span of training in an on–going program: initial training for CHWs and supervisors was allocated 10 life years when refresher training–mentorship took place, and 5 years in countries without refresher training. CHWs and supervisors attrition rates were applied. Incremental government and budget–holder economic costs are presented separately and combined (**Table 2**). Costs are presented in US dollars 2015, updating 2013 local currency with local inflation rate [12], then translated into US$, using the 2015 local US$ exchange rate [15].

Fixed costs per CHW, independent of the number of treatments: annualised set–up and 1 year implementation costs were combined to calculate annual fixed costs per CHW: CHW iCCM training, equipment, CHW salaries/stipends and allowances for meetings, supervision and management costs (iCCM training for CHWs' direct supervisors and district/zonal supervisors, share of supervisors' salary package, allowances for supervision and meetings, and bicycles or share of motorbike costs), and overheads of 5% of the annualised costs. The annualised fixed costs per CHW divided by the number of treatments per CHW in 2012/13 represent "the consultation cost".

Variable costs included drugs and RDTs used. Malaria positivity rate was used to calculate the number of RDTs used per child testing positive: with a 40% positivity rate, if 100 children are treated for malaria, 250 children have been tested; with a positivity rate of 60%, 167 children need to be tested. The average cost of consumables by treatment is weighted by the relative share of malaria, diarrhea and pneumonia treatments.

Financial costs per treatment are presented in **Figure 1**, highlighting the share of consultation cost per treatment.

### Affordability

We used financial costs to calculate the budgetary implications of the program: cost per CHW and per capita total population in study areas, which we then expressed as a percentage of the country 2013 public health expenditure (PHE) per capita (government + donors), as a proxy for affordability of the program. Data on health expenditure and 2013 total and rural population were obtained from the World Bank databank [16]. The number of under–fives in 2013 was extracted from the UNICEF statistical Tables [17].
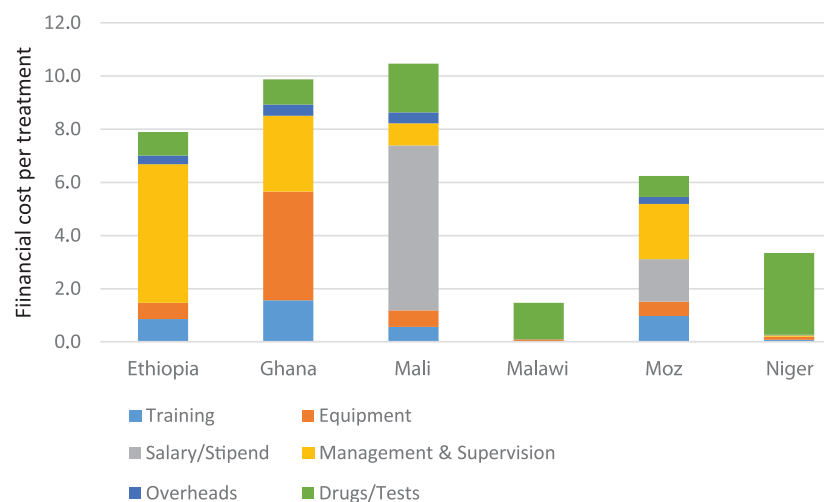


**Figure 1.** Financial cost per treatment (2015 US$).

## Sensitivity analysis

We modeled the impact of a 30% increase in demand, keeping the ratio of children per CHW observed in the CI districts and assessed the implications for CHW time, consultation cost, cost per treatment and cost per capita. We then modeled the national program cost if the program was scaled up to all under–fives living in rural areas.

## RESULTS

### Country contexts

In Niger over 80% of the trained CHWs operated in 2013, in Mali the majority of CHWs were trained in 2011 and in Ethiopia, Ghana, Malawi and Mozambique the CHWs had only been functioning at that level for about a year (**Table 1**).

Annual number of iCCM treatments per CHW ranged from 10 in Ghana to 603 in Niger, influenced by the number of under–fives per CHW, from 72 in Ghana to 632 in Malawi.

Time on iCCM was estimated between 3 hours a week or less per CHW in Ethiopia, Ghana, Mali and Mozambique to around 1 full day in Malawi and Niger (**Table 1**).

### Fixed costs per CHW and consultation cost

Annualised financial fixed costs per CHW ranged from US$ 811 in Mali to US$ 55 in Malawi, lower costs reflecting the pre–existence of community–based care with CHWs and supervisors salaries already paid by the state. Financial cost per consultation ranged from US$ 0.1 in Malawi to US$ 9 in Ghana. Annualised economic fixed costs per CHW (**Table 2**) ranged from US$ 128 in Ghana to US$ 870 in Mali (**Figure 1**), with an economic cost per consultation between under US$ 1 in Malawi and Niger with high utilization, and over US$ 11 in Ethiopia and Ghana.

Training costs are higher in Mali and Mozambique, with longer training (15 and 23 days respectively) compared to 6 days in other countries. Annualised equipment costs: bicycles, if relevant, and kits (excluding consumables) ranged from US$ 88 in Mali to US$ 13 in Ethiopia. Management and supervision cost represented a significant share of CHW fixed cost, from US$ 324 in Mozambique to US$ 51 in Ghana, largely reflecting the ratio of CHWs per supervisor (**Table 1**) and supervisors' daily allowance.

### Cost per treatment

Cost of consumables per condition varied, partly due to differences in protocols, with use of additional drugs (Paracetamol), or in Niger, using the more expensive drug ASAQ for malaria treatment. Positivity rates for malaria varied from 40% to 67%. Drug pricing systems also differed: in Mali, drugs distributed from clinics are 50% more expensive than at national level (distribution costs and revenue for the clinic) (**Table 3**).

Economic cost per malaria treatment ranges from US$ 3 in Malawi to US$ 14 in Ghana (financial cost US$ 2.4 to US$ 10.5 respectively), for diarrhea from US$ 1.3 to $12.9 (financial cost US$ 0.7 to US$ 9.3). User fees are implemented in two countries. In Mali patients pay US$ 0.2 per consultation and a weighted average of US$ 0.11 for drugs (excluding for malaria). In Ghana, patients contribute for drugs only, at a weighted average of US$ 0.34 per treatment (**Figure 1**).

### Affordability

Government paid from 5% of economic costs in Mali to under 20% in Mozambique and Niger, between 25% and 30% in Ghana and Malawi and 36% in Ethiopia (**Table 2**), while 100% of financial costs were paid by UNICEF. Financial costs range from US$ 0.06 per capita total population in Ethiopia to US$ 0.74 in Malawi and Niger, representing under 0.6% of the 2013 PHE per capita in Ethiopia, Ghana and Mozambique, but 1.8% in Malawi, 2.7% in Mali and 7.4% in Niger (**Table 4**), program cost per CHW ranges from US$ 101 in Ghana to US$ 2 047 in Niger (**Table 4**).

### Implications of increased utilization

With 30% higher utilization, time on iCCM would increase by 10% to just over 1 hour a week per CHW in Ghana, but in Niger would be 28% higher to 11 hours a week. A 30% increase in utilization could be

**Table 2.** Economic costs per provider and per treatment (2015 US$)

| UNICEF COST PER CHW | ETHIOPIA | GHANA | MALI | MALAWI | MOZAMBIQUEZ | NIGER |
|---|---|---|---|---|---|---|
| Training | 17 | 16 | 75 | 12 | 96 | 47 |
| Equipment | 13 | 44 | 88 | 36 | 57 | 74 |
| Salary/stipend | – | – | 834 | – | 160 | – |
| Management & supervision | 104 | 29 | 111 | 7 | 206 | 36 |
| Other Overheads 5% | 7 | 4 | 55 | 3 | 26 | 8 |
| % ICCM | 100 | 100 | 70 | 100 | 70 | 100 |
| *Sub–total Fixed Cost per CHW* | *134* | *89* | *776* | *55* | *363* | *156* |
| Supplies (Drugs/Tests) per CHW | 18 | 10 | 247 | 749 | 79 | 1859 |
| Budget holder cost per CHW | 152 | 99 | 1023 | 804 | 442 | 2015 |
| **Government cost per CHW:** | | | | | | |
| Training | 3 | 2 | 7 | – | 9 | 1 |
| Equipment | – | – | – | – | – | – |
| Salary/Stipend | 31 | 10 | – | 238 | – | 307 |
| Management & Supervision | 51 | 22 | 69 | 93 | 118 | 37 |
| Other Overheads 5% | 4 | 2 | 4 | 17 | 6 | 17 |
| % ICCM | 100 | 100 | 70 | 100 | 70 | 100 |
| *Sub–total Fixed Cost per CHW* | *85* | *33* | *53* | *332* | *89* | *345* |
| Supplies (drugs/tests) per CHW: | | | | | | |
| Government cost per CHW | 85 | 33 | 53 | 332 | 89 | 345 |
| **Combined costs per CHW:** | | | | | | |
| Training | 20 | 18 | 82 | 12 | 105 | 47 |
| Equipment | 13 | 44 | 88 | 36 | 57 | 74 |
| Salary/stipend | 31 | 10 | 834 | 238 | 160 | 307 |
| Management & supervision | 155 | 51 | 179 | 100 | 324 | 73 |
| Other Overheads 5% | 11 | 6 | 59 | 19 | 32 | 25 |
| % ICCM | 100 | 100 | 70 | 100 | 70 | 100 |
| *Sub–total Fixed Cost per CHW* | *219* | *122* | *828* | *386* | *452* | *502* |
| Supplies (drugs/tests) per CHW | 18 | 10 | 247 | 749 | 79 | 1859 |
| Total cost per CHW | 237 | 132 | 1075 | 1135 | 531 | 2360 |
| **Combined cost per treatment:** | | | | | | |
| Number of iCCM treatments/CHW/year | 20 | 10 | 134 | 546 | 99 | 603 |
| Consultation cost/treatment | 11.5 | 12.6 | 6.5 | 0.7 | 4.8 | 0.9 |
| Average consumable/treatment | 0.9 | 0.9 | 1.8 | 1.4 | 0.8 | 3.1 |
| Economic cost/treatment | 12.4 | 13.5 | 8.3 | 2.1 | 5.6 | 4.0 |
| Share consultation cost | 89 | 90 | 77 | 7 | 83 | 9 |
| **Share government cost** | **36** | **25** | **5** | **29** | **17** | **15** |
| **Share budget holder** | **64** | **75** | **95** | **71** | **83** | **85** |

CHW – community health worker, iCCM – integrated community case management

**Table 3.** Cost of consumables per iCCM treatment (2015 US$)

| | ETHIOPIA | GHANA | MALI | MALAWI | MOZAMBIQUE | NIGER |
|---|---|---|---|---|---|---|
| **Share of treatments (%):** | | | | | | |
| Malaria | 30 | 49 | 59 | 54 | 40 | 54 |
| Diarrhea | 41 | 32 | 20 | 13 | 29 | 18 |
| Pneumonia | 29 | 19 | 21 | 33 | 31 | 27 |
| Total | 100 | 100 | 100 | 100 | 100 | 100 |
| **Cost consumables per treatment (US$):** | | | | | | |
| Malaria including rapid diagnostic test | 1.74 | 1.56 | 2.73 | 2.32 | 1.51 | 4.84 |
| Diarrhea | 0.69 | 0.35 | 1.03 | 0.61 | 0.30 | 0.61 |
| Pneumonia | 0.26 | 0.39 | 0.09 | 0.13 | 0.33 | 1.24 |
| **Economic cost per treatment including consultation (US$):** | | | | | | |
| Malaria | 13.3 | 14.1 | 9.2 | 3.0 | 6.3 | 5.7 |
| Diarrhea | 12.2 | 12.9 | 7.5 | 1.3 | 5.1 | 1.5 |
| Pneumonia | 11.8 | 12.9 | 6.6 | 0.8 | 5.1 | 2.1 |

**Table 4.** iCCM impact on 2013 Public Health Expenditure (2015 US$)

| | Ethiopia | Ghana | Mali | Malawi | Mozambique | Niger |
|---|---|---|---|---|---|---|
| Current utilization: | | | | | | |
| Financial cost/CHW | 158 | 101 | 1058 | 804 | 458 | 2047 |
| Financial cost/capita total population | 0.06 | 0.20 | 0.57 | 0.23 | 0.11 | 0.74 |
| Share of 2013 Public Health Expenditure per capita (%) | 0.4 | 0.3 | 2.7 | 1.8 | 0.6 | 7.4 |
| Utilization +30%: | | | | | | |
| Financial cost/CHW | 163 | 104 | 1132 | 1029 | 482 | 2604 |
| Financial cost/capita total population | 0.07 | 0.20 | 0.61 | 0.29 | 0.11 | 0.94 |
| Share of 2013 Public Health Expenditure per capita (%) | 0.4 | 0.3 | 3 | 2.2 | 0.6 | 9.4 |
| If scaled up to all rural areas: | | | | | | |
| Share of 2013 Public Health Expenditure per capita (%) | 0.4 | 0.2 | 1.8 | 1.8 | 0.4 | 7.7 |

**Table 5.** Impact on time and costs of increased utilization

| | Ethiopia | Ghana | Mali | Malawi | Mozambique | Niger |
|---|---|---|---|---|---|---|
| Hours per week on iCCM: | | | | | | |
| Current utilization | 1.2 | 1.0 | 3.1 | 7.2 | 3.0 | 8.6 |
| Utilization +30% | 1.4 | 1.0 | 3.6 | 9.0 | 3.6 | 11.0 |
| Economic cost per treatment: | | | | | | |
| Current utilization | 12.4 | 13.5 | 8.3 | 2.1 | 5.6 | 4.0 |
| Utilization +30% | 10.0 | 10.7 | 6.8 | 2.0 | 4.5 | 3.9 |
| Decrease in cost per treatment | −19 | −21 | −18 | −4 | −20 | −2 |
| Increase in program cost | 5 | 3 | 7 | 25 | 4 | 27 |
| Additional financial cost/treatment: | | | | | | |
| Current utilization | 7.9 | 9.9 | 7.9 | 1.5 | 4.1 | 3.4 |
| Utilization +30% | 6.3 | 7.8 | 6.5 | 1.5 | 3.7 | 3.3 |
| Decrease in cost per treatment (%) | −20 | −21 | −19 | −3 | −21 | −2 |
| Increase in program cost (%) | 4 | 2 | 6 | 26 | 3 | 27 |

absorbed by the existing CHWs. In Ethiopia, Ghana, Mali, and Mozambique economic and financial costs per treatment would be about 20% lower. In Malawi and Niger, where consultation cost represents a small share of cost per treatment, the decrease is small (2 to 4%). Total costs of the program increase, however, due to additional consumables (**Table 5**). Financial costs of the program with higher utilization would remain under US$ 1 per capita.

### Affordability of scale–up

If the program with 30% increased utilization was scaled–up to cover all the country under–fives living in rural areas, the cost per CHW would remain the same, iCCM would represent between 0.4% and 7.7% of the country PHE.

## DISCUSSION

Utilization of iCCM services in UNICEF supported districts varied from 0.05 MDP treatment per year per under–five in Ethiopia to over 1 in Niger. Low utilization does not appear to be mainly related to availability of services (supply side), but to demand, as documented in many countries [9]. In Ethiopia around 80% did not seek treatment for the 3 conditions, 60% in Ghana, 50% in Mozambique, and 40% in Niger, but much lower in Malawi at 13%. All countries reported low levels (10–15%) of care seeking from informal providers [9]. Demand does not seem linked to the size of the under 5 population per CHW, a proxy for availability of iCCM services: 377 children per CHW in Ethiopia and 576 in Niger. Medicine stock–outs were most marked in Malawi [9] but at 0,5 the number of treatments per child per year, was 10 times that of Ethiopia with low levels of stock outs. User fees contribute to low demand: user fees were reduced by two–thirds in an iCCM district in Mali, translating into demand more than doubling [18]. In Ghana patients registered for National Health Insurance received free treatment at clinics but paid for treatment by CHWs (half of the payment was used for CHW incentives), almost certainly deterring use. Utilization rates, through consultation cost, impacts directly on cost per treatment. They were the high-

est contributor to the efficiency, and likely effectiveness, of the programs, pointing to the necessity of pro-active strategies to increase demand for existing programs before moving to scale–up.

Economic cost per consultation was US$ 12.6 in Ghana and US$ 0.7 in Malawi, representing 93% of cost per treatment in Ethiopia and Ghana but only 22% in Niger. Similar findings were reported in another multi–country assessment of iCCM costs [19].

Estimating CHWs time on the program is important to ensure that adding iCCM to CHWs' workload does not squeeze out other existing activities and that increased utilization is manageable. Estimated time from 1 to 9 hours a week, represents a small portion of CHWs' time whose main focus is mother and child health. A 30% increase in utilization would add under 1 to 2 hours a week, indicating that iCCM can be combined with other community–based activities: Across countries, communities requested that services be extended to older children, while CHWs indicated the difficulty of denying treatment to children over five in the same family.

iCCM training duration also impacted on costs: from 6 days in 3 countries to 23 in Mozambique. However it was only 3 days in Ghana for often illiterate volunteers without previous IMCI training, which may have contributed to low utilization.

Attrition rate has cost implications for training. It was under 4% for paid CHWs, except for Niger at 7% (clear career pathing to become a nurse may have contributed), and at 8% among Ghana volunteers. Similar differences between paid workers and volunteers were observed in another multi–country iCCM costing [19].

Management and supervision were a significant cost driver. Most countries however report recurrent challenges with consistent supervision including insufficient funding for supervisors travel and overwhelmed resource capacity; some of these could be addressed through mentorship at facility level, integrated supervision visits and use of simple supervision checklists [20].

The assumption that volunteers cost little, so many can be recruited, was contradicted by the Ghana example with the highest cost per treatment, due to fixed costs per volunteer and low utilization. With 2 CHWs per village, each covered an average of 72 children, compared to over 360 in the other countries. With one CHW per village, s/he would spend 1.2 hours a week on iCCM, average cost per treatment would be 47% lower, and incentive payments per CHW would double, emphasizing the need for more considered CHW deployment even in volunteer–based programs.

Scaling up the program to cover all rural areas would amount for all countries to under US$ 0.8 per capita total population, in most countries a small percentage of the PHE per capita: under 0.5% in Ethiopia, Ghana and Mozambique, under 2% in Malawi and Mali but 8% in Niger with the lowest PHE per capita. These countries are likely to remain dependent on foreign assistance to maintain and scale–up iCCM services which threatens their sustainability.

A systematic review of iCCM effectiveness reported a reduction in all–cause mortality in under–fives by up to 63% [21]. To sustain this, proactive support by governments is needed. Although iCCM has been recognized at policy level in these six countries, few have committed domestic resources. A survey of iCCM policy and implementation in sub–Saharan Africa reported that only 9 out of 33 countries had a budget line in government budget and CHW salaries were paid by government in only 5 countries [8]. In Mali there is uncertainty as to whether CHWs will be paid from user fees or funded by government/municipalities; the Mozambican government is reluctant to include CHWs as a new staff category of the public service (a pre–condition to allocate funds for their stipends). In Ghana CHWs are not included in the NHI.

In 2014 UNICEF, the Global Fund and the Reproductive, Maternal, Newborn and Child Health Trust Fund announced a unified plan to scale–up iCCM, with increased resources to expand in the near term [22].

iCCM costs need to be considered in light of expected savings from possibly reduced workload at clinics and from averting serious illness through early treatment. Families also experience time and cost savings with care closer to home. There is also increasing evidence of CHWs cost–effectiveness compared to increasing coverage of fixed health facilities staffed with nurses [23,24]. In Niger CHWs addressed unmet needs rather than replacing facility care seeking [25]. Costing of iCCM activities must also acknowledge that delivery of curative services strengthens the preventive role of CHWs [26].
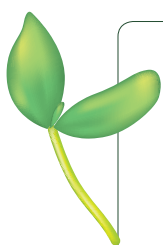
## Limitations

This economic analysis has several limitations: first, in its scope: it focuses on resource implications of iCCM and affordability and does not include an analysis of value for money, a pre–requisite, but the programs were mostly too recent to assess effectiveness. Additionally, CHWs work was supported by multi–programs volunteers whose cost has not been included. Second, in its measurement methods: implementation costs were measured for 1 year, recent guidelines suggest that a wider window of implementation costs should be measured [27], however in this evaluation there was only 1 common year of implementation at scale. In addition, the normative approach used for calculating commodities and supervision costs has the benefit of estimating costs as per protocol, but does not reflect variations in actual implementation. CHW time on the program was based on the same assumptions of length of visit and meetings for all countries rather than on observation. However informal observation during country visits showed that our assumption of 30 minutes per visit is unlikely to be an underestimation. Another limitation is that the modeling of extending the program to all rural areas was made by extrapolating CI districts data and did not reflect other iCCM districts with potentially different cost profiles. Additionally affordability is based on per capita spending and does not include possible savings/costs to other levels of the health system as a consequence of the program in a way a Budget Impact Analysis would do [28].

A strength of this analysis is the separation of economic from financial costs to avoid double–counting in the calculation of budgetary implications. Second, rather than separating set–up costs from recurrent costs, annualised set–up and implementation costs are combined since over time equipment has to be replaced and training redone, and cannot be considered as one–off costs.

## CONCLUSIONS

By addressing at community level the three main causes of deaths of children aged 2–59 months, iCCM can service unmet needs and contribute to reductions in under 5 mortality. While the programs were mostly too recent to assess effectiveness, a financial cost in this study of under US$ 1 per capita per year, highlights that iCCM can represent a very sound investment. Once services have been built–up, strengthening demand must become the priority.

Aligning funding and support with national priorities, along with political will and commitment of governments is central for sustainability of iCCM and CHW platforms. Benefits from strategies such as iCCM is dependent on country context and economic outlook. Continued donor support is required for the foreseeable future and should have a concurrent focus on strengthening integration of iCCM as an essential platform of care within national health systems.

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PAPERS

# Alcohol–attributed disease burden and alcohol policies in the BRICS–countries during the years 1990–2013

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**Background** We aimed to assess alcohol consumption and alcohol–attributed disease burden by DALYs (disability adjusted life years) in the BRICS countries (Brazil, Russia, India, China and South Africa) between 1990 and 2013, and explore to what extent these countries have implemented evidence–based alcohol policies during the same time period.

**Methods** A comparative risk assessment approach and literature review, within a setting of the BRICS countries. Participants were the total populations (males and females combined) of each country. Levels of alcohol consumption, age–standardized alcohol–attributable DALYs per 100 000 and alcohol policy documents were measured.

**Results** The alcohol–attributed disease burden mirrors level of consumption in Brazil, Russia and India, to some extent in China, but not in South Africa. Between the years 1990–2013 DALYs per 100 000 decreased in Brazil (from 2124 to 1902), China (from 1719 to 1250) and South Africa (from 2926 to 2662). An increase was observed in Russia (from 4015 to 4719) and India (from 1574 to 1722). Policies were implemented in all of the BRICS countries and the most common were tax increases, drink–driving measures and restrictions on advertisement.

**Conclusions** There was an overall decrease in alcohol–related DALYs in Brazil, China and South Africa, while an overall increase was observed in Russia and India. Most notably is the change in DALYs in Russia, where a distinct increase from 1990–2005 was followed by a steady decrease from 2005–2013. Even if assessment of causality cannot be done, policy changes were generally followed by changes in alcohol–attributed disease burden. This highlights the importance of more detailed research on this topic.

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Alcohol consumption has been causally linked to approximately 30 diseases and injuries [1,2], and is an important risk factor to the global burden of disease [3]. Although the level of alcohol consumption varies between countries and regions, the highest per capita consumption is still found in the economically developed world [1]. However, as a result of increased economic growth, alcohol consumption is expected to increase in several low– and middle–income countries (LMIC), as has been observed in eg, Brazil and India [4].

The BRICS countries (Brazil, Russia, India, China and South Africa) are all emerging economies that have experienced increased economic growth, reduced poverty and strengthening of their health systems during the past decade [5,6]. These countries, accounting for 40% of the world's population [5], are important and influential in global health development [7,8]. Although they have not officially signed a document declaring "we are the

BRICS", they have embraced the term and are taking steps to further develop their collaboration [8]. In 2014, the BRICS countries reiterated their commitment to prevent and control non–communicable diseases (NCDs) and to reduce the impact of risk factors on NCDs, one being harmful use of alcohol [9].

The impact of alcohol policies is well studied in several high–income countries [2,4], where eg, limited physical availability and high prices are well–established tools used to reduce alcohol consumption and related harm [2]. In contrast, such research is scarce in LMIC settings [4], and several studies focusing on the BRICS countries are calling for increased policy action to tackle alcohol consumption and subsequent harm [10,11]. This is also highlighted in the WHO Global strategy to reduce harmful use of alcohol where it is urged for action with regards to eg, drink–driving policies and countermeasures; availability of alcohol and pricing policies [12].

One increasingly used way to examine alcohol–attributed disease burden in a population and/or country, is by estimating disability adjusted life years (DALYs) [13], developed within the global burden of disease study (GBD). DALYs combine premature death or years of life lost (YLL) with years lived with disability (YLD), and thus allow for a more comprehensive assessment of disease burden. Moreover, the GBD enables comparisons across countries and over time as the disease burden is systematically and uniformly defined, and the latest methods are continuously applied for all data collected.

To date, there is no study summarizing alcohol consumption, alcohol–related disease burden and alcohol related policies in the BRICS countries. Thus, by using results from the Global Burden of Disease and Injuries and Risk Factors 2013 study, we aimed at 1) assessing overall alcohol consumption and alcohol attributed disease burden by DALYs in the BRICS countries between 1990 and 2013, and 2) identifying possible temporal linkages between evidence–based alcohol policies and alcohol consumption and alcohol–related harm.

## METHODS

### The Global Burden of Disease Study 2013

The GBD 2013 and the methods used therein have been described in detail elsewhere [13–16]. In short, GBD comprises estimates of 306 diseases and injuries, and 2337 sequelae (non–fatal health consequences of diseases and injuries) for men and women in 20 age groups, and uses DALY as measure of population health. DALYs assess years of healthy life lost by different causes and are calculated by summing YLLs (years of life lost to premature death) and YLDs (years lived with disability).

The burden of disease attributed to alcohol is estimated using a comparative risk assessment approach known as the population attributable fraction, which has been described in detail elsewhere [15,16]. Alcohol consumption has been identified as a risk factor for alcohol use disorder, self–harm and violence, transport injuries, unintentional injuries, cirrhosis, neoplasms, cardiovascular diseases, diabetes, epilepsy, pancreatitis, lower respiratory infections and tuberculosis [15].

The calculations are based on the effect of different levels of alcohol consumption on disease and injury outcome, ie, relative risks (RRs), and the prevalence of alcohol consumption at the population level. The RRs in the exposure–outcome associations are based on scientific systematic reviews and meta–analyses [16], while the distribution of alcohol consumption is based on the average all–age consumption per capita from the Food and Agriculture Organization of the United Nations (FAO) and WHO Global Information System on Alcohol and Health (GISAH) data, as well as survey data to obtain age patterns of consumption and the prevalence of drinkers, former drinkers and abstainers [16]. The RRs for some of the risk–outcome pairs for alcohol use in Russia are different from the rest of the BRICS based on evidence from a recent cohort study [16]. The contribution of alcohol to disease burden is estimated by comparing the risk of diseases or injuries under the current exposure distribution in the population (at different levels of alcohol use), to a theoretical counterfactual distribution where no one is exposed to alcohol. This population attributable fraction is then applied to the overall disease specific burden (YLLs and YLDs to later be summed, generating the DALYs).

### Evidence–based alcohol policies

Evidence–based alcohol policies, regarded as 'best practice' have been summarized by eg, Babor et al. (2010) [1], and include alcohol taxes, minimum legal drinking age, restriction on density of outlets, drunk driving countermeasures, and government monopoly on sales of alcohol. Information on each country's

existing alcohol policies was achieved through literature searches in the World Health Organization database, PubMed, Google Scholar and Web of Science using the following search words: 1) [(country) AND (alcohol OR alcohol consumption) AND (policy)], 2) [(BRICS) AND (alcohol OR alcohol consumption) AND (policy)].

## Analytical approach

We used the results from the Global Burden of Disease and Injuries and Risk Factors 2013 study [16] to present the age–standardized rates of DALYs attributed to alcohol, per 100 000, between 1990 and 2013 at five year intervals. Age–standardized rates adjust for total population and changes in age–specific population sizes over time, and allow comparison of alcohol–attributed health outcomes across countries. Estimates of alcohol consumption and alcohol–attributed disease burden were extracted from the GBD database provided by the Institute for Health Metrics and Evaluation (IHME) (http://www.healthdata.org/). Each policy identified through the literature searches was assessed in relation to patterns of alcohol–attributed DALYs.

## RESULTS

### Alcohol consumption and alcohol–attributable disease burden

**Figure 1** summarizes alcohol consumption and the alcohol–attributed DALYs in the BRICS countries. The alcohol–attributable disease burden of Brazil, Russia and India mirrors their level of alcohol consumption. This is however, not the case for China and South Africa. A decreasing disease burden is observed in China and South Africa from 2000 to 2013, while, at the same time, they have rising alcohol consumption levels (ie, from 2005 an onwards for China). This is opposite to the pattern Brazil, Russia and India depict.

### Alcohol policies

The implemented evidence–based alcohol policies in each country are summarized in **Table 1**. All BRICS countries have implemented excise tax on alcohol and drink–driving countermeasures. All countries also have regulations on exposure (advertisement, product placement etc.). India is the only country out of the five BRICS where restrictions on density of outlets are implemented and all countries barring Brazil have time and day restrictions on sales. China is the only country that has not implemented a legal minimum drinking age. None of the countries has a government monopoly on the sale of alcohol.
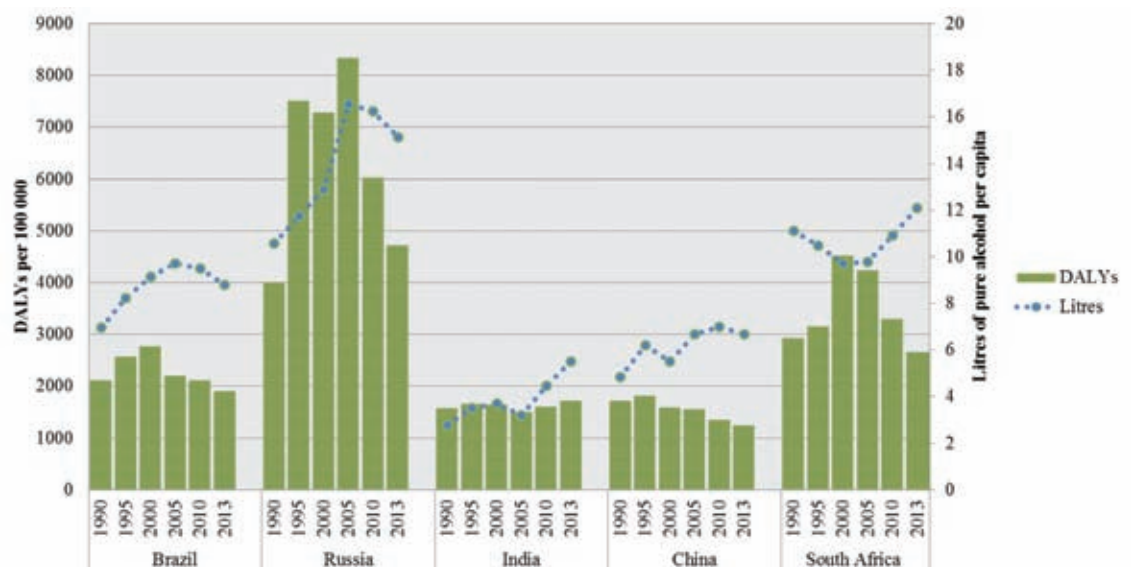


**Figure 1.** Alcohol–attributable DALYs (age–standardized per 100 000) and alcohol consumption in liters of pure alcohol in BRICS countries 1990–2013.

**Table 1.** The identification of implemented evidence–based polices in the BRICS countries (year of implementation in brackets)*

| POLICY | BRAZIL | RUSSIA | INDIA | CHINA | SOUTH AFRICA |
|---|---|---|---|---|---|
| Alcohol taxes | Yes (2004) [17] | Yes (2000), (2008) [18] | Yes (2004) [17] | Yes (2002) [19] | Yes (2003) [20] |
| Minimum legal drinking age | Yes (1999) | Yes (2001) [18] | Subnational (2004) [17] | No | Yes (2004) [17] |
| Time and day restrictions on sales | No | Yes, time (2005), (2006) [18] | Yes (2004) [17] | Yes (2004) [17] | Yes, time (2003) [20] |
| Restrictions on density of outlets | No | No | Yes (2004) [17] | No | No |
| Drink–driving countermeasures | Yes (2008) [11] | Yes (1999) [21] | Yes (1999) [21], (2004) [17] | Yes (2007) [19] | Yes (1999) [21] |
| Legal restriction on exposure | Yes, ads (1996) [21] | Yes, ads (1993), (1995), (2001) [18] | Yes (2004) [17] | Yes, ads (2010) [22] | Yes, ads (2004) [20] |
| Government monopoly | No | No (removed 1992) [18] | No | No | No |

*Where year of implementation is not available; year when policy is noted to be in place is used instead.

## Alcohol policies in relation alcohol–attributable disease burden

In 1992, Russia removed the state monopoly and in 1995 there was an increase in alcohol–attributable DALYs (**Figure 2**). Bans on advertisement and alcohol taxes were implemented (1993–2000), and from 1995–2000 the DALYs were rather constant. Between 2000 and 2005 there was a slight increase in DALYs (from 7288 to 8349 DALYs per 100 000). Russia implemented further alcohol policies on requirements on licensing and restriction on sales (2005–2006), after the legal drinking age was set in 2001, and then increased taxes (in 2008). Between 2005 and 2013 there was a substantial decrease in alcohol attribut-able DALYs (8349 to 4719 DALYs per 100 000).

In 1991, Brazil increased the flexibility of regulating sales and at this time DALYs were modestly increas-ing (2124 to 2771 DALYs per 100 000 between the years 1990–2000) (**Figure 2**). In the year 1997, the blood–alcohol concentration limit while driving was lowered, and from the year 1998 to 2008 the limit was set to zero ("Prohibition"), to later in 2008 be re–established and set to 0.02 g/L (grams per liter).

In South Africa, policies on taxes and restriction on sales were implemented in 2003 and advertisement was restricted in 2004. In 2008, a liquor bill was implemented, which regulated the physical availability of alcohol and in 2009 messages on container labels came into place. The DALYs peaked in the year 2000 in South Africa (4527 DALYs per 100 000), and an overall decrease was observed over the studied time period (2926 to 2662 DALYs per 100 000 between the years 1990–2013).
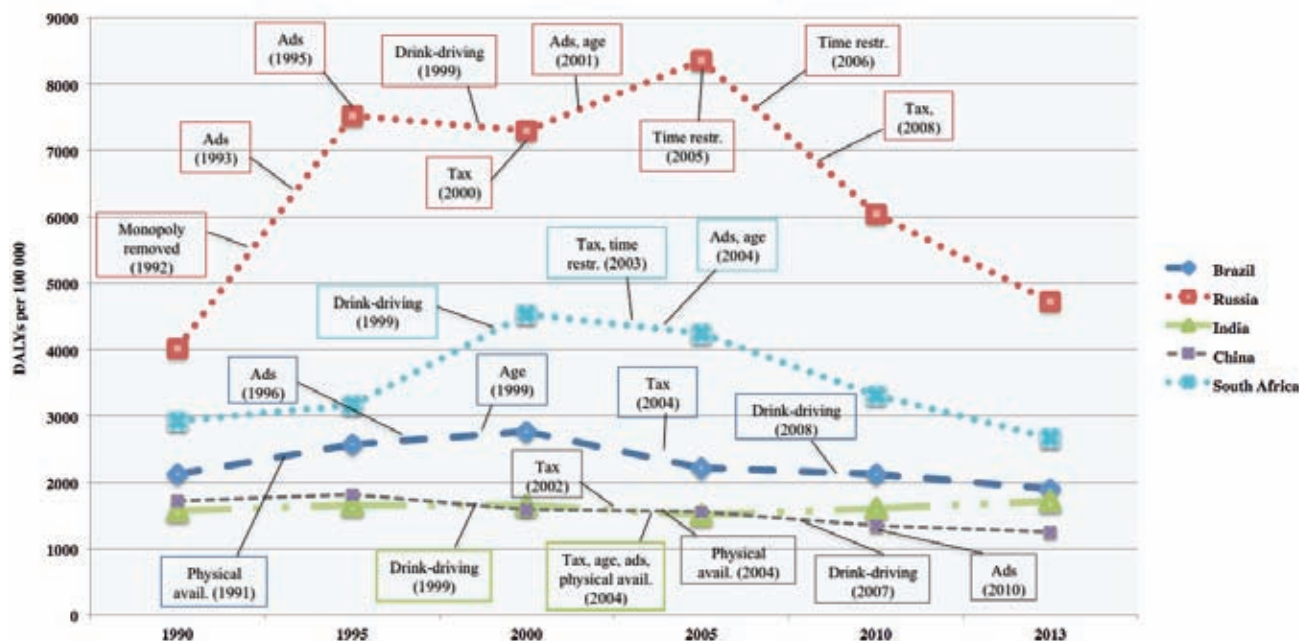


**Figure 2.** Change in alcohol attributable DALYs over time and implemented policies (year).

In China, the taxes on alcohol increased in 2002, and in 2004 restrictions on sales and licensing were in place. In 2007, measures on drunk driving were implemented and in 2010 restrictions in advertisement were in place. As in South Africa, an overall decrease in alcohol–attributable DALYs was observed in China (1719 to 1250 DALYs per 100 000 between the years 1990–2013).

In India, alcohol policies were observed to be in place for the years 1999 (the blood alcohol concentration while driving was set as 0.10 g/L) and 2004 (taxes, minimum legal age and limitations on physical availability and exposure). The DALYs increased over time in India (from 1574 to 1722 DALYs per 100 000 from 1990–2013) with a modest decline between the years 2000 and 2005 (from 1647 to 1512 DALYs per 100 000).

## Discussion

Our study showed an overall decrease of age–standardized disability adjusted life years (DALYs) in Brazil, China and South Africa, while an overall increase was observed in Russia and India when comparing 1990 to 2013. Most notably is the change in DALYs in the case of Russia, where a distinct increase between 1990 and 2005 was followed by a steady decrease from 2005 to the year 2013. For Brazil, India and Russia, levels of alcohol consumption were in line with levels of alcohol–attributed disease burden, while in China these levels separated from 2005 and onwards, and in South Africa the levels are totally the opposite of each other during the entire time period. Alcohol policies are implemented in all the BRICS countries, although types of policies differ. Furthermore, our results show that policy changes are generally followed by changes in alcohol–attributed disease burden.

Although Russia is part of the BRICS, their economic development is quite different [5] from the rest of the BRICS countries, as is their alcohol history; from the fall of the Soviet Union with the removal of state monopoly in 1992 [23], the recovering economic development in Russia in 2000, when alcohol consumption and alcohol–attributed disease burden increased, to the alcohol policies implemented in 2006 followed by a drop in alcohol–attributable DALYs in 2010. The major causes of deaths in Russia in the late 90s were cardiovascular diseases, cancer and violent causes [24]; ie, conditions where alcohol consumption is a known risk factor. Through the transition period in the beginning of 1990, alcohol related deaths increased the most [25]. The distinguished change of alcohol–related deaths in Russia has been observed earlier [24] and the history of Russia in the early 90s is worth highlighting when comparing the results to the other BRICS countries. It has been suggested that the drop seen in DALYs (year 2005 and onwards) was a result of Gorbachev's reform in 1985 (ie, raising prices and restricting sales). Some additional positive changes in alcohol consumption seem to be a result of the 2006 policy changes in Russia (eg, restricting sale locations and regulations on licensing for producers and distributors) [18,23,26].

India was the one country besides Russia that experienced an overall increase in alcohol–attributable DALYs between 1990 and 2013. India is a large and diverse country with regards to both age and gender compositions across the country and with vast differences in drinking patterns as well as adopted policies in different areas [27,28]. Of the few studies conducted on this topic in India, prevalence reports on alcohol consumption differ largely [29]. Consequently, as suggested by Girish et al. [28], different strategies to prevent and control alcohol are needed in different areas. At the national level, the policies in India (eg, taxes, minimum legal drinking age and drunk driving measures) were found to be in place in 1999 and 2004, slightly before the observed increase in disease burden, which might partially be explained by the increase in alcohol consumption from 2005 and onwards.

In the case of Brazil, the alcohol–attributable burden of disease decreased over time. Drinking and driving limitation and age restrictions are among the implemented alcohol policies in Brazil. A previous study showed that the 2008 policy implementation in Brazil (drunk driving) had a significant impact on reduction of traffic injuries and fatalities [30]. Other studies conducted in Brazil have emphasized comprehensive and effective alcohol and drug policy [11] since so far policies have been fragmented and poorly enforced [31]. As shown by our results, the alcohol consumption and the attributable disease burden mirror each other and the implemented policies fit the trend of the decreasing disease burden.

Although the alcohol–attributable DALYs in China have decreased over the decades, recent studies show an alarming increase in alcohol consumption and related harms [10,32], as well as an expansion of the alcohol production [10]. The lack of comprehensive alcohol policies [19,32] has been emphasized, as has the limited research on alcohol policy in China for the past decades [19]. Since DALYs have decreased in China despite the fact that the country has rather few implemented policies, it seems relevant to raise the question of a possible lagging effect of the implemented policies on the alcohol–attributable burden of disease.

Like Brazil and China, South Africa has experienced a decrease in alcohol–attributable DALYs. In South Africa there are similar diversities within the country as in India and drinking patterns differ largely in different areas or states [33,34]. An increase in alcohol consumption especially among youth, and an increase in traffic accidents and violence have been observed in the past two decades [34]. In South Africa, the development in alcohol consumption is almost the exact opposite to the DALY development. This peculiar trend can be explained by several phenomena. First, the consumption estimates plotted are total per capita, while the burden estimates are age–standardized. Second, in the comparative risk assessment approach, age–sex–specific attributable fractions are applied to the outcome–specific total burden, so the total burden trends can affect trends in attributable burden if the attributable fraction component changes relatively less than the total burden. In South Africa, the total age–standardized rate of DALYs rose between 1990 and 2000 and fell between 2000 and 2013 for many causes in which alcohol is a risk factor (eg, transport injuries, cirrhosis, tuberculosis, stroke, hypertension, and self–harm and interpersonal violence). Hence, different patterns emerge when results are stratified by age, sex, outcome (eg, liver cancer, ischemic stroke, etc.) and metric (YLL/YLD).

## Strengths and limitations

The BRICS countries are some of the world's largest countries, both with regard to population size [6] and land coverage [35], and in some cases different legal and policy regulations in different states within the countries [10,11,27]. Our study provides a first step of a cross–country comparison within the field of alcohol research in these countries. To compare the results from this study with research conducted on alcohol consumption and alcohol policy in high–income countries, where established systems for surveillance and monitoring exists, might be quite simplifying and deceptive because of the different contexts. With that in consideration, this study is in line with previous studies conducted in LMIC, emphasizing the need for empirical research on levels of alcohol consumption and effects of, as well as adherence to, implemented policies [10,11,20,33,34].

We recognize that many factors contribute to and explain the alcohol related disease burden, and an assessment of causality between implemented policies, alcohol consumption and attributable burden obviously cannot be done. For one thing, we do not know to what extent the alcohol policies were adequately enforced. A recent study by Ferreira–Borges and colleagues [36] focusing on alcohol policies in 46 African countries highlighted the need for increased training and capacity building among government leaders and decision makers in the development and implementation of alcohol control policies. There is also the possibility of differences in time lags for the different policies with regards to effects on consumption and harm. For example, the implementation of drink–driving countermeasures and increased pricing may have more immediate effects on alcohol–related harm than restrictions on advertisements.

Furthermore, there are limitations regarding the quality and validity of data. Per capita consumption tends to be underestimated and for this purpose a correction factor is used in the GBD calculation to account for unrecorded consumption [16]. Also, alcohol–attributed deaths tend to be underreported in registers due to difficulties in making accurate diagnoses. Coding practices also differ across countries and although the GBD study uses a general approach to assess causes of deaths from all countries, little is known about to what extent differences in coding may affect the estimates.

Our information on policies derives from published literature only and it is possible that we lack information on some alcohol policy changes that may have taken place in the BRICS countries during this time period. The alcohol policies included in this study are only those that have been documented to be effective [2]. However, most research building the evidence–based compilation [1] is based on studies in high–income countries (HIC). There may be context–specific factors in LMIC demanding different alcohol policies or interventions, as opposed to what has been shown in HIC. The lack of evaluations of current policies in the BRICS highlights the importance of further research.

The comparison carried out in this study is, to our knowledge, the first to be made. A key strength with the GBD methodology is that disease burden due to alcohol is systematically and uniformly defined and thus estimates can be compared across countries and over time. The results from this study illustrate a pattern in the development of alcohol–attributable disease burden and alcohol policy over time for the BRICS countries. Country specific studies on overall disease–burden have been conducted in Germany [37], the Kingdom of Saudi Arabia [38], Spain [39], and the United Kingdom [40], and specifically on alcohol–related disease burden in the Nordic countries [41] where GBD data for each country has been utilized to assess cross–country similarities and differences in relation to policy (eg, alcohol). Similar studies are yet to be conducted in LMIC. As regional differences have been highlighted in our study, the on–

going subnational burden of disease analyses conducted in Brazil, China, India, and South Africa are highly relevant, where regional differences in alcohol–attributable disease burden are more likely to be captured, in turn shedding more light on this topic.

## CONCLUSIONS

The alcohol–attributable DALYs changed between the years 1990–2013, with an overall increase in Russia and India and a decrease in Brazil, China and South Africa. This reflected the alcohol consumption development quite well for Brazil, Russia, and India, but only partly for China. However, the alcohol consumption in South Africa was roughly the opposite of the disease burden development for several reasons. Types of implemented alcohol policies varied between the countries, however all countries had policies on alcohol taxes, drink driving and advertisement.

Our study provides a first step of a cross–country comparison within the field of alcohol research in these countries, highlighting the need for further empirical research on levels of alcohol consumption and subsequent harm, and effects of, as well as adherence to, implemented policies.
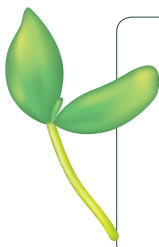
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# Psychosocial stimulation interventions for children with severe acute malnutrition: a systematic review

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**Background** The WHO *Guidelines for the inpatient treatment of severely malnourished children* include a recommendation to provide sensory stimulation or play therapy for children with severe acute malnutrition (SAM). This systematic review was performed to synthesize evidence around this recommendation. Specifically, the objective was to answer the question: "In children with severe acute malnutrition, does psychosocial stimulation improve child developmental, nutritional, or other outcomes?"

**Methods** A review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO 2016: CRD42016036403). MEDLINE, Embase, CINAHL, and PsycINFO were searched with terms related to SAM and psychosocial stimulation. Studies were selected if they applied a stimulation intervention in children with SAM and child developmental and nutritional outcomes were assessed. Findings were presented within a narrative synthesis and a summary of findings table. Quality of the evidence was evaluated using the Cochrane risk of bias tool and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

**Findings** Only two studies, both non–randomized controlled trials, met the selection criteria for this review. One was conducted in Jamaica (1975) with a follow–up period of 14 years; the other was done in Bangladesh (2002) with a six–month follow–up. At the individual study level, each of the included studies demonstrated significant differences in child development outcomes between intervention and control groups. Only the study conducted in Bangladesh demonstrated a clinically significant increase in weight–for–age z–scores in the intervention group compared to the control group.

**Conclusions** The evidence supporting the recommendation of psychosocial stimulation for children with SAM is not only sparse, but also of very low quality across important outcomes. High–quality trials are needed to determine the effects of psychosocial stimulation interventions on outcomes in children with SAM.

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Malnutrition, particularly in the first 1000 days of life, is known to be associated with serious outcomes including increased vulnerability to infection and disease, compromised development, as well as mortality [1–3]. In this same period of time, evidence suggests that inadequate psychosocial stimulation (ie, physical, sensory, and/or emotional input) inhibits infants from achieving developmental potential [3–5]. Malnutrition combined with

psychosocial deprivation can have considerable implications on child development that last throughout life including reduced intellectual capacity, and at a larger scale this can result in reduced societal contribution [5–7]. Because of the importance of early child development for country–level progress, the Sustainable Development Goals (SDG) have now included a focus for children younger than five years to achieve developmental milestones: "By 2030 ensure that all girls and boys have access to quality early childhood development, care and pre–primary education so that they are ready for primary education" (Target 4.2) [8].

Children with severe acute malnutrition (SAM) are at exceptionally high risk of poor growth outcomes and are also thought to be at high risk for motor and cognitive delays, as brain development is further inhibited with increasing severity of malnutrition [3,9,10]. SAM is defined by weight–for–length z–scores (WLZ) or weight–for–height z–scores (WHZ) at least three standard deviations below the median, a mid–upper arm circumference (MUAC) less than 115 mm, and/or nutritionally–induced bilateral pitting edema [11]. Children with WLZ or WHZ and/or MUAC meeting the above criteria are indicative of marasmus or severe wasting, while the presence of bilateral pitting edema is indicative of kwashiorkor [11]. Current guidelines recommend that SAM is treated through Community–Based Management of Acute Malnutrition (CMAM) [12,13]. In critical cases, inpatient treatment is required for children with SAM. This includes children with severe bilateral pitting edema, loss of appetite, or medical complications in addition to SAM [11,13].

Emotional and physical stimulation was first recommended for children with SAM by the World Health Organization (WHO) in the 1999 *Management of severe malnutrition: a manual for physicians and other senior health workers* [14]. The 2003 *Guidelines for the inpatient treatment of severely malnourished children* include ten principles for routine care; one of those is to establish a stimulating environment for children, along with involvement of primary caregivers in caring for and playing with children whenever possible [15]. Specifically, structured play therapy for 15–30 minutes per day is recommended with examples of activities related to language skills and motor development with the use of simple toys [15]. This recommendation was not described or evaluated in the 2013 *Guideline: updates on the management of severe acute malnutrition in infants and children*, but still remains as one of the ten steps of routine inpatient care for children with SAM [15,16]. On the contrary, the CMAM approach does not include recommendations around psychosocial stimulation in children with SAM in the community [12,13].

Psychosocial stimulation in children with SAM has not been evaluated in a rigorous manner in relation to child developmental and nutritional outcomes. Therefore, the primary objective of this systematic review was to synthesize evidence related to the question, "In children with severe acute malnutrition, does psychosocial stimulation improve child developmental, child nutritional, or other child outcomes?"

## METHODS

A review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO 2016:CRD42016036403). For reporting of this review, the standard guidelines by the Preferred Reporting Items for Systematic reviews and Meta–Analyses (PRISMA) were followed (see Table S1 in **Online Supplementary Document**) [17].

### Search strategy

The search strategy for this review was designed in consultation with a hospital research librarian at the Hospital for Sick Children to ensure a comprehensive search of the literature. The search included terms related to SAM, psychosocial interventions or therapy, and deprivation of psychosocial stimulation, specified in Table S2 in **Online Supplementary Document**. There were no language, location, or publication period restrictions applied. Four electronic bibliographic databases were searched up to March 29, 2016: MEDLINE(R) In–Process & Other Non–Indexed Citations (1946 to present), Embase Classic+Embase (1947 to present), CINAHL (1937 to present), and PsycINFO (1806 to present). Reference lists of included studies were also evaluated to identify any potential studies for inclusion.

### Inclusion and exclusion criteria

#### Studies

There were no restrictions on the study time periods or design types eligible for inclusion.

*Participants*

Children (0 to 18 years) with SAM were included; children had to have kwashiorkor (identified by bilateral pitting edema) and/or severe wasting (identified by WLZ or WHZ below –3 SD or MUAC less than 115 mm) [11]. The currently accepted criteria for identification of SAM were developed in 2006 [11], thus for studies conducted prior to 2006, anthropometric measures of children were compared to the current measures for SAM by examining previous and recent cut–off values for weight–for–length or –height [18]. If an alternative identification of SAM was used and there was confidence that children enrolled in these studies had anthropometric measures that did not match with the current definition of SAM, these studies were excluded. Studies that focused on children with other types of malnutrition, such as moderate acute malnutrition (MAM), were also excluded.

*Interventions*

Psychosocial stimulation (ie, physical, sensory, and/or emotional input), play therapy, or responsive parenting interventions in any setting (eg, community or hospital–based) were included.

## Controls

Intervention groups were compared to no intervention or alternative intervention groups.

## Primary outcomes

Child developmental (eg, cognitive, language, motor, and social–emotional measures) and nutritional outcomes (eg, anthropometric measures) were specified as the primary outcomes. Anthropometric measures of interest included weight–for–length or –height (ie, indicators of wasting), length– or height–for–age (ie, indicators of stunting), and weight–for–age (ie, indicators of underweight). Body mass index was not defined as an important nutritional outcome for this review because its implications for children and adolescents are indeterminate [19].

## Secondary outcomes

Child quality of life outcomes, morbidities, and mortality were included as secondary outcomes.

## Study selection and data extraction

Two authors (AD and MvdH) independently screened the titles and abstracts, followed by the full texts of potentially eligible studies, for eligibility as per the pre–specified selection criteria. Articles that were not in English (ie, French and Spanish) were translated. Finally, a third author (RB) was consulted to resolve any discrepancies between the two reviewers. Results from the screening process were summarized in a flow diagram as per the PRISMA guidelines [17]. Data from the selected studies were extracted by each of the two reviewers independently, including study information and methods, participant characteristics, intervention properties, and child outcomes.

## Assessment of evidence quality

Each of the two authors independently assessed risk of bias for each study using the Cochrane Handbook for Systematic Reviews of Interventions [20]. Although none of the included studies were randomized–controlled trials, the Cochrane risk of bias tool was deemed suitable because both included studies were experimental and controlled [20]. In addition to the standard six criteria for assessing risk of bias according to the Cochrane Handbook for Systematic Reviews of Interventions, risk of bias from confounding was also examined to account for the fact that participants were not randomized [20]. A risk of bias summary was created using Review Manager 5.3 [21]. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was then used to assess the body of evidence for each outcome [22].

Both studies were non–randomized controlled trials, thus they were considered observational studies in the context of GRADE, and started as low quality of evidence. The quality could have been downgraded for study limitations (risk of bias), inconsistency of results, indirectness of evidence, imprecision, publication bias, or could have been upgraded for large magnitude of effect, confounding, and dose–response gradient [22]. Clinical heterogeneity of outcome measures was qualitatively assessed based on the discretion of authors of this review.

## Analysis

A narrative synthesis was done of all eligible studies. Data were analyzed using Review Manager 5.3 [21]. To summarize findings across studies that included an intervention and comparison group, quantitative analyses were conducted in which mean differences or standardized mean differences with 95% confidence intervals (CI) were calculated for continuous outcomes and risk ratios with 95% CI were calculated for dichotomous outcomes. When outcomes were similar, results across studies were pooled. A summary of findings table was created in GRADEpro 3.6 in which the most important outcomes were included [23]. Results were considered statistically significant if 95% CI did not cross 0. A meta–analysis and subgroup analyses were not conducted, as there were too few studies identified from the search, without similar outcome measures.

## RESULTS

### Study selection

The database search yielded 554 articles, which were narrowed down to 411 articles after duplicates were removed. The results were confined to 18 articles that could potentially meet the inclusion criteria. These remaining articles were assessed in full, with two studies being selected to be included in the systematic review, one of which was published as five separate articles meeting the inclusion criteria [24–29]. No additional studies were identified from the reference lists of included studies. This is summarized as a flow diagram in **Figure 1**. Reasons for excluding studies are listed in Table S3 in **Online Supplementary Document**.

### Study characteristics

Two studies met the selection criteria for this review. The first study was conducted in Jamaica by Grantham–McGregor et al. beginning in 1975. Five papers that met the inclusion criteria for this review were published on the same study population. For the purpose of this review, these papers will be referred to as Grantham–McGregor 1980, the first paper published for this study. The second study meeting the inclusion criteria for this review was conducted in Bangladesh by Nahar et al. starting in 2002, and henceforth it will be referred to as Nahar 2009, the year it was published. Grantham–McGregor was also an author of the Nahar 2009 study.

The Grantham–McGregor 1980 study included children with marasmus (identified by authors as having weight below 60% of expected weight for age), marasmic–kwashiorkor (weight below 60% of expected weight for age with edema), or kwashiorkor (weights below 80% of expected weight for age with edema) in the intervention and control groups receiving standard inpatient nutritional care per hospital guidelines, although it is unclear whether these guidelines align with WHO guidelines for SAM treatment. This study also included a third comparison group of non–malnourished children who did not participate in any type of intervention program or treatment.

The Nahar 2009 study compared two malnourished groups of children, including children with marasmus (identified by authors as having weight–for–age below 50% or weight–for–length below 70% of expected values) and kwashiorkor (children with edema), or a combination of the two. Children in both groups received inpatient nutritional care according to the 1999 WHO guidelines for treatment of SAM [14]. Both groups were followed up at seven hospital visits over six months after receiving inpatient care, in which health and nutrition education was done and micronutrient supplements were provided.



**Figure 1.** Study flow diagram.

The two studies used a similar type of psychosocial intervention with a focus on activities that would stimulate a child's development including the involvement of mothers to play and talk with their children. In both studies, the intervention started in the hospital and was continued at home. This included one hour per week for two years and one hour every two weeks for the third year after hospital discharge in the McGregor 1980 study, and 18 supervised play sessions (7 play sessions in the hospital and 11 sessions at home) within six months of discharge in the Nahar 2009 study.

The Grantham–McGregor 1980 study used different developmental and IQ tests that were not developed or standardized in Jamaica. The Nahar 2009 study used the Bayley Scales of Infant Development (BSID–II) to assess psychomotor development. The BSID–II is not standardized in Bangladesh, however a strong interobserver reliability of r=0.99 (P<0.001) was reported. The main characteristics of the two studies, including the developmental assessment tools and the anthropometric measures used, are further described in **Table 1**.

## Evidence quality of included studies

For the Grantham–McGregor 1980 study, there was high risk of selection bias (random sequence generation) and reporting bias at the study level, since all tests were conducted by a tester blind to the participants' groups only from the 12–month session onwards; importantly the tester was not blinded at earlier assessment time points. There was also a high risk of attrition bias for all outcomes because of a lower number of children included in the non–intervention group in the 1987 publication than in the subsequent 1994 publication of this study. There was unclear risk for all other types of bias at the study and outcome levels (**Figure 2**).

There was a high risk of selection bias (random sequence generation) for the Nahar 2009 study as well due to the lack of randomization, in addition as high risk of attrition bias for all outcomes due to a high loss to follow–up. For all outcomes in the Nahar 2009 study, there was low risk of detection bias, as the tester was unaware of the participants' groups, and confounding bias because covariates were specified and controlled for (**Figure 2**). The types of bias for both studies are listed in Table S4 and Table S5, respectively, in **Online Supplementary Document**.

Overall, for each of the primary outcomes for this review and for mortality, evidence was of very low quality. Upgrading the quality of evidence because of a large magnitude of effect, confounding, or dose–response gradient was not admissible for any outcomes.



**Figure 2.** Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

## Effects of psychosocial stimulation interventions

### Child developmental outcomes

#### COGNITIVE DEVELOPMENT

Short–term cognitive outcomes (ie, at six months and two years after discharge from hospital) were significantly higher in children that received the intervention compared to the control group of malnourished children in the Grantham–McGregor 1980 study based on mean developmental quotients (DQ) from the Griffiths Mental Development Scales. The intervention group had the same DQ as the non–malnourished comparison group at two years' follow–up. At five years' follow–up, the Griffiths Mental Development Scales and the Stanford–Binet were both used to evaluate cognitive function. Results indicated that the intervention group had significantly higher DQ scores and intelligence quotients (IQ) compared with the control group, however the non–malnourished comparison group had the highest IQ scores (see **Table 2**). 14 years after leaving hospital, the Wechsler Intelligence Scale for Children was used to test the IQ of the participants. The intervention group had a significant higher IQ than the

**Table 1.** Study characteristics and primary outcomes

| Reference | Design, sample size, mean age (months, SD) | Follow-up | Developmental outcomes (mean, SD)* | | | Nutritional outcomes* | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Cognitive | Language | Motor | Weight expected for height (%, SD) | Height expected for age (%, SD) | Height for age (mean z-scores, SD) | Weight for age (mean z-scores, SD) |
| Grantham-McGregor 1980 [27] | Quasi-experimental study, Jamaica; Enrolment: 1975–1977; INT n=21, 12.7±3.0; C n=18, 12.9±4.5; NM n=15, 12.2±4.4<br><br>**Intervention:** *Activities*: home-made toys were used for play sessions. *Time and frequency*: 1 h per day in hospital, 6 days per week; 1 h per week at the family home over 2 years after hospital treatment followed by 1 h per week over year 3 after hospital treatment. *Personnel*: nurse or health worker with limited training | 1, **6** months | *Griffiths Mental Scales DQ:* INT 96±11.3, C 82±12.1, NM 105±11.2 | *Griffts Hearing & Speech:* INT 97±17.6; C 74±13.5; NM 93±8.2 | *Griffiths Locomotor:* INT 98±17.4; C 90±15.6; NM120±20.5; *Hand & eye:* INT 101±10.5; C 85±14.6; NM 105±13.0 | | | | |
| Grantham-McGregor 1983 [26] | | 18, **24** months | *Griffiths Practical Reasoning:* INT 93±9.5; C 78±12.1; NM 94±14.3 | | | | | | |
| Grantham-McGregor 1987 [25] | | 36, 48, 60, **72** months | *Stanford–Binet Test:* INT 71±8.3; C 64±6.4; NM 76±9.5 | *PPTV:* INT 43±4.6; C 39±9.9; NM 47±5.5 | | INT 92±7.5; C 95±8.4; NM93±68 | INT 95±2.5; C 94±4.5; NM 101±3.8 | | |
| Grantham-McGregor 1994 [24] | | 7, 8, 9, **14** years | *WISC full scale:* INT 65±12.4; C 56±9.4; NM 74±12.7. *WISC performance:* INT 64±14.9; C 58±12.5; NM 78.3±11.2 | *PPVT:* INT 71±11.9; C 64±7.2; NM 77±13.3. | | | | INT 0.8±0.6; C 1.0±0.9; NM 0.3±0.8 | |
| Nahar 2009 [28] | Quasi-experimental study, Bangladesh. Enrolment: 2002–2003; INT n=33 12.8±4.7; C n=37 12.0±4.6<br><br>**Intervention:** *Activities*: children were taught about size, shapes, and numbers with visual aids mothers were shown feeding, bathing, and play activities during hospital stay; at home visits, toys were given and replaced at each visit. *Time and frequency*: daily 30 min group play sessions and daily 30 min individual sessions during 14 day hospital treatment; 11 sessions at family homes and 7 sessions at hospital within 6 months of discharge. *Personnel*: health workers with two weeks training. | **6** months | *BSID–II Mental raw score:* INT 103±12.1; C 94±8.8 | | *BSID–II Psychomotor raw score:* INT 67±8.1; C 63±8.2 | | | | INT 3.1±0.9; C 3.6±1.2 |

SD – standard deviation, INT – malnourished intervention group, C – malnourished control group, NM – non-malnourished intervention comparison group, DQ – development quotient, PPVT – Peabody Picture Vocabulary Test, WISC – Wechsler Intelligence Scale for Children, BSID–II – Bayley Scales of Infant Development, Second Edition
*Development and nutritional outcomes described in this table are from the latest follow-up times in the references (indicated in bold at the column 'follow-up'). Some data was only presented in figure form in the different articles from Grantham–McGregor et al., and therefore could not be used in this table. The Grantham–McGregor 1989 paper is not included in table because this article presented only observational data.

control group (mean IQ 65 ± 12.4 vs 56 ± 9.4, respectively), but lower than the non–malnourished comparison group (mean IQ 74 ± 12.7). In the Nahar 2009 study, the children in the intervention group had significantly higher mental raw scores of the Bayley Scales of Infant Development, Second Edition (BSID–II) than those of the children who did not receive the intervention at the six–month follow–up.

Short–term academic performance was assessed in Grantham–McGregor 1980 study with Griffiths Mental Development; specifically, the performance subscale, indicating the speed of working an precision, and the practical reasoning subscale, describing the ability to solve problems, were used [30,31]. At two and five years' follow–up, children in the intervention group scored in between the control group and the non–malnourished comparison group on the performance subscale. On the practical reasoning scale, children in the intervention group had similar scores to the non–malnourished children and had scores significantly ahead of the control group at two and five years' follow–up. At 9 and 14 years' follow–up, academic performance (ie, spelling and reading) was tested with the Wide Range Achievement Test; the intervention group scored intermediate between the control and non–malnourished comparison groups, although the difference in scores between the intervention and control groups was not significant.

Table 2 shows short– and long–term cognitive development included as important outcomes. Since both studies reported on cognitive development at six months' follow–up, results were pooled and the standardized mean difference was calculated. The standardized mean difference was 0.95 on cognitive development at six months between the two studies.

### Language development

The intervention group in Grantham–McGregor 1980 study scored better than the control group at short–term language outcomes. They also scored significantly higher on the Griffiths Mental Development hearing and speech scale than the non–malnourished comparison group at two years' follow–up. However, long–term follow–up scores on this scale were no longer significantly ahead of the control group.

Between three and six years' follow–up in the Grantham–McGregor 1980 study, both the intervention and non–malnourished comparison groups had similar language scores on the Peabody Picture Vocabulary Test with significantly higher scores than the control group. At the 14–year follow–up, verbal performance was tested with the verbal scale of the Wechsler Intelligence Scale for Children; the intervention group scored significantly higher than the control group and had similar scores as the non–malnourished comparison group. Long–term language development results were included in Table 2.

### Motor development

In the Grantham–McGregor 1980 study, motor development was tested with the locomotor subscale (ie, gross motor skills) and eye and hand coordination subscale (ie, fine motor skills) of the Griffiths Mental Development Scales [30,31]. At the two–year follow–up time, the intervention group had higher scores on gross motor skills compared to the control group, yet these scores were lower than the non–malnourished comparison group. At four years' follow–up, the intervention and control groups scored similarly for gross motor skills.

In terms of fine motor skills, the intervention group in the Grantham–McGregor 1980 study had scores similar to those of the non–malnourished group at the two–year follow–up. The intervention group remained significantly ahead of the malnourished control group for fine motor skills at the three–, four–, and five–year follow–up times, and scored similarly to the non–malnourished children. In the Nahar 2009 study, motor development was assessed at the six–month follow–up time with the Psychomotor Developmental raw scores of the BSID–II. The intervention group had significantly better psychomotor raw scores than the control group. However, the difference in scores was lower than that of the mental raw score of the BSID–II, and the functional importance was not clear. Short–term motor development was described in Table 2 yet results could not be pooled because of the differences in outcome measures, with the Nahar 2009 study only presenting psychomotor development raw scores including both fine and gross motor development. Since the Grantham–McGregor 1980 study used only figures to describe long–term motor development data, these results could not be included in Table 2.

### *Social–emotional outcomes*

In the Grantham–McGregor 1980 study, behavior was assessed at the three–year follow–up time. The behavior of the mother and child was observed during a play situation. A non–standardized questionnaire was used for this observation. There was no significant difference identified between the intervention group and the non–malnourished comparison group. The control group of malnourished children stayed

**Table 2.** Summary of findings table

| Outcomes | Illustrative comparative risks* (95% CI) Assumed risk (control) | Illustrative comparative risks* (95% CI) Corresponding risk (psychosocial stimulation) | Relative effect (95% CI) | No of Participants (studies) | Quality of the evidence (GRADE)† |
|---|---|---|---|---|---|
| **Cognitive development (1):** Bayley Scales of Infant Development, Second Edition (Mental Development Index raw scores) and Griffiths Mental Development Index Follow–up: 6 months (short–term) | | The mean cognitive development in the intervention groups was **0.95 SD higher** (0.55 to 1.35 higher) | | 109 (2 studies) | ⊕⊝⊝⊝, **very low**‡,§ |
| **Cognitive development (2):** Wechsler Intelligence Scale for Children Follow–up: 14 years (long–term) | The mean cognitive development in the control groups was **56.1** | The mean cognitive development in the intervention groups was **8.6 higher** (1.3 to 15.9 higher) | | 35 (1 study) | ⊕⊝⊝⊝, **very low** ‡,# |
| **Language development:** Peabody Picture Vocabulary Test Follow–up: 14 years (long–term) | The mean language development in the control groups was **63.9 (raw score)** | The mean language development in the intervention groups was **6.9 higher** (0.4 to 13.4 higher) | | 35 (1 study) | ⊕⊝⊝⊝, **very low**‡,# |
| **Motor development:** Bayley Scales of Infant Development, Second Edition (Psychomotor Development Index, raw scores) and Griffiths Mental Development Scales (locomotor subscale and eye and hand coordination subscale) Follow–up: 6 months (short–term) | Not pooled | Not pooled | Not estimable | 104 (2 studies) | ⊕⊝⊝⊝, **very low**‡,§ |
| **Weight–for–length or weight–for–height:** | Not measured | Not measured | Not estimable | | |
| **Length–for–age or height–for–age:** Z–scores. Scale from: –4 to 4. Follow–up: 14 years (long–term) | The mean length–for–age or height–for–age in the control groups was **–1.0 SD** | The mean length–for–age or height–for–age in the intervention groups was **0.2 higher** (0.3 lower to 0.7 higher) | | 35 (1 study) | ⊕⊝⊝⊝, **very low** ‡,#¶ |
| **Weight–for–age:** Z–scores. Scale from: –4 to 4. Follow–up: 6 months (short–term) | The mean weight–for–age in the control groups was **–3.1 SD** | The mean weight–for–age in the intervention groups was **0.5 higher** (0.006 to 1.0 higher) | | 70 (1 study) | ⊕⊝⊝⊝, **very low**¶,*** |
| **Mortality:** Number of deaths Follow–up: 6 months to 14 years | | | RR 2.5 (0.5 to 12.3) | 112 (2 studies) | ⊕⊝⊝⊝, **very low**‡,# |

GRADE – Grading of Recommendations Assessment, Development and Evaluation, CI – confidence interval, RR – risk ratio

*The basis for the **assumed risk** (eg, the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

†GRADE Working Group grades of evidence. **High quality**: Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality**: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality**: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality**: We are very uncertain about the estimate.

‡Selection bias, attrition bias, and reporting bias are all likely.

§Clinical heterogeneity of outcome measures.

#Wide CI.

¶Z–scores according to the 1977 NCHS reference standards.

**Selection bias and attrition bias are likely.

nearer to their mothers and stopped playing with their toys sooner. During the developmental assessments in the Nahar 2009 study, activity level, emotional tone, vocalization, and cooperation were observed with nine–point Likert scales adapted from Wolke et al [32]. There was no significant treatment effect identified in any of these behavior ratings in the Nahar 2009 study.

### Child nutritional outcomes

In the Grantham–McGregor 1980 study, anthropometric measures including length– or height–for–age and weight–for–age, expressed as percentage of expected values for age and sex, were not significantly different between the groups six months and two years after hospital stay. There were also no significant differences in reported weight–for–height and height–for–age across the malnourished intervention and control groups at assessment time points between three and 14 years after hospital stay using percentage of expected values or z–scores based on the 1977 NCHS reference standards. Malnutrition relapse and readmission rates were not described.

In the Nahar 2009 study, duration of hospital stay was not significantly different between groups, indicating that inpatient nutritional recovery was similar. Weight–for–age z–scores (WAZ), WLZ, and length–for–age z–scores were reported at enrolment and at discharge. At the six–month follow–up time, only WAZ scores were reported. The mean difference in WAZ between the intervention group compared to the control group was clinically significant at follow–up, at a value of 0.4 SD higher in the intervention group ($P = 0.029$). No data on recurrence of malnutrition or readmission rates were reported. Long–term anthropometric outcomes are reported in **Table 2**, but for WAZ only short–term measures were done.

## Secondary outcomes

Mortality rates at the end of the 14 years of the Grantham–McGregor 1980 study were 14.2% in the intervention group, and there were no deaths in the control group ($P = 0.11$). It was reported that children in the intervention group died from accidents. In the Nahar 2009 study, mortality rates were 5.1% in the control group and 5.7% in the intervention group ($P = 0.91$); reasons were not specified. Other secondary outcomes, including quality of life and morbidities, were not described in either study.

## DISCUSSION

This systematic review contributes to the literature and demonstrates that the evidence supporting the WHO guidelines around provision of psychosocial stimulation during and after hospitalization is of very low quality across important outcomes in children with SAM. Neither of the included studies are randomized controlled trials, and there were high risks of different types of bias in both studies. Both studies examined hospital–based psychosocial intervention programs yet no studies that examined psychosocial stimulation interventions in children with SAM in the community were identified.

At the individual study level, each of the included studies showed significant differences between intervention and control groups of children with SAM in terms of child development. Cognitive development was significantly higher at short–term follow–up in the Nahar 2009 study and long–term follow–up in the Grantham–McGregor 1980 study in children with SAM who received psychosocial interventions. These children also had better language development at both short– and long term follow–up in the Grantham–McGregor 1980 study. These results are in line with a recent systematic review by Aboud & Yousafzai that evaluated psychosocial stimulation interventions in children under the age of two years who in low– and middle–income countries [5]. This recent review demonstrated a medium effect size of 0.42 and 0.47 on cognitive and language development, respectively [5]. However, at the 14–year follow–up period in the Grantham–McGregor 1980 study, both the malnourished intervention and control groups had poorer levels of academic performance compared to their non–malnourished peers, even after controlling for social background and hospitalization, possibly indicating long–term neurodevelopmental delays in children with SAM [24].

For motor development, there were mixed results between the two included studies. The psychosocial stimulation intervention did not have an effect on gross motor skills, but did improve fine motor skills in Grantham–McGregor 1980 study. The Nahar 2009 study also demonstrated significantly improved motor development scores, although the authors were not clear about whether or not this effect would be clinically significant. Both interventions used play activities and materials to stimulate fine motor development, which could explain the mixed outcomes for gross and fine motor development.

Both the Grantham–McGregor 1980 and Nahar 2009 studies used developmental assessment tools that were not culturally validated or locally standardized. Additionally, there is controversy about the validity of the Griffiths Mental Development Scales, which was used the most amount of times for the Grantham–McGregor 1980 study [33]. The BSID–II was used in the Nahar 2009 study; although it is a validated tool, it has since been replaced by the Bayley Scales of Infant Development, Third Edition [34]. Many children scored very low (ie, <50) on the BSID–II, and therefore the authors were not able to use standardized mental and psychomotor scores.

Nutritional outcomes did not change as a result of the psychosocial stimulation intervention in the Grantham–McGregor 1980 study. The Nahar 2009 study, on the other hand, did show statistically and clinically significant increases in WAZ scores in the intervention group compared to the control group six months after hospital stay. Authors hypothesized that psychosocial stimulation could improve mother–child interaction, which could lead to better feeding techniques [28]. Future research should evaluate the nutritional outcomes of psychosocial stimulation interventions in children with SAM and also explore possible mechanisms in more detail.

It is important to note that both studies included in this review applied interventions that differ from the current WHO recommendations of 15–30 minutes per day of psychosocial stimulation for children admitted to hospital with SAM [15]. Feasibility of the types of interventions tested in both included studies is of concern. For example, an intervention for three years after hospital stay, which was done in the Grantham–McGregor 1980 study, may not be feasible in most resource–constrained settings. During hospital stay, participants in the intervention group of the Grantham–McGregor 1980 study were involved in hour–long play sessions six days per week based on a semi–structured curriculum. This was followed by weekly home–based sessions for the first two years and bi–weekly sessions for an additional year. In the Nahar 2009 study, daily hour–long intervention sessions were done with participants during hospital stay, based on a child development manual with specific activities according to developmental milestones. There were also 18 follow–up visits with play activities as well as health and nutrition education (for hospital–based follow–up visits only), but after discharge there was a loss to follow–up of 39% of the children in the intervention group, vs 23% and 14%, respectively, in the control group.

Results from the two individual studies in this review showed important improvements in child development, indicating that further research is urgently needed to strengthen the case for psychosocial stimulation in children with SAM. Another important area to explore for improving child development outcomes in children with SAM is the added value of nutrition–specific interventions. Two recent systematic reviews in low– and middle–income countries in children under two years of age, not specifically in children with SAM, have found small benefits of nutritional interventions on child development outcomes, but the mechanisms explaining this relationship still need to be explored [5,35]. Additionally, the feasibility of psychosocial interventions should be investigated, especially since there is no data on how the basic WHO recommendations for play and stimulation activities for children with SAM in hospitals and health centers are currently practiced [12,15,36]. Compliance to psychosocial stimulation programs, and factors influencing their effectiveness such as maternal mental health, are also unknown. Last, in order to justify psychosocial interventions in areas with limited resources, the location (ie, hospital and/or community settings) and the optimal duration of psychosocial interventions should be a focus of further investigation with the use of reliable measures to understand if these interventions help to achieve the SDG for child development and other outcomes [8,12,37].
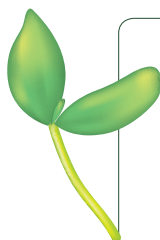
## Limitations

A limitation of this systematic review is that because there were few studies included and there was clinical heterogeneity of outcomes, it was not possible to conduct sub–group analyses and a meta–analysis.

To date, there are no randomized–controlled trials assessing psychosocial stimulation for children with SAM. Given that psychosocial interventions could be classified as behavioral interventions, it would be difficult to randomize individuals to groups and to conceal personnel at the study level. Authors of the Nahar 2009 study also explained that they also felt it would be unethical to provide the intervention to certain participants in the same hospital wards using randomization, and therefore used a time–lagged controlled design. This is one reason that the risk of bias is considered high and the quality low for the existing evidence. However, there are other possible strategies for randomization, such as block randomization of participant groups at frequent time intervals.

## CONCLUSIONS

Due to very low quality of evidence, there is currently insufficient direct evidence to recommend the provision of psychosocial stimulation in children with SAM. With SAM affecting millions of children worldwide, this is an important evidence gap. Results from the two individual studies in this review showed important improvements in child development in children with SAM, indicating that these interventions could be of benefit. More research is urgently needed to strengthen the case for psychosocial stimulation in children with SAM in the community and hospital settings. New studies also need to explore feasibility and implementation of psychosocial stimulation interventions in children with SAM.

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# Maternal mortality as a Millennium Development Goal of the United Nations: a systematic assessment and analysis of available data in threshold countries using Indonesia as example

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**Background** In 2015 the proposed period ended for achieving the Millennium Development Goals (MDG) of the United Nations targeting to lower maternal mortality worldwide by ~75%. 99% of these cases appear in developing and threshold countries; but reports mostly rely on incomplete or unrepresentative data. Using Indonesia as example, currently available data sets for maternal mortality were systematically reviewed.

**Methods** Besides analysis of international and national data resources, a systematic review was carried out according to Cochrane methodology to identify all data and assessments regarding maternal mortality.

**Results** Overall, primary data on maternal mortality differed significantly and were hardly comparable. For 1990 results varied between 253/100 000 and 446/100 000. In 2013 data appeared more conclusive (140–199/100 000). An annual reduction rate (ARR) of –2.8% can be calculated.

**Conclusion** Reported data quality of maternal mortality in Indonesia is very limited regarding comprehensive availability and methodology. This limitation appears to be of general importance for the targeted countries of the MDG. Primary data are rare, not uniformly obtained and not evaluated by comparable methods resulting in very limited comparability. Continuous small data set registration should have high priority for analysis of maternal health activities.

In 2000 governments from 189 countries agreed on the Millennium Explanation (Millennium Development Goals – MDG) at one of the largest summits of the United Nations (UN). Eight global development objectives were defined and the world community aimed to achieve these goals until 2015. In addition to the fight against poverty and starvation, for equalization of nations and individuals the fifth MDG contains the aim to improve the health care of mothers. The maternal mortality has been considered as an important indicator for the health of the population and the economic as well as social development. Based on this prioritization the targeted worldwide reduction of maternal mortality rates was targeted to be reduced by about 75% [1].

Major problems related to high maternal mortality currently occur in Africa, but also in Asia, in particular in South–East and South Asia. However, comparison between countries and over time requires sufficient data qual-

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ity based on standardized definitions and data availability with satisfying representability. Here, we systematically examined available data quality of maternal mortality in Indonesia as one of the largest countries worldwide with high impact on the achievements of the Millennium Goals. The aim of this analysis was the evaluation, critical review and summary of all available primary data about maternal mortality in Indonesia during the MDG time period. Specifically, we reviewed data resources and their acquisition before the Millennium Explanation and at the end of the proposed timeframe for their achievement. The critical review focused especially toward coverage of available data for the whole population of the country, reliability and potential biases of data acquisition. Comparable to other countries, such as Cambodia [2] and India [3], different record sets and a large gap of primary data were identified for Indonesia.

### Definition of maternal mortality

For maternal mortality, the World Health Organization (WHO) defines a maternal death as the death of a woman during pregnancy or within 42 days after its end regardless of duration or place of the pregnancy. It is distinguished between direct and indirect cause of death. A direct death is caused by complications directly related to the pregnancy, childbirth and puerperium including interventions, omissions, insufficient treatments or their combinations. An indirect death originates from preexisting illnesses which have worsened by physiological changes of the pregnancy [4]. A systematic WHO study investigating the causes of the maternal mortality worldwide raised that more than one quarter of these deaths are due to indirect causes. The systematic analysis showed that main direct causes of death (overall 73%) were bleeding (27%), followed by hypertension (14%) and sepsis (11%) [5].

### Methods to measure maternal mortality

Different methods to determine the risk of a motherly death have been used so far: maternal mortality ratio (MMR, for distinction also MMRatio) determines the number of the mothers' deaths per 100 000 live births per time period. Maternal mortality rate (for differentiation MMRate) defines the number of the maternal mortality in a certain period per 100 000 women at reproductive ages. The lifetime risk considers the likely hood to become pregnant and the likelihood of mothers' mortality at the reproductive ages (WHO, 2011) [4]. As alternative indicator for maternal mortality the percentage of pregnancy related deaths divided by all deaths with women at the age of from 15 to 49 years (PMDF) has also been implemented. Overall, to reliably obtain indicators for maternal mortality remains a difficult challenge mainly due to context–specific interrelations of various required information [6]. The industrial nations often dispose efficient registration systems enabling them to raise sufficient reporting. However, in the developing and threshold countries these data are often not documented in a reliable and complete manner. Due to the lack of real life data information are often used based on (randomly) selected subpopulations. For example, this includes specific questions within the scope of national censuses, budgetary questionnaires or more specific family interviews [7].

## METHODS

### Data sources

A comprehensive analysis of known international health care reporting resources combined with a systematic review according to the Cochrane method was carried out to identify the available primary data and studies that provide maternal mortality information for Indonesia. The elevated data, acquisition techniques, calculation methods and study designs were validated and compared between the various reports and for the proposed MDG period.

As initial step international and national health care reporting resources were searched for available data about mothers' mortality including:

- WHO
- United Nations Population Fund
- Worldbank
- Badan Pusat Statistik Indonesia
- The Organization for Economic Co–operation and Development (OECD)

To verify the results found at the international reporting platforms and to identify other data about the MMR a systematic review was subsequently carried out using the search criteria: "maternal mortality" and

"Indonesia". All obtained published paper were evaluated according to the criteria of the Cochrane Collaboration for meta–analyses [8]. Although this review is not based on clinical trials the principles and structure of this method have been adapted accordingly.

## Targets for evaluation

The targeted questions or aims of the primary reports refer to the central issue of this critical review. It was carefully looked for the different types of indicators for maternal mortality and for the types of data acquisition. This was of high importance since Indonesia (as most other threshold countries) does not provide a full–coverage and nationwide registration system. Specifically, the following criteria were used for upfront comparison:

- Targeted indicator
- Targeted population (if applicable selection criteria)
- Measured data, secondary resources (eg, family reporting) or estimations.

According to the scope of this review and in order to avoid secondary referencing effects primary reports were included in this evaluation exclusively. Data acquisition performance was evaluated and compared regarding the used baseline data, elevation methods, study design and kind of reporting. An assessment of the statistical calculation models was not done, but descriptions are given for completeness of the analysis.

## Inclusion and exclusion criteria

For this review full–paper publications and studies in English–speaking journals were primarily used. These publications were checked if they provide primary information and/or estimates about the Indonesian maternal mortality. Reports only based on references were expelled from the evaluation but will be included in the discussion. If the identified references did not contain MMR data for Indonesia and/or data were only referenced from other publications those were excluded.

## Literature search

A systematic search for Medical Subject Headings (MeSH)"Maternal Mortality" and "Indonesia" was carried out. The search was limited to the period of the years 2000 to 2014. Secondary literature was included if those references fulfilled the inclusion criteria. In addition, resources in Indonesia (especially governmental) supplemented the evaluation of the available data.

## Data extraction

All reports that were suitable for detailed review were analyzed regarding the following information.

- Type of data acquisition
- Whole coverage versus selected population
- Direct or indirect measurement
- Methods of data assessment and aggregation
- Inclusion of cofactors

## Validation and comparability

To evaluate the reported data, their inter–observer and longitudinal comparability for all selected publications the following aspects were considered.

- Representability of data
- Potential selection bias
- Reliability of obtained data
- Reproducibility of maternal mortality indicators

## Search for publications and reports

With respect to the review of literature, DIMDI and PubMed were searched, with DIMDI accessing approx. 30 international databases, such as MEDLINE, EMBASE, SciSearch and Cochrane Library. In doing so, a total of 262 publications were identified, 56 relevant publications of which found in PubMed. Sub-

sequently, titles and abstracts were read, while relevant literature was further investigated by reading and analyzing the full text.

Numerous publications could be found in both DIMDI and PubMed, and identical writings were identified and collated. Apart from methodically searching the above–mentioned databases, a non–systematic search was carried out, reviewing the results of the methodical literature search by snowball procedure. In doing so, another nine publications were determined. Accordingly, a total of 327 abstracts were identified. Five publications were considered after the selection.

## RESULTS

As shown in **Table 1** it is evident that different data and methods for maternal mortality calculations in various primary reports were applied. This resulted in variations of the reported MMR for 1990: 253–446/100 000, for 2000: 265–420/100 000 and for 2010: 165–346/100 000. In addition, the "Indonesian Demographic and Health Surveys" (IDHS) in 2012 even reported 359/100 000 [14]. Subsequently, the identified primary data reports will be described.

At national level, household IDHS survey data could be identified. Data acquisition of maternal mortality was done as "sister's survey". To receive different records on the maternal mortality, siblings of surviving relatives were interviewed using a detailed questionnaire about surviving relatives of all living born children of the questioned mother. The MMR in 1997 IDHS was 390/100 000. Unpublished analysis of data from the IDHS show a slight decline to 334/100 000 births for the period 1993–1997. Subsequent surveys showed further declined MMR until 2007 (228/100 000), but a subsequent increase in 2012 to 359/100 000 [7]. According to the authors, IDHS suffer from selection bias and high confidence intervals

**Table 1.** Reported MMR data for Indonesia since 1990

| Author | Title | 1990 | 1995 | 1997 | 2000 | 2002 and 2003 | 2005 | 2007 | 2008 | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Statistics Indonesia; National Population and Family Planning Board; Ministry of Health | Demographic and Health Surveys (Indonesia), 1987, 1991, 1994, 1997, 2002–2003, 2007 and 2012 | | | 390 | | 307 | | 228 | | | | 359 | |
| MMEIG (WHO, UNICEF, UNFPA and The World Bank) | Trends in Maternal Mortality, 1990–2008,1990–2010, 1990–2013 (data for 2013) | 430 | 360 | | 310 | | 250 | | | | | | 190 |
| United Nations | The Millennium Development Goals Report, 2008, 2009, 2010, 2011, 2012, 2013, 2014 (data for 2014) | 446 | 326 | 299 | 265 | 241/231 | 212 | 190 | 181 | 165 | 156 | 148 | 140 |
| Central Bureau of Statistics (BPS) of Indonesia | Sensus Penduduk, 2010 | | | | | | | | | 346 | | | |
| Harvard Center for Population and Development Studies (Hill et al.); 2007 [9] | Estimates of maternal mortality worldwide between 1990 and 2005: an assessment of available data | | | | 420 | | | | | | | | |
| Institut für Health Metrics and Evaluation (Hogan et al.); 2010 [10] | Maternal mortality for 181 countries, 1980—2008: a systematic analysis of progress toward Millennium Development Goal 5 | 253 | | | 290 | | | | 229 | | | | |
| Institut für Health Metrics and Evaluation (Lozano et al.) 2011 [11] | Progress toward Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis | 404 | | | 333 | | | | | | 248 | | |
| Institut für Health Metrics and Evaluation (Kassebaum, et al.); 2014 [12] | Global, regional, and national levels and causes of maternal mortality during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013 | 368 | | | | 262 | | | | | | | 199 |
| Ronsmans et al.; 2008 [13] | Professional assistance during birth and maternal mortality in two Indonesian districts | | | | | 435 | | | | | | | |

of the survey data. However, the general increased rate of reported adult female mortality in Indonesia appears to be consistent with this MMR increase. One important selection bias should be considered due to the fact that until 2007 only married women were questioned, but in 2012 unmarried women were also interviewed. In addition, in 2007 siblings of both genders were included whereas in 2012 only female siblings were interviewed. According to these primary data from the period 1993–1997 to 2012 the annual rate of reduction (ARR) would only be 0.4%.

At supranational level two reports were raised by the United Nations. The "Trends in Maternal Mortality" reports are a number of analyses published by the WHO, UNICEF, UNFPA, the World Bank and United Nations [15]. Headed by the Maternal Mortality Estimation Group (MMEIG) maternal mortality estimates were developed [16]. In 2008 and 2010 included countries have been classified into groups A – C according to the availability and quality of maternal mortality data to evaluate estimation methods of MMR for each country. Countries which had data from civil registration systems were classified as Group A (countries with no available national–level data on maternal mortality) and B (countries that lack complete registration systems but for which other nationally representative data are available for measuring maternal mortality) whereas group C consists of countries for which multi–level regression models were applied for lack or incomplete registration data. This model uses socioeconomic information including fertility, birth attendants and Gross Domestic Product (GDP) as well as available national maternal mortality data. Nearly half of all countries including Indonesia belong to group B. Therefore, in this critical overview the authors consider Indonesia as example of the majority of threshold countries. Only data from IDHS until 1994, from 2002 to 2003, 2007 and 2012 were used. This is in line with the data limitations, modeling assumptions and quit large uncertainty intervals around global maternal mortality estimates that have been recognized by MMEIG [17].

The MDG Reports are based on a set of comprehensive official statistics compiled by the Inter–Agency and Expert Group (IAEG) on MDG indicators led by the Statistics Division of the Department of Economic and Social Affairs [18]. The reports use population adjusted means of official data provided by governments, international agencies and, if available, Demographic and Health Surveys. Transparency of data resources is ensured by IAEG (http://mdgs.un.org), but data quality relies on national publication policies. For South East Asia apart from Indonesia, the following countries are summarized in Southeast Asia: Brunei Darussalam, Cambodia, Lao People's Dem Republic, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor–Leste. For Indonesia the web–based publication refers to data and rather methodology of the WHO's report "Trends in maternal mortality" [IAEG]. The UN's ARR being at –4.9% between 1990 and 2013 is higher than the decline obtained by MMEIG (–3.5%) during the same period.

"Sensus Penduduk" (SP) is a national census and grasps socioeconomic and demographic information like age, religion, impediment, ethnic origin, language, migration, education, marital status, employment, fecundity, mortality and residential facilities of the population. SP results in 2010 are still incompletely published, originally reporting MMR of 259/100 000 live births, after recalculation being 346 per 100 000 live births [19,20].

Using Cochrane search strategy five additional publications could be found (**Table 2**). However, these publications do not contain primary data and include multinational summaries. For Indonesia different types of data were considered reaching from siblings' surveys, case-control studies and estimations. Different types of calculations were used and indicators were also not comparable throughout the reports.

Hill et al. utilized a number of different data records to generate an estimate for 125 countries, and international sources (local data collections) as well as WHO, UNICEF, UNFPA information and further national sources were considered. In 2005, there were an estimated 402 global maternal deaths in 100 000 live births (confidence interval CI 216–654). They applied a concept similar to MMEG's: According to availability and quality of the data (civil registration or complete registration of deaths, direct sisterhood or reproductive age mortality surveys, estimates based on sample registration, population census or empirical data), countries were classified into eight groups (A to H). In groups C, F and H, maternal mortality was assessed according to the PDMF. The acquisition period was 1985 to 2005. Indonesia as well as another 27 countries with incomplete data records were rated group C. Via statistical models, the MMR for Indonesia for the period 1998 – 2003 was estimated 420 (240–600)/100 000 [9]. Many threshold countries, such as India, Brazil, Egypt, and few southeast countries, among others, belong to groups C–E where at least limited primary data were available. Indonesia may serve as example for these kind of countries regarding data availability.

The estimates of Hogan et al. showed large differences compared to Hill et al. These authors already pointed out their different methods, such as larger database and a systematic search for references resulting in consideration of DHS data, WHO estimates and two subnational verbal autopsies. Their assessment was

**Table 2.** Results of Cochrane–based data evaluation

| Author | Title | Number of countries | Number of data | Data used from Indonesia | Period | Method | HIV | Statistical calculate model |
|---|---|---|---|---|---|---|---|---|
| Hill et al.; 2007 [9] | Estimates of maternal mortality worldwide between 1990 and 2005: an assessment of available data | 125 | 858 | 63 sisterhood studies for group C | 1985–2005 | PMDF | yes | random–effects time–series regression model for group A+B; for the groups C until H a model of PM with 2 coefficients |
| Hogan et al.; 2010 [10] | Maternal mortality for 181 countries, 1980—2008: a systematic analysis of progress toward Millennium Development Goal 5 | 181 | 2651 | 2 verbal autopsies, 5 sibling histories, 4 WHO estimates | 1980–2008 | PMDF | yes | Linear model an spatial–temporal local regression with 6 covariates |
| Lozano et al.; 2011 [11] | Progress toward Millennium Development Goals 4 and 5 on maternal and child mortality: an updated systematic analysis | 187 | 3793 | 9 verbal autopsies, 8 survey/census, 60 sibling histories | 1980–2011 | MMRatio | yes | Linear model an spatial–temporal local regression with 11 covariates |
| Kasse-baum, et al.; 2014 [12] | Global, regional, and national levels and causes of maternal mortality during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013 | 188 | 7065 | 3 verbal autopsies, 6 IDHS, 2 surveys/census | 1980–2013 | MMRatio | yes | Codem–Model with 9 covariates |
| Ronsmans et al.; 2008 [13] | Professional assistance during birth and maternal mortality in two Indonesian districts | | | Sample: 458 cases, 1234 controls | 01/2004 – 12/2005 | MMRatio | no | Capture–recapture method |

based on a two–step regression model considering various covariates (total fertility rate, GDP per capita, HIV sero–prevalence, neonatal mortality, age–specific female education, skilled birth attendance) and indicators for 5–year age groups [10].

Lozano et al. apply a concept similar to Hogan, but included more data and observations, such as 60 sibling histories that are roughly comparable with 5–year intervals in IDHS surveys. They included more covariates (age–specific fertility rate, in–facility delivery, total fertility rate, skilled birth attendance, antenatal care coverage, female education by age, HIV prevalence, health system access, neonatal death rate, malnutrition, income) for their linear regression with random effects by country or as the mean function in a Gaussian Process Regression [11].

Kassebaum et al. applied the most extensive study, but for Indonesia these authors used a smaller data set compared to Lozano et al. [11]. Continuing the concept of Lozano et al. they used the Cause of Death Ensemble model (CODEm) to model maternal mortality and considered 9 covariates (age–specific fertility rate, total fertility rate, age–standardized HIV death rate for female individuals aged 15–49 years, neonatal death rate, GDP per person, proportion of deliveries occurring in facilities, proportion of deliveries overseen by skilled birth attendants, coverage of four visits of antenatal care, and malnutrition in children younger than 5 years) [12]. The calculated decline in MMR was comparable for Lozano et al. (ARR 1990–2011: –2.4%) and Kassebaum et al. (ARR 1990–2013: –2.6%).

In contrast to the other model–based MMR estimations Ronsmans et al. carried out a regional case-controlling study with a randomly selected 458 cases and 1.234 controls. This group reported a MMR of 435/100 000 with large differences between rural regions (706/100 000) and urban areas (232/100 000). The authors, however, already discussed some advantages and limitations of their effort to gain retrospective primary data. The quality of delivery documentation may be inaccurate. However, this limitation they considered less relevant in Indonesia, where birth attendants are usually midwives or physicians compared to countries with usually traditional birth attendants. MMR estimates produced by the capture–recapture method used in this evaluation are likely to be less biased than crude death counts regarding missing events. Finally, the applied asset–based classification of the population into wealth quartiles may not overlap with the governmental method the government uses to stratify population cohorts [13].

## Discussion

In this review we systematically analyzed the available data about maternal mortality in Indonesia as an example to validate the achievements regarding the Millennium Goals of the UN. **Figure 1** shows how different the data of the MMR are.
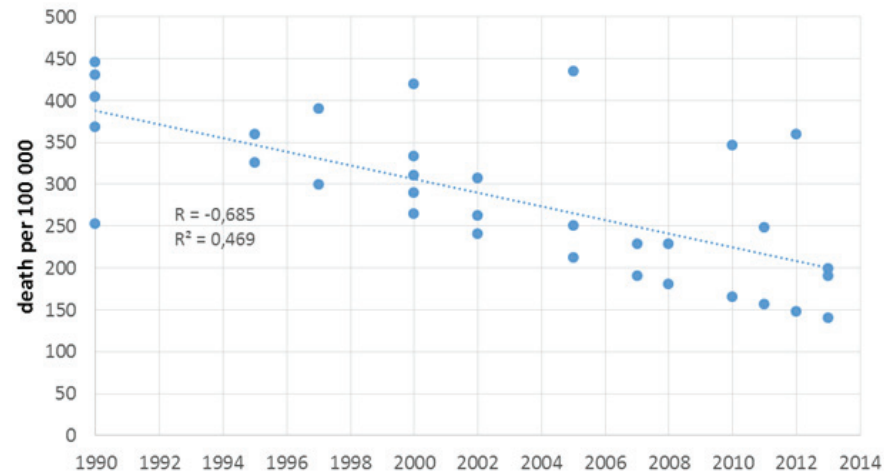
**Figure 1.** Time course of reported MMR data. Due to the very limited amounts of investigations confidential intervals are not calculated. An overall sufficient trend line can be estimated, but variability of data are remarkable.

Taken together the very limited amount of available primary data, their overall data quality, heterogeneity in data acquisition, selection biases, variability in data evaluation and calculation methods as well as lack of sufficient reporting intensively limit evidence based evaluation of the maternal mortality throughout the MDG time frame. Going back to the acquired primary data it became clear that for Indonesia, and very likely for most of developing and threshold countries, reliable estimations of MMR or comparable indicators remains difficult.

Almost all authors use the IDHS–Data for their calculation which has shown to have limitations. Furthermore, due to low frequencies of maternal deaths and the sample size used for DHS surveys standard errors were high for estimates leading to volatile maternal mortality indicators. In addition, the majority of non–sampling errors were also rather under– than overestimated [21,22]. Therefore, reported MMR seem to be not suitable for controlling achievement of MDG targets. Primary data and subsequent maternal mortality models suffer from many restrictions, random and systematic errors resulting in very high uncertainty internals that are most prominent in threshold countries, such as in Southern Asia and Oceania.

However, with exception of one outlier in 2012 the overall correlation coefficient of $R = -0.685$ ($R^2 = 0.469$) seems to support an estimation of the development over time (**Figure 1**). The applicable ARR of the respective data which could be used has been shown in **Table 3**. The ARR obtained by the different data resources is highly variable between 0.6% and 4.9%, but the obtained linear regression of all identified MMR data provides an assumption of an $ARR = -2.8\%$ for the whole period of 1990–2014. This regression with an overall reduction of about 50% during the MDG period is in line with the recently published estimates by the UN Maternal Mortality Estimation Inter–Agency Group [16]. Considering these results Indonesia belongs to the vast majority of countries that have been grouped into the medium achievers by the WHO group that made significant progress but did not fully reach initial reduction goals.

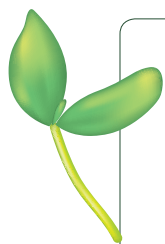**Table 3.** Calculation of annual rate of reduction (ARR) as published in available reports*

| Author/Source | MMR | | | | ARR | Years |
|---|---|---|---|---|---|---|
| | 1990 | 2008 | 2011 | 2013 | | |
| MMEIG | 430 | | | 190 | –3.5% | 1990–2013 |
| UN | 446 | | | 140 | –4.9% | 1990–2013 |
| Hogan et al.; [10] | 253 | 229 | | | –0.6% | 1990–2008 |
| Lozano et al.; [11] | 404 | | 248 | | –2.4% | 1990–2011 |
| Kassebaum et al.; [12] | 368 | | | 199 | –2.6% | 1990–2013 |
| Overall regression | | | | | –2,8% | 1990–2013 |

MMEIG – Maternal Mortality Estimation Group, UN – United Nations

*Overall regression was done using all identified data (compare with Figure 1).

Data availability with sufficient coverage of the regions and data quality including standardized reporting formats remain a key issue for a sufficient evaluation of maternal mortality in these countries. Central population statistics with information about births, deaths and causes of death are obligatory data requirements for the improvement of the health care systems. To build up such databases suitable reporting systems, such as web–based solutions or other types of online reporting and telemedicine may provide achievable ways for developing and threshold countries. In addition, capture–recapture sampling has been recommended as reliable technique to obtain MMR estimates for Indonesia and comparable countries [23], but as a survey alternative it also lacks complete coverage of the whole country and maternal mortality cases resulting in high potential sampling errors [16]. We would therefore not consider this method as alternative for the required data quality, especially in the clinically required context. Therefore, the health care policy conclusions drawn by the UN Maternal Mortality Estimation Inter–Agency Group towards clinical efforts to extent achievements of the MDG into a Sustainable Development Goal (SDG) should be broadened with inclusion of efforts to improve health care reporting systems. For example, according to current plans of the "Indonesian Ministry of Foreign Affairs" a central registration system shell be implemented in Indonesia until 2024 [24]. Nevertheless, these data are of considerable relevance for the development of care structures for the improvement of the maternal health but need to be complemented with a basic data set for the delivery process including pre–, peri– and postpartal indicators. Only these types of data would enable detailed conclusions about required actions to achieve SDGs.

Valid data about important cofactors, such as age at delivery of the mothers, number of the exemptions (experience of the obstetric institution), cause of death, etc. are necessary for the improvement of the maternal health and to carry out suitable measures for the medical care development according to the real local/regional/national requirements.

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# Evolving treatment implementation among HIV–infected pregnant women and their partners: results from a national surveillance study in Italy, 2001–2015

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**Background** The current global and national indications for antiretroviral treatment (ART, usually triple combination therapy) in adolescent and adults, including pregnant women, recommend early ART before immunologic decline, pre–exposure chemoprophylaxis (PrEP), and treatment of HIV–negative partners in serodiscordant couples. There is limited information on the implementation of these recommendations among pregnant women with HIV and their partners.

**Methods** The present analysis was performed in 2016, using data from clinical records of pregnant women with HIV, followed between 2001 and 2015 at hospital or university clinics within a large, nationally representative Italian cohort study. The study period was divided in three intervals of five years each (2001–2005, 2006–2010, 2011–2015), and the analysis evaluated temporal trends in rates of HIV diagnosis in pregnancy, maternal antiretroviral treatment at conception, prevalence of HIV infection among partners of pregnant women with HIV, and proportion of seronegative and seropositive male partners receiving antiretroviral treatment.

**Results** The analysis included 2755 pregnancies in women with HIV. During the three time intervals considered the rate of HIV diagnosis in pregnancy (overall 23.3%), and the distribution of HIV status among male partners (overall 48.7% HIV–negative, 28.6% HIV–positive and 22.8% unknown) remained substantially unchanged. Significant increases were observed in the proportion of women with HIV diagnosed before pregnancy who were on antiretroviral treatment at conception (from 62.0% in 2001–2005 to 81.3% in 2011–2015, $P<0.001$), and in the proportion of HIV–positive partners on antiretroviral treatment (from 73.3% in 2001–2005 to 95.8% in 2011–2015, $P=0.002$). Antiretroviral treatment was administered in 99.1% of the pregnancies that did not end early because of miscarriage, termination, or intrauterine death, and in 75.3% of those not ending in a live birth. No implementation of antiretroviral treatment was introduced among male HIV–negative partners.

**Conclusions** The results suggest good implementation of antiretroviral treatment among HIV–positive women and their HIV–positive partners, but no implementation, even in recent years, of Pre–Exposure Prophylaxis (PrEP) among uninfected male partners. Further studies should assess the determinants of this occurrence and clarify the attitudes and the potential barriers to PrEP use.

The recent global HIV guidelines expanded the use of antiretroviral treatment (ART) to include early ART before immunologic decline, pre–exposure chemoprophylaxis (PrEP), and treatment of HIV–negative partners in serodiscordant couples [1–3]. All these situations apply to women with HIV who are planning a pregnancy or are already pregnant, and to their partners. An effective implementation of these measures is necessarily dependent on knowledge of HIV status in both partners, and a good implementation of HIV diagnosis is necessary to ensure effectiveness in the "cascade" process that link different steps of diagnosis and care of HIV (testing, implementation of treatment, adherence with treatment, effective suppression of viral load) [4]. If both the woman and the partner are infected, both should be on treatment according to the expanded indications of the new guidelines, irrespective of the level of immunological deterioration. Treatment is however also now recommended, although less stringently, for the HIV–uninfected male partners of HIV–positive women. In this context, it is important to quantify to what extent the new guidelines on treatment of HIV positive pregnant women and their HIV positive partners, or PrEP among HIV–negative partners in serodiscordant couples is implemented. In order to quantify this, we used data from a large national cohort of pregnant women with HIV to explore temporal trends in the proportion of HIV diagnoses that occurred in pregnancy, maternal antiretroviral treatment at conception, prevalence of HIV infection among partners of HIV positive pregnant women, and proportion of seronegative and seropositive male partners receiving antiretroviral treatment.

## METHODS

Data from the Italian National Program on Surveillance of Antiretroviral Treatment in Pregnancy were used [5]. This is an ongoing observational study established in Italy in 2001, which covers, based on available prevalence data [6], roughly 30–40% of live births from women with HIV in Italy. Site participation is voluntary, and at present is based on more than 30 clinicians reporting from Obstetrics, Infectious Diseases, and Paediatrics departments across the country. Only HIV–positive pregnant women are included, and treatment of HIV infection is decided by the treating physician, usually according to national guidelines. Laboratory and clinical data are collected from hospital records, following the women's consent based on a patient information sheet approved by the competent Ethics Committee. Information and measurements are collected at routine pregnancy visits, at delivery, and during a follow–up of mothers and newborns for up to 18 months. Timing of HIV diagnosis is calculated using the date difference between HIV diagnosis and last menstrual period. Gestational age at birth is determined on the basis of the last menstrual period, ultrasound biometry, or both. Information on HIV status of the partners is based on women's report. Women provide consent based on a patient information sheet approved by the competent Ethics Committee (deliberation 578, September 28, 2001, I.N.M.I. Lazzaro Spallanzani Ethics Committee, Rome). For the current analysis, all pregnancies with available date of HIV diagnosis were considered eligible. The study period (2001–2015) was divided in three intervals of five years each (2001–2005, 2006–2010, 2011–2015), and temporal trends were analyzed using the chi–square test for trend. $P$ values <0.05 were considered significant. All statistical analyses were performed with the SPSS software, version 22 (IBM Corp, released 2013, Armonk, NY, USA).

## RESULTS

As of 19 August 2016, 2755 pregnancies in HIV–infected women had available information and were included in the analyses. The temporal trends are summarized in **Table 1**. Across the three time periods studied, the rate of HIV diagnosis in pregnancy remained stable (overall: 643/2755, 23.3%), with no significant changes over time ($P = 0.908$). Conversely, the proportion of women with HIV diagnosed before pregnancy who were on ART at conception increased significantly from 62.0% in 2001–2005 (557/899), to 81.3% (312/384) in 2011–2015 ($P < 0.001$). Subsequent ART coverage in pregnancy was roughly universal, involving 99.1% (2306/2326) of the pregnancies that did not end early because of miscarriage, termination, or intrauterine death (proportion on ART in this group with no live births: 75.3%, 235/312).

The distribution of HIV status of male partners remained substantially unchanged during the entire period (overall: 48.7% HIV–negative, 28.6% HIV–positive and 22.8% unknown). None of the HIV–negative partners received antiretroviral treatment during the entire time of observation, while the proportion of HIV–positive partners receiving treatment increased significantly from 73.3% in 2001–2005 to 95.8% in 2011–2015 ($P = 0.002$, **Table 1**).

**Table 1.** Temporal trends in HIV and treatment status of mothers and partners (2001–2015)

|  | 2001–2015 | 2001–2005 | 2006–2010 | 2011–2015 | P VALUE* |
|---|---|---|---|---|---|
| **Diagnosis of HIV in current pregnancy (%)** | 23.3 (643/2755) | 22.9 (268/1172) | 24.2 (261/1079) | 22.6 (114/504) | 0.908 |
| **Mothers on treatment at conception (%):** | | | | | |
| Overall | 51.8 (1414/2728) | 47.8 (557/1166) | 51.0 (545/1068) | 63.2 (312/494) | <0.001 |
| HIV known before pregnancy | 67.6 (1414/2093) | 62.0 (557/899) | 67.3 (545/810) | 81.3 (312/384) | <0.001 |
| **HIV status of the partner† (%):** | | | | | |
| HIV–positive | 28.6 (593/2077) | 29.4 (262/892) | 28.3 (228/807) | 27.2 (103/378) | 0.423 |
| HIV–negative | 48.7 (1011/2077) | 50.4 (450/892) | 46.0 (371/807) | 50.3 (190/378) | 0.562 |
| Unknown | 22.8 (473/2077) | 20.2 (180/892) | 25.8 (208/807) | 22.5 (85/378) | 0.120 |
| **HIV–positive partners on treatment† (%)** | 77.0 (291/378) | 73.3 (121/165) | 71.8 (102/142) | 95.8 (68/71) | 0.002 |
| **Guidelines recommendations for treatment in pregnancy** | | Recommended (usually mono–or dual therapy) | Recommended (combination therapy) | Recommended (combination therapy) | |
| **Guidelines recommendations for treatment in all HIV–infected individuals** | | <200–350 CD4 or symptomatic disease | <350–500 CD4 or symptomatic disease | Progressive shift to any CD4 level | |
| **Guidelines recommendations for treatment in HIV–negative partners** | | Not recommended | Not recommended | PrEP (since 2012) | |

*$\chi^2$ for trend.
†Women with HIV infection diagnosed before pregnancy only. No HIV–negative partner was receiving anti–HIV treatment across the entire period of observation.

## CONCLUSION

This analysis provided information on several aspects of the cascade of HIV diagnosis and treatment among pregnant women with HIV and their partners that can be relevant for health care providers. At first, we showed a stable rate of HIV diagnosis during pregnancy in the last 15 years. Although this rate (23%) is similar or even lower compared to other national and international studies [7,8], this suggests no improvement in the proportion of cases in which HIV infection was already known before pregnancy, a condition that represents the target for an optimal management of pregnancy. Similarly, no temporal changes were observed in the distribution of HIV status of the partners, with roughly half of the pregnancies occurring in a context of HIV–serodiscordant couples (with an HIV–uninfected male partner), and no less than 20% of cases (overlapping the proportion of maternal HIV diagnosis in pregnancy) characterized by an unknown HIV status of the partner, suggesting frequent occurrence of no HIV testing for both members of the couple before pregnancy. These findings indicate that there is still the need to improve the rate of HIV testing among people of child-bearing age through information campaigns and facilitated access to testing and prenatal counselling services. Such services should be targeted not only to women who are planning pregnancy or who present in early pregnancy, but also to their partners. This not only would improve management of pregnancy but also clinical HIV outcomes.

The analysis of temporal trends showed significant improvements in treatment coverage in the population with HIV already known before pregnancy. In 2011–2015, more than 80% of the women diagnosed before pregnancy were on treatment at conception, and almost all their HIV–positive partners (95.8%) were receiving ART. These figures indicate good implementation of the expanded indications to ART among people with HIV in Italy, confirming a good response to the recent guidelines that have progressively expanded the indication to treatment to any person with HIV, irrespective of the level of immune deterioration [1,2,9,10]. A wide effort is ongoing worldwide to ensure equal access to antiretroviral treatment to all infected people, with the aim to obtain the 90–90–90 target (90% diagnosed, 90% treated and 90% virally suppressed), and ultimately end the HIV/AIDS epidemics by 2030. Encouraging results have been achieved, even in countries with lower resources, with more than 17 millions of people on antiretroviral treatment in 2016, although large disparities exist between countries [4]. Current challenges in this pathway involve reaching and diagnosing the millions of people who do not know that they have HIV, and effectively retaining in care those who start ART, in order to achieve a prolonged viral suppression [11].

Even more challenging may be providing treatment as prophylaxis to HIV–uninfected partners. In our study, none of the HIV–uninfected males in the serodiscordant couples, even in recent years, received antiretroviral treatment as a potential prophylaxis against HIV transmission. The absence of

any PrEP among uninfected males indicates no implementation of the recently recommended use of antiretroviral treatment as a preventive measure in uninfected partners. We are unable to define the possible basis for this occurrence, that may include preference for barrier methods compared to antiretroviral treatment as preventive measures against HIV transmission in sexually active serodiscordant couples, with use of self–insemination techniques (in which the woman inserts semen into the vagina herself, without medical intervention) when attempting to conceive. The implementation and efficacy of guidelines may be affected by several factors that influence the attitudes of both health care providers and people with HIV. The efficacy of PreP, in particular, is conditioned by adherence, perceived level of HIV risk, and access and availability of health services [12]. All these factors may show important differences among male and female heterosexuals, sex workers, men who have sex with men, and injection drug users [13,14]. Several studies have shown the difficulty to enrol partners of HIV–infected pregnant women into programs of HIV testing and care [15,16]. Our results indicate the need for further studies that investigate the potential barriers to PrEP implementation in uninfected partners of HIV–infected women, including the specific attitudes and expectations on PrEP use among prescribing physicians and people with HIV.

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PAPERS

PAPERS

# Increasing use of mental health services in remote areas using mobile technology: a pre–post evaluation of the SMART Mental Health project in rural India

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**Background** About 25% of the Indian population experience common mental disorders (CMD) but only 15–25% of them receive any mental health care. Stigma, lack of adequate mental health professionals and mental health services account for this treatment gap, which is worse in rural areas. Our project evaluated task shifting and mobile–technology based electronic decision support systems to enhance the ability of primary care health workers to provide evidence–based mental health care for stress, depression, and suicidal risk in 30 remote villages in the state of Andhra Pradesh, India.

**Methods** The Systematic Medical Appraisal Referral and Treatment (SMART) Mental Health project between May 2014 and April 2016 trained lay village health workers (Accredited Social Health Activists – ASHAs) and primary care doctors to screen, diagnose and manage individuals with common mental disorders using an electronic decision support system. An anti–stigma campaign using multi–media approaches was conducted across the villages at the outset of the project. A pre–post evaluation using mixed methods assessed the change in mental health service utilization by screen positive individuals. This paper reports on the quantitative aspects of that evaluation.

**Results** Training was imparted to 21 ASHAs and 2 primary care doctors. 5007 of 5167 eligible individuals were screened, and 238 were identified as being positive for common mental disorders and referred to the primary care doctors for further management. Out of them, 2 (0.8%) had previously utilized mental health services. During the intervention period, 30 (12.6%) visited the primary care doctor for further diagnosis and treatment, as advised. There was a significant reduction in the depression and anxiety scores between start and end of the intervention among those who had screened positive at the beginning. Stigma and mental health awareness in the broader community improved during the project.

**Conclusions** The intervention led to individuals being screened for common mental disorders by village health workers and increase in mental health service use by those referred to the primary care doctor. The model was deemed feasible and acceptable. The effectiveness of the intervention needs to be demonstrated using more robust randomized controlled trials, while addressing the issues identified that will facilitate scale up.

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Mental disorders is a major global public health problem and accounts for 8.5% of the total years of life lost due to premature death and years lived with disability globally [1]. Between 13–50% of Indians suffer from common mental disorders (CMD) such as depression, stress and suicidal risk [2], but majority receive little or no care, with estimates from low– and middle–income countries (LMICs), such as India, suggesting that only 15–25% of affected individuals receive any treatment for their mental illness [3], resulting in a large 'treatment gap'. The reasons for this gap are numerous, but include poor awareness about mental health, personal and community stigma related to mental illness and help seeking, lack of appropriate mental health services and trained mental health professionals [4,5]. Treatment gaps are more in rural populations [6], especially in Scheduled Tribe (ST) communities in India, which have particularly poor infrastructure and resources for health care delivery in general, and almost no capacity for providing mental health care.

The ST communities are identified as culturally or ethnographically unique by the Indian Constitution. They are populations with poorer health indicators and fewer health care facilities compared to non–ST rural populations, even when within the same state [7], and often live in demarcated geographical areas known as ST areas. In Andhra Pradesh, the state where the current study is based, infant mortality rate in ST areas and non ST areas was 94.1 and 54.0, respectively; and under–5 mortality rate was 112 and 63.2, respectively [7]. Primary health care systems in ST areas are similar to those available in other rural areas with a tiered model involving sub–centers, primary health centers (PHCs) and district hospitals. Non–physician health care workers, called Accredited Social Health Activists (ASHAs), are a key resource for providing health care in rural settings. These female health care workers are community members with an average of 8–10 years of formal education, who mainly focus on maternal and child health by visiting households regularly and systematically. Each ASHA is responsible for about 1000 villagers. Primary care doctors are in–charge of the activities of a PHC which covers 20 000–30 000 population. They provide primary health care and refer any condition that they cannot manage, including mental disorders, to the next level of care at district hospitals.

One way to reduce treatment gap is by addressing the lack of trained mental health professionals in rural areas by using task shifting and training primary care health workers in the villages to manage CMD. A systematic review found that task shifting involving non–physician health workers is beneficial for a number of chronic conditions including mental disorders [8]. The process can be facilitated by using screening and management protocols that could be used by them easily. Task shifting for ASHAs and primary care doctors involve training and provision of basic skills to identify and manage CMD, which otherwise would have been the responsibility of trained mental health professionals. Task shifting for ASHAs involves training on concepts about mental health and screening for CMD; and providing skills in basic mental health care. Task shifting for primary care doctors involve training in interviewing, diagnosing, and managing CMD using standardized guidelines and algorithms.

Integrating standardized protocols into algorithm based electronic decision support systems (EDSS) could facilitate task shifting, by making the protocols easier to administer. A number of systematic reviews have outlined the effectiveness of EDSS to deliver appropriate health care [9–13]. Computer–based decision support systems are effective in bringing about positive change [14], and provision of individualised recommendations using an EDSS have been found to be useful [12]. Mobile technology based EDSS using commercial mobile networks leverages the increasing penetration of mobile phones across India, including rural India, increasing 3G connectivity that allows faster data sharing, and availability of cheaper smart phones/tablets. Prior research has highlighted the use of mHealth in communicable diseases and maternal and child health, but its research on use in mental illness is limited [15].

Another way to reduce treatment gap and increase demand for mental health services is by increasing knowledge about mental health and reducing stigma related to mental illness and help–seeking [4,5,16]. Research has shown that interventions especially those involving social contact with people with mental illness are effective in reducing stigma [17,18].

This paper reports on a "proof of concept" project – Systematic Medical Appraisal Referral and Treatment (SMART) Mental Health project – conducted in rural Andhra Pradesh, India. The project used task shifting supported by a mobile technology based mental health services delivery model for screening, diagnosing, and managing CMD. A campaign to increase mental health awareness and reduce stigma related to mental health and help–seeking was also implemented as part of the intervention. The aim was to ascertain the acceptability, feasibility and preliminary impact of the intervention, specifically on mental health services use, using mixed evaluation methods. This paper focuses on the key quantitative results.

# METHODS

The methods used have been outlined earlier [19], and are summarized below.

## Objectives

The project had two key objectives:

1. The development of a multifaceted intervention using training, task shifting, and mobile–based decision support to increase the screening and referral of individuals with CMD in one area of rural Andhra Pradesh.

2. To evaluate the feasibility and acceptability of the intervention amongst community members, health workers, and other stakeholders, and document preliminary evidence and lessons learned about the intervention for future study and scale up.

The primary outcome of the evaluation was to assess the change in proportion of mental health services use by individuals who were suffering from CMD. Other quantitative outcomes included changes in depression and anxiety scores, number of individuals screened, and number of screen positive individuals referred to the primary care doctor. The feasibility and acceptability of the intervention including process evaluation were assessed using qualitative interviews conducted at post–intervention, and will be reported separately.

## Site

The project was implemented in 30 villages associated with two PHCs, located in an ST area of the West Godavari district of Andhra Pradesh. All villages served by the PHCs were listed and a random selection of 15 villages from each PHC was made. The eligibility criteria for selecting villages were that all villages should have ASHAs and the population should be proportionate to the number of ASHAs. One village with a population >3000, was replaced by another one with a smaller population, keeping in mind that the average population was ~400. The main source of livelihood was farming. In Andhra Pradesh, 5.5% of the total population belong to ST communities. The West Godavari district of Andhra Pradesh, where this project was conducted, has 3.4% ST population living in ST areas (http://aptribes.gov.in/statistics.htm), which are in the interior or more remote areas of the district. On extrapolating recent Census data from 2011 (http://censusindia.gov.in/pca/cdb_pca_census/Houselisting–housing–AP.html) and data collected through the government led Anganwadi program, more than two–third of the population belonged to the ST communities and other backward communities in the 30 villages.  All eligible adults ≥18 years of age who gave consent to participate, were able to understand the questions and instructions, and were not limited by any severe physical disorder from accessing mental health services were invited to participate.

## Duration

24 months, from May 2014 to April 2016.

## Ethical considerations

Ethics approval was received from the Independent Review Committee of the Centre for Chronic Disease Control, New Delhi, India. Informed written consent was obtained from all participants and data were collected according to the Declaration of Helsinki on ethical research. Approval for conducting the project was obtained from the Health Department, Government of Andhra Pradesh, and the Integrated Tribal Development Agency was informed about the project. Approval was also obtained from all the local village administrations. Data are reported as per STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for reporting observational studies [20].

## Development of the multifaceted intervention

### 1. Development of mobile technology based EDSS

A single screening and management algorithm was developed for use by the doctors and ASHAs. The screening tool used by ASHAs was based on standard screening tools – Patient Health Questionnaire (PHQ9) [21] and Generalized Anxiety Disorder questionnaire (GAD7) [22]. The diagnosis and management guidelines used by the doctors was based on the Mental Health Gap – Intervention Guide (mhGAP–IG) [23]. The system was developed on an OpenMRS platform and allowed clinical data to be shared between the ASHA and doctor using cloud computing. The algorithm and user interface were programmed

for use as an application on a 7 inch Android tablet. Both the PHQ9 and GAD7 provide diagnoses of mild/moderate/ severe levels of depression/anxiety based on scores 5–9, 10–14. ≥15, respectively [24]. Only scores ≥10 on either scale, or a positive response to the question on self–harm in the PHQ9, were considered as screen positive for this project. As anxiety is commonly associated with depression, GAD7 scores were also considered as indicative of depression. The tool for the ASHAs was developed in Telugu, whereas the mhGAP–IG tool was in English. The algorithms were developed for a mobile platform and finalized iteratively using simulated data. Subsequently, mock clinical data were validated against a psychiatrist's diagnosis. As a final step, the applications were tested in one village as part of a formative process, for user acceptability and identification of issues related to functionality [25].

### 2. Interactive voice response system (IVRS)

An algorithm based IVRS sent out pre–recorded messages to the screen positive individuals to continue care as advised by the ASHA or the doctor; and to the ASHAs and doctors to screen and followup individuals as per guidelines.

### 3. Stigma Reduction Campaign

A stigma reduction campaign was conducted at the outset to increase knowledge about mental health in the community and reduce stigma related to mental health. This was perceived as a key step to ensure that the services were availed and the importance of CMD was understood. The campaign's objective was to increase mental health knowledge and reduce stigma in the community, and was conducted for 8 weeks prior to the baseline survey across all villages. It included a number of strategies: sharing brochures and posters on mental health awareness and information with the community using a door–to–door campaign; showing a video of a person talking about his own mental illness and a video of a film actor talking about CMD; staging live performances or video recordings of a drama on mental disorder and help–seeking. Two instruments were used; the first was the Knowledge, Attitude and Behaviour about mental health instrument [26] and the second was Barriers to Access to Care Evaluation – Treatment Stigma Subscale (BACE–TS) [27]. They were administered at baseline and at post–intervention. They are a 16–item and 12–item questionnaire, respectively, with Likert type responses. Mean scores for each item can be calculated, with lower scores indicating lower knowledge and lower stigma, respectively.

## Demonstrating feasibility, acceptability and potential impact of the intervention

### 4. Baseline household survey (September – October 2015)

A baseline survey of the whole community (all households in all 30 villages) was conducted by trained interviewers using tablets. The survey enquired about socio–demographic details, stressors, social network, CMD, past history of mental disorders and its treatment, family history of mental disorders, and perceptions about stigma related to mental health.

### 5. Intervention (3 months– November 2015–January 2016)

Both ASHAs and PHC doctors were provided training on identification and management of CMD using EDSS. The ASHAs received classroom training from research staff for one week and then received additional supervised field training for an additional day, followed by feedback. The total period of training was 10 days. Concepts conveyed included mental health, CMD, treatment needs and a basic understanding about treatment modalities using medicines or counselling. Each doctor was trained individually by the Principal Investigator for one day and then additional support was provided to them by the field staff to sensitize them to the tablets and application. The doctors were trained using the mhGAP modules and were provided guidance on interviewing skills, diagnosis, and treatment guidelines. For both ASHAs and doctors, the research staff provided continued support and feedback on the tools over the whole course of the study on a needs basis. The ASHAs used the PHQ9/GAD7 to screen the population in their homes for CMD. They referred all those who screened positive to the PHC doctor. The doctor used another EDSS based on the mhGAP–IG tool to diagnose and manage those cases, either at PHCs or at health camps organized in villages. The mhGAP–IG tool provided the doctors a suite of recommended treatments for managing patients they diagnosed with CMD. The doctors followed those recommendations to provide treatment as needed. Health camps were organized in selected villages, so that patients could visit the doctor closer to home. The PHC doctor and ASHAs were available at this camp. The doctor not only saw patients with CMD, but also any other medical conditions. People from all neighbouring villages were asked to visit the health camp and ASHAs informed people screened positively for CMD about the time

and location of the camp. Individuals with severe mental disorders or any other complications were referred to mental health professionals at district hospitals. Treatment data were shared electronically between the ASHAs and the PHC doctors, and an algorithm–based mechanism helped ASHAs to plan follow–up schedules and prioritize individuals who needed prompt follow–up to ensure treatment adherence. The screen positive individuals, ASHAs and doctors also received IVRS messages to facilitate followup and treatment adherence. The project staff monitored the work of ASHAs and doctors and responded to any project or application specific problems faced by them.

*6. Post–intervention phase (February – March 2016)*

All screen–positive individuals identified by ASHAs were re–interviewed at the end of the intervention by trained interviewers, using a questionnaire. Process evaluation of the project was done using focus group discussions and in–depth interviews of key stakeholders – community members, ASHAs, primary care doctors, village leaders and field staff – to identify barriers and facilitators in implementing the project.

## Data management and statistical analyses

All data were captured electronically, encrypted and stored on secure servers at the George Institute office in Hyderabad. All tablets and servers were password protected. Data on tablets could be accessed by user defined login. Additionally all applications were locked by the administrator so that only data and applications relevant to the project were accessible to ASHAs and doctors, and once data were submitted by ASHAs or doctors it could be changed only by the administrator in case of any errors. All data were cleaned by the data management team. Most of the coding was predefined at the time of developing the electronic data capture tools by the software developers in consultation with the researchers. Further modifications, as per need, were made by researchers. Only de–identified data were shared with researchers for analyses.

## Sample size calculation

Villages in the ST areas are smaller in size compared to other rural villages in the West Godavari district; for 30 villages we estimated the population would be around 10 000. We anticipated that approximately 7500 individuals will be aged ≥18 years based on the demographic profile. Based on our extensive previous work, we expected a response rate of 75%, or about 5600 participants. It was conservatively estimated that about 15% of consenting participants at baseline will have a CMD as determined by the screening tools, representing approximately 850 individuals. Studies have estimated that in developing countries only 15–25% of those with severe mental disorders receive treatment, and these numbers are even less for CMD [4]. We conservatively assumed that 10% of individuals who screened positive will have sought medical care for mental disorders in the previous 12 months at baseline.

With these assumptions, a project involving 360 screen positive individuals would have 80% power at 2–tailed $\alpha = 0.05$, to detect a relative increase of mental health care utilization by as little as 30% (ie, from 10% to 13%) at follow–up. This further assumes up to 4% of discordant results between baseline and follow–up; that is, up to 0.5% who switch from utilizing services at baseline to no longer accessing services at follow–up. Other studies on provision of mental health services in primary care in India have found an intracluster correlation (ICC) of 0.03 [28]. After adjusting for the ICC and 30 clusters/villages a sample size of 545 individuals (on average 18 per cluster) was estimated to provide 80% power.

## Outcomes of interest

The proportionate change in mental health services use following intervention was the primary outcome. Depression and anxiety scores among those who had scored ≥10 (cut off score for screening positive) on either the PHQ9 or GAD7 at the beginning of the intervention were compared with their scores at post–intervention phases using paired t–test. The cluster impact (village as a cluster) was explored by adding village as a random effect to a mixed model of change from baseline anxiety and depression score.

## RESULTS

**Table 1** outlines the population base and participants screened at different phases of the project. Training was provided to 21 ASHAs and 2 PHC doctors in managing CMD.

The socio–demographic and basic health parameters of the 5167 individuals screened at baseline is presented in **Table 2**. There were 775 (15.0%) individuals with a score of ≥5 for either depression/anxiety,

**Table 1.** Population screened at different stages of the project

| STAGE OF PROJECT | POPULATION SCREENED AT EACH STAGE | N/N (%) |
|---|---|---|
| Total population in the villages | 10676 | – |
| Total adult population (≥18 year) | 8182 | 8182/10676 (76.6) |
| Baseline survey: | | |
| Adult population contacted during baseline survey | 7152 | 7152/8182 (87.4)* |
| Adult population screened at baseline following informed consent | 5167 | 5167/7152 (72.2)† |
| Population who "screened positive" at baseline | 339 | 339/5167 (6.6) |
| Screening at start of intervention: | | |
| Adult population screened by ASHAs during intervention | 5007 | 5007/5167 (96.9) |
| Adult population who 'screened positive' at intervention | 238 | 238/5007 (4.8) |

ASHAs – Accredited Social Health Activists

*Those not contacted had moved out of the village in search of seasonal jobs and none in the household could be identified.

†Reasons for not being screened were that even after 3 attempts they could not be contacted because they had temporarily moved out of the village and were unavailable; had died or were unwell; people less than 18 y were misclassified during the listing process as adults; 8 people refused.

corresponding to mild to severe depression/anxiety. At baseline, 200 (3.9%) individuals had a score of ≥10 on the depression/anxiety scale corresponding to moderate/severe types of depression/anxiety, and 224 had responded positively to the question on suicide. All individuals who screened positive were advised to seek medical care from the nearest doctor or health facility (as the intervention had not been deployed at this time). Family members of those who screened positive for suicide were specifically told about the risk and the need for seeking urgent medical care, after obtaining permission from the individual. Eighty–five (42.5%) individuals out of the 200 who had a score of ≥10 on the depression/anxiety scale, had responded positively to the question on suicide.

The commonest stressful events in the past year, associated with moderate or severe depression/anxiety, were suffering financial problems, suffering from major illness/injury either to self or loved ones, and death of loved ones (**Table 3**).

During the intervention, the ASHAs re–screened all eligible adults and identified 238 individuals (4.75%) as 'screen positive' (72.7% female). There were only 38 individuals who were commonly identified as screen positive at both the baseline survey by interviewers and screening done by ASHAs at the beginning of the intervention.
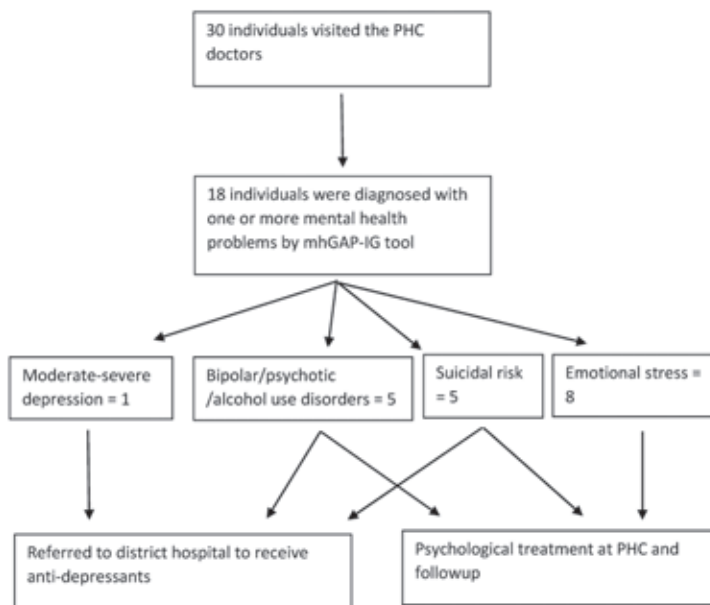


**Figure 1.** Final diagnosis of screen positive individuals and treatment provided.

Thirty of the individuals identified as screen positive by ASHAs visited a doctor, with 19 visiting camps and 11 visiting the PHCs. Of these, 24 (80%) were female. Eighteen of these 30 individuals were diagnosed with a confirmed mental health problem by the mhGAP–IG tool (**Figure 1**). Due to non–availability of anti–depressant medication, the individual with moderate depression was referred to the district hospital. Psychological therapy consisting of discussions on stressors, involving social networks, participating in pleasurable activities and work were provided to all individuals with emotional stress, 2 individuals with suicidal risk, and one with bipolar disorder. They were all asked to follow-up later to assess progress. Others were referred to the district hospital for specialist care. The ASHAs completed a follow–up visit for almost 80% of screen positive individuals.

Only 2 (0.8%) out of the 238 screen positive individuals had received mental health treatment in the past. The increase in mental health service use in this population was from 0.8% at the beginning of intervention to 12.6% at the end of intervention. Due to the small numbers, we had not adjusted for the clustering effect of villages for this analysis.

**Table 2.** Socio–demographic and health characteristics of baseline population (N = 5167)

| CHARACTERISTIC | BASELINE — N (%) |
|---|---|
| Gender: | |
| **Gender:** | |
| Female | 3026 (58.56) |
| Male | 2141 (41.44) |
| **Occupation:** | |
| Unorganized sector* | 3706 (71.72) |
| Organized sector | 224 (4.34) |
| Housewife/retired | 887 (17.17) |
| Other | 350 (6.77) |
| **Education:** | |
| No school | 2408 (46.60) |
| Primary school | 1438 (27.83) |
| High school | 938 (18.15) |
| Graduate/post–graduate | 362 (7.01) |
| Other | 21 (0.41) |
| **Marital status:** | |
| Never married | 741 (14.34) |
| Currently married | 3882 (75.13) |
| Separated/divorced/widowed | 544 (10.53) |
| **Age (years):** | |
| Mean (SD) | 39.7 (14.69) |
| Range | 18–92 |
| **Past history of physical/mental illness based on doctor's diagnosis:** | |
| Angina | 139 (2.69) |
| Stroke | 75 (1.45) |
| Diabetes | 232 (4.49) |
| Cancer | 7 (0.14) |
| Mental disorder | 27 (0.52) |
| Family history of mental illness: | |
| Presence of a family history | 95 (1.84) |
| **Substance use in lifetime:** | |
| Tobacco (cigarettes, bidi, gutka, cigars, etc.) | 1502 (29.07) |
| Alcohol (beer, wine, spirits, etc.) | 1781 (34.47) |
| Others (cannabis, cocaine, opioid, sedatives, hallucinogens, amphetamine, inhalants) | 30 (0.59) |
| **Severity of depression (PHQ9):** | |
| Score 5–9 (mild) | 442 (8.55) |
| Score 10–14 (moderate) | 98 (1.90) |
| Score ≥15 (severe) | 55 (1.06) |
| Severity of anxiety (GAD7): | |
| Score 5–9 (mild) | 367 (7.10) |
| Score 10–14 (moderate) | 82 (1.59) |
| Score ≥15 (severe) | 22 (0.43) |
| **Stressful events (number):** | |
| 0 | 2891 (55.95) |
| 1 | 1527 (29.55) |
| 2–3 | 692 (13.39) |
| ≥4 | 57 (1.10) |

*Agricultural laborer, manual laborer, skilled worker, farmer and business are reported under unorganized sector.

Post–intervention data were collected from 232 out of the 238 individuals who had screened positive during the intervention (**Table 4**). Three people had died due to natural causes (none due to self–harm) and 3 could not be contacted even after repeated attempts.

**Table 5** shows that both depression and anxiety scores reduced significantly at the end of the intervention, among those who had a score ≥10 on the depression/anxiety scales at the beginning of the intervention, as identified by ASHAs. After adjusting for clustering, there was a significant reduction in score of depression by 3.6 (SE 0.6, $P < 0.0001$) and a reduction in anxiety score by 1.3 (SE 0.4, $P = 0.004$), at the end of intervention.

The results from the anti–stigma campaign show that during the project period, the communities' knowledge, attitude and behavior related to mental health [26] had consistently shown an improved lower score, especially for the attitude and behavior related questions (**Table 6** and Table S1 in **Online Supplementary Document**). The responses on the BACE–TS [27] are indicative of low baseline stigma which reduced even further during the project period (**Table 7** and Table S2 in **Online Supplementary Document**).

## DISCUSSION

We found that about 5% individuals suffered from common mental health disorders in a rural, remote community in India. This population is considered to be particularly vulnerable due to remote location making traveling for help–seeking difficult, poorer health facilities and limited mental health facilities. The rates of CMD are somewhat lower than reported in a recent national mental health survey from India found that in community settings, CMD prevalence is around 10%, and it includes substance use disorders [29]. The SMART Mental Health Project did not include substance use disorders under its definition for CMD. Moreover it included only moderate to severe depression/anxiety, hence the rates were even lower. If we Include mild depression/anxiety, the prevalence for CMD increases to 15%. This is similar to the lower value observed in earlier studies, where the prevalence of CMD was estimated to be between 13–50% [2], with the variability explained due to different study designs and instruments.

We implemented a mobile technology enabled mental health services model coupled with training of primary care health workers with the aim of increasing identification and referral of community members with CMD. We found the intervention of training, task shifting, and referral model to be feasible, acceptable to community and health care providers. It also led to identification of people with CMD in this rural community. Detailed qualitative process evaluation will be reported subsequently and will provide more details about feasibility and acceptability, but the fact that these could be implemented in this population and the intervention could be delivered using a predetermined strategy, provides preliminary indication about the feasibility and acceptability of the intervention. It appeared to lead to an increase in the proportion of individuals seeking mental health services. Few studies from India and other LMICs have focused on the mental health issues of ST communities leading to limited knowledge about the

**Table 3.** Summary of stressful events faced by individuals who had a depression or anxiety score ≥10 at baseline (N = 200)

| Question | Baseline n (%) |
|---|---|
| Did you get married in the last 1 year? | 2 (1.0) |
| Did you get separated/divorced in the last 1 year? | 1 (0.5) |
| Did your spouse die in the last 1 year? | 6 (3.0) |
| Did any of your loved ones die in the last 1 year? | 43 (21.5) |
| Did you have a baby in the last 1 year? | 2 (1.0) |
| Did you lose your job in the last 1 year? | 2 (1.0) |
| Did you retire in the last 1 year? | 2 (1.0) |
| Did you or your loved one suffer any major illness/injury in the last 1 year? | 48 (24.0) |
| Did you have any problems with your boyfriend/girlfriend in the last 1 year? | 21 (10.5) |
| Did you have any major problems with your school/college performance in the last 1 year? | 4 (2.0) |
| Did you have any major financial problems in the last year? | 97 (48.5) |
| Did you face any natural disaster or stolen livestock or death of livestock, or crop failure or forced migration leading to loss of income or property? | 36 (18.0) |
| Did you experience any major crime or were a victim of a major crime like robbery, assault/beating, murder/attempted murder, sexual violence? | 15 (7.5) |

**Table 4.** Characteristics of the screen–positive population identified by ASHAs (N = 238)*

| Characteristic | Post intervention — n/N (%) |
|---|---|
| **Gender:** | |
| Female | 169/238 (71.01) |
| Male | 63/238 (26.47) |
| Missing | 6/238 (2.52) |
| **Occupation:** | |
| Unorganized sector | 169/238 (71.01) |
| Organized sector† | 9/238 (3.78) |
| Housewife/retired | 41/238 (17.23) |
| Other | 13/238 (5.46) |
| Missing | 6/238 (2.52) |
| **Education:** | |
| No school | 144/238 (60.50) |
| Primary school | 52/238 (21.85) |
| High school | 21/238 (8.82) |
| Graduate/Post–graduate | 13/238 (5.46) |
| Other | 2/238 (0.84) |
| Missing | 6/238 (2.52) |
| **Marital status:** | |
| Never married | 20/238 (8.40) |
| Currently married | 173/238 (72.69) |
| Separated/divorced/widowed | 39/238 (16.39) |
| Missing | 6/238 (2.52) |
| **Age (years):** | |
| Mean (SD) | 44.1 (14.83) |
| Range | 19 – 92 |

ASHAs – Accredited Social Health Activists

*Out of 238 at the beginning of the intervention stage, 232 were interviewed at the post–intervention stage; out of the 6 missing at post–intervention stage 4 were women, all 6 had either no schooling or only primary levels schooling, 5 worked in the unorganized sector and 1 was housewife/retired, all were married, and the average ages were similar to that of the larger group

†Agricultural laborer, manual laborer, skilled worker, farmer and business are reported under unorganized sector.

prevalence of mental disorders or availability of mental health services in such communities. Remoteness of ST areas and difficulties in conducting research are some of the reasons for this. Studies show that ST populations seek care overwhelmingly through public sector, which highlights the importance of strengthening the public health sector in such areas [7]. To the best of our knowledge, this is the first project from India which reports on using innovative mobile–technology based mental health service delivery mechanisms in an ST area.

The project has a number of limitations. First, this is a pre–post design with no controls, hence the results need to be interpreted cautiously. Second, only 38 out of the screen positive individuals identified by interviewers at baseline were also identified by ASHAs. This suggests a poor inter–rater reliability. However, the reasons for such could be that some of the initial screen positive have had spontaneous remission. A systematic review showed that for major depressive disorder 23% have spontaneous remission within 3 months, and mild–to moderate depression has 20–30% higher remission than severe forms [30]. The time difference for the two assessments in this project was 2–3 months, and a number of screen positive individuals were suffering mild to moderate depression with suicidal risk. Another explanation is the 'retest effect' where results from psychiatric research show that retesting using the same instrument can lead to attenuated results due to a number of reasons [31]. Additionally, preliminary information from qualitative interviews of different stakeholders conducted at post–intervention stage reveal that some community members had not disclosed their symptoms to ASHAs due to apprehensions about the type of treatment they would be asked to undertake; fear that disclosing mental health symptoms to ASHAs could be inadvertently leaked within their community as ASHAs are part of the community; and lack of confidence in the PHC doctor's ability to manage mental disorders (data not shown). Third, the 3–month intervention period was short and allowed only 30 screen positive individuals to access services. Our experience gained through ongoing research in other villages show that uptake of services increases gradually with time and 3 months was insufficient. The short time also prevented organizing more than 3 health camps, which were the main avenues to seek care by the community as they preferred to receive care closer to home which helped to reduce their traveling time and cost. Fourth, the short period of intervention also implies that while

**Table 5.** Change in depression/anxiety scores for those who had a score ≥10 at the beginning of the intervention as screened by ASHAs

| | DEPRESSION SCORE | | | |
|---|---|---|---|---|
| Descriptive statistic response | Beginning of intervention | Post intervention | Test statistics* | P–value |
| **Depression score:** | | | | |
| N | 73 | 69 | | |
| Mean (SD) | 13.84 (4.14) | 4.59 (5.35) | | |
| Median | 12 | 3 | | |
| Minimum | 10 | 0 | | |
| Maximum | 27 | 26 | | |
| **Change in depression score:** | | | | |
| n† | | 69 | –11.92 | <.0001 |
| Mean (SD) | | –9.20 (6.41) | | |
| Median | | –9 | | |
| Min | | –24 | | |
| Max | | 8 | | |
| Anxiety score: | | | | |
| N | 31 | 30 | | |
| Mean (SD) | 12.42 (2.84) | 3.73 (3.61) | | |
| Median | 12 | 3 | | |
| Minimum | 10 | 0 | | |
| Maximum | 21 | 15 | | |
| Change in anxiety score: | | | | |
| n† | | 30 | –9.562 | <.0001 |
| Mean (SD) | | –8.77 (5.02) | | |
| Median | | –9 | | |
| Minimum | | –21 | | |
| Maximum | | 3 | | |

*Paired t–test.

†Number of individuals who were assessed at both points in time.

**Table 6.** Change in mean scores for Knowledge, Attitude, and Behavior Questions from baseline to post–intervention*

| QUESTION | MEAN (SD), BASELINE, N | MEAN (SD), POST INTERVENTION, N | DIFFERENCE OF MEAN (SD), N | P–VALUE† |
|---|---|---|---|---|
| **Knowledge:** | | | | |
| Mentally ill people tend to be violent | 2.2 (1.34), 4401 | 1.6 (0.86), 193 | –0.5 (1.57), 167 | <.001 |
| People with mental illness cannot live a good, rewarding life | 1.9 (1.14), 4660 | 1.4 (0.68), 211 | –0.5 (1.34), 192 | <.001 |
| People with severe mental health problems can fully recover | 2.1 (1.25), 4694 | 1.7 (0.9), 215 | –0.2 (1.43), 189 | 0.020 |
| Medication can be an effective treatment for people with mental health problems. | 1.6 (1.01), 4800 | 1.5 (0.68), 223 | –0.2 (1.29), 204 | 0.067 |
| **Attitude:** | | | | |
| Mentally ill people shouldn't get married | 2.2 (1.4), 4591 | 1.4 (0.71), 205 | –0.7 (1.62), 176 | <.001 |
| People with mental health problems are far less of a danger than most people suppose | 1.8 (1.06), 4714 | 1.4 (0.65), 207 | –0.5 (1.21), 191 | <.001 |
| We need to adopt a far more tolerant attitude toward people with mental illness in our society | 1.6 (0.97), 4861 | 1.3 (0.64), 227 | –0.2 (1.11), 215 | 0.013 |
| People with mental health problems should not be given any responsibility | 1.9 (1.22), 4798 | 1.5 (0.81), 222 | –0.6 (1.58), 207 | <.001 |
| **Behavior:** | | | | |
| If you suffered from a mental health problem would you tell your family or friends? | 2.8 (0.61), 5167 | 2.8 (0.59), 232 | 0.1 (0.84), 232 | 0.139 |
| I would be willing to live with someone with a mental health problem | 2 (1.37), 4858 | 2.1 (1.3), 224 | 0.1 (1.89), 213 | 0.328 |
| I would be willing to work with someone with a mental health problem | 2 (1.26), 4862 | 1.6 (0.84), 224 | –0.3 (1.51), 213 | 0.004 |
| I would be willing to live nearby someone with a mental health problem | 1.9 (1.22), 4862 | 1.6 (0.9), 223 | –0.3 (1.57), 213 | 0.004 |
| I would be willing to continue a relationship with a friend who developed a mental health problem | 1.8 (1.11), 4857 | 1.5 (0.82), 227 | –0.3 (1.42), 213 | <.001 |

*Lower scores on the Knowledge, Attitude and Behavior questionnaire indicate that respondents are more agreeable to the statement.

†Difference in means includes only paired observation; P–value is calculated using paired t–test; n = observations for each analysis.

**Table 7.** Change in mean scores for each barrier in the Barriers to Access to Care Evaluation – Treatment Stigma Subscale, from baseline to post–intervention*

| Question | Mean (SD) Baseline, n | Mean(SD) Post Intervention, n | Difference of Mean (SD), n | *P-value |
|---|---|---|---|---|
| Concern that I might be seen as weak for having a mental health problem | 0.17 (0.45), 4416 | 0.07 (0.27), 232 | 0.16 (0.55), 216 | <.0001 |
| Concern that it might harm my chances when applying for jobs | 0.09 (0.35), 1690 | 0.06 (0.24), 17 | 0 (0), 10 | Not computed |
| Concern about what my family might think, say, do or feel | 0.17 (0.45), 4416 | 0.13 (0.36), 232 | 0.1 (0.64), 216 | 0.03 |
| Feeling embarrassed or ashamed | 0.13 (0.38), 4416 | 0.09 (0.30), 232 | 0.09 (0.56), 216 | 0.02 |
| Concern that I might be seen as crazy | 0.13 (0.38), 4416 | 0.13 (0.37), 232 | 0.02 (0.59), 216 | 0.56 |
| Concern that I might be seen as a bad parent | 0.12 (0.38), 3848 | 0.1 (0.34), 218 | 0.08 (0.54), 193 | 0.04 |
| Concern that people I know might find out | 0.13 (0.40), 4416 | 0.1 (0.33), 232 | 0.07 (0.59), 216 | 0.08 |
| Concern that people might not take me seriously if they found out I was having professional care | 0.12 (0.39), 4416 | 0.13 (0.41), 232 | 0.02 (0.63), 216 | 0.66 |
| Not wanting a mental health problem to be on my medical records | 0.13 (0.43), 4416 | 0.3 (0.79), 232 | –0.18 (0.84), 216 | 0.002 |
| Concern that my children may be taken into care or that I may lose access or custody without my knowledge | 0.12 (0.36), 3795 | 0.23 (0.71), 218 | –0.05 (0.8), 194 | 0.37 |
| Concern about what my friends might think, say or do | 0.15 (0.40), 4416 | 0.18 (0.46), 232 | –0.03 (0.61), 216 | 0.44 |
| Concern about what people at work might think, say or do | 0.14 (0.39), 4416 | 0.13 (0.38), 232 | 0.03 (0.55), 216 | 0.45 |
| Overall mean | 0.14 (0.27), 4416 | 0.14 (0.31), 232 | 0.03 (0.45), 216 | 0.39 |

*Lower scores on the BACE–TS suggest that the barrier is perceived less of an issue or none at all.

†P–value is calculated using paired t–test; n = observations for each analysis.

service contact information is available, information about adequacy and effectiveness of treatment is not available. While there was significant changes in depression/anxiety score, the sample size was small, making it difficult to generalize the results. This could also represent natural remission and regression to mean. Finally, though there was a need for anti–depressants in only one case, the lack of psychotropic medications at primary health center meant that the individual had to be referred to the district hospital.

More women were identified as screen positive compared to men and reflects the higher prevalence of depression in women found by others [32–34]. However, another reason could be that due to cultural norms, men are less likely to express symptoms of depression or anxiety leading to under–reporting [35]. Marital status, education, and age were significantly associated with CMD, as had been observed earlier [32]. Financial problems, illness/injury to self or to someone in the family, and death of a loved one were the commonest stressors associated with moderate/severe depression, similar to earlier research [32]. Lifetime alcohol use had a high prevalence and some reasons suggested for higher consumption among tribal populations are increased poverty, illiteracy, increased stress, and peer pressure [36].

The SMART Mental Health project used three key strategies to provide mental health care. The first involved task shifting, where ASHAs and PHC doctors were trained in screening and managing CMD. The second involved developing and implementing a mobile technology enabled EDSS for use by ASHAs and doctors, to screen, diagnose, and manage CMD. The third involved implementation of an anti–stigma campaign.

### Task–shifting

Task shifting combined with health system restructuring is effective for management of non–communicable disorders, though its cost–effectiveness is still inconclusive [8]. Task shifting is particularly relevant for mental health care in resource poor settings with few mental health professionals [37], and was reported to be effective and acceptable in an earlier study done in tribal areas [38]. But in that study majority of cases who sought treatment suffered from severe mental disorders, which are easier to identify in the community, hence more likely to be treated when compared to CMD [39]. Our project showed that ASHAs and PHC doctors were able to perform the task of screening and managing CMD using the EDSS.

### EDSS enabled mental health services delivery model

Using the EDSS the ASHAs were able to screen and refer individuals with CMD to the PHC doctors, who in turn used an EDSS with the mhGAP–IG tool to diagnose and manage such individuals. Overall there was an increase in accessing mental health care from PHC doctors. The results also appeared to be beneficial and showed a significant decrease in the depression/anxiety scores at post–intervention, for those individuals who had scored moderate–severe depression at the beginning of the intervention. The results showed that a mobile–technology based mental health services delivery strategy can be implemented in this community using existing government resources.
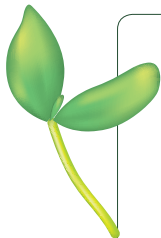
This project helps to provide mental health services in rural and remote areas and provides some preliminary evidence suggesting that task shifting coupled with a mobile technology enabled EDSS can be used is such areas after suitable adaptations. mHealth enabled health care models have been criticized [40] for a lack of appropriate scaled up projects to follow the initial pilot projects. The aim of this project was to use the learnings from a proof–of–concept project to develop more robust studies which could be scaled up across larger areas. The EDSS provided a platform that not only helped ASHAs to screen for CMD, but also allowed them to follow them up to ensure treatment adherence. It also enabled the doctors to use an evidence–based guideline to manage the cases. One review identified EDSS as an important strategy to improve health care delivery, especially where algorithms were used to provide treatment plans and included patient and provider prompts [14]. However, another review found that data from LMICs is limited, but a number of ongoing projects with a potential to provide valuable information about mHealth solutions in health care are available [41], and this project has the same potential.

### Anti–stigma campaign

Responses from the Knowledge, Attitude and Behavior questionnaire (**Table 6**) show that about 20% of the population knew someone with mental disorders and that may be a reason for the low level of baseline stigma in the population. About 7% of people responded that faith healers and religious leaders were the first point of contact for people with mental illness and this has been reported earlier from India [42]. During the intervention period people's attitudes and behaviors appeared to improve but not their scores on knowledge, and this is similar to other studies [17]. Stigma related to help–seeking was low and is similar to earlier research from LMIC [43].

## CONCLUSIONS

In conclusion, the SMART Mental Health project showed that the delivery of mobile based mental health services was possible in the community and preliminary evidence suggests an increase in mental health service use. Future research needs to use more robust randomized controlled trial methods to identify the effectiveness and cost–effectiveness of the program. In order to take this to scale, there needs to be greater involvement of the government at all levels and systems should be in place at PHCs to enable mental health services delivery including training of staff, provision of psychotropic medications, basic counselling services and a streamlined referral systems to the next level where specialist mental health services can be provided to those in need.

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# Cost–effectiveness analysis of revised WHO guidelines for management of childhood pneumonia in 74 Countdown countries

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**Background** Treatment of childhood pneumonia is a key priority in low–income countries, with substantial resource implications. WHO revised their guidelines for the management of childhood pneumonia in 2013. We estimated and compared the resource requirements, total direct medical cost and cost-effectiveness of childhood pneumonia management in 74 countries with high burden of child mortality (Countdown countries) using the 2005 and 2013 revised WHO guidelines.

**Methods** We constructed a cost model using a bottom up approach to estimate the cost of childhood pneumonia management using the 2005 and 2013 WHO guidelines from a public provider perspective in 74 Countdown countries. The cost of pneumonia treatment was estimated, by country, for year 2013, including costs of medicines and service delivery at three different management levels. We also assessed country–specific lives saved and disability adjusted life years (DALYs) averted due to pneumonia treated in children aged below five years. The cost-effectiveness of pneumonia treatment was estimated in terms of cost per DALY averted by fully implementing WHO treatment guidelines relative to no treatment intervention for pneumonia.

**Results** Achieving full treatment coverage with the 2005 WHO guidelines was estimated to cost US$ 2.9 (1.9–4.2) billion compared to an estimated US$ 1.8 (0.8–3.0) billion for the revised 2013 WHO guidelines in these countries. Pneumonia management in young children following WHO treatment guidelines could save up to 39.8 million DALYs compared to a zero coverage scenario in the year 2013 in the 74 Countdown countries. The median cost-effectiveness ratio per DALY averted in 74 countries was substantially lower for the 2013 guidelines: US$ 26.6 (interquartile range IQR: 17.7–45.9) vs US$ 38.3 (IQR: US$ 26.2–86.9) per DALY averted for the 2005 guideline respectively.

**Conclusions** Child pneumonia management as detailed in standard WHO guidelines is a very cost–effective intervention. Implementation of the 2013 WHO guidelines is expected to result in a 39.5% reduction in treatment costs compared to the 2005 guidelines which could save up to US$ 1.16 (0.68–1.23) billion in the 74 Countdown countries, with potential savings greatest in low HIV burden countries which can implement effective community case management of pneumonia.

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Globally, pneumonia is a leading cause of mortality and morbidity in young children accounting for about 0.935 million deaths in 2013 (15% of under–five mortality) [1] and 120 million episodes worldwide in 2010 [2]. Implementation of the World Health Organization (WHO) and United Na-

tions International Children's Emergency Fund (UNICEF) recommended integrated management of childhood illness (IMCI) strategy can potentially reduce 32 to 70% of pneumonia–specific under–five mortality [3–5]. However, treatment of childhood pneumonia places a large economic burden on families and the health care system, especially in resource–constrained countries. Severe acute lower respiratory infections (ALRI) places a substantial burden on health services worldwide and is a major cause of hospital referral and admission in young children [6]. The World Health Report (WHR) 2005 estimated that if a comprehensive package of child survival interventions was scaled up to 95% coverage in 74 high (child mortality) burden countries [7], by 2015 the costs for managing pneumonia would be equivalent to an *additional* US$ 1.48 per capita (2004 US$, inflated to 1.83 in 2013 US$) from public provider's perspective.

In 2013, WHO revised the guidelines for the management of childhood pneumonia [8–10]. The key change in the 2013 guidelines is that Human Immunodeficiency Virus (HIV)–uninfected children (aged 1 month – 4 years) with lower chest wall in–drawing (with or without tachypnoea) are classified as having pneumonia and recommended management at first level facilities (as out–patients) with oral dispersible amoxicillin instead of co–trimoxazole and no longer need to be treated at a hospital (see Box S1 in **Online Supplementary Document**). They also recommend that HIV–infected children with lower chest wall in–drawing should be considered as having severe pneumonia and referred for hospital admission and treatment with ampicillin plus gentamicin IM or IV. Several clinical trials in the past few years have suggested that the treatment protocols in the revised (2013) guidelines are as effective as those in the previous (2005) guidelines in terms of measured clinically–defined rates of treatment failure and from this it has been inferred that they should have at least a similar impact on mortality [11–18].

However, we are not aware of any studies to date that report country level cost estimates for the 2013 WHO treatment guidelines. Existing studies that report cost of treatment of pneumonia mainly focus on the cost of illness per episode for each individual patient and demonstrate a considerable degree of methodological heterogeneity [19]. This greatly limits the extent to which valid national and international economic analyses can be carried out to inform international child health policy on pneumonia.

We aimed to estimate the cost of pediatric pneumonia management (from a public provider perspective) using the 2013 WHO guidelines, estimate cost-effectiveness (and cost savings) compared to use of the 2005 guidelines and estimate the country–specific annual investment required for childhood pneumonia management in the 74 Countdown countries prioritised by the "Countdown to 2015" initiative. These countries account for 97% of the maternal and child deaths worldwide [7].

## METHODS

### Study design

We constructed a cost model using a bottom up approach to estimate the total cost of pneumonia management using the 2005 and 2013 WHO guidelines from a public provider perspective in the 74 Countdown countries. In the absence of information on the clients' preferred use of providers and challenges related to making predictions on private/public split, we applied public provider cost profiles to the analysis. We also used the WHO recommended template [20] to assess country–specific lives saved and disability adjusted life years (DALYs) averted in pneumonia cases (in children aged below five years receiving treatment in the 74 Countdown countries (comparing universal treatment coverage of cases to no treatment). DALYs for a disease were calculated as the sum of the Years of Life Lost (YLL) due to premature mortality in the population and the Years Lost due to Disability (YLD) for people living with the disease condition and its consequences. These 74 priority countries account for a population of 5.1 billion, with 520 million children aged below five years in 2013, and 97% of global pneumonia deaths [21].

We estimated the total cost of pneumonia treatment at a country level in the year 2013 assuming universal coverage (100%), including the total cost for medicine and service delivery at three different levels – community, first level health facility, and first referral hospital level. The total medicine cost and service delivery cost in each country were calculated for each delivery level based on the coverage and population in need. We used the standard treatment protocol recommended by the WHO including recommended dosage for antibiotics, supportive therapy and duration of treatment [8]. We estimated the cost of management of pneumonia in HIV–infected and uninfected children following the 2005 and 2013 WHO guidelines. In the absence of empirical data, we assumed that the proportion of pneumonia signs (ie, fast breathing, lower chest wall in–drawing and danger signs) are the same in HIV–infected and un-

infected children with pneumonia – 85% of children with pneumonia have fast breathing, 13% have chest wall in–drawing and about 2% have danger signs – based on the results of studies carried out at the community level [15,22,23].

## Cost model inputs

The 74 countries were categorised into four groups based on HIV prevalence and the presence or absence of an implemented pneumonia community case management (CCM) policy. Community case management refers to an integrated strategy to achieve high treatment coverage and delivering high–quality care to sick children in the community.by community health workers. A country was defined as "high HIV prevalence country" when the adult prevalence (15–49 years) was above 1% in 2012. The proportion of the adult population infected by HIV was obtained from UNAIDS (2012) [24]. The standard treatment procedure in children who are HIV positive and negative are different as per the WHO guidelines. Information on policy and implementation of CCM were obtained from the Countdown Reports for 2014 [25] and 2012 [7]; these influenced assumptions regarding the proportion of the rural population seeking treatment at first level facility or community level.

The estimated country–specific population in need for each level of intervention was calculated using three parameters: population size, pneumonia incidence and urban/rural distribution of the population. The exposed population in need was calculated using the country level population of children aged below five years from the UN World Population Prospects [21], and the most recent published country–specific estimates of incidence of pneumonia among children below five years [26]. The population living in rural areas was estimated using the UN World Urbanisation Prospects (2011) [27], and we estimated the population in need at the community and facility level for urban and rural areas separately. The number of pneumonia cases in HIV–infected children was obtained from recently published estimates [26].

We assumed universal coverage of pneumonia treatment with 100% children affected by pneumonia being treated either at community, first level health facility or first referral hospital level. Community level treatment implies a community health worker (CHW) treating the child at home. In countries with implementation of a CCM policy, we assumed that half of the rural population would be treated by CHWs and the remaining half would be treated at a health facility [15,19]. We assumed that the urban population would be treated at first level health facility and first referral hospital level. We conducted sensitivity analyses to examine the change in the overall cost of pneumonia treatment by varying the coverage of the rural population by CHWs. We considered two different types of direct medical costs – cost of medicines and costs related to service delivery. All costs are presented in US dollars (2013), and are estimated by level of intervention and country. We used median supplier prices from Management Sciences for Health (MSH) International Price Indicator (2012) [28], UNICEF supply division data, and UNICEF report for cost of medicines [29] for the list of drugs based on the previous and revised WHO guidelines. Costs were estimated for an average child weighing 10 kg (around one–year–old) due to lack of age disaggregated population data.

Country–specific service delivery costs (ie, costs for one inpatient day and one outpatient visit) were obtained from the World Health Organization Choosing Interventions that are Cost–Effective project (WHO–CHOICE) estimates [30] (which include operational costs such as health worker consultation time, electricity and maintenance of health facility buildings). We applied outpatient unit costs from WHO–CHOICE for service delivery at the first level facility and inpatient unit costs for service delivery at the first referral level hospital. For the community level service delivery, we used the salary received by CHWs in the published literature [31], which was supplemented by consultation with experts from WHO. The number of CHWs needed per country was obtained by assuming one CHW per 1000 rural population [31].

## Effectiveness of pneumonia treatment

The effectiveness of pneumonia treatment was measured in terms of country–specific disability adjusted life years (DALYs) averted by implementing WHO treatment guidelines relative to no treatment intervention for pneumonia, ie, implementation of 2005 guidelines vs no treatment and implementation of 2013 guidelines vs no treatment. Country–specific DALYs were computed using the WHO DALY Calculation Template [20,32]. We obtained country–specific population data by gender for children aged 0–4 years and the life expectancy at birth for both the sexes from the World Population Prospect (2013) [21], and used pneumonia specific incidence and mortality estimates published recently [1,2,26]. Deaths averted by pneumonia treatment were calculated based on the reported estimates of 70% child mortality reduc-

tion from universal coverage of community management of childhood pneumonia [33]. We assumed that the 2005 and 2013 guidelines have the same treatment effectiveness and that community management of fast breathing pneumonia and health facility management of fast breathing and lower chest in–drawing pneumonia with oral amoxicillin (based on the clinical trials [11–18]) have similar effectiveness in terms of mortality reduction. We assumed that the peak incidence of childhood pneumonia was at 1.5 months and that median age at death was 8.9 months based on unpublished data from Kilifi, Kenya, (Jay Berkley, personal communication); these were also supported by published literature and expert opinion [34,35]. Disability weight is a weighting factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead). For our analysis, we applied a standard disability weight of 0.21 for infectious disease (acute episode, severe) [36].

Cost-effectiveness is measured in terms of cost per DALY averted in each country. The thresholds for considering an intervention to be cost–effective were set following the recommendations of the Commission on Macroeconomics and Health [37]. Interventions that cost less than three times the average gross domestic product (GDP) per capita income per DALY averted were considered to be cost–effective and an intervention whose cost per DALY averted was less than the average per capita income for a given country was considered to be highly cost–effective.

### Sensitivity analysis

We simulated the cost estimates using several scenarios by varying unit cost, length of stay in hospital, level of coverage and population in need (Box S2 in **Online Supplementary Document**). We extracted an actual cost data scenario derived from a systematic review of the published literatures based on 34 cost studies, and incorporated these data into our model to compare the results with the standard prices model [19]. We also conducted sensitivity analyses assuming 100% rural coverage for CCM implementation, 36% of mortality reduction, 1 CHW per 5000 rural population and 9%–30% of effective access rate to health care in rural areas [38]. Additionally, we performed several analyses to examine a range of total costs and cost savings in each country to assess whether / within what parameter settings the intervention remained cost–effective.

We conducted the analyses using Microsoft Excel 2010 (Microsoft Corp., Redmond, WA, USA).

## RESULTS

### Total cost and cost savings

The total direct medical cost of management of all–cause childhood pneumonia in the 74 Countdown countries in 2013 using the 2005 IMCI guidelines was estimated to be about US$ 2.94 billion. However, implementation of the 2013 IMCI guidelines would cost approximately US$ 1.78 billion (**Table 1**). Thus, a total of US$ 1.16 billion could potentially be saved by implementing the 2013 guidelines in these countries. About 82% of these cost savings could be achieved in countries in the WHO South–East Asia, Africa and Western Pacific regions (**Figure 1**), which account for the majority of cases and deaths due to childhood pneumonia. These findings can be further broken down into cost at the three delivery levels
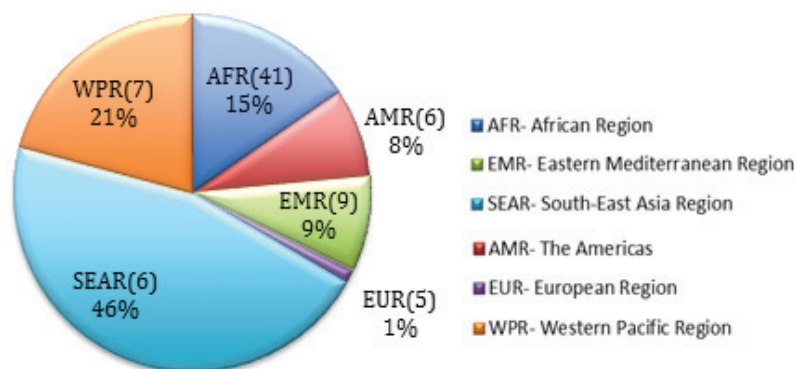


**Figure 1.** Percentage of Total Cost Savings by WHO Regions (number of countries in each region), total estimated cost savings in 2013: US$ 1.16 billion. Total cost savings (Unit: Billion) SEAR: 0.53; WPR: 0.24; AFR: 0.18; EMR: 0.099; AMR: 0.094; EUR: 0.014.

**Table 1.** Total cost of management of childhood pneumonia in 74 Countdown countries in 2013

| DELIVERY LEVEL | TOTAL COST FOR PNEUMONIA TREATMENT IN 2013 (BILLIONS, IN 2013 US$) | | | | |
|---|---|---|---|---|---|
| | 2005 Guidelines [10] | | 2013 Guidelines [8] | | 2013 Guidelines/2005 Guidelines % |
| | Total Cost | % Total | Total cost | % Total | |
| Community | 1.25 | 42.4 | 1.25 | 70.4 | 100.3 |
| First level facility | 0.18 | 6.1 | 0.23 | 12.8 | 126.0 |
| Hospital | 1.51 | 51.4 | 0.30 | 16.9 | 19.9 |
| Total cost | 2.94 | 100 | 1.78 | 100.0 | 60.5 |

– pneumonia management at community and first level facilities cost more per child with pneumonia when following the 2013 guidelines, but this was outweighed by the substantial reduction in costs at the hospital level (**Table 2**).

Our estimates of country–specific cost for the management of childhood pneumonia demonstrate that ten countries (Bangladesh, China, India, Mexico, Pakistan, Indonesia, Philippines, Brazil, Nigeria and South Africa) account for about three quarters of the total cost in the 74 Countdown countries (**Table 3**). Potentially up to US$ 933 million could be saved in these ten countries alone by fully implementing the 2013 guidelines which corresponds to about 80% of the total cost savings in the 74 countries.

## Cost savings by HIV prevalence

In low HIV prevalence countries, treatment costs for HIV–infected patients accounted for less than one percent of the total cost of pneumonia management. Countries with high HIV prevalence require a larger share (between 0.82% and 65.20%) of the total direct medical cost investment to manage pneumonia in young HIV–infected children. Following implementation of the 2013 guidelines, countries implementing CCM can achieve substantial cost savings of US$ 1.00 billion collectively compared to savings of only $0.16 billion in those not implementing CCM, particularly in low HIV burden settings (Table S1 in **Online Supplementary Document**).

## Total cost per capita

Globally, the total cost per capita for direct medical pneumonia costs of treatment (based on an assumed 100% treatment coverage) ranged from US$ 0.04 (in Brazil on one extreme) to US$ 2.13 (in Equatorial Guinea at the other extreme). Similarly, total health care expenditure per capita using the 2013 guidelines ranged from 0.0035% (Brazil on the lower end) to 12.47% (Somalia on the higher end) (**Table 2**). The median total cost per capita for the 2013 guidelines among 74 countries was US$ 0.38 (IQR: US$ 0.24–0.47), which represented 0.52% (IQR: 0.15%–1.14%) of total health care expenditure per capita. This is lower than that for the 2005 guideline – US$ 0.54 (IQR: US$ 0.40–0.75). In seven countries (Eritrea, Niger, Somalia, Burundi, Central African Republic, Madagascar, and Ethiopia), the estimated total cost of pneumonia treatment per capita exceeds 2% of the total health care expenditure per capita following the 2013 guidelines.

## Cost–effectiveness of 2005 and 2013 guidelines

Assuming that the two sets of guidelines are equally effective (see above) then adopting the 2013 guidelines should help many countries achieve a more cost–effective pneumonia management strategy and should result in substantial savings per DALY averted, compared to the 2005 guidelines. Following the parameters described above and 100% treatment coverage, our model estimates that up to 39.8 million DALYs could be averted in the 74 countries. We also estimate that the total Years of Life Saved would be 38.8 million and total deaths averted would be about 0.63 million. This yields a median cost–effectiveness ratio of $38.3 (IQR: US$ 26.2–86.9) and US$ 26.6 (IQR: 17.7–45.9) per DALY averted using the 2005 and 2013 guidelines respectively. The median cost per DALY averted for 74 countries was US$ 11.5 (IQR US$ 7.2–30.0). We estimated that nine countries with highest cost per DALYS averted – China, Mexico, Peru, Brazil, Gabon, Botswana, Equatorial Guinea, Azerbaijan and South Africa – could save between US$ 95.6 and US$ 284.8 per DALY averted if the 2013 guidelines were fully implemented (**Table 4**).

## Sensitivity analysis results

We conducted sensitivity analyses by varying the unit price of medicine (Tables S2–S4 in **Online Supplementary Document**), CHW/rural population ratio and CHW coverage (Tables S5–S7 in **Online Supplementary Document**), effective access to health care in rural areas (Tables S8–S10 in **Online Supplemen-**

**Table 2.** Total treatment cost by country for each level of service delivery*

| Country | Total treatment cost by delivery level for 2005 Guidelines [10] (thousands, 2013 US$) | | | Total treatment cost by delivery level for 2013 Guideline [8] (thousands, 2013 US$) | | | Total treatment cost ratio: 2013 Guidelines/2005 Guidelines (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Community | First level facility | Primary hospital | Community | First level facility | Primary hospital | Commu-nity | First level facility | Primary hospital | Total |
| Afghanistan | 11401.08 | 10460.50 | 12278.82 | 11516.61 | 13283.25 | 1794.78 | 101.01 | 126.98 | 14.62 | 77.90 |
| Angola | – | 1114.05 | 23277.54 | – | 1401.03 | 5088.23 | – | 125.76 | 21.86 | 26.60 |
| Azerbaijan | 2120.28 | 1286.70 | 6289.06 | 2125.15 | 1561.02 | 1274.37 | 100.23 | 121.32 | 20.26 | 51.16 |
| Bangladesh | 54523.08 | 2917.34 | 27298.93 | 54727.21 | 4065.44 | 4227.04 | 100.37 | 139.35 | 15.48 | 74.37 |
| Benin | 2764.68 | 128.71 | 2029.47 | 2775.73 | 190.67 | 358.01 | 100.40 | 148.13 | 17.64 | 67.53 |
| Bolivia (Plurinational State of) | – | 242.95 | 1709.18 | – | 297.57 | 316.86 | – | 122.48 | 18.54 | 31.47 |
| Botswana | – | 44.29 | 2430.51 | – | 57.19 | 766.37 | – | 129.11 | 31.53 | 33.28 |
| Brazil | – | 2295.24 | 26878.76 | – | 2888.23 | 5004.98 | – | 125.84 | 18.62 | 27.06 |
| Burkina Faso | 6066.40 | 964.40 | 5864.39 | 6116.28 | 1301.36 | 981.56 | 100.82 | 134.94 | 16.74 | 65.13 |
| Burundi | 4399.71 | 709.60 | 1123.25 | 4414.11 | 923.06 | 199.84 | 100.33 | 130.08 | 17.79 | 88.84 |
| Cambodia | – | 455.79 | 1666.49 | – | 559.87 | 288.41 | – | 122.83 | 17.31 | 39.97 |
| Cameroon | 5182.60 | 258.02 | 5652.74 | 5202.16 | 381.90 | 1298.54 | 100.38 | 148.01 | 22.97 | 62.04 |
| Central African Republic | – | 6789.37 | 1118.01 | – | 7794.68 | 267.34 | – | 114.81 | 23.91 | 101.96 |
| Chad | – | 720.47 | 4500.48 | – | 926.15 | 941.21 | – | 128.55 | 20.91 | 35.77 |
| China | 332126.14 | 4231.84 | 250139.39 | 332389.24 | 6056.05 | 48630.31 | 100.08 | 143.11 | 19.44 | 66.00 |
| Comoros | – | 448.69 | 213.26 | – | 522.36 | 33.25 | – | 116.42 | 15.59 | 83.94 |
| Congo | 786.08 | 127.92 | 2897.28 | 789.56 | 169.37 | 699.90 | 100.44 | 132.40 | 24.16 | 43.52 |
| Congo, Democratic Republic | 21593.58 | 1991.78 | 11753.02 | 21710.58 | 2730.74 | 1876.43 | 100.54 | 137.10 | 15.97 | 74.47 |
| Côte d'Ivoire | – | 2526.81 | 7952.09 | – | 3043.90 | 1740.60 | – | 120.46 | 21.89 | 45.66 |
| Djibouti | – | 40.93 | 266.28 | – | 51.46 | 53.53 | – | 125.74 | 20.10 | 34.18 |
| Egypt | – | 1466.52 | 13,334.03 | – | 1809.30 | 2479.44 | – | 123.37 | 18.59 | 28.98 |
| Equatorial Guinea | – | 14.07 | 5042.05 | – | 19.36 | 1591.47 | – | 137.59 | 31.56 | 31.86 |
| Eritrea | 2421.25 | 85.68 | 2007.63 | 2429.03 | 122.15 | 380.68 | 100.32 | 142.57 | 18.96 | 64.94 |
| Ethiopia | 37952.87 | 919.68 | 10635.81 | 38069.35 | 1359.98 | 1948.09 | 100.31 | 147.87 | 18.32 | 83.58 |
| Gabon | – | 49.79 | 2770.42 | – | 63.20 | 688.00 | – | 126.95 | 24.83 | 26.64 |
| Gambia | 384.33 | 87.02 | 388.63 | 386.11 | 111.45 | 70.00 | 100.46 | 128.08 | 18.01 | 66.00 |
| Ghana | 6053.11 | 350.63 | 4385.54 | 6067.41 | 474.13 | 866.40 | 100.24 | 135.22 | 19.76 | 68.66 |
| Guatemala | 3774.98 | 234.93 | 1857.80 | 3786.51 | 324.04 | 284.08 | 100.31 | 137.93 | 15.29 | 74.90 |
| Guinea | 3689.35 | 699.79 | 2357.00 | 3707.74 | 901.87 | 419.99 | 100.50 | 128.88 | 17.82 | 74.56 |
| Guinea–Bissau | – | 68.07 | 377.07 | – | 87.36 | 88.04 | – | 128.34 | 23.35 | 39.40 |
| Haiti | – | 517.71 | 1298.83 | – | 626.76 | 238.43 | – | 121.06 | 18.36 | 47.63 |
| India | 418239.33 | 16406.87 | 591463.73 | 419709.33 | 23682.25 | 112428.79 | 100.35 | 144.34 | 19.01 | 54.17 |
| Indonesia | 59799.61 | 4929.74 | 35865.47 | 59913.35 | 6346.30 | 6344.94 | 100.19 | 128.73 | 17.69 | 72.18 |
| Iraq | – | 9823.46 | 20550.40 | – | 11456.60 | 4154.23 | – | 116.62 | 20.21 | 51.40 |
| Kenya | – | 5337.83 | 7865.87 | – | 6275.86 | 1904.43 | – | 117.57 | 24.21 | 61.95 |
| Korea, Democratic People's Republic | 4795.55 | 145.40 | 4851.59 | 4802.07 | 204.49 | 912.74 | 100.14 | 140.64 | 18.81 | 60.45 |
| Kyrgyzstan | 1743.10 | 99.15 | 1107.97 | 1748.98 | 136.66 | 183.49 | 100.34 | 137.83 | 16.56 | 70.13 |
| Lao People's Democratic Republic | 2164.27 | 117.75 | 1909.82 | 2173.38 | 167.33 | 332.71 | 100.42 | 142.10 | 17.42 | 63.78 |
| Lesotho | – | 50.08 | 472.47 | – | 63.35 | 218.85 | – | 126.49 | 46.32 | 54.00 |
| Liberia | 1561.98 | 261.60 | 660.00 | 1566.95 | 332.13 | 101.53 | 100.32 | 126.96 | 15.38 | 80.55 |
| Madagascar | 7520.89 | 944.39 | 4473.18 | 7559.02 | 1253.21 | 687.17 | 100.51 | 132.70 | 15.36 | 73.42 |
| Malawi | 6705.06 | 732.96 | 1979.92 | 6724.64 | 934.94 | 669.24 | 100.29 | 127.56 | 33.80 | 88.44 |
| Mali | 4848.14 | 1647.53 | 4249.70 | 4878.90 | 2094.76 | 722.41 | 100.63 | 127.15 | 17.00 | 71.62 |
| Mauritania | 1107.71 | 478.22 | 1172.87 | 1113.42 | 597.55 | 207.50 | 100.51 | 124.95 | 17.69 | 69.54 |
| Mexico | 12994.34 | 1491.12 | 77172.09 | 13012.59 | 1921.17 | 15409.53 | 100.14 | 128.84 | 19.97 | 33.11 |
| Morocco | – | 4556.94 | 6606.32 | – | 5309.92 | 1237.23 | – | 116.52 | 18.73 | 58.65 |
| Mozambique | 8652.85 | 5520.45 | 6414.29 | 8700.73 | 6780.13 | 1999.95 | 100.55 | 122.82 | 31.18 | 84.91 |
| Myanmar | 17424.61 | 762.94 | 7406.96 | 17467.28 | 1041.27 | 1272.04 | 100.24 | 136.48 | 17.17 | 77.28 |
| Nepal | 11210.34 | 678.15 | 3103.69 | 11239.79 | 907.35 | 477.82 | 100.26 | 133.80 | 15.40 | 84.21 |
| Niger | 7138.68 | 2330.37 | 4913.61 | 7193.46 | 3030.11 | 741.45 | 100.77 | 130.03 | 15.09 | 76.24 |
| Nigeria | 42534.99 | 26108.57 | 59338.83 | 42732.87 | 31949.59 | 13508.53 | 100.47 | 122.37 | 22.77 | 68.91 |

**Table 2.** Continued

| Country | Total treatment cost by delivery level for 2005 Guidelines [10] (thousands, 2013 US$) | | | Total treatment cost by delivery level for 2013 Guideline [8] (thousands, 2013 US$) | | | Total treatment cost ratio: 2013 Guidelines/2005 Guidelines (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Community | First level facility | Primary hospital | Community | First level facility | Primary hospital | Commu-nity | First level facility | Primary hospital | Total |
| Pakistan | 56 508.00 | 16 699.70 | 46 987.80 | 56 741.27 | 21 059.19 | 7879.04 | 100.41 | 126.11 | 16.77 | 71.28 |
| Papua New Guinea | 3114.48 | 188.58 | 1986.34 | 3124.71 | 256.22 | 370.36 | 100.33 | 135.87 | 18.65 | 70.92 |
| Peru | 3352.26 | 124.13 | 9306.02 | 3356.20 | 181.53 | 1840.11 | 100.12 | 146.24 | 19.77 | 42.07 |
| Philippines | 24 463.96 | 3722.85 | 34 784.32 | 24 547.02 | 4779.18 | 6335.22 | 100.34 | 128.37 | 18.21 | 56.63 |
| Rwanda | 4627.50 | 308.74 | 1178.31 | 4638.29 | 405.88 | 224.79 | 100.23 | 131.46 | 19.08 | 86.17 |
| Sao Tome and Principe | – | 30.83 | 33.66 | – | 35.97 | 6.74 | – | 116.68 | 20.02 | 66.23 |
| Senegal | 3948.39 | 488.16 | 3059.40 | 3962.94 | 635.97 | 536.93 | 100.37 | 130.28 | 17.55 | 68.51 |
| Sierra Leone | 1801.09 | 248.21 | 1131.77 | 1810.32 | 327.56 | 189.91 | 100.51 | 131.97 | 16.78 | 73.18 |
| Solomon Islands | – | 78.99 | 126.27 | – | 92.97 | 22.40 | – | 117.69 | 17.74 | 56.20 |
| Somalia | 3185.18 | 1113.81 | 2841.88 | 3211.74 | 1431.19 | 410.91 | 100.83 | 128.50 | 14.46 | 70.77 |
| South Africa | – | 1275.60 | 49 053.75 | – | 1590.69 | 17 881.83 | – | 124.70 | 36.45 | 38.69 |
| Sudan | – | 11 281.13 | 22 475.25 | – | 13 405.65 | 3844.41 | – | 118.83 | 17.11 | 51.10 |
| Swaziland | – | 60.05 | 520.30 | – | 70.48 | 252.13 | – | 117.35 | 48.46 | 55.59 |
| Tajikistan | 2932.36 | 774.56 | 1777.77 | 2944.10 | 986.64 | 291.31 | 100.40 | 127.38 | 16.39 | 76.98 |
| Tanzania, United Republic of | – | 8832.22 | 7093.35 | – | 10 288.06 | 1676.30 | – | 116.48 | 23.63 | 75.13 |
| Togo | 2054.78 | 285.33 | 1198.07 | 2063.27 | 368.76 | 260.12 | 100.41 | 129.24 | 21.71 | 76.09 |
| Turkmenistan | 1305.42 | 85.85 | 2913.80 | 1308.94 | 115.77 | 566.89 | 100.27 | 134.85 | 19.46 | 46.26 |
| Uganda | 15 426.85 | 943.94 | 6083.92 | 15 480.64 | 1280.18 | 1522.94 | 100.35 | 135.62 | 25.03 | 81.43 |
| Uzbekistan | 8969.37 | 862.48 | 6421.00 | 8994.75 | 1121.98 | 1147.19 | 100.28 | 130.09 | 17.87 | 69.30 |
| Viet Nam | – | 4275.11 | 14 077.75 | – | 5150.35 | 2476.74 | – | 120.47 | 17.59 | 41.56 |
| Yemen | 8042.85 | 2660.84 | 11 772.38 | 8094.02 | 3398.63 | 2058.14 | 100.64 | 127.73 | 17.48 | 60.29 |
| Zambia | 4299.30 | 574.52 | 3296.80 | 4309.87 | 721.09 | 1172.36 | 100.25 | 125.51 | 35.56 | 75.92 |
| Zimbabwe | – | 643.02 | 2062.99 | – | 765.63 | 832.50 | – | 119.07 | 40.35 | 59.06 |
| Total | 1 247 712.75 | 180 231.49 | 1 511 555.44 | 1 251 337.59 | 227 059.41 | 300 210.04 | 100.42 | 125.98 | 19.86 | 60.51 |

*Total treatment cost ratio of Revised Guidelines vs Old guideline by treatment settings.

tary Document) and the proportion of pneumonia signs in HIV– infected children with pneumonia (Tables S11–S13 in **Online Supplementary Document**, higher cost from published studies but less effective scenario (Tables S14–S18 in **Online Supplementary Document**). This way we designed 6 likely scenarios (See Box S2 in **Online Supplementary Document**). These analyses demonstrated that the total direct medical cost of pneumonia treatment was US$ 1.9–4.2 billion based on universal coverage of the 2005 WHO guidelines and US$ 0.8–3.0 billion following the 2013 guidelines. The estimated cost savings (from a public provider perspective) by implementing the 2013 guidelines ranged between US$ 0.7 and US$ 1.2 billion, eg, in the effective access scenario, with a 9%–30% effective access rate applied to rural population, total cost saving was US$ 0.78 billion (Table S8 in **Online Supplementary Document**). The median cost–effectiveness ratio ranged from US$ 12.8 (IQR: 8.8–25.6) to US$ 56.0 (34.7–120.2) per DALY averted. Both 2005 and 2013 guidelines for the pneumonia treatment interventions remained highly cost–effective in all scenarios.

## Discussion

Treatment of childhood pneumonia poses a substantial economic burden in resource limited low–income countries. Our study is the first to estimate the direct medical cost to the public sector of pneumonia management at community, first level facility, and first referral hospital levels using the 2005 and 2013 WHO guidelines. In this analysis we have studied "pneumonia" as defined by WHO case management and realize that this case definition encompasses other acute lower respiratory conditions such as bronchiolitis. We have demonstrated that implementation of the 2013 IMCI guidelines for the treatment of childhood pneumonia is expected to result in substantial cost savings (up to 39.5% of the budget for pneumonia treatment) and saved 38.8 millions years of life globally (Table S19 in **Online Supplementary Document**). More than 80% of the estimated global savings would be made by implementing the 2013 guidelines in ten high burden countries alone (**Table 2**). Although implementation of these guide–

**Table 3.** Total cost of management of childhood pneumonia by HIV status

| Country | 2005 Guidelines [10] (thousands, 2013 US$) | | | 2013 Guidelines [8] (thousands, 2013 US$) | | | Total cost savings (thousands, 2013 US$) | 2013 Guidelines | |
|---|---|---|---|---|---|---|---|---|---|
| | HIV+ | HIV− | Total | HIV+ | HIV− | Total | | Total cost per capita | Proportion of national health care expenditure per Capita (%) |
| Afghanistan | 4.78 | 34135.63 | 34140.41 | 4.95 | 26589.69 | 26594.64 | 7545.77 | 0.87 | 1.56 |
| Angola | 588.79 | 23802.80 | 24391.59 | 808.42 | 5767.72 | 6576.13 | 17815.46 | 0.30 | 0.16 |
| Azerbaijan | 39.30 | 9656.73 | 9696.03 | 53.31 | 4907.24 | 4960.54 | 4735.49 | 0.53 | 0.15 |
| Bangladesh | 3.03 | 84736.32 | 84739.35 | 3.30 | 63016.38 | 63019.68 | 21719.66 | 0.40 | 1.52 |
| Benin | 43.96 | 4878.91 | 4922.87 | 48.47 | 3275.94 | 3324.41 | 1598.46 | 0.32 | 0.88 |
| Bolivia (Plurinational State of) | 4.06 | 1948.07 | 1952.13 | 5.10 | 577.56 | 582.66 | 1369.47 | 0.06 | 0.05 |
| Botswana | 270.49 | 2204.32 | 2474.81 | 388.96 | 480.84 | 869.80 | 1605.01 | 0.41 | 0.09 |
| Brazil | 15.10 | 29158.90 | 29174.00 | 19.46 | 7847.54 | 7867.01 | 21306.99 | 0.04 | 0.0035 |
| Burkina Faso | 132.04 | 12763.14 | 12895.19 | 140.12 | 8259.09 | 8399.21 | 4495.98 | 0.50 | 1.33 |
| Burundi | 75.95 | 6156.61 | 6232.56 | 76.33 | 5460.68 | 5537.02 | 695.55 | 0.54 | 2.33 |
| Cambodia | 24.87 | 2097.41 | 2122.28 | 27.60 | 754.28 | 781.88 | 1340.40 | 0.06 | 0.11 |
| Cameroon | 355.52 | 10737.84 | 11093.36 | 416.34 | 6466.27 | 6882.61 | 4210.75 | 0.31 | 0.45 |
| Central African Republic | 538.84 | 7368.55 | 7907.39 | 544.55 | 7521.47 | 8066.02 | −158.64 | 1.75 | 9.55 |
| Chad | 289.80 | 4931.14 | 5220.94 | 318.28 | 1563.37 | 1881.65 | 3339.29 | 0.15 | 0.41 |
| China | 83.52 | 586413.86 | 586497.37 | 116.07 | 386959.53 | 387075.60 | 199421.77 | 0.28 | 0.10 |
| Comoros | 0.25 | 661.70 | 661.95 | 0.26 | 487.15 | 487.41 | 174.54 | 0.76 | 1.78 |
| Congo | 140.61 | 3670.67 | 3811.28 | 185.79 | 1473.04 | 1658.82 | 2152.46 | 0.37 | 0.43 |
| Congo, Democratic Republic | 429.87 | 34908.51 | 35338.38 | 428.49 | 25889.25 | 26317.74 | 9020.64 | 0.39 | 1.98 |
| Côte d'Ivoire | 565.27 | 9913.63 | 10478.90 | 637.47 | 4180.08 | 4817.55 | 5661.34 | 0.24 | 0.30 |
| Djibouti | 10.07 | 297.13 | 307.20 | 11.72 | 94.00 | 105.72 | 201.48 | 0.12 | 0.11 |
| Egypt | 1.05 | 14799.49 | 14800.54 | 1.35 | 4072.57 | 4073.92 | 10726.63 | 0.05 | 0.04 |
| Equatorial Guinea | 514.83 | 4541.29 | 5056.12 | 776.24 | 935.46 | 1711.70 | 3344.42 | 2.13 | 0.17 |
| Eritrea | 17.15 | 4497.40 | 4514.55 | 21.54 | 2910.33 | 2931.87 | 1582.68 | 0.46 | 3.33 |
| Ethiopia | 552.14 | 48956.23 | 49508.37 | 567.44 | 40809.98 | 41377.42 | 8130.95 | 0.44 | 2.65 |
| Gabon | 127.20 | 2693.01 | 2820.21 | 185.24 | 588.53 | 773.77 | 2046.44 | 0.45 | 0.13 |
| Gambia | 13.10 | 846.88 | 859.98 | 14.09 | 553.47 | 567.55 | 292.43 | 0.31 | 1.12 |
| Ghana | 118.24 | 10671.04 | 10789.28 | 140.10 | 7267.84 | 7407.95 | 3381.33 | 0.29 | 0.38 |
| Guatemala | 16.60 | 5851.12 | 5867.72 | 17.41 | 4377.21 | 4394.63 | 1473.09 | 0.28 | 0.13 |
| Guinea | 99.32 | 6646.82 | 6746.14 | 103.90 | 4925.69 | 5029.59 | 1716.55 | 0.43 | 1.44 |
| Guinea–Bissau | 40.40 | 404.74 | 445.14 | 42.93 | 133.95 | 176.88 | 268.26 | 0.10 | 0.28 |
| Haiti | 54.97 | 1761.58 | 1816.55 | 58.94 | 808.36 | 867.31 | 949.24 | 0.08 | 0.15 |
| India | 1669.57 | 1024440.35 | 1026109.93 | 2193.12 | 553627.25 | 555820.37 | 470289.56 | 0.44 | 0.75 |
| Indonesia | 125.39 | 100469.43 | 100594.82 | 149.35 | 72455.25 | 72604.59 | 27990.23 | 0.29 | 0.31 |
| Iraq | 310.48 | 30063.38 | 30373.86 | 387.99 | 13745.27 | 14133.26 | 16240.60 | 0.46 | 0.14 |
| Kenya | 1064.89 | 12138.81 | 13203.70 | 1146.41 | 7074.75 | 8221.16 | 4982.54 | 0.18 | 0.51 |
| Korea, Democratic People's Republic | 0.21 | 9792.33 | 9792.54 | 0.27 | 5919.03 | 5919.30 | 3873.24 | 0.24 | 0.63 |
| Kyrgyzstan | 0.43 | 2949.80 | 2950.22 | 0.49 | 2068.64 | 2069.13 | 881.09 | 0.37 | 0.52 |
| Lao People's Democratic Republic | 8.92 | 4182.93 | 4191.84 | 10.47 | 2662.95 | 2673.42 | 1518.42 | 0.39 | 1.07 |
| Lesotho | 168.05 | 354.51 | 522.56 | 190.83 | 101.93 | 292.76 | 229.79 | 0.14 | 0.10 |
| Liberia | 17.86 | 2465.72 | 2483.58 | 17.99 | 1982.63 | 2000.62 | 482.96 | 0.32 | 0.59 |
| Madagascar | 54.14 | 12884.32 | 12938.46 | 56.38 | 9443.03 | 9499.41 | 3439.05 | 0.41 | 2.18 |
| Malawi | 543.94 | 8873.99 | 9417.94 | 556.83 | 7771.98 | 8328.82 | 1089.12 | 0.51 | 1.65 |
| Mali | 108.31 | 10637.06 | 10745.37 | 115.13 | 7580.94 | 7696.07 | 3049.30 | 0.50 | 1.13 |
| Mauritania | 18.69 | 2740.12 | 2758.81 | 20.91 | 1897.56 | 1918.47 | 840.35 | 0.49 | 0.85 |
| Mexico | 44.11 | 91613.44 | 91657.55 | 63.93 | 30279.36 | 30343.29 | 61314.27 | 0.25 | 0.04 |
| Morocco | 6.27 | 11156.99 | 11163.26 | 7.55 | 5847.48 | 5855.04 | 5308.22 | 0.20 | 0.11 |
| Mozambique | 1774.32 | 18813.27 | 20587.58 | 1841.68 | 15639.12 | 17480.80 | 3106.78 | 0.68 | 1.92 |
| Myanmar | 67.27 | 25527.24 | 25594.51 | 76.30 | 19704.29 | 19780.59 | 5813.92 | 0.37 | 1.65 |
| Nepal | 15.35 | 14976.83 | 14992.18 | 16.34 | 12608.62 | 12624.96 | 2367.23 | 0.45 | 1.38 |
| Niger | 80.04 | 14302.62 | 14382.67 | 81.83 | 10883.19 | 10965.02 | 3417.64 | 0.61 | 3.06 |
| Nigeria | 4233.83 | 123748.56 | 127982.39 | 4875.27 | 83315.73 | 88190.99 | 39791.39 | 0.51 | 0.64 |

**Table 3.** Continued

| Country | 2005 Guidelines [10] (thousands, 2013 US$) | | | 2013 Guidelines [8] (thousands, 2013 US$) | | | Total cost savings (thousands, 2013 US$) | 2013 Guidelines | |
|---|---|---|---|---|---|---|---|---|---|
| | HIV+ | HIV− | Total | HIV+ | HIV− | Total | | Total cost per capita | Proportion of national health care expenditure per Capita (%) |
| Pakistan | 21.97 | 120173.52 | 120195.50 | 24.95 | 85654.55 | 85679.50 | 34516.00 | 0.47 | 1.58 |
| Papua New Guinea | 20.99 | 5268.41 | 5289.40 | 25.47 | 3725.83 | 3751.30 | 1538.11 | 0.51 | 0.65 |
| Peru | 19.10 | 12763.31 | 12782.41 | 26.85 | 5350.99 | 5377.84 | 7404.57 | 0.18 | 0.06 |
| Philippines | 3.61 | 62967.52 | 62971.13 | 4.54 | 35656.88 | 35661.42 | 27309.71 | 0.36 | 0.38 |
| Rwanda | 62.14 | 6052.42 | 6114.56 | 65.85 | 5203.11 | 5268.96 | 845.59 | 0.45 | 0.71 |
| Sao Tome and Principe | 1.68 | 62.80 | 64.49 | 1.89 | 40.91 | 42.80 | 21.69 | 0.22 | 0.19 |
| Senegal | 37.10 | 7458.85 | 7495.95 | 42.18 | 5093.66 | 5135.84 | 2360.11 | 0.36 | 0.54 |
| Sierra Leone | 41.06 | 3140.00 | 3181.06 | 42.06 | 2285.72 | 2327.79 | 853.27 | 0.38 | 0.56 |
| Solomon Islands | 0.83 | 204.44 | 205.27 | 0.95 | 102.53 | 103.48 | 101.79 | 0.21 | 0.15 |
| Somalia | 47.85 | 7093.02 | 7140.86 | 47.93 | 5005.91 | 5053.84 | 2087.03 | 0.48 | 12.47 |
| South Africa | 7868.39 | 42460.96 | 50329.35 | 11230.10 | 9556.77 | 20786.88 | 29542.47 | 0.37 | 0.05 |
| Sudan | 126.39 | 33629.99 | 33756.38 | 142.23 | 17114.97 | 17257.20 | 16499.17 | 0.45 | 0.44 |
| Swaziland | 169.06 | 411.29 | 580.35 | 219.61 | 123.37 | 342.98 | 237.37 | 0.26 | 0.10 |
| Tajikistan | 5.36 | 5479.34 | 5484.70 | 5.92 | 4216.14 | 4222.05 | 1262.65 | 0.51 | 0.95 |
| Tanzania, United Republic of | 1243.91 | 14681.66 | 15925.57 | 1287.95 | 10703.65 | 11991.59 | 3933.98 | 0.24 | 0.65 |
| Togo | 105.00 | 3433.18 | 3538.18 | 110.67 | 2581.48 | 2692.15 | 846.03 | 0.39 | 0.88 |
| Turkmenistan | 4.00 | 4301.07 | 4305.08 | 5.50 | 1986.10 | 1991.60 | 2313.48 | 0.38 | 0.29 |
| Uganda | 788.10 | 21666.61 | 22454.70 | 816.27 | 17467.48 | 18283.75 | 4170.95 | 0.49 | 1.15 |
| Uzbekistan | 26.54 | 16226.31 | 16552.84 | 31.81 | 11232.11 | 11263.92 | 4988.92 | 0.39 | 0.44 |
| Viet Nam | 74.25 | 18278.60 | 18352.85 | 86.23 | 6906.74 | 6992.97 | 11359.88 | 0.08 | 0.09 |
| Yemen | 14.65 | 22461.41 | 22476.07 | 17.31 | 13533.47 | 13550.78 | 8925.28 | 0.56 | 0.63 |
| Zambia | 690.95 | 7479.67 | 8170.62 | 797.46 | 5405.86 | 6203.32 | 1967.29 | 0.43 | 0.49 |
| Zimbabwe | 709.98 | 1996.04 | 2706.02 | 760.05 | 865.22 | 1625.27 | 1080.74 | 0.11 | 0.29 |
| Total | 27566.10 | 2911933.58 | 2939499.68 | 33767.00 | 1743376.97 | 1777143.97 | 1162355.70 | | |

**Table 4.** Total DALYs averted and cost–effectiveness of implementing 2013 guidelines

| Country | Total DALY averted (thousands) | Cost per DALY averted (2013 US$) | | Percentage of cost per DALY averted in GDP per capita (%) | |
|---|---|---|---|---|---|
| | | 2005 Guidelines [10] | 2013 Guidelines [8] | 2005 Guidelines | 2013 Guidelines |
| Afghanistan | 875.44 | 39.00 | 30.38 | 6.29 | 4.90 |
| Angola | 971.25 | 25.11 | 6.68 | 0.46 | 0.12 |
| Azerbaijan | 45.64 | 212.44 | 108.68 | 2.87 | 1.47 |
| Bangladesh | 910.09 | 93.11 | 69.25 | 12.46 | 9.27 |
| Benin | 191.87 | 25.66 | 17.33 | 3.41 | 2.30 |
| Bolivia (Plurinational State of) | 81.97 | 23.81 | 7.50 | 0.92 | 0.29 |
| Botswana | 9.75 | 253.83 | 84.47 | 3.53 | 1.17 |
| Brazil | 167.92 | 173.73 | 47.00 | 1.53 | 0.41 |
| Burkina Faso | 390.63 | 33.01 | 21.50 | 5.20 | 3.39 |
| Burundi | 250.15 | 24.92 | 22.14 | 9.93 | 8.82 |
| Cambodia | 120.25 | 17.65 | 7.05 | 1.87 | 0.75 |
| Cameroon | 499.15 | 22.22 | 13.79 | 1.93 | 1.20 |
| Central African Republic | 113.76 | 69.51 | 70.87 | 14.71 | 14.99 |
| Chad | 516.30 | 10.11 | 3.62 | 1.14 | 0.41 |
| China | 1752.85 | 334.60 | 220.83 | 5.41 | 3.57 |
| Comoros | 13.03 | 50.80 | 42.64 | 6.12 | 5.13 |
| Congo | 37.44 | 101.79 | 44.30 | 3.23 | 1.40 |
| Congo, Democratic Republic | 1770.31 | 19.96 | 14.87 | 7.34 | 5.47 |
| Côte d'Ivoire | 391.80 | 26.75 | 12.21 | 2.15 | 0.98 |
| Djibouti | 11.01 | 27.90 | 9.54 | 2.63 | 0.90 |
| Egypt | 227.57 | 65.04 | 18.85 | 2.04 | 0.59 |

**Table 4.** Continued

| Country | Total DALY averted (thousands) | Cost per DALY averted (2013 US$) | | Percentage of cost per DALY averted in GDP per capita (%) | |
|---|---|---|---|---|---|
| | | 2005 Guidelines [10] | 2013 Guidelines [8] | 2005 Guidelines | 2013 Guidelines |
| Equatorial Guinea | 14.30 | 353.62 | 112.66 | 1.47 | 0.47 |
| Eritrea | 98.98 | 45.61 | 29.62 | 9.04 | 5.87 |
| Ethiopia | 1568.40 | 31.57 | 26.38 | 6.71 | 5.61 |
| Gabon | 16.33 | 172.73 | 46.01 | 1.51 | 0.40 |
| Gambia | 29.69 | 28.96 | 19.11 | 5.66 | 3.73 |
| Ghana | 352.92 | 30.57 | 20.99 | 1.90 | 1.31 |
| Guatemala | 132.69 | 44.22 | 33.12 | 1.32 | 0.99 |
| Guinea | 224.05 | 30.11 | 22.45 | 5.09 | 3.80 |
| Guinea–Bissau | 41.79 | 10.65 | 4.20 | 1.97 | 0.78 |
| Haiti | 172.73 | 10.52 | 5.01 | 1.36 | 0.65 |
| India | 8522.64 | 120.40 | 65.22 | 8.08 | 4.38 |
| Indonesia | 1137.93 | 88.40 | 63.80 | 2.49 | 1.79 |
| Iraq | 265.05 | 114.60 | 58.90 | 1.78 | 0.91 |
| Kenya | 817.99 | 16.14 | 10.00 | 1.87 | 1.16 |
| Korea, Democratic People's Republic | 82.09 | 119.29 | 72.11 | 23.58 | 14.25 |
| Kyrgyzstan | 24.97 | 118.16 | 82.87 | 10.19 | 7.15 |
| Lao People's Democratic Republic | 124.61 | 33.64 | 21.46 | 2.40 | 1.53 |
| Lesotho | 24.95 | 20.94 | 11.31 | 1.76 | 0.95 |
| Liberia | 64.60 | 38.45 | 30.97 | 9.12 | 7.34 |
| Madagascar | 370.93 | 34.88 | 25.61 | 7.80 | 5.72 |
| Malawi | 215.99 | 43.60 | 38.56 | 16.27 | 14.39 |
| Mali | 515.92 | 20.83 | 14.92 | 3.00 | 2.15 |
| Mauritania | 80.87 | 34.11 | 23.72 | 3.08 | 2.14 |
| Mexico | 212.37 | 431.59 | 142.88 | 4.43 | 1.47 |
| Morocco | 151.78 | 73.55 | 43.13 | 2.53 | 1.49 |
| Mozambique | 423.41 | 48.62 | 41.29 | 8.40 | 7.13 |
| Myanmar | 327.07 | 78.25 | 60.48 | 6.84 | 5.29 |
| Nepal | 165.78 | 90.43 | 76.15 | 12.80 | 10.78 |
| Niger | 635.69 | 22.63 | 17.25 | 5.91 | 4.51 |
| Nigeria | 4499.06 | 28.45 | 19.60 | 1.83 | 1.26 |
| Pakistan | 3212.46 | 37.42 | 26.67 | 2.90 | 2.07 |
| Papua New Guinea | 96.55 | 54.79 | 38.86 | 2.51 | 1.78 |
| Peru | 57.94 | 220.62 | 92.82 | 3.36 | 1.41 |
| Philippines | 595.98 | 105.66 | 59.84 | 4.08 | 2.31 |
| Rwanda | 174.96 | 34.95 | 30.11 | 5.64 | 4.86 |
| Sao Tome and Principe | 2.46 | 26.25 | 17.38 | 1.87 | 1.24 |
| Senegal | 165.98 | 45.16 | 30.94 | 4.38 | 3.00 |
| Sierra Leone | 184.08 | 17.28 | 12.65 | 2.72 | 1.99 |
| Solomon Islands | 4.47 | 45.92 | 25.81 | 3.02 | 1.70 |
| Somalia | 476.59 | 14.98 | 10.60 | 0.20 | 0.14 |
| South Africa | 320.65 | 156.96 | 60.73 | 9.93 | 3.84 |
| Sudan | 772.94 | 43.67 | 22.32 | 1.43 | 0.73 |
| Swaziland | 15.91 | 36.47 | 20.27 | 4.18 | 2.32 |
| Tajikistan | 107.30 | 51.12 | 39.35 | 8.40 | 6.46 |
| Tanzania, United Republic of | 634.76 | 25.09 | 18.85 | 4.37 | 3.28 |
| Togo | 117.10 | 30.21 | 22.99 | 0.67 | 0.51 |
| Turkmenistan | 46.83 | 91.93 | 42.53 | 1.41 | 0.65 |
| Uganda | 654.10 | 34.33 | 27.95 | 6.28 | 5.11 |
| Uzbekistan | 241.88 | 67.19 | 46.57 | 3.91 | 2.71 |
| Viet Nam | 214.59 | 85.53 | 35.54 | 5.36 | 2.23 |
| Yemen | 303.25 | 74.12 | 44.68 | 4.96 | 2.99 |
| Zambia | 311.04 | 26.27 | 19.94 | 1.79 | 1.36 |
| Zimbabwe | 238.01 | 11.37 | 6.71 | 1.44 | 0.85 |
| Total | 39 613.61 | | | | |
| Median (IQR) | 212.37 (82.00–493.51) | 38.45 (26.25–87.68) | 26.67 (17.75–46.43) | | |

DALYs – disability adjusted life years, GDP – gross domestic product

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lines will result in slightly higher costs (per patient) at community and first level facility levels due to the use of oral amoxicillin (**Table 2**), the substantial reduction in costs at the hospital level would substantially decrease the overall economic burden on the health care system in low–income countries (**Table 2**) and save monies. However, the cost savings are comparatively lower in high HIV–burden settings (**Table 3**).

This study shows the significant financial and social benefits that would accrue and the substantial reduction in burden on inpatient hospital services that would result from full implementation of the 2013 WHO guidelines. The difference in direct medical costs of pneumonia management is mainly due to the reduction in costs at the hospital level, because most of the pneumonia cases with lower chest in–drawing will NOT be admitted but will be treated on an outpatient basis at the first level facility. Implementing the revised guidelines will thus result in reduction in hospitalization that will reduce the burden on already overcrowded and poorly resourced hospitals. Fewer beds will be utilized by these (less severely ill) children so benefiting more severely ill children (with pneumonia or other severe illness) for whom those beds (and consequent care from in–patient hospital staff) will become available. There will also result in less pressure on over–stretched inpatient staff, limited resources (such as oxygen which can then be targeted better at children with hypoxaemia), a reduced risk of hospital infections and fewer injection related serious adverse events. In addition, the reduction in hospitalization rates can be expected to reduce non–medical costs and the social and financial burden on families by avoiding family costs associated with hospitalisation. Implementing the 2013 WHO guidelines will also make effective treatment with less expensive medicines more locally available to families nearer their homes. This will act to reduce transport costs, loss of wages and other opportunity costs.

Although WHO and UNICEF issued joint statements supporting community case management of pneumonia, diarrhea (and later malaria) in 2004 [39], CCM as an integrated package was introduced only in 2012 [40]. Despite there being clear scientific evidence and an established global consensus regarding benefits of integrated community services for childhood illnesses, the uptake of CCM has been limited. Presently, integrated CCM guidelines are being implemented in only 47 of the 74 Countdown countries [25]. The potential savings in the annual recurrent cost by implementing the 2013 WHO guidelines (as demonstrated in this paper), could be used to support the costs in starting–up the CCM strategy and/or scaling–up the coverage of CCM.

Our estimates have several limitations. First, due to lack of empirical evidence, we have assumed that the proportion of children with pneumonia who have tachypnoea and those who have lower chest wall in–drawing and / danger signs remains same in HIV negative and HIV positive children. This is unlikely to be the case, as children with HIV who are not on anti–retroviral therapy, are more likely to develop (very) severe disease and die. Preliminary large–scale data from Malawi (high HIV burden with integrated CCM implementation) indicates that in program settings, as many as 13% of the children with pneumonia have been reported by CHW to have danger signs compared to 2% in our model (Tim Colbourn, personal communication). In the model, treatment procedures and cost implications for HIV positive patients with chest in–drawing and danger signs are the same in 2005 and 2013 guidelines (Box S1 in **Online Supplementary Document**). Thus as long as the total percentage of patients with chest in–drawing and danger signs remains the same, the proportion of the subgroups does not influence the total management cost. While this does not alter the total direct medical costs much in our study, with regards to implementation of the 2013 IMCI guidelines, this does indicate the need for further research on community–based case ascertainment of pneumonia in high HIV burden settings. Moreover, in this study, we estimated the cost of childhood pneumonia caused by viruses or bacteria, and did not include complications of pneumonia, such as pleural effusion and empyema, lung abscess and pneumothorax. Children presenting other conditions with wheeze (such as bronchiolitis and asthma), with stridor (such as viral croup or diphtheria) or chronic cough (such as tuberculosis and pertussis) were not included.

Second, we have assumed that in integrated CCM implemented settings, 50% of the rural population would be covered by CHWs and the number of CHWs needed per country was obtained by assuming one CHW per 1000 rural population. Available data indicate that this may be difficult to achieve. Therefore, we conducted sensitivity analysis assuming a coverage among rural populations of 9% (when no CCM is implemented), and 30% when CCM is fully implemented (Tables S8–10 in **Online Supplementary Document**). We also considered a scenario with one CHW per 5000 rural population. We found cost savings in all these scenarios (Tables S11–13 in **Online Supplementary Document**). In the extreme scenario with 100% of the rural population were treated by community health workers the results remain cost–effective (Tables S2–S4 in **Online Supplementary Document**).

Third, we only measured "one–off" direct medical cost from a health care provider's perspective. Direct non–medical costs, such as transportation, over the counter medicines, food for patients and accompanying family members, and other out–of–pocket expenses were not considered in this model. Indirect costs (productivity loss and opportunity costs for caregivers) were also not included in this analysis. The recurrent costs and program costs of introducing a new policy in a country were not estimated here. These costs can often be substantial.

Fourth, we applied a public provider cost profile only. Recent surveillance data in Guatemala, Kenya and Thailand found that private physicians treated up to 36% of severe respiratory illness [41]. However, the cost information for private care is difficult to obtain and estimate in these countries. By considering only a public provider profile our estimated costs are likely to under–estimate true resource needs, especially in settings in which private providers are more commonly consulted for treatment of pneumonia.

Fifth, we assumed the same clinical effectiveness for 2005 and 2013 guidelines (ie, they achieved 70% mortality reduction). However, there is some debate as to whether the 2013 guidelines can achieve the same effectiveness as the previous one [42]. We undertook a sensitivity analysis varying the clinical effectiveness estimate and found that the 2013 guidelines remained cost-effective when the mortality reduction from pneumonia management for 2013 guideline was only 36% (ie, roughly half that when following 2005 guidelines) (Table S16 in **Online Supplementary Document**).

Our research demonstrates that implementing the WHO 2013 guidelines for pneumonia management is not only cost–effective, but can also generate substantial cost–savings for each country (compared to current costs implementing 2005 WHO guidelines). Estimation of these avoidable costs is highly relevant and should be of great interest to policy makers in developing countries and donor agencies. Our estimates provide a vital piece of evidence from an economic perspective, to encourage policy makers at the national level and external funding bodies to make informed decisions in setting priorities and budget lines for pneumonia treatment within national programmes. Additionally, the use of scarce resources could be maximized toward the development and advancement of integrated CCM where referral is not possible and improving the quality of care at the primary, secondary and tertiary level health facilities. We also postulate that the cost savings are mainly in low HIV settings. Therefore, further research is required into more cost-effective treatment strategies for pneumonia in high HIV burden settings, especially where there is good coverage with anti–retroviral therapy.

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# Emotional abuse of girls in Swaziland: prevalence, perpetrators, risk and protective factors and health outcomes

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**Background** Research on emotional child abuse in sub–Saharan Africa is scarce. Few studies thus far have examined prevalence, risk and protective factors for emotional child abuse or the associations between emotional abuse and girls' health.

**Methods** A nationally representative two–stage, cluster–sampled, household survey of females aged 13–24 years (n = 1244) on childhood abuse victimisation was conducted. Participants completed interviewer–assisted questionnaires. Associations between emotional abuse and putative risk, and protective factors and health outcomes were analyzed using separate logistic regression models accounting for sampling design. Marginal effects of cumulative risk factors for emotional abuse victimisation were examined.

**Results** Lifetime prevalence of emotional abuse was 28.5% with 58.3% of these girls reporting many abusive incidents. The most common perpetrators were female (27.8%) and male (16.7%) relatives and, more rarely, biological parents. Risk factors associated with emotional abuse were frequent caregiver changes (odds ratio (OR) 1.42, 95% confidence interval (CI) 1.03–1.970, poverty (OR 1.51, 95% CI 1.12–2.03), physical abuse (OR 1.98, 95% CI 1.45–2.71) and sexual abuse (OR 2.22, 95% CI 1.57–3.10) victimisation. Being close to one's mother was a protective factor (OR 0.88, 95% CI 0.80–0.97). Risk for emotional abuse increased from 13% with no risk factors present to 58.4% –with all four risk factors present. Health outcomes associated with emotional child abuse were suicidal ideation (OR 1.85, 95% CI 1.30–2.63) and feeling depressed (OR 1.89, 95% CI 1.31–2.71).

**Conclusions** Girls in Swaziland experience high levels of emotional abuse victimisation. Emotional abuse is associated with economic disadvantage, family factors, other types of abuse victimisation and poor mental health. Therefore, a holistic approach to prevention is needed, incorporating poverty reduction and programmes to improve parent–child relationships, reduce the use of harsh criticism, and change parenting social norms.

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Worldwide, millions of children are victims of abuse and neglect [1], with children in the sub–Saharan African region suffering from particularly high rates of abuse [2,3]. Child maltreatment in the region is associated with a large range of negative outcomes including substance use [4], mental health problems [5], re–victimisation [6], and HIV–risk behavior [7].

A recent systematic review of risk factors for child abuse victimisation in Africa found a growing body of evidence on factors associated mainly with

physical and sexual abuse victimisation [8]. Factors pertaining to emotional child abuse, however, are understudied. In fact, across the sub–Saharan region, only a few quantitative studies have investigated determinants or consequences of emotional child abuse, mostly in conjunction with other adverse childhood experiences [5,9–11]. Available research on emotional abuse alone presents a range of findings depending on the measurements used: living or having lived with a step–father [12], witnessing domestic violence [13], having a caregiver who is ill with AIDS or being AIDS–orphaned [7,11], living with someone who is chronically ill, poverty [14], poor family functioning [15] and poor caregiver mental health [13,15]. Countries across sub–Saharan Africa are culturally and socioeconomically diverse with differing services available to children and abuse victims. Therefore, country–specific research on prevalence and factors associated with emotional child abuse is important for the design of prevention and care policies and programs.

In Swaziland, research on emotional abuse has mostly focused on abuse perpetrated by teachers [16] and the use of humiliating punishment [17]. Some studies have identified drivers of physical and emotional violence against children in Swaziland such as poverty [17,18], orphanhood and moving to live with a different caregiver [18]. However, none of these studies used a nationally representative sample of children to investigate factors associated with emotional child abuse.

The current study had four aims: 1) to estimate the prevalence of childhood emotional abuse and frequency of victimisation, along with the most common perpetrators of emotional abuse among girls in Swaziland; 2) to investigate potential risk and protective factors for emotional abuse 3) to examine whether there is a cumulative risk for emotional abuse when more than one risk factor is present; and 4) to identify associations between emotional abuse and health outcomes.

## METHODS

The analyses presented below are part of the Violence Against Girls Study in Swaziland. The Government of Swaziland had the responsibility for the overall study design and management of the national survey with technical leadership provided by the Central Statistical Office in collaboration with UNICEF Swaziland and the United States Center for Disease Control and Prevention (CDC). The study's overarching aim was to describe epidemiological patterns of sexual violence, identify risk factors, assess knowledge and utilization of services available to victims of sexual violence and to improve awareness of sexual violence against girls [19]. It is to date the only nationally representative survey of girls in Swaziland.

### Procedure

From May 2007 to June 2007, a nationally representative household survey of 13–24 year–old females was conducted using a two–stage, cluster survey design. In the first stage, 40 enumerator areas were selected. In the second stage, a systematic sample of 48 households in each enumerator area with a random start was selected. The sampling frame was provided by the Central Statistics Office of Swaziland based on the 1997 population census. A total of 1900 households were visited, of which 68% (1292) had an eligible female (aged 13–24 years). Overall response rate was 96.3% with 1.1% (n = 14) refusals and 2.6% (n = 34) unavailability [19], which is comparable to other studies in the region [20], and resulted in data from 1244 individuals. One eligible participant was interviewed per household. Where more than one eligible girl was resident, a single participant was randomly selected using the Kish Method [20]. The interview schedule was developed using standardised questionnaires with the help of local informants and were pre–tested through piloting. Interviews were carried out in SiSwati and no incentives were provided. More information on sampling and methodology are available from previous publications on Violence Against Girls in Swaziland [21–23].

Ethical approval was granted by the CDC's Institutional Review Board, and ethics and safety guidelines for studies on violence against women were followed [24,25]. Voluntary consent was obtained from all participants and their head of household. Questionnaires were completed with the help of female interviewers who had received extensive training on privacy, confidentiality and talking about sensitive themes. Participants could stop the interview at any time or skip questions and were given a list of organisations that provide services for women and children.

### Measures

*Emotional abuse* was measured using one item: "When you were growing up, did any adults scare you or make you feel really bad because they called you names, said mean things to you, or said they didn't want

you?" Any emotional abuse that was carried out by an adult such as a biological parent, another relative, a partner, teacher, community or church leader when the participant was aged <18 was included in this analysis.

*Physical abuse* was measured using one item on being kicked, bitten, slapped, hit with a fist or an item, or threatened with a weapon. Contact *sexual abuse* was measured using five items on forced sexual intercourse, coerced sexual intercourse, attempted forced intercourse, and forced sexual touching. The participant had to be <18 years old when the first such incident occurred.

*Abuse frequency* was measured for each perpetrator with a response code of "never; once; few; and many".

*Orphanhood* was defined as having lost one or both parents during childhood [26]. Participants were also asked how *close to their biological mother or father* they felt.

*Overcrowding* was measured asking for the largest number of people who lived in the home at any point in time and defined as >5. *Frequent caregiver changes* were measured using one item establishing how many different families the participant had lived with in their lifetime and defined as having moved family >3. *Poverty* was measured using the proxy food insufficiency which was defined as going hungry often or sometimes. *Community trust* was measured using an item on trusting people in the neighborhood/community/village. *School trust* was measured using one item establishing how trusting the child was of teachers and school administrators.

*Mental health and health risk behaviors* were not comprehensively measured in this interview, although indicators of possible mental health problems included one item on *depression* ("have you ever felt depressed?"), two items on *suicidal ideation* ("have you ever thought about suicide and attempted suicide?"), one item on *smoking* cigarettes, and ever drinking *alcohol,* ever having had a *sexually transmitted disease,* and being *HIV–positive.*

Other socio–demographic information was also collected: the *importance of religion*, *faith, highest level of education, marital status,* whether they lived in *urban/peri–urban or rural locations*, and their *age.*

Most of the items used in this survey have been used successfully in multiple Violence Against Children (VAC) studies [23,27,28].

## Analysis

Four analyses steps were conducted using Stata 13 (StataCorp, College Station, Texas, USA), each accounting for the clustered sampling design. First, descriptive statistics for emotional abuse, risk factors, health outcomes and covariates were obtained (**Table 1**). Second, bivariate regressions were used to investigate associations among emotional abuse, hypothesized risk factors and health indicators (**Table 2**). Third, all significant

**Table 1.** Socio–demographic characteristics of the sample of girls in Swaziland, 2007 (n = 1224)*

| Characteristics | Percentage (n) | Confidence Interval (95%) |
|---|---|---|
| Child emotional abuse | 28.5% (355) | 25.8–31.4% |
| Child sexual abuse | 49.3% (613) | 46.2–52.5% |
| Child physical abuse | 25.6% (319) | 22.5–27.8% |
| Orphanhood | 43.7% (544) | 40.6–47.9% |
| Paternal orphanhood | 33.0% (411) | 30.4–36.4% |
| Maternal orphanhood | 10.8% (134) | 9.0–12.9% |
| Community trust: | | |
| –Strongly disagree | 13.7% (170) | 11.7–16.1% |
| –Disagree | 39.6% (493) | 36.6–42.7% |
| –Neither agree nor disagree | 18.8% (234) | 16.4–21.5% |
| –Agree | 22.0% (274) | 19.6–24.6% |
| –Strongly agree | 5.7% (71) | 4.5–7.4% |
| School trust: | | |
| –Not at all trusting | 9.0% (112) | 7.3–11.0% |
| –Somewhat trusting | 31.1% (387) | 28.2–34.1% |
| –Very trusting | 59.9% (745) | 56.8–62.9% |
| Religious practice: | | |
| –Not important | 7.2% (90) | 5.8–9.0% |
| –A little important | 5.4% (67) | 4.1–7.0% |
| –Somewhat important | 16.0% (199) | 13.8–18.5% |
| –Very important | 71.4% (888) | 68.5–74.1% |
| Poverty | 58.5% (728) | 55.5–61.4% |
| Overcrowding | 87.8% (1092) | 85.8–89.5% |
| Close to mother | 75.9% (944) | 73.2–78.9% |
| Close to father | 46.6% (580) | 43.5–49.7% |
| Frequent caregiver changes | 26.1% (325) | 23.5–28.9% |
| Age (years) | 17.9 (SE 0.10) | 17.8–18.1 |
| Relationship status: | | |
| –Married | 9.7% (120) | 8.1–11.7% |
| –Living with partner, not married | 3.4% (42) | 2.5–4.4% |
| –Not living with partner | 86.8% (1079) | 84.7–88.7% |
| Urban or peri–urban area | 15.3% (190) | 14.5–16.3% |
| Ethnicity African | 99.8% (1241) | 99.2–99.9% |
| Highest level of education: | | |
| –Some primary | 43.4% (538) | 40.3–46.5% |
| –Some secondary | 55.2% (687) | 52.0–58.3% |
| –Some tertiary | 1.4% (17) | 0.7–2.4% |
| Religion: | | |
| –Zionist Christian Church | 41.0% (510) | 38.1–44.1% |
| –Catholic | 5.4% (67) | 4.2–6.9% |
| –Protestant | 52.7% (656) | 49.6–55.8% |
| –Muslim | 0.1% (1) | 0.002–0.04% |
| Suicidal ideation | 17.7% (220) | 15.5–20.0% |
| Feeling depressed | 67.8% (843) | 64.8–70.6% |
| Sexually transmitted diseases | 5.0% (62) | 3.7–6.6% |
| Alcohol | 10.3% (128) | 8.6–12.4% |
| HIV–positive | 12.0% (149) | 8.7–16.2% |
| Smoking | 2.0% (25) | 1.3–3.0% |

SE – standard error
*Some variation in numbers across variables due to a small amount of missing data.

**Table 2.** Factors associated with emotional abuse victimisation among girls in Swaziland, 2007 using bivariate logistic regressions (n = 1244)

| Factor | Odds ratio (95% confidence Interval) | P-value |
|---|---|---|
| Physical abuse | 2.55 (1.89–3.44)‡ | 0.001 |
| Orphanhood | 1.44 (1.09–1.90)† | 0.009 |
| Sexual abuse | 2.11 (1.59–2.80)‡ | 0.001 |
| Community trust (very low ref): | | |
| –Low | 0.70 (0.46–1.07) | 0.103 |
| –Undecided | 0.61 (0.37–1.00)* | 0.049 |
| –High | 0.73 (0.46–1.15) | 0.180 |
| –Very high | 0.93 (0.47–1.83) | 0.838 |
| School trust (low trust ref): | | |
| –Medium trust | 0.89 (0.53–1.48) | 0.640 |
| –High trust | 0.97 (0.60–1.58) | 0.782 |
| Religious practice | 0.94 (0.80 –1.10) | 0.451 |
| Poverty | 1.48 (1.12–1.96)* | 0.005 |
| Overcrowding | 1.18 (0.78–1.78) | 0.428 |
| Close to mother | 0.85 (0.77–0.92)‡ | 0.001 |
| Close to father | 0.94 (0.88–1.01) | 0.119 |
| Frequent caregiver changes | 1.64 (1.21–2.22)‡ | 0.001 |
| Age | 0.97 (0.94–1.01) | 0.147 |
| Level of education primary (ref): | | |
| –Some secondary | 0.84 (0.63–1.12) | 0.229 |
| –Some tertiary | 0.10 (0.01–0.78)* | 0.028 |
| Relationship status: | | |
| –Married | 1.31 (0.85–2.04) | 0.225 |
| –Living with partner, not married | 1.17 (0.63–2.20) | 0.614 |
| –Not living with partner (ref) | | |
| Urban or peri–urban area | 0.72 (0.50–1.02) | 0.066 |
| Faith: | | |
| –Catholic (Ref Zionist Christian) | 0.56 (0.30–1.02) | 0.062 |
| –Protestant | 0.83 (0.62–1.10) | 0.197 |
| –No religion | 1.62 (0.42–6.27) | 0.480 |
| HIV–positive | 0.96 (0.47–1.99) | 0.918 |
| Drinks alcohol | 1.25 (0.79–1.96) | 0.335 |
| Smoking | 0.91 (0.38–2.18) | 0.839 |
| Suicide ideation | 2.23 (1.61–3.07)‡ | 0.001 |
| Feeling depressed | 2.15 (1.55–2.97)‡ | 0.001 |
| Sexually transmitted disease | 2.39 (1.29–4.41)† | 0.006 |

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

risk factors (at $P < 0.05$) obtained from the bivariate regression were included in two multivariate models with controls for age, urban/rural location and faith. This resulted in five regression models: risk factors for emotional abuse (**Table 3**, Models 1, 2 and 3) and health outcomes (**Table 4**, Models 1 and 2) showing model selection through backward elimination of non–significant risk factors until all remaining factors were associated with emotional abuse ($P < 0.05$) [29]. The first risk factor model includes all significant factors ($P < 0.05$) from the bivariate regressions (Model 1). The second includes all factors significant at $P < 0.1$ and the third includes all factors significant at $P < 0.05$. For the health outcome models, the first includes all risk factors significant at $P > 0.1$. The second includes all factors significant at $P < 0.05$. Finally, cumulative risk of associated factors was tested. For all risk factor variables and covariates that were included in **Table 3** Model 3, marginal effects for emotional abuse – based on the logistic regression model – were calculated with all covariates held at their mean value (average marginal effect). This determined how the predicted probability of the outcome changes for different risk factors (and combinations of risk factors; see **Figure 1**).

## RESULTS

1244 girls (mean age 17.9 years, 99.8% Black African) were interviewed in this study. Sample characteristics showed high levels of deprivation: 43.7% were orphaned, 58.5% experienced poverty to the point where there was insufficient food in the household, 26.1% experienced frequent caregiver changes and 87.8% lived in overcrowded accommodation. Of the participants, 67.8% reported feeling depressed, 17.7% suffered from suicidal ideation, 12.0% were HIV–positive and 5.0% had a sexually transmitted disease in the past (**Table 1**).

### Prevalence of emotional abuse in childhood

Nearly three in every ten participants (28.5%, 95% CI 25.8%–31.4%) reported experiencing emotional abuse at least once
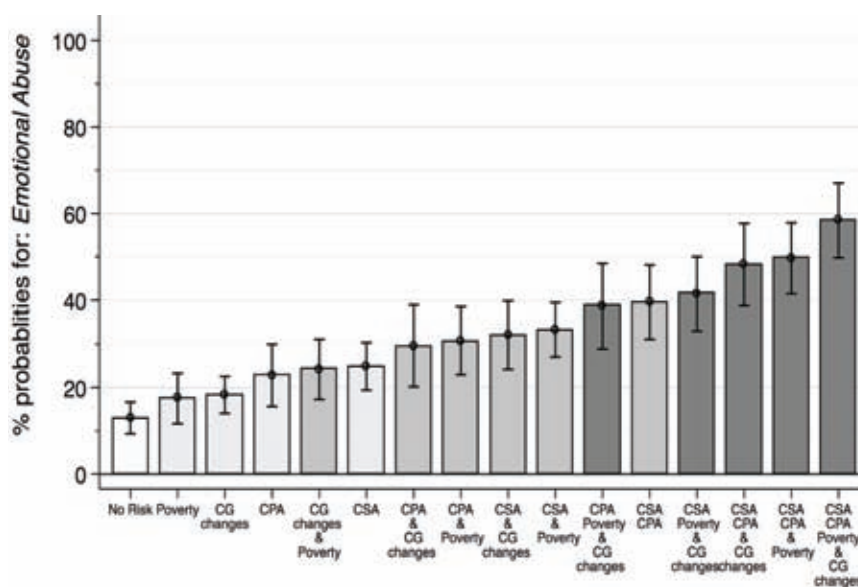


**Figure 1.** Predicted cumulative risk for emotional abuse victimisation among girls in Swaziland, 2007. Data source: VACS Swaziland, n=1224.

**Table 3.** Multivariate logistic regressions of factors associated with emotional abuse among girls in Swaziland, 2007 (n = 1244)

| | Model 1 | | Model 2 | | Model 3 | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95% CI | Odds ratio | 95% CI | Odds ratio | 95% CI |
| Orphanhood | 1.26 | 0.94–1.70 | | | | |
| Close to mother | 0.91† | 0.82–1.00 | 0.88† | 0.80–0.89 | 0.88‡ | 0.80–0.97 |
| Frequent caregiver changes | 1.40† | 1.00–1.97 | 1.41† | 1.01–1.97 | 1.42† | 1.03–1.97 |
| Poverty | 1.45† | 1.07–1.96 | 1.52‡ | 1.13–2.05 | 1.51‡ | 1.12–2.03 |
| Physical abuse | 2.00§ | 1.45–2.75 | 1.98§ | 1.44–2.72 | 1.98§ | 1.45–2.71 |
| Sexual abuse | 2.19§ | 1.55–3.09 | 2.14§ | 1.52–2.01 | 2.22§ | 1.57–3.10 |
| Tertiary education | 0.17* | 0.02–1.32 | 0.16 | 0.20–1.22 | | |
| Urban or peri–urban area | 0.64* | 0.43–0.96 | 0.64† | 0.43–0.96 | 0.65† | 0.44–0.96 |
| Age | 0.92§ | 0.88–0.97 | 0.92‡ | 0.88–0.97 | 0.92§ | 0.88–0.97 |
| Faith | 0.93 | 0.80–1.08 | | | | |

CI – confidence interval
*Statistically significant at $P < 0.1$.
†Statistically significant at $P < 0.05$.
‡Statistically significant at $P < 0.01$.
§Statistically significant at $P < 0.001$.

in their childhood. Of those who reported emotional abuse, 16.8% (95% CI 13.4%–21.0%) reported one incident, 24.8% (95% CI 20.7%–29.5%) reported few incidents and 58.3% (95% CI 53.2%–63.2%) reported many incidents. Girls in rural areas reported higher levels of emotional abuse compared to those in urban and peri–urban areas but this was not statistically significant.

## Emotionally abusive acts by family members compared to "others"

The majority of emotionally abusive acts were carried out by extended family members. The most frequent perpetrators were female relatives (27.8%, 95% CI 23.4%–32.6%), followed by male relatives (16.6%, 95% CI 13.0%–20.8%), biological mother (11.1%, 95% CI 8.45–14.5%), biological father (9.8%, 95% CI 7.0%–13.4%), brother (4.7%, 95% CI 2.9%–7.5%) and sister (4.3%, 95% CI 2.5%–7.4%). Less frequent perpetrators were ex–partners (1.2%, 95% CI 0.4%–3.5%), step–mothers (6.5%, 95% CI 4.5%–9.5%), teachers (2.5%, 95% CI 1.4%–4.6%) and community leaders (2.1%, 95% CI 1.2%–3.7%).

## Risk factors associated with emotional child abuse victimisation

Using bivariate regressions, childhood emotional abuse was associated with physical and sexual childhood abuse, orphanhood, poverty, and frequent caregiver changes. Being close to one's mother was found to be protective against childhood emotional abuse as was being educated at tertiary level. Community trust, school trust, being close to one's father, relationship status, overcrowding and religious practice were not associated with emotional abuse (**Table 2**).

Using multivariate regressions controlling for age, location, faith, frequent caregiver changes (OR 1.42, 95% CI 1.03–1.97), poverty (OR 1.51, 95% CI 1.12–2.03), childhood physical abuse (OR 1.98, 95% CI 1.45–2.71) and sexual abuse (OR 2.22, 95% CI 1.57–3.10) continued to be associated with an increased risk for childhood emotional abuse. Being close to one's mother (OR 0.88, 95% CI 0.80–0.97) continued to be protective of emotional abuse. Orphanhood and tertiary–level education were no longer significant and therefore dropped from the model (**Table 3**, Model 3).

## Combinations of risk factors

For female youth in Swaziland, the predicted probability of childhood emotional abuse victimisation was 13.0% (95% CI 9.3%–15.6%) when none of the included risk factors of frequent caregiver changes, poverty, childhood physical and sexual abuse were present. One risk factor at a time was then included in a model, followed by a set of combinations of two, three and all four risk factors to establish which girls are at highest risk of emotional abuse.

Results for individual risk factors show the following predicted probabilities of emotional abuse expressed in percentages: 17.5% (95% CI 11.6%–23.3%) for poverty; 18.3% (95% CI 14.1%–22.4%) for frequent caregiver changes; 22.8% (95% CI 15.6%–30.0%) for physical child abuse; and 24.9% (95% CI–19.4%–30.0%) for sexual child abuse. When two risk factors were combined the predicted probabilities increased:

24.2% (95% CI 17.3%–31.1%) for frequent caregiver changes and poverty, 30.7% (95% CI 23.0%–38.5%) for child physical abuse and hunger, 29.5% (95% CI 20.2%–39.0%) for child physical abuse and frequent caregiver changes, 32% (95% CI 24.2%–40.0%) for child sexual abuse and frequent caregiver changes, 33.3% (95% CI 27.1%–39.5%) for child sexual abuse and poverty and 39.6% (95% CI 31.1%–48.1%) for child sexual and physical abuse. The combination of three risk factors showed an increase of predicted probabilities as well: 38.7% (95% CI 29.0%–48.5%) for physical abuse, frequent caregiver changes and poverty; 41.5% (95% CI 33.0%–50.0%) for sexual abuse, frequent caregiver changes and poverty; 48.3% (95% CI 38.8%–57.7%) for sexual abuse, physical abuse and frequent caregiver changes; and 49.7% (95% CI 41.5%–57.9%) for sexual abuse, physical abuse and poverty. Finally, among girls who reported experiencing all four risk factors, predicted probability for childhood emotional abuse victimisation increased to 58.4% (95% CI 49.8%–67.1%; **Figure 1**).

### Mental and sexual health outcomes associated with emotional abuse

Using *bivariate regressions*, childhood emotional abuse was associated with the following health risks: suicide ideation, feeling depressed and having suffered from a sexually transmitted disease. Being HIV–positive, consuming alcohol and smoking were not associated with emotional abuse (**Table 2**).

Using multivariate regression analyses, suicidal ideation (OR 1.85, 95% CI 1.30–2.63) and feeling depressed (OR 1.89, 95% CI 1.31–2.71) were associated with emotional childhood abuse when controlling for location, age, faith, physical abuse and sexual abuse. Having a sexually transmitted disease was no longer significant and was therefore dropped from the model (**Table 4**, Model 2).

**Table 4.** Logistic regression analyses of health factors associated with emotional abuse among girls in Swaziland, 2007 (n = 1244)

| | MODEL 1 | | MODEL 2 | |
|---|---|---|---|---|
| | Odds ratio | 95% CI | Odds ratio | 95% CI |
| Suicide ideation | 1.79* | 1.25–2.56 | 1.85* | 1.30–2.63 |
| Feeling depressed | 1.87* | 1.30–2.69 | 1.89* | 1.31–2.71 |
| Sexually transmitted disease | 1.78 | 0.90–3.55 | | |
| Physical abuse | 1.89* | 1.38–2.58 | 1.92* | 1.40–2.62 |
| Sexual abuse | 2.04* | 1.45–2.86 | 2.08* | 1.48–2.92 |
| Urban or peri–urban area | 0.78 | 0.53–1.16 | | |
| Age | 0.88* | 0.84–.93 | 0.89* | 0.84–94 |
| Faith | 0.91 | 0.78–1.06 | | |

CI – confidence interval
*Statistically significant at *P* < 0.05.

## DISCUSSION

To the best of the authors' knowledge, this is the first and only nationally representative study of emotional child abuse victimisation in Swaziland. This study adds to the literature on the epidemiology of emotional child abuse victimisation in sub–Saharan Africa by investigating prevalence, risk factors and health outcomes associated with emotional child abuse. It finds high prevalence of emotional abuse and significant associations with hypothesized risk factors and indicators of poor health. In addition, a cumulative effect of risk factors for emotional abuse could be established.

Prevalence of emotional child abuse was high, with 28.5% of girls reporting at least one incident and 58.3% of these reporting many incidents. Results also show that physical and sexual child abuse are strongly associated with emotional child abuse, suggesting many instances of multiple abuse victimisation. This finding corresponds to reports from other cross–sectional studies in sub–Saharan Africa showing associations between emotional and physical and sexual child abuse [8]. Poly–victimisation affects large numbers of children across the world [30]. Children affected by one type of violence are often susceptible to other types of violence as these are mediated by common individual, family and social vulnerabilities [31]. In a recent study from South Africa, 35.5% of children experienced more than five lifetime events of violence [32]. Factors associated with increased poly–victimisation in South Africa included parental substance use, parental absence due to illness, child substance use, child sexual risk behavior, single–parenting and living in urban areas [32].

Contrary to other research from the region [33], this study found female relatives to be the most common perpetrator of emotional abuse victimisation, followed by male relatives and biological parents. This may be due to family caregiving arrangements influenced by the high number of orphaned children in Swaziland, also found by this study. A large, national qualitative study on the drivers of violence affecting children in Swaziland, which included focus groups and interviews with 373 respondents, found that of all the interpersonal–level risk factors for violence against children suggested by respondents, family structure was the most cited. This is because "not living with biological parents" was perceived by many to almost guarantee negative differential treatment – which would be emotionally abusive at the least, but was also likely to result in a child being given a disproportionate number of household chores and harsher punishment [34]. While orphanhood was not associated with higher risk for emotional abuse in multivariate regressions, orphaned girls reported higher percentages of violence victimisation than non–orphans. This finding is consistent with a number of studies from sub–Saharan Africa [11,28,35,36]. However, these associations tend not to hold up in multivariate regressions controlling for other potential risk factors, which may drive risk for abuse more strongly than orphanhood alone. A recent systematic review examining risk for violence victimisation among orphaned and non–orphaned children found little or no difference in risk for abuse between the groups [37]. More research on the vulnerabilities of orphans is needed to better understand how orphanhood and violence interlink, particularly in countries with large numbers of orphans like Swaziland.

In line with high numbers of orphaned children, large numbers of girls reported frequent caregiver changes, and this type of social disadvantage is associated with emotional abuse. Conversely, being close to one's mother was a protective factor. The association between frequent caregiver changes and emotional abuse in Swaziland is particularly interesting considering that relatives in the extended family but not biological parents were the most commonly reported perpetrators of emotional abuse. This pattern contrasts with some findings in South Africa [33]. Future research should investigate whether these relatives are the primary caregivers of the child and, if so, how the child came to be in their care (ie, through orphanhood, abandonment, work or migration) as well as whether these abusive events occurred while the child was in the primary care of her biological parents or outside the household setting. Caregiving arrangements for girls should also be investigated to determine whether having kinship caregivers as opposed to non–kinship carers increases the odds of emotional abuse victimisation as has been found in qualitative research in Swaziland [34].

Overall, the findings correspond with research from South Africa where multiple victimisation, poverty and frequent caregiver changes were found to be associated with emotional abuse [11]. It is also likely that the specific context of Swaziland compounds these problems. Swaziland has a population of 1.3 million, 59.1% of whom live on less than US$ 2 per day [38] and an estimated population of 120 000 orphaned children [39]. The HIV prevalence in Swaziland is 27.4%, which is the highest prevalence worldwide [40]. It is therefore likely that families experience multiple severe stressors such as extreme poverty, illness and death, resulting in insufficient care, disruption of social norms, and overburdened and under–resourced systems for child protection [14,41-43]. Violence prevention interventions could thus be linked to HIV–prevention efforts through comprehensive social protection and social welfare efforts [44-46].

Contrary to other studies, overcrowding was not associated with emotional abuse in the multivariate analyses [8], which may be a result of the way in which this variable was measured. Establishing the highest number of residents in the household throughout one's lifetime may not be sensitive enough to establish whether the overcrowding was short–term or long–term.

Cumulative effects of risk factors on emotional abuse victimisation were found. Without any of the three significant risk factors, a girl's probability of experiencing childhood emotional abuse was 13%, while girls who reported frequent moves, hunger, and physical and sexual childhood abuse had a probability of 58.4%. The connections between adverse childhood experiences such as orphanhood, parental mental illness or childhood abuse, and putative outcomes have long been established in high income countries [47] with a growing evidence–base in low– and middle–income countries [48,49]. In particular, adults who experienced a combination of four or more adverse events in childhood are at risk for negative health outcomes.

Feelings of depression and suicidal ideation were also found to be associated with emotional abuse in this study. While more robust measures on mental health would need to be used in future studies to explore this relationship, this association has also been found in the evidence from the sub–Saharan African region [5] and across the globe [50]. Emotional childhood abuse may contribute to the salience of suicide as a leading cause of death for young people in southern Africa [51]. Sub–Saharan Africa experiences a high burden of child and adolescent mental health problems with a recent systematic review of commu-

nity–based studies establishing a psychopathology prevalence rate of 14.3% [52] but with little nationally representative data available from the region [53].

The results of this study suggest a need for comprehensive child abuse prevention and protection strategies for girls in Swaziland. Girls experiencing multiple adverse conditions are at high risk of abuse, and humiliating punishment of children is an accepted form of discipline in many Swazi households [17]. Holistic social support interventions that promote positive parenting behaviors of primary caregivers may be useful [54] and help to build stronger relationships between children and their caretakers, particularly mothers. A recent study from South Africa found adolescent health risks were linked to family disadvantage via abusive parenting and caregiver mental health problems, suggesting a need for combined parenting assistance, poverty alleviation and mental health support [10]. In particular, adolescent mothers are at high risk for harsh parenting [55], struggle with parenting stress [56], and experience high levels of poverty [56,57] and low levels of education [58]. Considering the high risk for re–victimisation in victims of childhood violence [50,59] and the possibility of inter–generational violence transmission to these girls' children [60], the high prevalence of abuse victimisation in this sample suggests that an entire society is persistently at risk for poor outcomes. Programmes are thus needed for both adult and adolescent mothers to reduce household stress and increase parenting capacity. Emerging evidence on parenting programmes with financial strengthening components for caregivers and teenagers shows clear reductions in physical and emotional abuse victimisation [61], also in the context of high levels of caregiver changes [62] in South Africa.

In light of the high levels of physical and sexual violence found in this study, a holistic approach to prevention is needed. As described in the INSPIRES framework, the seven strategies with the best available evidence for the reduction and prevention of violence against children across contexts are implementation of enforcement laws, changing of norms and values, safe environments, parent and caregiver support, income and economic strengthening, response and support services, and education and life skills, which should be implemented as part of a comprehensive and multi–sectoral plan [63]. However, each of these strategies need to be adapted and evaluated for the contexts in which there are to be used. Emerging research from other sub–Saharan countries suggests that prevention of violence against girls should incorporate asset–based approaches. Protective assets can be income generating activity, friendship networks, specific knowledge of one's community, services and rights, enabling girls to make safety plans, and creating safe spaces [64]. In Swaziland specifically, a school–based intervention of "Safer Spaces" showed stark increases in girls' protective assets and in knowledge about gender–based violence. Furthermore, changes in gendered attitudes were observed, which is often the first stage in normative transformations around violence. However, reporting of violence increased and no reductions in victimisation were shown [65]. Early results from other countries in sub–Saharan Africa show a potential for using protective assets to prevent gender–based violence [64], early child marriage [66] and HIV–risk [67]. However, further research and large–scale intervention evaluation are needed in order to verify the impact of parenting interventions and protective assets on child abuse prevention.

Research in sub–Saharan Africa has consistently shown the impact of violence on educational attainment [68,69] as well as the protective effect of secondary education on harsh parenting in adulthood [70] and exposure to intimate partner violence [71]. A case could thus be made that secondary schooling – provided the school setting is safe and protective as indicated in the Safe Spaces Intervention – is another important child abuse prevention intervention.

In order to address the multiple needs of young women and children in Swaziland, an integrated, early intervention approach may be effective. This holistic approach could give ample opportunity for different services providers to collaborate and address multiple forms of violence using gender–sensitive approaches. Where strong links are built between services for women and children as well as between school–based and parenting programmes, complex family dynamics may be addressed, and continued programming for adolescent health and development with gender–sensitive content could be facilitated.

## Limitations and future research

This study had a number of limitations. First, an all–female sample was recruited so no assumptions regarding the victimisation of boys can be made. Second, data were cross–sectional and therefore did not allow for causal inferences. Further, it is impossible to say in what temporal order risk factors and putative health outcomes occurred. In other words, we cannot know if children experience suicidal ideation because they were victims of violence or if they are more vulnerable to experience violence. Third, the study used retrospective self–report which may be subject to recall bias due to under–reporting of abusive events [72]. Furthermore, the study used interviewer–guided questionnaires, which may have resulted in some under–reporting due to social desirability bias in particular with regards to sensitive ques-

tions such as parental aggression and sexual violence. However, official records are not kept reliably in Swaziland, and few child abuse victims access services [73], thus making self–report a more reliable source of information. Further, the study did not use internationally validated measures of child abuse victimisation and mental health. For example, emotional abuse was measured using one item that grouped many emotionally abusive acts in one question. While different abuse measures use differing definitions of emotional abuse, there is large overlap between the abusive incidents queried in the single–item question and the most common child abuse measures. However, including four types of abusive behavior in a single question might have made this question too complex and thus led to over– or under–reporting of abusive events. Depression was measured with only one question about whether the participant had felt depressed. Validity of these single items as indicators of complex constructs is not established. Although these single–item measures have been used in multiple VAC studies in sub–Saharan Africa and elsewhere [27] since the completion of this study and the basic trends in prevalence may be similar to regional surveys that used more comprehensive measures, ie, Optimus Study in South Africa [74], future research should develop and utilize validated and standardised measures. Finally, there is a strong likelihood for unmeasured confounding in this study. Even though models adjusted for potential confounding, no such adjustment was possible for caregiver–related variables commonly associated with emotional abuse victimisation (ie, mental health problems, drug abuse) or community factors (ie, social norms, service availability, girls' knowledge of services).

## CONCLUSIONS

Overall, the findings of this study demonstrate the magnitude of girls' exposure to emotional abuse in Swaziland. It highlights particularly vulnerable groups such as victims of multiple types of abuse, those who experienced frequent caregiver changes and those most affected by poverty. The findings are relevant to social policy and intervention programmes. Holistic child abuse prevention programmes targeting poverty, unstable family environments and parenting—such as cash transfers and programmes focused on keeping girls in education, teaching parenting skills and delaying marriage—are needed to reduce the burden of emotional abuse and associated adverse mental health outcomes.

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# Solar powered oxygen systems in remote health centers in Papua New Guinea: a large scale implementation effectiveness trial

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**Background** Pneumonia is the largest cause of child deaths in Papua New Guinea (PNG), and hypoxaemia is the major complication causing death in childhood pneumonia, and hypoxaemia is a major factor in deaths from many other common conditions, including bronchiolitis, asthma, sepsis, malaria, trauma, perinatal problems, and obstetric emergencies. A reliable source of oxygen therapy can reduce mortality from pneumonia by up to 35%. However, in low and middle income countries throughout the world, improved oxygen systems have not been implemented at large scale in remote, difficult to access health care settings, and oxygen is often unavailable at smaller rural hospitals or district health centers which serve as the first point of referral for childhood illnesses. These hospitals are hampered by lack of reliable power, staff training and other basic services.

**Methods** We report the methodology of a large implementation effectiveness trial involving sustainable and renewable oxygen and power systems in 36 health facilities in remote rural areas of PNG. The methodology is a before–and after evaluation involving continuous quality improvement, and a health systems approach. We describe this model of implementation as the considerations and steps involved have wider implications in health systems in other countries.

**Results** The implementation steps include: defining the criteria for where such an intervention is appropriate, assessment of power supplies and power requirements, the optimal design of a solar power system, specifications for oxygen concentrators and other oxygen equipment that will function in remote environments, installation logistics in remote settings, the role of oxygen analyzers in monitoring oxygen concentrator performance, the engineering capacity required to sustain a program at scale, clinical guidelines and training on oxygen equipment and the treatment of children with severe respiratory infection and other critical illnesses, program costs, and measurement of processes and outcomes to support continuous quality improvement.

**Conclusions** This study will evaluate the feasibility and sustainability issues in improving oxygen systems and providing reliable power on a large scale in remote rural settings in PNG, and the impact of this on child mortality from pneumonia over 3 years post–intervention. Taking a continuous quality improvement approach can be transformational for remote health services.

Pneumonia is the largest cause of child deaths in Papua New Guinea (PNG), as it is globally [1,2]. Hypoxaemia is the major complication causing death in childhood pneumonia and is highly prevalent in highlands region of

PNG. In provincial hospitals in PNG the mortality rate for pneumonia and severe pneumonia are 5% and 10%, respectively [2]. In previous studies in PNG we showed that improved oxygen systems, which include a reliable source of oxygen therapy using concentrators, and pulse oximetry for detection of hypoxaemia, can reduce mortality from pneumonia by up to 35% [3]. Hypoxaemia occurs in many other common conditions: bronchiolitis, sepsis, asthma, tuberculosis, HIV–related lung disease, malaria, perinatal problems, trauma, obstetric emergencies, and chronic respiratory and cardiac disease in adults and children [4–7]. A reliable oxygen system is therefore a critical minimum input for adequate health care in all settings where such emergencies present and such conditions are managed.

However, in PNG and in low and middle income countries throughout the world, improved oxygen systems have only been implemented where it is relatively easy to do so; in larger provincial or referral hospitals with adequate power supplies and staff capacity [3,8,9]. In these countries, including those with the largest shares of the global burden of childhood pneumonia deaths such as Ethiopia and PNG, a high proportion of the population live in rural areas, where access to urban centers and referral health care facilities is limited or non–existent. Improved oxygen systems have not been implemented at scale in such settings, and do not reach smaller rural hospitals or district health centers that serve as the first point of referral for acute illness. Many children with severe pneumonia present to these small rural hospitals and district health centers where hypoxaemia often goes undetected or untreated. Barriers to improving oxygen systems in these settings include the lack of adequate power, uncertain long–term reliability of equipment in remote settings, logistics of implementation, lack of preventive maintenance, lack of recognition of the importance of oxygen or identification of hypoxemia using pulse oximetry, limited training of health workers in the recognition of hypoxaemia, and lack of financial investment in quality health services in rural and remote areas. Oxygen concentrators have previously been run using solar power, but only on a small scale in a single health facility [10,11].

We report the steps needed to implement basic oxygen systems in 36 health facilities in remote rural areas of PNG. The decisions and steps involved included: defining the criteria for facilities where such an intervention is appropriate, assessment of power supplies and power requirements, the optimal design of a solar power system that can address both oxygen equipment load and for other essential health facility equipment, specifications for oxygen concentrators and other oxygen equipment that will function in remote and tropical environments, implementation logistics in remote settings, the role of oxygen analyzers in monitoring oxygen concentrator performance, the engineering capacity required to sustain a program at scale, clinical guidelines and training on oxygen equipment and the treatment of children with severe respiratory infection and other critical illnesses, program costs, and measurement of processes and outcomes to inform continuous quality improvement.

These steps to scaling up oxygen systems in the most challenging environments have not previously been actioned in a large field trial. We describe this model of implementation in the hope that other countries will build on this.

### The project

Previous research has been conducted to understand the epidemiology of hypoxaemia in PNG [4,12,13], the quality of care provided in rural and district hospitals [14], and the effect of oxygen on case fatality rates from pneumonia [3]. What has not been demonstrated until now is the sustainable implementation at large scale in the most difficult environments, and the steps required to achieve this. This project is funded by the Bill and Melinda Gates Foundation and other partners. Project funding, which also included support for trialing the implementation of oxygen concentrators in 12 urban hospitals in Nigeria [15], was provided in 2014. Preparatory work for this project occurred in 2014 and 2015.

## METHODS

### The process for identifying suitable facilities

Criteria for selecting suitable health facilities was determined by wide stakeholder consultation between representatives of the National Department of Health, provincial health, nurses and doctors, administrators and technicians. Broad principles for selection were set out and suitability was ascertained by on–site assessments and review of the available routine data. Selection of participating health facilities was on the basis of clinical need and the capacity for benefiting that community. The need for sources of oxygen and

power are high for health facilities that are located within large population areas (even if that population is dispersed over a wide area) where the prevalence of pneumonia and other acute respiratory infections is high, and where access to a provincial referral hospital is limited or transportation is likely to be hazardous for seriously ill patients. Other principles for health facility selection were that the health facility had difficulty gaining access to a reliable source of oxygen; that the facility was open and functioning; and staff were motivated to participate. In PNG while some primary health centers are closed or not functioning, many, particularly district health centers fulfilled these criteria, are functioning to the best of their capacity and have staff who are enthusiastic and committed.

Baseline data were collected on all proposed health facilities. This involved routine recording of admissions, deaths and referrals for the previous 3 years (Table 1).

Data were also collected on characteristics of the health services: the number of health personnel, levels of training and recent continuing education, health facility bed capacity for children, availability of oxygen equipment, existing power sources, security issues at the health facility, and essential medicines, equipment, commodities and procedures for infection control, and laboratory tests.

## Assessment of power supplies and power requirements

We have previously assessed the power supplies in five district hospitals using an Electrocorder [14]. This demonstrated that even in facilities that are connected to mains power, power supplies are erratic, with many outages, fluctuations and surges. These abrupt changes in power have the high likelihood of damaging oxygen concentrators and other equipment, and may be one of the key reasons for concentrator failure in previous studies. In this current field trial we did not reproduce Electrocorder readings as the health facilities included were at an even lower level than the previously assessed 5 district hospitals, and were either without mains power, with known unreliable power, or with an alternative source of renewable power, such as hydropower. If a health facility only had a diesel backup generator this was not considered sufficient, as the costs, availability and logistics of diesel fuel are an obstacle to using electrically powered equipment.

## The optimal design of a solar power system

Considerations in the design of the solar panel included the efficiency of the system, the peak sun hours for the specified tilt angle (4.53 hours), a 25% oversupply of power, and the total daily energy demand. The system was designed to supply 11.44kWh/d daily average load, using eighteen 240W panels. This was based on the power requirements for a rural health facility for treating common childhood illnesses [16]. A battery backup system was designed to provide 3 days autonomy at 80% depth of discharge. Other solar equipment calculations are included in **Online Supplementary Document.**

## Specifications for oxygen concentrators and other oxygen equipment that will function well in remote environments

The choice of oxygen equipment was based on over a decade of trial and error, in PNG and in other countries [8,17–20]. The principles are that concentrators needed to be robust, standardized, and able to function well at high temperature and high humidity, and have a relatively low power requirement. Concentrator specifications follow the now published WHO guidelines for oxygen concentrators [21]. We use Airsep Elite 5 l/min concentrators (Chart Industries, New York NY, USA) and Lifebox pulse oximeters (Lifebox, London, UK), both of which have been successfully used in larger hospitals in previous field trials in PNG and other developing countries. Busy district hospitals are receiving three concentrators, and smaller health centers are receiving two. Theoretically, several patients can be treated at any one time

**Table 1.** Baseline data in 36 health centers and district hospitals

| Year | Paediatric admissions | Paediatric deaths | CFR (%) | Pneumonia | Pneumonia deaths | Pneumonia CFR (%) | Births | NND | NMR (per 1000) | Children referred out |
|---|---|---|---|---|---|---|---|---|---|---|
| 2014 | 8511 | 309 | 3.63 | 3510 | 146 | 4.16 | 10933 | 98 | 9.0 | 687 |
| 2013 | 7193 | 236 | 3.28 | 2849 | 125 | 4.39 | 10329 | 88 | 8.5 | 695 |
| 2012 | 5104 | 216 | 4.23 | 2447 | 86 | 3.51 | 10284 | 84 | 8.2 | 791 |
| Total | 20808 | 761 | 3.66 | 8806 | 357 | 4.05 | 31546 | 270 | 8.6 | 2173 |

NND – neonatal deaths, CFR – case fatality rate

using a concentrator using a flow meter assembly which splits flow to several patients (Sureflow meter, Airsep FM069–1, Chart Industries, Galveston USA). Typically two patients at any one time can be safely managed using one concentrator, even if they are each severely hypoxic and requiring standard flow rates of 2 L/min. Sometimes very unwell children will require higher flows in the initial treatment period and may need a single concentrator [19,22].

### Installation logistics

This project involves implementation teams and provincial monitoring teams. Implementation consisted of several skilled teams of 4–5 workers. The team leaders were trained in installing the solar power system, and in commissioning and use of oxygen concentrators. Large transport logistics were required to haul equipment from wharf up the PNG highlands highway, and smaller vehicles were required on un-made feeder roads to remote health centers. The installations were preceded by site visits, to discuss with the community and health workers, to ensure facilities fulfilled the criteria for inclusion, and to plan the siting of solar panels for maximal effectiveness. The installations typically took 2–3 days in each center, occurring between March and October 2016.

The implementation teams followed up to assess whether the equipment was being properly used and cared for.

### Monitoring oxygen concentrator performance using oxygen analysers

Health care workers, particularly in remote settings, have an important role in maintaining equipment. For decades many oxygen concentrator projects have failed the test of even medium term sustainability because of technical faults that were detected late or not at all, leading to entire oxygen system failure. In most health facilities throughout the world qualified engineers do not monitor equipment regularly (as engineers may be stationed at a major hospital rather than a district hospital or health center). Therefore preventative maintenance of oxygen concentrators (apart from occasional external filter cleaning) is limited or non–existent. Use of simple oxygen analyzers (Maxtec $O_2$ analyzer, Maxtec, Utah USA) by health care workers to monitor the performance of concentrators (fraction of oxygen produced, to ensure it is >85%), and the flow rate, and training health workers to understand the meaning of alarms on the concentrator will enable early detection of developing faults or parts wearing, and early communication with provincial engineers. Given the limits of current concentrator technology this is a key to addressing the problems of all previous research in concentrators in low resource settings. We taught all health staff how to use oxygen analyzers and provided one for each health facility.

### The engineering capacity required to sustain a program at scale

Previous oxygen projects have had centralized engineering capacity, but these have floundered because technicians change roles, move into the private sector, or because of over–reliance on one or two busy persons. In this project we have decentralized the technical capacity as much as possible, by optimizing what nurses in health centers can do in preventative maintenance and monitoring of equipment performance, and training provincial and district level technicians, and having spare parts available in provincial locations which are at most 2–5 hours' drive away.

### Clinical guidelines and training on oxygen equipment and the treatment of children with severe respiratory infection and other critical illnesses

We use the WHO guidelines for the Clinical Use of Oxygen in Children [22], and the WHO Hospital Care for Children for training [23]. The training is practical, initially workshop based, and repeated on several occasions and reinforced on health center visits by the provincial pediatricians. The training combines clinical and technical teaching and experience, and the messages are heard in more than one forum and more than one way – direct facilitator led teaching, peer and facilitator supervised practical examples, breaking complex tasks and skills into component parts and modeling each component, and presenting a holistic approach to the management of sick children. Training covers an understanding of hypoxaemia in pneumonia, other acute respiratory infections and non–respiratory diseases, respiratory clinical signs, principles and practical use of pulse oximetry, oxygen concentrators and how they work, preventative maintenance and trouble–shooting, use of oxygen analysers for assessing performance of concentrators, safe use of oxygen therapy in newborns, resuscitation, and the concept and practical aspects of continuous quality improvement. The curriculum is based on the WHO guidelines [22].

For many health care workers, the health technologies we introduce are new and sometimes daunting. Oxygen concentrators, like all technologies, may fail because people cannot understand them, or are wary of them, or cannot competently perform the practical tasks of checking and maintenance. A considerable part of this project on the sustainability of better oxygen systems in remote low resource settings involves a novel technology–clinical interface. Until now, these health care settings have been a technology–free zone and the integration of technology into clinical medicine in these settings is unproven and experimental. The elements of a successful technology–clinical interface, if it can be achieved, need to be better understood. If health care workers and technicians have not physically performed a given procedure during training, it is not likely they can do it in their own health care setting (eg, changing oximeter probes, replacing oximeter batteries, replacing concentrator filters, testing concentrator alarms and using an oxygen analyzer). Clinical and technical training tools are available at http://www.hospitalcareforchildren.org/.

### Program costs

It is relatively inexpensive to provide oxygen concentrators, however solar power is expensive. The cost per health facility is approximately US$ 50 000, including oxygen and solar equipment, installation and logistics, and training. Over the course of the formal training, on–site support and continuous quality improvement, all health workers who manage children in these 36 facilities will have training and hands on assessment of skills.

## RESULTS

### Baseline data on logistics and health services

Of 36 health facilities originally proposed, 6 were unsuitable because of poor road conditions that would not allow a vehicle carrying equipment to access the health center (n = 3) or the health center was in a state of disrepair (n = 3). Six more health facilities which fulfilled the criteria were selected to replace these. The catchment population of these 36 health facilities was 1 223 755 in the last (2011) National census, out of a total PNG population of 7.013 million. The median number of beds for children was 10 (interquartile range IQR 5–13), and newborns was 4 (0–8). Only 10 of the 36 health facilities have doctors. The median number of nurses on staff was 4 (IQR 2–10), and 29 had one or more midwives (12 health facilities had only one midwife). Only 16 of the health facilities had a trained pediatric nurse, with the other 20 having general trained nurses. Community health workers were present in all health facilities, with the median number of 7 (IQR 3–17). Only 16 health facilities were connected to mains power, 21 had a petrol generator. Running water was available in 30 health facilities (83%). Most health facilities had simple antibiotics for the treatment of pneumonia, either amoxycillin (n = 33) or penicillin (all health facilities). 34 had vaccine refrigerator, and most were stocked with vaccines: measles vaccine (n = 34), Pentavalent (32), but BCG was less available (25 health facilities). All but one had infant weighing scales and safe sharps disposal, but a minority (10) could check blood glucose, hemoglobin (10), or had x–ray facilities (7). Malaria tests were available in 28 and sputum smear for tuberculosis in 20.

### Baseline data on outcomes

In the 36 participating health centers we gathered data on over 20 000 admissions in the 3 years prior to the installations (Table 1). Over 8000 admissions were for pneumonia. The overall case fatality rate was 3.7% and the case fatality rate for pneumonia was 4.1%. Just over 10% of admissions required referral to provincial hospitals. These baseline data were collected from health facility admission record books, which are historically meticulously kept by nursing staff in PNG.

A sample size calculation was based on the primary outcome of reducing pneumonia mortality – from 4% to 3%, with 90% power = 7295 in each arm. The study was also adequately powered to detect a different of 20% in overall mortality rate, and a 20% reduction in referrals to tertiary centers. Other outcomes are listed in Table 2.

### Assessing continuous quality improvement outcomes

Continuous quality improvement (CQI) involves regular monitoring and supervision by provincial supervisory teams; each team consists of the provincial pediatrician and a technician trained in oxygen and solar equipment. These reviews will occur every 4 months after implementation, will be carried out by

**Table 2.** Outcomes, research questions, sources of data and specific metrics

| Outcome category | Research questions | Sources of data | Metrics |
|---|---|---|---|
| 1 Deaths from pneumonia; overall pediatric deaths in health facility | Is there a difference in pneumonia case fatality rates and overall pediatric CFR from pre to post implementation of improved oxygen therapy and solar power? | Admission record books | **Pneumonia case fatality rate**: Pneumonia deaths / pneumonia admissions (%). **Paediatric case fatality rate**: Paediatric deaths / all pediatric admissions (%). |
| 2 Referral / transfer | Is there any difference in referral rates from pre to post intervention? | Admission record books | Paediatric transfers / all pediatric admissions (%). |
| 3 Patient characteristics and response to oxygen therapy – effectiveness of oxygen therapy using the method we have designed to treat hypoxaemia | What are the conditions associated with hypoxaemia in remote rural health facilities? What is the response to oxygen therapy when oxygen is given using solar–powered oxygen concentrators? What is the duration of hypoxaemia in children managed in remote rural health facilities? | Standardised admission record data | Diagnoses associated with hypoxaemia (proportions) disaggregated for neonates and children >1 mo. Response to oxygen therapy (median change in $SpO_2$ in the first 30 min; and proportion responded / not responded, ie, proportion with persisting $SpO_2 < 90\%$, or severe signs of respiratory distress 30 min after commencing oxygen). Days of oxygen therapy. Duration of hypoxaemia for neonates and children >1 month. |
| 4 Maintenance of oxygen equipment | Are concentrators maintained well, are problems identified and is appropriate action taken? What proportion of concentrators undergo weekly maintenance and performance checking? What problems are identified? What proportion of concentrators are functioning well after 1, 2 and 3 years since installation? | Oxygen concentrator performance log–books. On–site checks on support and monitoring visits | What proportion of oxygen concentrators undergo weekly maintenance and performance checking? List of problems identified and action taken. Number / proportion of concentrators providing >85% oxygen and reliable flow rates as checked by oxygen analyzer at 1, 2 and 3 years. |
| 5 Health workers knowledge and skill of oxygen therapy | What is the oxygen knowledge and skill of the health workers in remote health facilities? Does this improve with training and CQI | Oxygen competency tests – repeated measures | Repeating oxygen knowledge and skill tests at 12 monthly intervals. |
| 6 Reliability, efficiency and adequacy of solar power | Solar power output (quantitative kW hours per day), adequacy of this power for running concentrators and other equipment needed by the health facility, and any problems identified. | Tristar 60 Amp controller | **Solar power output**: average kW hours per day produced by each solar system in the previous 6 mo. Occurrence of breakdown of solar output, such that concentrators are unable to function. |
| 7 Training outcomes | What training was done and what are the perceived training needs? | Project records | Record of training courses conducted: formal; in–house as part of CQI |
| 8 Sustainable processes | Is it sustainable in PNG to have concentrators run off solar power as the source of oxygen in remote areas? | Mixture of the above data sources, and documentation of relevant events, meetings and occurrences | How would we measure sustainability? **Equipment sustainability** (ie, proportion of concentrators and oximeters still functioning well at 1, 2, 3 years). **Energy sustainable** (proportion of solar power systems still functioning well at 1, 2, 3 years). **Health worker sustainability** (proportion with good oxygen knowledge and skills at 1, 2, 3 years). **Financial sustainability** (examples where national, provincial or local governments have invested in other facilities in a similar way). **Policy sustainability** (occurrence of a national oxygen policy that incorporates these principles). Documentation of other examples of engagement by policy makers. |
| 9 Wider benefits | Does CQI in rural health facilities improve wider outcomes? Care seeking by parents? Health worker morale? | Above data and qualitative assessments | **Care seeking**: Number of children brought to health facilities (admission activity number per year for 3 years, compared with pre–intervention baseline data). **Women having confidence in the health services:** Number of babies born at health facilities (births per year for 3 years, compared with pre–intervention baseline data). **Qualitative assessment** of what health workers think of the oxygen project, whether and how it helps them in their work, what problems it may have resulted in, what could be done to help them better serve their communities, how they feel about their work, what their hopes are for their careers. |

CQI – continuous quality improvement, CFR – case fatality rate, $SpO_2$ – arterial oxygen saturation

the provincial teams and will include on–site training, collection of data on functioning of equipment, utilization, maintenance needs, and trouble–shooting of problems identified. There will be multiple assessments during these visits over the 3 years, including for example, whether nurses can accurately use oxygen analysers to effectively monitor the performance of concentrators, and whether the solar power capacity is sufficient for energy demand. The CQI approach involves feedback by the provincial monitoring teams – feedback is to the health center staff, the district and provincial authorities, and the National Department of Health. CQI outcomes also include whether interventions occurs in response to feedback, and the effect of these responsive interventions. An assessment of sustainability processes, including policy maker engagement, and the wider effects of this project on care seeking, health facility functioning and health worker morale is under way (**Table 2**).

## DISCUSSION

Over the past two decades mortality from childhood pneumonia has decreased significantly. While much effort has been put into vaccines and first line antibiotics for pneumonia, there is still a need for scaling up broader prevention and treatment initiatives. Even if severe pneumococcal infection could be markedly reduced by vaccination, realistically there will still be a myriad of respiratory viruses, particularly respiratory syncytial virus, and other viruses such as influenza, human metapneumo virus, parainfluenza; non–vaccine type pneumococci and *Haemophilus*; tuberculosis and other bacteria, which cause lower respiratory tract infections and fill up hospitals in low– and middle–income countries, as is the case in developed countries. The residual mortality, regardless of etiology will likely rest in those with more than a need for antibiotics alone. The population will likely be a more complex, comorbid, undernourished population where supportive care is increasingly important, including a role for oxygen therapy. The challenge of how to provide services in primary care and regional centers is not unique to PNG or to even to developing countries, the same drive to improve quality and reduce the need for referral is a focus in wealthy countries also. But the challenges are greater in rural, low income settings.

This implementation paper documents the steps to scaling up oxygen therapy in remote rural settings. Many steps are involved and this is a complex health care intervention. Previously oxygen has been thought of as an essential drug [24], but it is also an essential *service*. With the drive to increase facility births in low income, high mortality countries, health facilities have to reach a certain standard to signal to the community that they can provide a greater level of service than delivering at home – these essential services include power, clean water, oxygen, and infection control and prevention. As more and more births in countries like India, Ethiopia and Nigeria are happening in health facilities, there has been an ecological and foundational shift in care at these facilities. It is important to understand the importance of oxygen as a relatively simple yet essential service to maintain a minimum standard of quality in the redefined roles of primary health care and first referral facilities. Other investments, such as building sleeping quarters for staff to allow them to stay overnight, have to be prioritized also, and where oxygen, power, and running water fit into these priorities is a matter of judgement, but they all can be regarded as essential. PNG still has low rates of facility delivery (40%), but further increases will require explicit attention on ensuring that minimum services are in place close to where communities live.

We emphasize the importance of a holistic health systems approach, community engagement, and continuous quality improvement. To be sustainable and maximally effective such interventions should integrate into routine health system functioning, and the benefits must be cross–cutting for maximum adoption and effect. For example, there is limited value in installing solar power to run an oxygen concentrator if there is no light in the delivery room, as women will not want to deliver babies overnight. Lack of basic services effect the health center's reputation and have adverse effects on community demand and care seeking (such as when an infant is unwell with pneumonia). However addressing such conditions, for example by providing power to run a light, and the vaccine refrigerator, and oxygen, can be transformational [16,25]. To be maximally efficient, such interventions should be based on a holistic and systematic approach to improving health service quality, with the provision of basic oxygen technology and adequate power as an entry point. Along with transforming a community's perception of a health center, essential services like oxygen and a reliable power system, and training to match, can boost health workers confidence and morale.

PNG is an expensive place to do such work, as the terrain is difficult, and distances far. Many concentrator programs only report the oxygen concentrator costs, but we have previously shown that the implementation and training costs are at least as much again as the costs of concentrator and other oxygen

equipment [1]. Sustainability and expansion of such programs require an accurate estimation of true costs and benefits, so that health administrators and governments can order priorities according to their needs and program according to their available resources. In a decentralized system where provinces and districts have to decide on their health spending priorities, this project leaves no doubt as to the full costs of such a health facility service upgrade. There are many health priorities for child health in the sustainable development era, including health facility quality improvement, and each have real costs that have to be weighed [26].

Over the next 3 years we will measure clinical effectiveness and what is required to sustain this program, from simple things like whether nurses can accurately use oxygen analysers to effectively monitor the performance of concentrators, to whether the solar power capacity is sufficient for energy demand. And we will monitor, beyond effectiveness in the field, the administrative and political steps required for decisions about involvement of other provinces in the program, and how such interventions can be seen as cross–cutting, and part of a greater whole – quality services at district hospitals and rural health centers. A serious problem for many such rural health services and primary health care workers in the past has been low expectations, and showing that appropriate and essential technology such as this can be effective and sustained may just raise expectations to the level needed in the era of sustainable development.

## CONCLUSIONS

This study will evaluate the feasibility and sustainability issues in improving oxygen systems and providing reliable power on a large scale in remote rural settings in PNG, and the impact of this on child mortality from pneumonia over 3 years post–intervention. Taking a continuous quality improvement approach may be transformational for remote health services.

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# Costs of hospitalization with respiratory syncytial virus illness among children aged <5 years and the financial impact on households in Bangladesh, 2010

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**Background** Respiratory syncytial virus (RSV) is the leading cause of acute respiratory illness in young children and results in significant economic burden. There is no vaccine to prevent RSV illness but a number of vaccines are in development. We conducted this study to estimate the costs of severe RSV illness requiring hospitalization among children <5 years and associated financial impact on households in Bangladesh. Data of this study could be useful for RSV vaccine development and also the value of various preventive strategies, including use of an RSV vaccine in children if one becomes available.

**Methods** From May through October 2010, children aged <5 years with laboratory–confirmed RSV were identified from a sentinel influenza program database at four tertiary hospitals. Research assistants visited case–patients' homes after hospital discharge and administered a structured questionnaire to record direct medical costs (physician consultation fee, costs for hospital bed, medicines and diagnostic tests); non–medical costs (costs for food, lodging and transportation); indirect costs (caregivers' productivity loss), and coping strategies used by families to pay for treatment. We used WHO–Choice estimates for routine health care service costs. We added direct, indirect and health care service costs to calculate cost–per–episode of severe RSV illness. We used Monte Carlo simulation to estimate annual economic burden for severe RSV illness.

**Findings** We interviewed caregivers of 39 persons hospitalized for RSV illness. The median direct cost for hospitalization was US$ 62 (interquartile range [IQR] = 43–101), indirect cost was US$ 19 (IQR = 11–29) and total cost was US$ 94 (IQR = 67–127). The median out–of–pocket cost was 24% of monthly household income of affected families (US$ 143), and >50% families borrowed money to meet treatment cost. We estimated that the median direct cost of RSV–associated hospitalization in children aged <5 years in Bangladesh was US$ 10 million (IQR: US$ 7–16 million), the median indirect cost was US$ 3.0 million (IQR: 2–5 million) in 2010.

**Conclusion**: RSV–associated hospitalization among children aged <5 years represents a substantial economic burden in Bangladesh. Affected families frequently incurred considerable out of pocket and indirect costs for treatment that resulted in financial hardship.

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Globally, an estimated 34 million new episodes of respiratory syncytial virus (RSV)–associated acute respiratory infection occurred among children aged <5 years in 2005, of which 2.8–4.3 million episodes required hospi-

talization [1]. The incidence of RSV–associated ARI among young children in low–income countries is believed to be more than twice than that of the high–income countries (59 vs 24/1000 per year) [1]. RSV has been reported as an important viral contributor to the pneumonia burden among young children in both rural and urban settings in Bangladesh [2,3] and is the leading viral pathogen for hospitalization of children aged <5 years with severe acute respiratory illness [4].

The annual direct health care cost of hospitalization because of RSV illness among young children in high–income countries was estimated at US$ 24–394 million [5–8]. For those countries, the annual economic burden of illness provides an estimate of government expenditures due to the illness that can inform implementation of appropriate cost–effective prevention strategies. In contrast, in most low–income countries, including Bangladesh, where the majority of health care cost is paid out–of–pocket in the absence of public health insurance systems [9], an annual economic estimate of a particular illness reflects the financial impact of the illness on households. There is little information about the economic burden of RSV illness in low–income countries such as Bangladesh where the RSV–associated disease burden is high [1]. In 2007, a cost of illness study conducted at the largest pediatric hospital in Bangladesh estimated that the mean medical cost for a hospitalized child with pneumonia was US$ 94 per illness episode and nearly two–thirds of families in this study had to spend more than half of their monthly expenditure for treatment [10]. Although the previous cost study lacks cost estimates for viral respiratory illness, the findings suggested that costs for hospitalization with RSV pneumonia could be catastrophic for affected families because of existing high RSV burden.

While there is currently no licensed vaccines to protect against RSV, a number of vaccines are in development [11]. Palivizumab, an intramuscular monoclonal antibody is recommended for young infants with high risk conditions including congenital heart disease, congenital lung disease or prematurity to prevent severe RSV infection, but is not currently cost-effective for use in Bangladesh because of its high cost (US$ 6000 per child per season) [12,13]. Using 2010 cost data from hospitalized persons with laboratory–confirmed viral illnesses, we aim to analyze the costs associated with severe RSV hospitalization among children aged <5 years in Bangladesh. Specifically, the objective is to estimate out–of–pocket, health care system and indirect costs from the societal, provider and family perspectives as well as the financial hardship imposed on families of sick children. These data may be used to evaluate the value of various preventive strategies, including use of an RSV vaccine in children if one becomes available.

## METHODS

### Surveillance settings

We conducted this study in the catchment areas of ongoing sentinel childhood respiratory illness surveillance at three public and one private hospital in four districts in Bangladesh [14]. As part of the surveillance activity, two days per month, a surveillance physician in each hospital enrolled all children aged <5 years residing in the catchment area who were hospitalized with any two of the following symptoms during admission: reported or measured fever, cough or difficulty breathing. Nasal and throat swabs were collected from enrolled children. The specimens were kept in liquid nitrogen and transported to icddr,b virology laboratory fortnightly to test for the presence of RSV using real time reverse transcription polymerase chain reaction (rRT–PCR) [15].

### Study population and enrolling case–patients

We conducted this study during the influenza epidemic period, May through October, as the primary objective of the original study was to estimate economic burden of influenza in Bangladesh. The seasonality of RSV in Bangladesh is well defined but we anticipated finding laboratory–confirmed RSV cases at the sentinel hospitals during those months as well [2,3,16]. During May through October, 2010, investigators identified all children aged <5 years from the sentinel childhood respiratory illness surveillance database who had laboratory–confirmed RSV infection and defined them as case–patients. Research assistants telephoned each case–patient's parents, informed them that their child had laboratory–confirmed viral respiratory illness and obtained verbal consent for a home visit to administer a standard questionnaire about the cost associated with the hospitalization. Then, research assistants visited each case–patient's home and if any parents were unavailable during the first visit, field research assistants made two more visits to that dwelling in an attempt to collect cost information.

## Data collection

We used the same data collection tool to capture direct and indirect costs, previously used for influenza cost estimation in this setting [17]. Research assistants interviewed case–patients' parents using a structured questionnaire to obtain socio–economic information such as the highest household educational attainment, monthly household income, accumulated household assets, source of water supply, cooking fuel and latrine type, self–reported costs incurred at other health care service facilities prior to visiting the sentinel hospital for that illness episode, cost associated with hospitalization at sentinel hospitals, impact of treatment cost on household economy and the coping strategies that each household used to pay treatment cost [17]. In cases when parents reported about borrowing money as coping strategy, research assistants collected data on the lender and interest rate. The interest rate was standardized into per annum rate.

## Cost components

### Direct costs

We categorized the direct cost into medical and non–medical costs [18]. Cost incurred for hospital registration fees, bed rent, medicine, laboratory tests, and informal payments (comprised payments to hospital support staff for arranging beds for admitted children on the floor of the ward, obtaining oxygen cylinders for children). for the illness were considered as medical costs. The respondent identified which medications and laboratory tests they received from the hospital free of charge (hospital subsidized cost) and which they purchased out–of–pocket. Research assistants collected cost information for hospital registration fees and bed rent from hospital receipts. Research assistants also collected self–reported non–medical cost such as caregivers' food, lodging and transportation costs. We used WHO–Choice estimates for routine health care service costs per bed–day for any hospitalized patients at tertiary level hospitals in Bangladesh [19] to calculate costs for that illness episode from providers' perspectives. WHO–choice estimates the routine health care service cost that includes health–care providers and support staffs salary, capital cost and patients' food cost. WHO–Choice data excludes cost of any drugs and laboratory tests, whether subsidized or paid out–of–pocket, which were collected from the patients' caregiver.

### Indirect costs

We collected self–reported daily wage and number of work days lost by each family caregiver due to the illness event. For employed caregivers, loss of work days excluded weekends or leave days. For caregivers who were daily–wage earners or homemakers (mothers), we considered any day lost for caring for sick children as a lost work day. We did not assign an indirect cost for days of restricted activity such as half a day of work or when a caregiver reported that the illness episode did not interrupt their regular activity.

## Cost calculation

We calculated prescribed medicine and laboratory test costs using price lists collected from local drug stores and laboratories during the study period. We calculated hospital subsidies cost and out–of–pocket cost for medicine and laboratory tests. We then added medical, non–medical and health care service cost to estimate the direct cost–per–episode. We estimated indirect cost (ie, work time lost) of caregivers using the human capital approach [20]. We assigned monetary value to the time lost by caregivers by multiplying missed work days by self–reported daily wages. To calculate the value of work time lost by unemployed caregivers such as mothers and grandparents, we used the minimum wage in Bangladesh during 2010 [ie, Taka 100/d or US\$ 1.4/d] [21] and multiplied this rate by the number of work days missed. This approach was previously used by other researchers in measuring economic burden of illness [22]. For multiple caregivers of the hospitalized child, we calculated work time loss of each caregiver and then summed these to estimate the total indirect cost–per–episode for each hospitalized child. We added cost incurred at other health care facilities to total direct and indirect cost–per–episode to obtain the total cost–per–episode of RSV–associated hospitalization. Initially, we estimated each cost in Bangladeshi currency (Taka) and then converted our estimates into US\$ according to the average exchange rate during the time of data collection (US\$ 1 = Taka 70) [23]. We multiplied the incidence rate for RSV hospitalization (8.3/1000 children year) from a recent study in Bangladesh [16] by the estimated national population of children <5 years during 2010 to estimate the annual number of children aged <5 years with RSV–associated hospitalization in Bangladesh in 2010 [24]. We then multiplied the median cost of an episode

for RSV hospitalization by the estimated number of RSV–associated hospitalizations per year to obtain the annual economic burden for RSV–associated hospitalization among children aged <5 years in Bangladesh in 2010. We used a Monte Carlo simulation to resample from empirical distribution of our cost components 1000 times to generate a 95% confidence interval of the estimates [25,26].

## Principal component analysis

We performed a principal component analysis using information about household assets (eg, table, chair, radio, television, and refrigerator) and access to household services (eg, electricity, source of water, fuel and latrine type) to construct a wealth index [27]. We divided the households into two groups on the basis of their median principal component score. Families below the median were categorized as poor and those who had median scores at or above the median were categorized as wealthier.

## Ethical consideration

We obtained written informed consent from the parents of hospitalized child. The study protocol was reviewed and approved by an icddr,b institutional review committee.

## RESULTS

### Characteristics of study respondents

During May through October 2010, 47 hospitalized children aged <5 years with laboratory–confirmed RSV illness were identified from the surveillance database. Research assistants interviewed parents of 39 (83%) case–patients and were unable to reach the remaining eight (17%) after multiple visits to their dwellings. The monthly household income of participating households was US$ 143 (interquartile range [IQR] = 114–257). The mean duration between case–patients' hospital discharge and their parents' interview was 26 days (range = 8–47 days). The median age of the 39 case–patients was 4 months (IQR = 2–7 months) (**Table 1**). Most recruited children (82%, 32/39) had already sought health care before reaching the study hospitals; 41% (13/32) visited doctors with a Bachelors of Medicine and Surgery, 25% (8/32) visited other health facilities, 22% (7/32) visited village doctors, 16% (5/32) visited homeopath doctors and 9% (3/32) visited pharmacies. The median out–of–pocket cost incurred for treatment at other health care providers before reaching the sentinel hospitals was US$ 3.6 (IQR = US$ 1.5–7.2).

### Costs of RSV hospitalization

#### Direct costs

The median direct cost of RSV hospitalization was US$ 62 (IQR = US$ 43–101). The median direct cost in the private hospital was higher than in the public hospitals (US$ 90 vs US$ 48) ($P$ = 0.0038) (**Table 2**). Nearly two–thirds (16/25) of case–patients in public hospitals received at least one medicine and/or diagnostic test from the hospital free of charge whereas none of 14 case–patients in the private hospital

**Table 1.** Characteristics of children hospitalized with respiratory syncytial virus (RSV)–associated illnesses and their families, by hospital type, Bangladesh, May–October, 2010

| Characteristics | Public hospital | Private hospital | Total |
|---|---|---|---|
| Number of case–patients | 25 | 14 | 39 |
| Male (%) | 18 (72) | 9 (64) | 27 (69) |
| Age of case–patients in months: | | | |
| ≤6 (%) | 17 (68) | 11(79) | 28 (72) |
| 7–12 (%) | 6 (16) | 2 (14) | 8 (20) |
| 13–59 (%) | 2 (8) | 1 (7) | 3 (8) |
| Median (IQR) | 5 (3–7) | 3.5(2–6) | 4 (2–7) |
| Monthly household income, median (IQR) US$ | 143 (100–214) | 201 (129–343) | 143 (114–257) |
| Number of household members, median (IQR) | 5 (4–7) | 6 (4–9) | 5 (4–7) |
| Days from symptom onset to hospital admission, median (IQR)* | 4 (3–5) | 2 (1–4) | 3 (2–5) |
| Days hospitalized, median (IQR) | 5 (3–6) | 4.5 (4–5) | 5 (3–6) |

*Comparisons are between public hospital and private hospital; $P$ = 0.01.

**Table 2.** Direct cost–per–episode (in US$) of respiratory syncytial virus (RSV) hospitalization in four hospitals, Bangladesh, May–October 2010

| PARAMETER | PUBLIC HOSPITALS | | PRIVATE HOSPITAL | | TOTAL | |
|---|---|---|---|---|---|---|
| | N (%) | Median (IQR) | N (%) | Median (IQR) | N (%) | Median (IQR) |
| Medicine cost | 25 (100) | 21(15–25) | 14 (100) | 20 (12–27) | 39 (100) | 22 (15–27) |
| Diagnostic cost | 9 (36) | 5(1.5–7.5) | 11 (79) | 2.6 (2.5–4.0) | 20 (50%) | 2.7 (2.5–6.6) |
| Transportation cost† | 23 (92) | 4.2 (2.6–7.3) | 14 (100) | 8.9 (6.4–17) | 37 (95) | 6.4 (3.0–11) |
| Healthcare service cost | 25 (100) | 23 (14–27) | 14 (100) | 20 (18–23) | 39 (100) | 23 (14–27) |
| Other costs‡ | 25 (100) | 1.7 (0.6–4.1) | 13 (93) | 33 (26–37) | 38 (97) | 3.7 (0.8–27) |
| Total direct cost/episode* | 25 | 48 (36–64) | 14 | 90 (71–112) | 39 | 62 (43–101) |

*Comparisons are between public hospital and private hospital, $P = 0.0038$.

†Transportation costs included round trip cost of case–patient from home to hospital and care–givers travel cost for hospital visit.

‡Other costs included cost for hospital registration, informal payment, food, hospital bed and lodging of caregiver.

received any hospital subsidized medicine or diagnostic test. The remaining nine (36%) case–patients in public hospitals and all case–patients in private hospitals paid 100% of medicine and diagnostic costs out–of–pocket. The cost of medicine, on average, constituted 60% (range: 11–92%) of the total direct cost of hospitalization.

### Indirect costs

During the illness, children obtained care from an average of three family caregivers (range: 1–6). Mothers were invariably the primary caregiver (39/39, 100%) with grandmothers also providing some care (21/39, 54%). Caregivers lost a median of 12 days of productivity (IQR = 8–17 days) and a median of US$1.4 (IQR = US$ 1.4–1.6) loss per day during the illness episodes. The median indirect cost of RSV hospitalization was US$ 19 (IQR = US$ 11–29).

### Total cost

We estimated that the median total cost per episode of RSV hospitalization was US$ 94 (IQR = 67–127) and that direct cost constituted, on average, 67% (95% CI = 62–72) of this total cost.

## Financial impact on affected families

The median out–of–pocket cost for hospitalization with laboratory–confirmed RSV represented 24% of the monthly household income among participating families, 32% among the poorer families and 17% among wealthier families (Table 3). None of the families reported having health insurance to cover the treatment cost. More than 50% (20/39) of the families borrowed money to pay for their child's treatment (Table 3). Of 20 families who obtained loans, 13 (65%) obtained interest–free loans from relatives and seven (35%) obtained loans from community lenders at annual interest rates of 50–120%. Four (31%) of the 13 who obtained interest free loans had repaid them whereas none of the seven families who took loans with interest had repaid the loan a month after hospital discharge. Fourteen (70%) of the poorer families and 6 (32%) wealthier families decreased their monthly expenditures on food because of costs incurred during illness.

**Table 3.** Per–capita income per month of case–patient's family (in US$), out–of–pocket costs per episode of RSV hospitalization as a percentage of monthly household income and the coping strategies, Bangladesh, May–October 2010

| PARAMETER | HOUSEHOLD CATEGORY | |
|---|---|---|
| | Poorer, N = 20 | Wealthier, N = 19 |
| Per capita income per month, median (IQR) | 23 (17–25) | 38 (29–64) |
| Out–of–pocket costs as percentage of monthly income, median (IQR) | 32 (19–53) | 17 (12–27) |
| Coping strategy: | | |
| Received contribution from relatives, n (%) | 3 (15) | 2 (11) |
| Borrowed money, n (%) | 13 (65) | 7 (37) |

IQR – interquartile range

## National cost

We multiplied the rate of RSV hospitalization in children aged <5 years (8.3/10 000 children year) [16], by the census population of children aged <5 years in Bangladesh during 2010 and estimated that approximately 160 500 children aged <5 years were hospitalized with RSV illness in Bangladesh in 2010. We estimated that the median direct cost of RSV–associated hospitalization in children aged <5 years in Bangladesh was US$ 10 million (IQR: US$ 7–16 million), the median indirect cost was US$ 3.0 million (IQR: 2–5 million) in 2010.

## DISCUSSION

RSV is the leading viral cause of acute lower respiratory infections in children, particularly in children younger than 5 years and 99% of RSV–associated deaths occur in low–income countries [1]. RSV vaccines are in development but there is little information about the cost of RSV illness to inform cost–benefit models of RSV vaccination programs. Our data illustrates that RSV–associated hospitalization among children aged <5 years represents a substantial economic burden in Bangladesh and families caring for children with severe RSV illness frequently incur substantive out of pocket and indirect costs that result in financial hardship, particularly among the poorer. Our estimated cost of an episode of severe RSV illness (US$ 94) was similar to a previously published cost estimate for hospitalized pneumonia among children in Bangladesh [10]. We estimated the annual direct and indirect economic burden for RSV–associated hospitalization in Bangladesh; however, if non–hospitalized disease were included the amount might be twice as high because only 51% of children aged <5 years with severe acute respiratory illness are brought to hospitals for evaluation [4,28].

Our data showed that the health care costs associated with RSV hospitalization were primarily paid out–of–pocket, irrespective of type of health facility, public or private. The out–of–pocket costs were as high as one–third of the monthly income of poor families excluding the substantial work time lost for caregivers. The high out–of–pocket expenditures for health care service was somewhat expected as there is no insurance scheme to cover health care costs in Bangladesh, similar to many low–income countries [29,30] and previous cost studies in Bangladesh also had similar findings [10,17]. We found that the direct cost for RSV hospitalization in private hospitals was higher than in public hospitals although the median days of hospitalization in public and private hospitals were similar. Hospital registration, food for patients, and hospital bed charges are subsidized in public hospitals but paid by families in private hospitals. In addition, none of the patients in private hospitals received any hospital supported medicine and/or laboratory tests, which resulted in higher out–of–pocket costs when compared with those in public hospitals.

We found that affected families frequently obtained loans, either interest free from relatives or at usurious rates from local money lenders to meet treatment cost. Similar coping strategies were previously documented in other resource–poor settings to pay for health care costs of ill family members [10,31]. In Bangladesh, the annual interest rate for loans obtained from the informal sectors, such as local money–lenders, is around 180–240% and is much higher than from commercial banks where the rates are ~10–13% per annum [32]. Nevertheless, people in rural settings rely on the informal sector to obtain loans because such loans are available quickly and the majority of these poor people are ineligible to get loans from formal sectors as they do not own adequate assets to guarantee their ability to repay the loan [32]. Families in our study who obtained loans from local money lenders were also unable to repay their loan nearly a month after hospital discharge. Loans obtained from the informal sector at extremely high interest rates for RSV treatment could result in long–term debits and may propel families into vicious cycles of poverty [33–35].

A study on out–of–pocket expenditure for health care services in neighboring India suggested the impact of health care payments on families food and children's education purchasing capacity can be substantial [36]. The parents of this study also mentioned reduction of monthly food expenditure as the foremost impact of treatment cost for their child's illness. These data also highlight how an episode of severe RSV illness that resulted in hospitalization could have an indirect impact on the food availability in affected households, which is concerning for a country like Bangladesh where nearly half of the children aged <5 years are malnourished [37].

Our study had several limitations. We identified RSV–cases from an ongoing surveillance for respiratory illness which seemed to use less sensitive case–definition for RSV illness and thus we likely missed cases of RSV–illness. We estimated the cost of an episode of RSV hospitalization using data from only 39 labo-

ratory–confirmed cases. A more sensitive case–definition might have resulted in the enrollment of patients with a different presentation, treatment profile, and cost of illness. Cases were identified from four rural hospitals and our cost–estimates may not be generalizable to urban areas where 25% of the population lives. Although the study sample size was relatively small and cost estimates largely represented rural population, these cost estimates were similar to previously published pneumonia hospitalization costs at other sites in Bangladesh [10], supporting the representativeness of our cost estimation. Our cost estimates could be underestimates for several reasons. We collected expenditure data from study respondents retrospectively. Some of the respondents were interviewed after a month of hospital discharge and may have forgotten some expenses incurred during illness. In order to improve recall, we went through all billing records, prescriptions and discharge reports of hospitals and also cross–checked claimed medicine cost with local drug stores. To ensure the representativeness of drug prices, research assistants collected the brand name of the drug used by the child during the illness. Because the price of drug of a specific brand is likely to be fixed in most pharmacies in Bangladesh (as set by the producing company), these estimates are likely reliable. We did not count days with restricted activity as it would over–report the productivity loss. To calculate the work time lost by caregivers, we used wage rates self–reported by caregivers which may not have been generalizable. However, the monthly household income of the study families (US$ 143) was similar to the monthly income of a typical rural household in Bangladesh (US$ 138) [38], suggesting that our data might be representative of the whole country. Our estimates of annual direct and indirect cost of RSV–associated hospitalization at the national level was based on an incidence estimate from a single year and RSV burden has been found to vary substantially from year to year in Bangladesh [16]. However, a recent paper on RSV hospitalization from 2010–2014 in Bangladesh showed that RSV hospitalization rate was the highest in 2010 than other years [16], suggesting that the estimated cost represented the economic burden of a season with high RSV activity in Bangladesh.

Severe RSV illness requiring hospitalization of young children seemed to result in a significant annual economic burden in Bangladesh during 2010. Most of the hospitalization costs were paid out–of–pocket and often led families to incur loans. In the absence of government–sponsored health insurance, community–based health insurance programs could help to reduce the household–level economic impact of childhood hospitalization for severe respiratory infection [39]. Cost data for RSV hospitalization from low–income settings, where the disease burden is highest, could be used as a baseline to evaluate the cost–benefit of ongoing efforts to develop affordable RSV vaccines for resource poor settings and also to evaluate the effect of non–pharmaceutical preventive interventions, such as hand washing which have been found effective in reducing RSV transmission [40].

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# Initiating a participatory action research process in the Agincourt health and socio–demographic surveillance site

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**Background** Despite progressive health policy, disease burdens in South Africa remain patterned by deeply entrenched social inequalities. Accounting for the relationships between context, health and risk can provide important information for equitable service delivery. The aims of the research were to initiate a participatory research process with communities in a low income setting and produce evidence of practical relevance.

**Methods** We initiated a participatory action research (PAR) process in the Agincourt health and socio–demographic surveillance site (HDSS) in rural north–east South Africa. Three village–based discussion groups were convened and consulted about conditions to examine, one of which was under–5 mortality. A series of discussions followed in which routine HDSS data were presented and participants' subjective perspectives were elicited and systematized into collective forms of knowledge using ranking, diagramming and participatory photography. The process concluded with a priority setting exercise. Visual and narrative data were thematically analyzed to complement the participants' analysis.

**Results** A range of social and structural root causes of under–5 mortality were identified: poverty, unemployment, inadequate housing, unsafe environments and shortages of clean water. Despite these constraints, single mothers were often viewed as negligent. A series of mid–level contributory factors in clinics were also identified: overcrowding, poor staffing, delays in treatment and shortages of medications. In a similar sense, pronounced blame and negativity were directed toward clinic nurses in spite of the systems constraints identified. Actions to address these issues were prioritized as: expanding clinics, improving accountability and responsiveness of health workers, improving employment, providing clean water, and expanding community engagement for health promotion.

**Conclusions** We initiated a PAR process to gain local knowledge and prioritise actions. The process was acceptable to those involved, and there was willingness and commitment to continue. The study provided a basis from which to gain support to develop fuller forms of participatory research in this setting. The next steps are to build deeper involvement of participants in the process, expand to include the perspectives of those most marginalized and engage in the health system at different levels to move toward an ongoing process of action and learning from action.

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Estimates suggest that over 1 billion people, the majority from low and middle–income countries (LMICs), experience barriers to access of good quality health care [1]. The problem can be related to a lack of information about the needs of those who are excluded from access. Health policy and planning that does not account for those who are excluded can give rise to a self–sustaining situation in which the health system, albeit inadvertently, is organized to maintain their exclusion [2–4]. The first step toward overcoming this situation requires reliable evidence about those who are excluded in order to inform the equitable organization of care [5–7].

In the absence of complete vital health data, pragmatic alternatives such as Verbal Autopsy (VA) has become an important source of information on population health. VA is a survey based method frequently used to investigate deaths identified as part of the routine operations of health and demographic surveillance sites (HDSSs). In a VA, final carers of deceased persons are interviewed about their relatives' terminal symptoms using a standard, validated questionnaire [8]. Data are then interpreted to determine probable medical causes of death [8]. Approximately 48 million deaths are unregistered worldwide, three–quarters of which occur in LMICs [7]. In this context, VA has become a critical source of information for vital statistics and health systems strengthening [4,9–11].

Avoidable mortality among disadvantaged groups is strongly influenced by social conditions. Information on how the social determinants of health inequalities influence access to health services and health outcomes is therefore necessary to prioritize equity in health policy and planning [12]. An extension of this school of thought prioritizes participatory research as an approach to elicit information on the social determinants of health inequalities by enabling the perspectives of disadvantaged populations.

Participation is a broad term encompassing a range of interpretations from non– and marginal participation to fuller forms concerned with power and empowerment [13,14] (**Figure 1**). Narrower forms of participation are characterized by activities such as information sharing and consultation, considering participation as a means to an end in which: "donors or governments [use] community resources (land, labour, money) to offset the costs of providing services" [15].

Broader views of participation consider it as an end in itself, where communities own the process and its development, where: "local communities [take] responsibility for diagnosing and working to solve their own health and development problems" [15]. In this scenario, active participation is related to community control and empowerment [13]. Here, the process aims to redresses power and information asymmetries between communities and the political and administrative forces that shape health policies [16,17].

Participatory action research (PAR) is an approach concerned with fuller forms of participation. In PAR, knowledge is co–created, acted on, and learning from action is sought to bring about and sustain change [17]. PAR methods change the usual way of doing research that emphasizes a divide between the researchers and the researched, transforming the subjects of research toward roles as active researchers and agents of change [18].

The research was conducted in a rural province of South Africa. Described as one of the most unequal societies in the world, the South African health system faces a complex 'quadruple' burden of socially patterned mortality comprising: chronic infectious diseases (characterized by HIV/AIDS and tuberculosis), non–communicable conditions, maternal and child mortality, and mortality owing to injury and violence [19]. The burden of HIV is high and highly unequal. Prevalence in black populations is 40–50 times that of white and in adolescents, risks are eight times higher in females than males [20].

Despite entrenched inequalities, the post–apartheid policy context in South Africa is progressive and inclusive. There is a constitutional commitment to the right to health and community participation for Primary Health Care (PHC) [21], and in 2011 National Health Insurance (NHI) was launched as a bold commitment to Universal Health Coverage (UHC) [22–24]. Significant gaps exist between policy and implementation however, in a system characterized by chronic underinvestment, a human resource crises, widespread corruption, poor stewardship and deteriorating infrastructure [25].

## Aims and objectives

Robust evidence on context, health and risk for groups excluded from health and information systems is crucial to inform equitable health systems responses. The overall aims of the research were to initiate a PAR process with communities in a health and socio–demographic
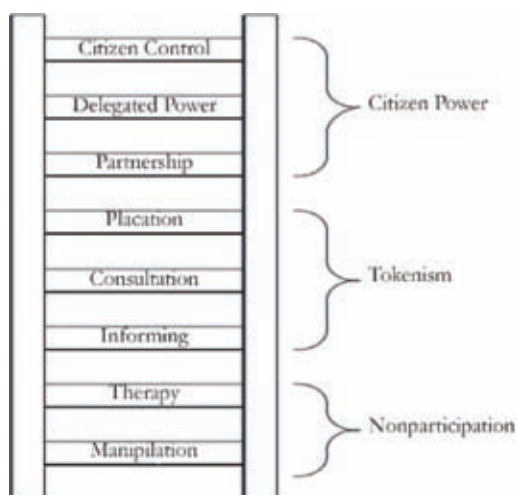


**Figure 1.** Ladder of citizen participation [13].

surveillance site (HDSS) and produce evidence of practical relevance. The objectives were to engage with communities to examine VA data from HDSS, develop local knowledge around the VA data, and set priorities for local services.

## METHODS

### Study setting

The study was conducted at the MRC/Wits Rural Public Health and Health Transitions Research Unit, which oversees the Agincourt HDSS located in rural Mpumalanga, a province of 4 million people in rural northeast South Africa. Established in 1992, the HDSS covers a population of approximately 115 000 people, over 450 km², 31 villages, and 20 000 households [26,27] (**Figure 2**). A dedicated Public Engagement Office works to enhance community and health systems engagement at different levels. The office regularly provides data and discusses research findings with the community and health system at different levels.

Serving the Agincourt study area within a radius of 20–60 km, is a network of ten government run PHC clinics that provide free basic outpatient health services during regular working hours. Services include routine maternal and child health interventions (including integrated management of childhood illnesses, well child visits, growth monitoring, routine immunizations), sexual and reproductive health services, testing and treatment for sexually transmitted infections, including HIV, minor trauma and routine care for chronic illnesses [28]. In 2015, attendance at antenatal care (ANC) clinics before 20 weeks of pregnancy in Mpumalanga was 56%, 80% of children one year and below had complete immunization, and the facility–based under–5 mortality rate was 8.3% against a target of 5% [29]. There are also limited private health care services in the area.

### Initiating PAR

We developed a process based on PAR. PAR is a non–linear, context specific process, with cycles of observing, reflecting, acting and learning from action. The repeated cycles build a sustained process that enables community ownership [30]. Within the time and resources available, it was possible to initiate the process and so the following description offered by Loewenson et al was adopted: "start by obtaining an insight into the communities and their conditions. This provides the information to support inclusion in the work, to systematize experience and to draw out priorities for attention" [30] (**Figure 3**).

We defined communities geographically, as residents of a specific area with shared social and health conditions. To prioritize and maintain prior linkages, we attempted to re–engage participants involved in a previous community–based participatory research (CBPR) pilot study in the Agincourt HDSS [31]. In the previous study, three village–based discussion groups had been convened. Villages had been selected on
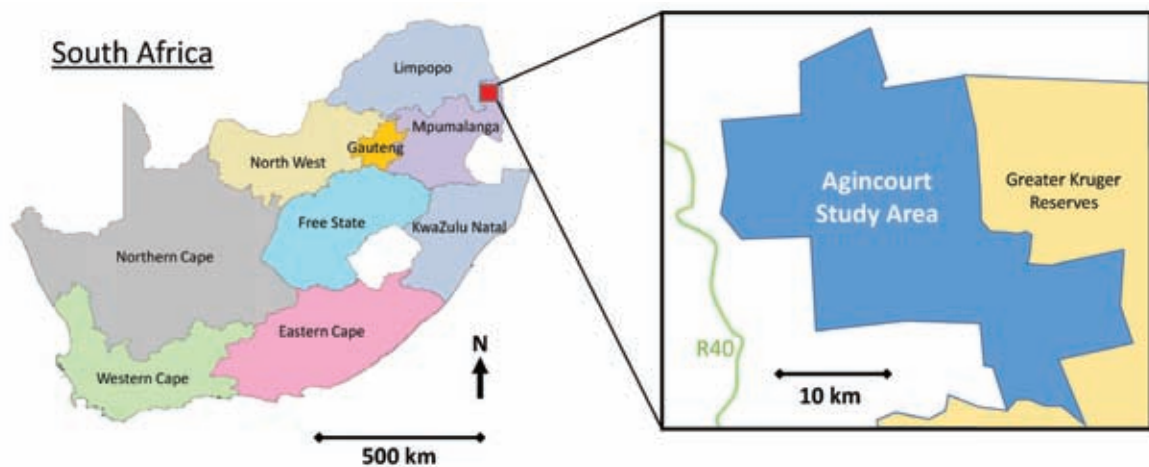


**Figure 2.** Map of Agincourt HDSS in rural northeast South Africa.
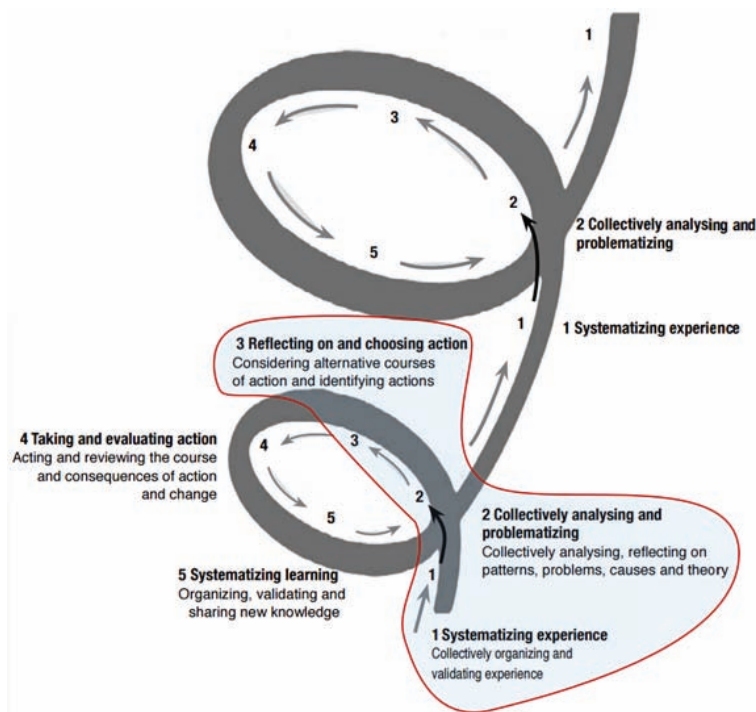
**Figure 3.** PAR process, with the initial elements highlighted [30].

the basis of demographic variation and feasibility (**Table 1**) and in each village, discussion groups comprised women of reproductive age, family members, traditional healers, religious leaders, community health volunteers, health workers and community leaders. To mitigate any potential biases due to power differentials, in one village, the group consisted of women only (**Table 2**).

Public Engagement Office staff approached individuals involved in the earlier CBPR study in villages, and described the current study, activities and intended outputs. Written consent forms and information sheets were provided, and participants were invited to ask questions at the time, or afterwards by telephone. For those willing to be involved, a convenient time was arranged for the first meeting at which participants were asked to sign and return the consent forms. Through this process, all participants from the prior study agreed to be involved.

## Data collection

In the first meeting, and to encourage participant control over how the topics for discussion were framed, we asked people's opinions about conditions to examine. We also consulted the Directorate for Maternal Child, Women and Youth Health and Nutrition (MCWYH&N) in the provincial Department of Health (including co–authors BS and MVDM) and considered conditions with high prevalence rates identified in Agincourt HDSS. Through this approach, under–5 mortality and HIV–related mortality were selected. The discussion groups then embarked on a series of six weekly meetings to consider the conditions in terms of causes, contributory factors, and actions to address the identified issues (**Table 3**). This paper reports on the process as it related to under–5 mortality, the results on HIV–related mortality are reported elsewhere [33].

**Table 1.** Characteristics of selected villages

| | VILLAGE-BASED DISCUSSION GROUP | | |
|---|---|---|---|
| | **A** | **B** | **C** |
| Number of households | 1178 | 932 | 647 |
| Population, total | 6158 | 4827 | 3705 |
| Population, male | 3005 | 2305 | 1781 |
| Population, female | 3147 | 2522 | 1924 |
| Population, children under 5 | 647 | 513 | 458 |
| Population, children of school age | 1911 | 1410 | 1167 |

Source: [32].

**Table 2.** Composition of village based discussion groups

| Participants* | Group | | | Total |
|---|---|---|---|---|
| | A | B | C | |
| Women of reproductive age (WRA) | 1 | 1 | 2 | 4 |
| Family members† | 2 | 2 | 2 | 6 |
| Traditional healers | 1 | 1 | 2 | 4 |
| Religious leaders and elders | 1 | 2 | 2 | 4 |
| Community health volunteers‡ | 1 | 1 | | 2 |
| Community/village officials‡ | 1 | 1 | | 2 |
| Community/village health workers‡ | 1 | 1 | | 2 |
| Total | 8 | 8 | 8 | 24 |

*All participants recruited were 18 years of age or older. Although participants are likely to be categorized by more than one role in the community, one role per individual was considered for the purposes of convening the focus groups. We agreed roles with participants to identify what they feel to be their primary role in the community.

†Close relative: parents, grandparents, siblings, children, in–laws, nieces, nephews and cousins.

‡We acknowledged that people with working arrangements, particularly village health workers and village officials may not be available for a series of six weekly meetings. We also acknowledged the ethical imperative of engaging participants who would otherwise be involved in earning income and or the provision of public services. The groups were therefore based on these compositions, with careful consideration of minimizing disruption to local services.

**Table 3.** Schedule of village–based meetings

| | Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 |
|---|---|---|---|---|---|---|
| | | Under–5 mortality | | HIV–related mortality | | |
| | Introduction and recruitment | Life histories and collective analysis | Collective analysis (continued) and action agendas | Life histories and collective analysis | Collective analysis (continued) and action agendas | Preliminary feedback and reflections on process |
| Group: | | | | | | |
| A | A, 1 | A, 2 | A, 3 | A, 4 | A, 5 | B, 6 |
| B | B, 1 | B, 2 | B, 3 | B, 5 | B, 5 | B, 6 |
| C | C, 1 | C, 2 | C, 3 | C, 5 | C, 5 | C, 6 |
| Total number of meetings | | | | | | 18 |

## Subjective perspectives: VA data and life histories

In the second meetings, VA data on under–5 deaths were presented. 110 such deaths had been recorded by Agincourt HDSS in 2012 and 2013. The leading causes of death were acute respiratory infection (including pneumonia), HIV/AIDs–related death and malaria accounting for 18%, 15% and 13% of the total burden respectively. Overall, 61% of deaths were due to infectious causes. Furthermore, 49% of deaths occurred among children 1–4 years of age, 30% to infants and 21% to neonates (**Table 4**). The VA data also contained indicators on the circumstances of mortality, developed in the same project [35]. These data indicated multiple problems with access to care at and around the time of death. Specific issues identified were: families not calling for help (34% of all problems reported), not going to a facility at the time of death (29% of all problems reported), and that the overall costs of care were unaffordable (14% of all problems reported) (**Table 5**).

After presenting the VA data, we invited participants to share their knowledge and experiences in an open discussion. Participants were prompted to share views on symptoms, modern and traditional therapies, health service responses, and what happens in the village in acute situations. Issues that arose were recorded on a flip chart that was visible to all participants. When a sufficient amount of discussion had occurred in the time that was available, and no new issues were identified, the facilitator (co–author SN) summarized the discussion and checked the list with participants for completeness.

## Collective analyses: ranking and diagramming

We then undertook a process to systematize individual views and experiences into shared accounts using ranking and diagramming. For the ranking, the flip chart with the initial long list was put on a table in

**Table 4.** Cause–specific mortality fraction (CSMF): all under–5 deaths, age/sex sub–groups

| CAUSE OF DEATH | AGE GROUP | | | SEX | | |
|---|---|---|---|---|---|---|
| | Neonate (<28 days) | Infant (1–11 months) | Under 5 (1–4 years) | Female | Male | n (%) |
| **Infectious:** | | 27 | 40 | 38 | 29 | 67 (61) |
| Acute respiratory infection including pneumonia | | 9 | 11 | 15 | 5 | 20 (18) |
| HIV/AIDS related death | | 2 | 14 | 7 | 9 | 16 (15) |
| Malaria | | 6 | 8 | 5 | 9 | 14 (13) |
| Diarrheal diseases | | 8 | 5 | 9 | 4 | 13 (12) |
| Meningitis and encephalitis | | 1 | 1 | 1 | 1 | 2 (2) |
| Pulmonary tuberculosis | | | 1 | 1 | | 1 (1) |
| Other and unspecified infectious disease | | 1 | | | 1 | 1 (1) |
| **Neonatal:*** | 16 | 2 | 1 | 9 | 10 | 19 (17) |
| Neonatal pneumonia | 7 | | | 6 | 1 | 7 (6) |
| Congenital malformation | 1 | 2 | 1 | 1 | 3 | 4 (4) |
| Prematurity | 3 | | | 1 | 2 | 3 (3) |
| Birth asphyxia | 3 | | | 1 | 2 | 3 (3) |
| Neonatal sepsis | 1 | | | | 1 | 1 (1) |
| Other and unspecified neonatal cause of death | 1 | | | | 1 | 1 (1) |
| **Indeterminate** | 7 | | 2 | 6 | 3 | 9 (8) |
| **External:** | | 2 | 6 | 3 | 5 | 8 (7) |
| Accidental drowning/submersion | | | 3 | 2 | 1 | 3 (3) |
| Road traffic accident | | | 2 | 1 | 1 | 2 (2) |
| Other and unspecified external cause of death | | 2 | | | 2 | 2 (2) |
| Assault | | | 1 | | 1 | 1 (1) |
| **Non–communicable:** | | 2 | 5 | 2 | 5 | 7 (6) |
| Acute abdomen | | 1 | 1 | 1 | 1 | 2 (2) |
| Asthma | | | 2 | | 2 | 2 (2) |
| Epilepsy | | 1 | | | 1 | 1 (1) |
| Severe malnutrition | | | 1 | 1 | | 1 (1) |
| Severe anemia | | | 1 | | 1 | 1 (1) |
| Total number (%) | 23 (21) | 33 (30) | 54 (49) | 59 (54) | 51 (46) | 110 (110) |

*Deaths due to congenital malformations include conditions that have their origin in the perinatal period even though death or morbidity occurs later [34].

**Table 5.** Frequencies of responses to new Verbal Autopsy indicators on circumstances of mortality

| | AGE GROUP | | | |
|---|---|---|---|---|
| | Neonate (<28 days) | Infant (1–11 months) | Under 5 years (1–4 years) | Total responses to new Verbal Autopsy indicators on circumstances of mortality, n (%) |
| **Recognition:** | | | | |
| Doubts about the need for care | 2 | | 3 | 5 (3) |
| Use of traditional medicine | 3 | 8 | 8 | 19 (13) |
| **Access:** | | | | |
| >2 hours to hospital/health facility | | | | |
| Overall costs prohibitive | 3 | 7 | 10 | 20 (14) |
| Did not use mobile phone | 13 | 12 | 25 | 50 (34) |
| Did not travel to hospital/ health facility | 13 | 9 | 20 | 42 (29) |
| Did not use motorised transport* | | 5 | 5 | 10 (7) |
| **Quality of care:** | | | | |
| Problems with admission* | | | | |
| Problems with treatment* | | | | |
| Problems with medications* | | | | |
| Total number of deaths, n (%) | 23 (21) | 33 (30) | 54 (49) | |

*The denominator is the number of respondents who reported traveling to hospital/health facility. Respondents were able to indicate more than one 'circumstance of mortality' indicator for each death reported.

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**Figure 4.** Systematising subjective perspectives – ranking.



**Figure 5.** Validating by consensus – diagramming.



**Figure 6.** Participatory photography.

the center of the group, and participants were invited to interrogate it. Participants were given adhesive markers to nominate issues they considered to have the highest priority (**Figure 4**). Two rounds of ranking were conducted to ensure the issues were re–visited and re–checked and to validate the list before recording the flip chart in a photograph and closing the meeting. In the subsequent meetings (meeting three) we used diagramming to revisit the ordered list. We adopted a 'problem tree' diagram to organize issues identified into proximate determinants, mid–level systems factors, and social and structural causes of under–5 mortality [30] (**Figure 5**).

One discussion group used a visual participatory technique called Photovoice to explore the use of contemporary methods employing mobile and digital technologies. We selected the remotest, all–female discussion group (Group C) for the Photovoice method. Participants in Group C were provided with digital cameras to take photographs of their physical environments as a further input to the discussions [36,37]. We provided basic training on photography, explained why and how to secure release permissions from subjects of photographs, and provided consent forms for permission releases. In the subsequent weekly meetings, we projected the photographs taken by group members during the discussions. Photographers were invited to describe and explain their images and the group considered the issues they represented as additional inputs to the discussion (**Figure 6**).

### Priority setting

In the final meetings on under–5 mortality, a summary of the process was fed back to each group to verify content and meaning, upon which discussions were held about actions to address the issues identified. This involved re–visiting and re–checking the outputs of the prior process, and moving from causes and contributory factors toward remedial actions. We used ranking to identify priorities for action through which only issues that were nominated by the group were registered. We also indicated that the outputs of the process would be provided to the local health authority.

All discussions were facilitated by a senior qualitative researcher (co–author SN) with knowledge of the local area, assisted by a qualitative field research assistant and co–researchers (co–author LD). The focus group discussion (FGD) method was employed [38] using topic guides to structure the discussions in meetings lasting 90–120 minutes. With separate permissions, the discussions were audio recorded and transcribed verbatim. Transcripts were translated from the local language, xi–Tsonga, into English. SN oversaw and performed transcription and translation with the field assistant. Observational notes were also taken (SN, LD and field assistant) and analyzed.

### Data analysis

The visual and narrative data were thematically analyzed to complement the collective analyses. Thematic analysis was conducted in parallel to, and following completion of, data collection. NVivo Version 10

was used for data entry and management [39]. Transcripts were analyzed based on combined inductive/deductive framework analysis (co–authors OW and LD). This involved a sequence of steps of increasing abstraction from data to findings [40,41]. The transcripts were read several times to familiarize researchers with the main ideas, paying attention to recurring patterns and themes. Initial themes and sub–themes were noted as codes. Transcripts were re–read, re–checking for themes, how themes supported the data and vice versa, identifying relationships within and between themes. This was done iteratively until thematic saturation. The visual data were cataloged and a 'word cloud' was generated though which frequencies of terms were graphically represented.

## Ethical considerations

Informed consent was sought from all participants. Participants were provided with information in the local language and contact details for the research team, and given time to consider this before agreeing to be involved. Separate consents were gained for audio recordings. All participants were assured anonymity, and that taking part would have no influence on care available to themselves or their families. Participants were also assured that they were free to leave the process at any time and for any reason. Participants were reimbursed with travel expenses, provided with refreshments in meetings, and given a voucher of ZAR300 (approx. US$ 23) at the end to reimburse for time spent participating and as a token of appreciation. All identifiable data were anonymized. Institutional review boards at the Universities of Aberdeen, Scotland, and Witwatersrand, South Africa, and the provincial health authority in Mpumalanga, reviewed and approved the study protocol.

## RESULTS

The collective analysis is presented below according to two overall categories: a) social and structural root causes and b) contributory mid–level systems factors related to under–5 mortality. The results are illustrated with verbatim quotes and visual Photovoice images from the thematic analysis.

### Social and structural root causes

#### *Lack of education, unemployment and poverty*

Unemployment and poverty linked to lack of education were identified as root causes of under–5 mortality. Despite free public health care for children under–5, the indirect costs of care seeking were unaffordable for people without regular paid employment. The consequences for service utilization and ultimately health outcomes were clearly stated. Lack of education was referred to as 'a problem of black people' more generally, with the need for community health education and activities such as the PAR process noted.

*"…when they say money to take the child to the hospital she would tell you that she doesn't have money [to travel to the clinic]. And then you find that the child might be unlucky and then die."* (Woman 3; Village B; Discussion 4)

*"…they are not educated … even this workshop is teaching people about diseases … If there are workshops like this, they are few."* (Woman 5; Group B; Discussion 4)

*"The bottom line is … our black people need a lot of education."* (Man 2; Group B; Discussion 4)



**Figure 7.** Lack of clean drinking water (Photovoice image).

#### *Lack of clean water*

Lack of clean drinking water was a further fundamental root cause identified. Participants described using rivers and animal water supplies as drinking sources during periods of drought and when pipe–borne water fails (**Figure 7**). Participants also recounted knowledge of children drowning while fetching water in these circumstances.

*"…look carefully… this place is dirty, even our livestock drinks water there, also people drink water there."* (Woman 5; Group C; Discussion 5)

*"…we are suffering because of water; we go to the streams to dig to get water. Meanwhile the water that we get when we dig it's not right."* (Woman 2; Group A; Discussion 9)

**Figure 8.** Unsafe domestic environments (Photovoice image).



**Figure 9.** Overcrowding and poor housing (Photovoice image).

### Unsafe environments and inadequate housing

Unsafe environments and inadequate housing were verified across the groups (**Figure 8**). Further domestic hazards related to water were noted, such as drowning in water storage cans and ingestion of chemicals mistaken for water. Road traffic accidents and sexual assaults were also noted.

*"That child drowned in the water while there are people in the house, they were at home."* (Woman 5; Village B; Discussion 4)

*"If I have bought 2 litres of paraffin, I have to hide it… the child was thirsty and then he took that 2 litre and drank it."* (Woman 6; Group C; Discussion 8)

*"…The child can walk into the bush and find snakes and cruel people … there are lots of people in the bush that might rape the child."* (Man 1; Group C; Discussion 8)

Furthermore, inadequate housing and overcrowding were reported to result in children contracting infectious conditions (**Figure 9**).

*"…the cold was coming into the house until my child had pneumonia."* (Woman 4; Group B; Discussion 4)

### Malnutrition

Malnutrition was identified as a common cause of ill–health and death in younger children. Malnutrition was also linked to poverty and unemployment, with reference to the inability of parents to purchase nutritious food.

*"… young children died because of hunger."* (Woman 1; Group B; Discussion 4)

*"… how would I buy milk … the father of my child is not working."* (Woman 1; Group A; Discussion 6).

### Perceived parental neglect

The neglect of infants, particularly by young, single mothers was repeatedly noted in the discussions. Specifically, views on the misuse of child support grants (CSGs) were recounted in detail. Discussions also centered on how grandmothers are left with children whose mothers are seeking employment or engaging in vices. Grandmothers were described as unable to properly care for under–5s, further compounding exposure to risk.

*"[Single mothers] receive R330 Child Support Grant … She takes that money and uses it or spend it on alcohol, buys pants and cool drink [participants laugh]."* (Woman 1; Group B; Discussion 4)

*"Children … can get infections because the way a young person and a granny nurse the child it's not the same…"* (Woman 1; Group A; Discussion 6)

Lack of recognition of the severity of symptoms on the part of parents (generally young, single mothers) was also identified and related to incomplete health education and limited understandings of health protection and promotion. According to participants, this resulted in the worsening of child health and sometimes death.

*"Another thing is negligence, you find that a child has started diarrhoea and then the parent say it's nothing and it will pass. And then when the child is too weak it's when they try the hospital whereas it's already late."* (Woman 5; Group C; Discussion 5)

### Traditional medicines, witchcraft

Participants described how some traditional treatments are harmful to children and delay presentation in clinics and hospitals. However others expressed views that certain illnesses are only curable with tradi-

tional medicines. Although there were some differences in views on the use of traditional medicine within the groups, a pervasive lack of faith in modern medicine was identified as a strong influence on its use.

*"…they take rat's faeces and grind it and put it on the child's belly button, do you see that I am killing the child when I do that?"* (Woman 5; Group C; Discussion 8)

*"…when a child is sick… just take what we give* [traditional medicine]*… you don't go to hospitals."* (Man 2; Group B; Discussion 4)

Witchcraft was also identified as a deterrent to care seeking. Participants recounted how mothers believe that illnesses in children are due to spells cast by neighbors and so conceal and/or do not act on signs and symptoms.

*"There is lots of witchcraft and we don't trust one another… she won't help you with anything, which is why there is lots of death because I hide from my neighbour that I have a child who is sick…"* (Woman 2; Group A; Discussion 6)

## Contributory mid–level systems factors

### Unavailable emergency transport

An unreliable ambulance service was identified as a major problem linked to adverse outcomes. Ambulance delays for several hours after being called were described. Participants reported how unavailable emergency transport results in worsening of children's conditions and, on occasion, death in the acute situation.

*"…when you call the ambulance it doesn't come from* [hospital 30 km away] *but from* [hospital 150 km away]. *Even the time my child was sick I called an ambulance and they told me that they are busy … I asked my sister to take my child to the hospital because I saw that she would die."* (Woman 2; Group B; Discussion 4)

### Delays in facilities

Delays in health facilities was a further issue identified. Specific issues included: overcrowded clinics, long queues and waiting times, and long breaks taken by health workers. Participants described whole days spent waiting and knowledge of situations where children had died while waiting to be seen.

*"When you get to the clinic you have to queue … even when they see that the child is very sick they don't help you immediately … the child dies because of queuing."* (Woman 2; Group A; Discussion 9)

### Poor quality care

Poor quality of care, particularly care provided by nurses, was ascertained as a major contributory factor across the groups. Specific issues included lack of respect for patients and disclosures of HIV status. Participants noted how fear of status disclosure leads to avoidance of ANC, in turn increasing risks to new–borns.

*"If there was confidentiality, people would …go to the clinic when they are pregnant… they are scared to go to the antenatal clinic."* (Woman 3; Group B; Discussion 7)

*"She never went for antenatal clinic … when she gave birth the child was born infected with HIV."* (Woman 2; Group A; Discussion 6)

Accounts of nurses treating patients poorly, giving preferential treatment to friends and relatives, not performing triage, and lack of a sense of urgency in acute situations were also verified. Again, fear and avoidance of health services were corroborated among participants.

*"She's scared to take the child to the hospital because…they are not treating us well."* (Woman 2; Group A; Discussion 6)

There was some acknowledgment of broader system influences on provider behaviors. Participants noted that health workers are overworked and clinics understaffed. Several also shared knowledge and experience of good nurses.

*"*[Nurses] *are tired because they work with many people…"* (Man 1; Group A; Discussion 6)

**Figure 10.** Word cloud of discussion narratives on causes and contributors of under–5 mortality.

### Lack of medicines

Lack of medicines was a further factor identified that discouraged parents from taking children to clinics. Nurses taking medicines for personal use and further depleting supplies was also noted between the groups.

*"…make sure that the nurses don't take the medication….that is why we don't get it sometimes."* (Woman 3; Group B; Discussion 7)

*"… the child might die because I went where I was supposed to get help but they tell me that there are no medications."* (Woman 1; Group C; Discussion 8)

The word cloud illustrates the frequency of references to fear of negative consequences from interacting with the health system, quality of care from nurses, transport problems, the effects of poverty, and perceived neglect of children by their parents (**Figure 10**).

## Priority setting

Participants identified areas for action to address the issues identified. These were validated via ranking and arranged according to the two overall categories – "social and structural" and "mid–level systems" priorities (**Table 6**).

### Social and structural priorities

Considering the influence of poverty – on housing, nutrition, care–seeking, access to clean water, and the combined effects of these on under–5 mortality – participants identified employment as a priority area for action. Participants described how this would empower people to generate income, thereby enabling family health promotion.

*"…they fall pregnant just because they want the money for Child Support Grant. And that grant is little, so I think they can be helped by employment. So everyone could work and end poverty."* (Woman 2; Group A; Discussion 6)

Expanding health promotion and health education were also prioritized, and approaches to achieve this, for example via media campaigns and local radio were suggested. Participants also stated that the PAR process itself could serve as a vehicle for health education and promotion.

*"… the government needs to help us to broadcast everything that we talk about on television, radio and teach parents so they can be responsible for their children."* (Woman 4; Group B; Discussion 4)

**Table 6.** Collective analysis on causes, contributors and priority actions to reduce under–5 mortality

| Causes/contributors | Actions |
| --- | --- |
| **Social and structural root causes:** | |
| Lack of education, unemployment and poverty | Generate employment; increase social amenities related to primary and secondary education |
| Lack of clean water | Provide access to clean water |
| Unsafe environments/ inadequate housing | Increase social amenities related to road safety |
| Malnutrition | Implement community based health promotion |
| Parental neglect | Health education and health promotion campaigns (eg, through PAR process) |
| Traditional medicine and witchcraft | Encourage medical and traditional healers to work together |
| **Mid–level contributory systems factors:** | |
| Transport problems | Build and expand clinics |
| Delays in facilities | Employ more health workers |
| Poor quality care | Improve attitudes toward patients; ensure confidentiality; monitor health workers |
| Lack of medicines | Increase medicines and supplies |

## Mid–level systems priorities

The need for basic functionality in clinics was highlighted, with the respecting of patient confidentiality around HIV status in ANC identified as a primary priority within this. In addition, the expansion and/or building of more clinics and encouraging medical and traditional healers to work together were further priority areas defined.

*"…at the clinic they have to teach themselves to have confidentiality."* (Woman 3; Group B; Discussion 7)

*"They have to extend that clinic because there are many people who use that clinic and that clinic is small. People wait outside."* (Woman 2; Group B: Discussion 8]

*"… make traditional healers and western doctors work together because even what others do it's working and also the doctors what they do it's working. Not to say: 'don't use other things' when you use [traditional] treatment … it's working and most people do use it."* (Man 1; Group A; Discussion 6)

## DISCUSSION

We initiated a PAR process to gain local knowledge and prioritize actions with communities in an established HDSS. This section reflects on these aims, considers the findings, and discusses implications for further application of the method.

### Substantive findings

Poverty, unemployment, inadequate housing, unsafe environments and shortages of clean water were clearly identified as fundamental root causes of under–5 mortality. Considering the high proportion of under–5 deaths due to infectious diseases, it is reasonable to assert that critical risk is introduced from the environmental conditions identified. It is also noteworthy that the priorities identified to respond to these issues (improving employment, providing clean water and improving road safety) are beyond the remit of the Department of Health. We re–visit this point in the methodological reflections below.

Despite the clear acknowledgment of the influence of social conditions on under–5 mortality, marked criticism was expressed toward young single mothers for the neglect of children and infants and the misuse of the CSG. CSG is a social protection intervention which covers 12 million children in South Africa. It is available to primary carers earning below a means–tested benchmark. At the time of data collection, the CSG provided ZAR330 (approx. US$ 25) per month per child [42,43]. Studies have linked the scheme to increased quality of life, better access to services, and reductions in adolescent pregnancy with little perverse incentive [44,45]. Others however assert that such schemes may have limited benefits for those already engaged in risky behaviors, noting influences other than material deprivation on loss of responsibility [46–48]. The findings highlight both the limitations on parents' abilities to protect and promote family health, and local views on individuals' accountability for these situations.

A series of mid–level health systems factors were also identified as contributory to adverse outcomes. Lack of confidentiality around HIV status, disrespect and abuse of patients, and misuse of medications on the part of clinic nurses were identified as deeply problematic. Poorly staffed and equipped clinics, long waiting times and overcrowded facilities were also ranked as key influences. The expressions of fear and avoidance of services due to poor quality care supports ideas of how repeated interactions between providers and users of services shape, and are shaped by, social norms of eligibility for services [49]. Again, the blame directed toward clinic nurses was expressed with simultaneous acknowledgment of wider systems constraints.

The health system in South Africa faces far–reaching challenges. Service provision is distinctly two–tiered with over 70% of physicians working in the private health sector catering for an affluent 16% of the population [19,50,51]. The public arm of the system is described as fragmented and dysfunctional, with systemic failures in leadership, stewardship and implementation [52]. Clinics are acutely resource–constrained, and staff are chronically over–worked as a result [19,25]. The two–tier system was explicitly acknowledged in the recent White Paper for NHI in a bold move toward universal access to a basic minimum package of essential health care services available on the basis of need and without financial hardship [22].

The White Paper commits to substantial reorganization of the health system in a phased 14–year implementation comprised of three phases: (1) strengthening quality of care; (2) registering the population,

distributing NHI cards and procuring services and; (3) assessing functionality and sustainability via audit, demographic and epidemiological population profiling [22]. A policy of PHC Re–engineering was introduced in 2011 to support the first phase. The policy focuses on improving connections between services and communities through community (ward) based outreach teams, health promotion in schools, and scaled up attention to maternal and child health [53]. PHC Re–engineering is an opportunity to develop the relationships between health authorities and communities to inform decentralized PHC, to foster more positive care contexts and interactions. The recommendations for action on enlarging community engagement for health promotion and education are consistent with the aims of PHC Re–engineering. Participants also noted that the PAR process was a suitable means for expanded engagement.

The work developed an initial understanding of context and common conditions. Priority actions were specified, fed back to the provincial directorate [54], and subsequently a feedback forum was held between the Department of Health and participants in the Agincourt HDSS [55,56]. Within the time and resources, it was not possible to develop the process into taking action, and reflecting on and learning from action, and so PAR was not fully achieved. Through the activities undertaken however, willingness and commitment were expressed by participants and health authorities to continue the process into taking action, and reflecting and learning from this action [57]. Extending the process will add a crucial link to understand how change occurs in health systems, by which means, for whom, and on the role of evidence in the process. We consider these points further below.

## Methodological reflections

### Participation for whom?

As the process continues, who participates is a key consideration. In the introductory work, we sought to convene village–based discussion groups with shared social and health conditions. We developed a geographically defined group as residents of a specific area and varied the constituency of the groups to be more or less homogenous. There were no overt differences observed in the dynamics between the groups in the discussions on under–5 mortality, underscoring ideas that no group is entirely homogenous [30].

A prominent finding common to all the discussions was the blame and negativity expressed toward clinic nurses and young single mothers – two females at the care interface who arguably have limited control over the wider conditions identified. Despite several participants being young mothers themselves, the blame and negativity was clearly directed toward the behaviors of "others". Similar dynamics have been observed in participatory research elsewhere, whereby initially blaming views, over time, gave way to sophisticated multi–level interpretations of complex problems [58].

The importance of maintaining links with the groups convened to date as well as expanding the process to include the perspectives of child–headed households, young mothers and clinic nurses will be central to considerations of whose voices count in the process in future. Close attention is also required on whether and how views around blame, responsibility and accountability develop in the longer term.

### By which means?

The importance of actively disrupting hierarchies between researchers and participants is a further feature to be developed in future application of the method [59]. Promoting and building participants' capacities as co–researchers, decision makers, action takers and influencers of institutional decision makers is necessary for communities to own the process and the development of the process.

In this research, we made efforts to foster a sense of control by encouraging participants to determine how the topics were selected and framed, and which issues would be referred to the health authority. As the process continues, increasing participant control over the design, process, choice of topics, how outputs are discussed, communicated, acted on and learned from will help build roles related to community ownership and capacity [30,60,61].

Photovoice is a capacity building process in which participants gain skills that can be used to earn income [36]. In this study, Photovoice fostered participation, was a low–cost means of generating powerful evidence and strengthened the process as a whole. The use of Photovoice to investigate quality of care in health facilities however may be more contentious, and is an area that requires further consideration with providers and participants.

Photovoice was one of a range of analytical approaches employed in the initialized process. The thematic analysis was performed to fully interrogate the data collected and illustrate the collective analysis. It identified the paradoxical blame. The different approaches have supported one another, triangulated findings, and helped to identify relevant divergences.

### How change occurs in health systems

Connecting the process to the means for action is critical [61,62]. The initialized process was developed in close collaboration with the Public Engagement Office of the Agincourt HDSS, a group that has strong and sustained links with communities and health authorities at different levels. Through these links it was possible to connect communities, health authorities and researchers to develop and address common research questions and adopt roles as co–researchers.

We plan to extend what has been achieved to date into an ongoing cycle of reflection and action inclusive of district, sub–district and clinic level to facilitate and increase the co–production of policy–relevant evidence to understand and respond to priorities. The importance of engagement with sectors adjacent to health – such as labor, housing, and sanitation as well as the local authority – will help to foster an integrated approach to using the information generated to achieve change in health systems [63].

### The role of evidence

This work adds to the literature on researching the social determinants of mortality in HDSSs. Verbal and social autopsy surveys have collected data on social determinants of child mortality in the INDEPTH Network (International Network for the Demographic Evaluation of Populations and Their Health), HDSSs [64,65] and at district and national level [66,67]. The latest version of the WHO VA tool also includes questions on circumstances of mortality that have been developed as part of, and used within, the current project [35].

These efforts reflect the need for methods to provide better understandings of the contextual determinants of mortality in low income settings. Providing PAR methods and data to HDSSs in other settings is also prioritized to promote further application of the method to provide complementary perspectives gained from local knowledge and oriented toward action [68,69]. This is relevant in South Africa as the government consolidates and expands national HDSS infrastructure as a means to inform public policy in the country [70].

## CONCLUSIONS

*"Health systems can, in the way they function, strengthen the capabilities of individuals and social groups, for example by including opportunities for people to participate in planning services, from individual care plans to community health interventions."* (page 11 in [30])

We initiated a PAR process to gain local knowledge and prioritize actions. This study provides evidence that consulting communities provides rich and textured information on the social and health systems dimensions of avoidable mortality. Widespread poverty, unemployment, poor housing and inadequate water were repeatedly identified as direct causes of death within and between the village–based discussion groups. Health systems factors were also clearly identified as contributing to mortality.

The process also helped to establish a commitment to partnerships between communities, health authorities and researchers. The study provided a basis from which to gain support to develop fuller forms of participatory research in this setting. The next steps are under way to build deeper involvement of participants in the process, expand to include the perspectives of those most marginalized and to further develop engagement with health systems stakeholders to enable action, and learning from action. In combination with routine HDSS, the use of PAR to elicit local knowledge on health problems has the potential to connect communities, researchers and health authorities to develop robust evidence for service delivery, policy and planning.

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# Mapping the global research landscape and knowledge gaps on multimorbidity: a bibliometric study

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**Background** To summarize global research trends and activities on multimorbidity; then to assess the knowledge gaps and to identify implications for knowledge exchange between high income countries (HICs) and low– and middle– income countries (LMICs).

**Methods** A comprehensive search was conducted to identify research publications on multimorbidity in the Web of Science™, as well as diabetes, depression, hypertension, and Chronic Obstructive Pulmonary Disease (COPD). The time frame for the search was from 1900 to June, 2016. Information (such as publication date, subject category, author, country of origin, title, abstract, and keywords) were extracted and the full texts were obtained for the co–citation analysis. Data were linked with the life expectancy at birth (years) and Gross National Income (GNI). Co–citation and hierarchal clustering analysis was used to map the trends and research networks with CiteSpace II (JAVA freeware, copyright Chaomei Chen, http://cluster.cis.drexel.edu/~cchen/citespace/).

**Findings** We identified 2864 relevant publications as at June 2016, with the first paper on this topic indexed in 1974 from Germany, but 80% were published after 2010. Further analysis yielded two knowledge gaps: (1) compared with single conditions (diabetes, hypertension, depression, and COPD), there is a mismatch between the high prevalence of multimorbidity and its research outputs (ratio of articles on multimorbidity vs other four single conditions is 1:13–150); (2) although a total of 76 countries have contributed to this research area, only 5% of research originated from LMICs where 73% of non–communicable disease (NCD) related deaths had occurred. Additional analysis showed the median year of first publication occurred 15 years later in the LMICs compared with HICs (2010 vs 1995); and longer life expectancy was associated with exponentially higher publication outputs (Pearson correlation coefficient $r=0.95$) at the global level. The life expectancy at the median year (1994) of first publication was 66.1, with the gap between LMICs and HICs 7.9 (68.4 vs 76.3).

**Conclusions** This study confirms substantial knowledge gaps in the research agenda on multimorbidity, with input urgently needed to move us forward worldwide, especially for and in LMICs. There is the possibility that LMICs can learn from and collaborate with HICs in this area.

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Noncommunicable diseases (NCDs) have accounted for 68% of the world's 56 million deaths in 2012 [1], with half of the people with NCDs having two or more conditions (multimorbidity) [2,3]. Multimorbidity is a comparatively new concept and a challenging area in medical practice globally. Although it is simply defined as "the coexistence of multiple chronic conditions in a given individual" [4,5], based on the research to date [2,3], there is no consensus on which conditions should be considered; or on the method used for measuring multimorbidity. This makes comparisons between– or among studies difficult.

With increasing population and life expectancy, the disease burden of multimorbidity to both individuals and society are increasing. Multimorbidity is already, and will be in the future, a great challenge for both developed– and developing country settings [3,5]. A staggering toll of about 80% of NCDs deaths occurred in low income settings [6], and the most socioeconomically deprived areas have substantially more multimorbidity, that happens earlier (10–15 years) than do their most affluent peers [2], however, evidence from low income settings is limited [3,7–9]. The identification and implementation of innovative approaches are essential for tackling this growing epidemic, especially for and in LMICs.

Better understanding of the whole picture of global research trends, activities and identification of the knowledge gaps on multimorbidity is necessary to move the research agenda forward, and especially for LMICs. This has coincided with the World Health Organization (WHO) global health and research priority on healthy aging [3,10]. While some studies have pointed to the mismatch between the importance of multimorbidity and research outputs in this area [11–13], only a few studies have comprehensively evaluated the research trends, knowledge gaps, and inequality among countries. We aimed to use a comprehensive bibliometric analysis to document these gaps at a global level.

## METHODS

### Data sources and search strategy

A comprehensive search was conducted to identify research publications on multimorbidity including its various spellings (multiple chronic diseases, multiple chronic conditions, polymorbidity, polypathology, pluripathology, and multipathology) in the Web of Science™, Core Collection database, one of the world largest databases of peer–reviewed literature provided by the Thomson Scientific Institute. The time frame for the search was from 1900 to June, 2016. Detailed search strategies can be found in Appendix S1 in **Online Supplementary Document**. The same search strategies were performed on four other leading causes of death: diabetes, depression, hypertension, and COPD. We included all publication types (such as, article, meeting abstracts, review, editorial, letter, etc.).

We also collected the life expectancy at birth (years) and gross national income (GNI) per capita from the website of the World Bank to examine the relationship between these variables and research outputs. The income groups included low–income (US$ 1025 or less), lower middle–income (US$ 1026 to US$ 4035), upper middle–income (US$ 4036 to US$ 12 475), and high–income (US$ 12 476 or more) economies based on per capita gross national income.

### Data analysis and visualization

All publications were included with the following variables extracted: publication date, subject category, document type, author, organization of origin, funding agency, language, country of origin, title, abstract, and keyword. In addition, the full texts were obtained for the co–citation analysis. The retrieved results were exported to both Microsoft Office Excel (Microsoft, Seattle, WA, USA) and plain text for further analysis.

Data were linked with the life expectancy at birth (years) and GNI in Microsoft Office Excel. The Pearson correlation coefficient ($r$) between life expectancy at birth (year) and annual publications (on the logarithmic scale) was calculated.

CiteSpace II [14] was used to conduct co–citation and hierarchal clustering analysis to map the trends and research networks.

### Ethical issues

The research used published data from secondary sources and did not involve any interactions with human subjects. Hence it is exempt from the institutional review board (IRB) approval process.

## RESULTS

### Characteristics of research landscapes on multimorbidity worldwide
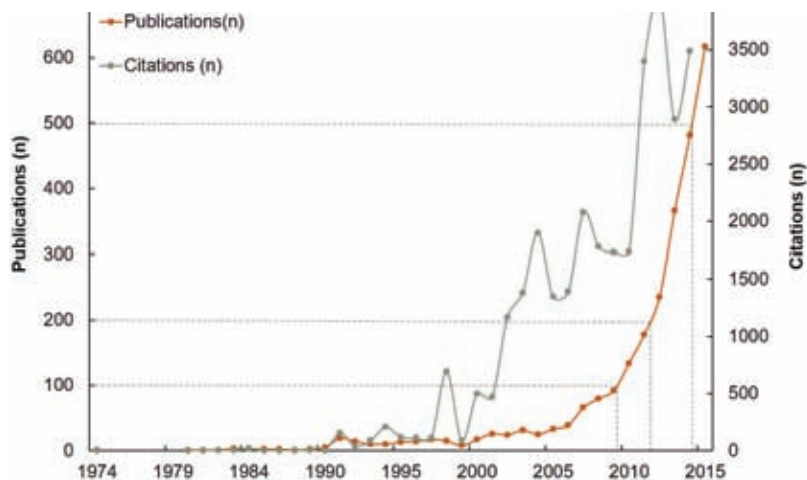


**Figure 1.** Trends of the annual publications and citations on multimorbidity worldwide.

A total of 2864 articles on multimorbidity were retrieved from the database, with the first indexed in 1974 from Germany. As shown in **Figure 1**, the publications appeared sporadically before 1990, and increased slowly up to the early 2000s, with a transition to exponential growth after 2005. Of the 2864 articles, 80% were published after 2010, while only 9% appeared between 1974 and 2004. Regarding the development of annual total citations, **Figure 1** shows a similar trajectory to the publication data with a total of 31 669 citations. However, the exponential growth started around 2000.

The primary type of publication was research article (74%) (see Appendix S2 in **Online Supplementary Document**). There were 12 publication languages, 87% were reported in English, followed by German (10%), Spanish (1.3%) and French (1.0%) (see Appendix S3 in **Online Supplementary Document**). The publications covered 897 journals, and we identified the top 20 journals had published around or more than 20 articles between 1974 and 2016. Journals with the most articles on multimorbidity include the *Journal of the American Geriatrics Society* (n = 74), *PLOS One* (n = 74) and *BMC Family Practice* (n = 67). Further details on the top 20 journals can be found in Appendix S4 in **Online Supplementary Document**. Of the 20 most prolific authors, 15 were from Europe, four were from North America, and one was from Australia, with none from LMICs (see Appendix S5 in **Online Supplementary Document**).

Overall, the three leading research institutions (Johns Hopkins University, Harvard University, and University of California System) were from the US, followed by Germany and UK institutions (see Appendix S6 in **Online Supplementary Document**). Visualization of the institutions performance and collaborative networks can be seen in Appendix S7 in **Online Supplementary Document**. Nine of the top 15 funding agencies from US sponsored the most publications (see Appendix S8 in **Online Supplementary Document**).

A total of 117 different subject categories were involved in this research area, with the leading three subject categories: Medicine General Internal (691 papers), Health Care Sciences Services (422 papers), and Geriatrics Gerontology (381 papers). The top 20 subject categories are listed in Appendix S9 in **Online Supplementary Document**. The different subject categories connected broadly, imply that multimorbidity research is an interdisciplinary area (see Appendix S10 in **Online Supplementary Document**).

### Knowledge Gap 1. Mismatch between the high prevalence of multimorbidity and its publication outputs

Compared with other high prevalence single chronic condition (diabetes, hypertension, depression, and COPD), there is a mismatch between the high prevalence of multimorbidity and its research outputs. Although the median prevalence of multimorbidity is 63%, the number of articles on the other four single conditions is 13 to 150 times that of multimorbidity (**Table 1**).

Further analysis demonstrated both physical and mental disorders are contained in the research framework of multimorbidity. **Table 2** shows the top 10 featured conditions and leading risk factors mentioned in the keywords list. Similar findings were also found in other research types, such as systematic review [18], and longitudinal cohort study [19]. The leading disease and risk factor was cardiovascular and heart disease, and physical activity, respectively.

**Table 1.** Prevalence of certain conditions and number of related articles published to date

| Conditions | Prevalence (year) | Publications | Ratio of articles on multimorbidity vs on other four conditions |
|---|---|---|---|
| Multimorbidity | 13%–83% (1989–2012) [15]* | 2864 | 1:1 |
| Diabetes | 9% (2014) [1] | 431 009 | 1:150 |
| Depression | 5.9–14.6 (2000s) [16] | 360 666 | 1:126 |
| Hypertension | 22% (2014) [1] | 346 894 | 1:121 |
| COPD | 11.7% (2010) [17] | 36 866 | 1:13 |

*A systematic review included articles from 1989 to 2012, with median prevalence 63%.

**Table 2.** Featured conditions and risk factors mentioned in the keywords list

| Rank | Conditions or risk factors | Appearance (N) |
|---|---|---|
| **Diseases:** | | |
| 1 | Cardiovascular and heart disease | 340 |
| 2 | Depression | 195 |
| 3 | Diabetes mellitus | 94 |
| 4 | Dementia | 85 |
| 5 | COPD | 78 |
| 6 | Cancer | 70 |
| 7 | Hypertension | 56 |
| 8 | Alzheimer disease | 41 |
| 9 | Chronic kidney disease | 34 |
| 10 | Cognitive impairment | 33 |
| **Risk factors:** | | |
| 1 | Physical activity | 51 |
| 2 | Obesity | 45 |
| 3 | Body mass index | 30 |

## Knowledge Gap 2. Imbalance in publications among countries and the roles of economics and life expectancy

Table 3 outlines indicators to demonstrate the imbalance in research outputs on multimorbidity and NCD disease burden and life expectancy. Compared with 73% NCD related deaths that occurred in LMICs, only 5% of publications on multimorbidity originated from LMICs. Onset of the median year of first publication occurred 15 years later in the LMICs compared with HICs (2010 vs 1995.), and at that time point, the life expectancy at birth (years) was 66.1, with the gap between LMICs and HICs 7.9 (68.4 vs 76.3).

We analyzed the year of first publication and total number of publications by country. **Figure 2** shows the distributions and trends of publications between 1974 and 2016 plotted according to the level of GNI
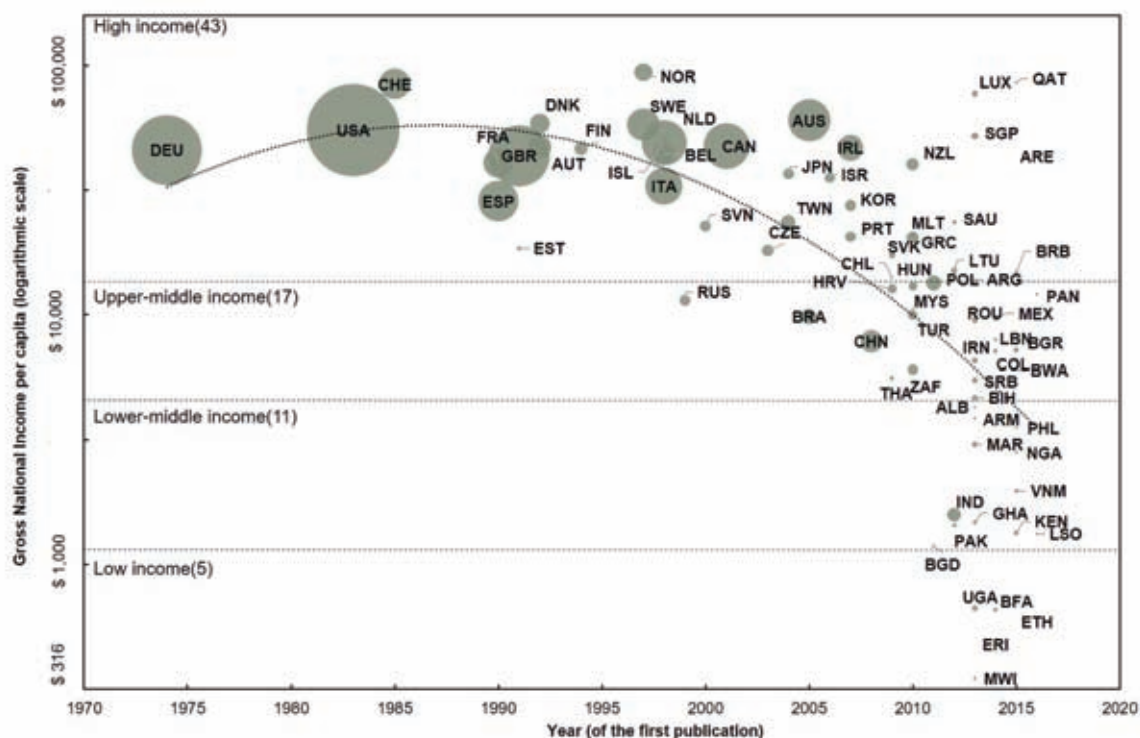


**Figure 2.** Publications distribution and changes in high, middle, and low income countries, 1974–2016. Marker size is proportional to the total publications between 1990 and 2016. The full results of the above figure can be found in Appendices S11 and S12 in **Online Supplementary Document.**

**Table 3.** Research outputs on multimorbidity vs NCD deaths and life expectancy in LMICs and HICs, 1974–2016

| INDICATORS | INCOME GROUP | |
|---|---|---|
| | LMICs | HICs |
| Multimorbidity publications (%) | 176 (5) | 3510 (95) |
| NCD deaths (%)* | 27 733 (73) | 10 159 (27) |
| Median year of the first publication | 2010 | 1995 |
| Life expectancy at birth (years) at the median year of the first publication | 68.4 | 76.3 |

LMIC – low– and middle–income countries, HIC – high–income countries
*Data sources: World Health Organization [20].

b) High income countries

c) Low and middle income countries

● Life expectancy at birth (years)  ● Publications(n)

**Figure 3.** The relationship between life expectancy at birth (years) and annual publications (logarithmic scale), 1974–2014.

per capita in 2015 for the 76 countries with at least one publication indexed in the Web of Science™. The GNI data sources for **Figure 2** are from the World Bank [21]. The chart illustrates the substantial knowledge gaps with a direct gradient apparent by income country status, especially compared with the disease burden (**Table 3**).

Among the income groups, there is a great deal of heterogeneity in the year of first publication and total number of publications. The number of countries in high income, upper–middle income, lower–middle income, and low–income countries is 43, 17, 11, and 5 respectively. Although Germany published earlier (1974), US holds the most publications (n=895), followed by Germany (n=511) and UK (n=389). All the top 15 countries were HICs; the first LMIC being China with 52 publications, ranked 16th. The median year of the first publication in high income, upper–middle income, lower–middle income, and low income countries was 1995, 2010, 2013, and 2014 respectively. The first LMIC publication was in 2005 by Brazil, which is ranked 25th.

**Figure 3** shows the relationship between life expectancy at birth (years) and annual publications (on the logarithmic scale) from 1974 through 2014. Longer life expectancy was associated with higher publication outputs in both HICs and LMICs (r=0.95 and 0.91, respectively). The life expectancy at the median year (1994) of first publication was 66.1, with a gap between LMICs and HICs of 7.9 (68.4 vs 76.3). The data sources for **Figure 3** are from the World Bank [22].

## Applications: research topics evolution over time and potential collaborations between HICs and LMICs

Terms from keywords were used to explore the emerging research trends and evolution topics [14]. 152 distinct topics from keywords of publications were obtained between 1990 and 2016 to illustrate the rapidly advancing research area. **Figure 4** shows the research topics evolution over the years, with topics beginning with depicting epidemiology characteristics (such as "prevalence", "age", "disease", "disorders", "chronic disease" and "mortality"), then moving to exploring risk factors, the impact of multimorbidty on individuals and the health system (such as "determinants", "quality of life", "family practice", "self management", "guideline", "polypharmacy", and "adherence"), and more recently examining interventions and how to improve the management (such as "intervention", "education", "comprehensive geriatric", "collaborative and integrated care").

**Figure 5** shows the featured research topics (based upon the top cited publications from each income group in each year) evolution in each income group between 2000 and 2016, in an attempt to illustrate the knowledge gaps and potential collaboration among countries (the full results of the featured publications and the top 15 cited publications can be found in Appendices S13 and S14 in **Online Supplemen-**
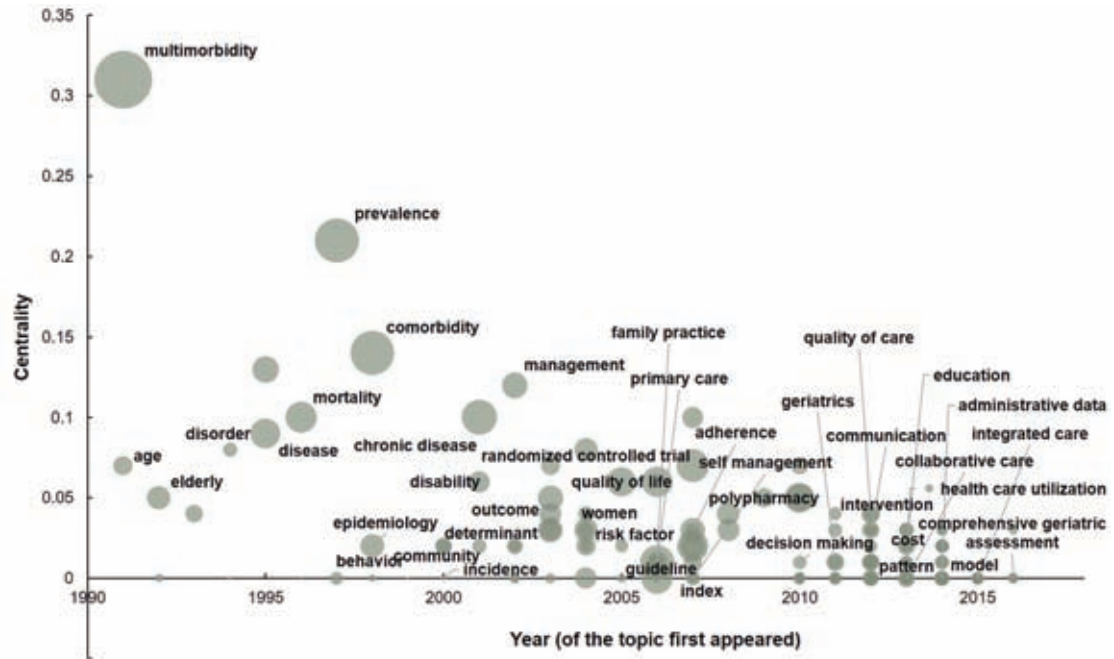


**Figure 4.** Research topics evolution on multimorbidity, 1990–2016. A node of high centrality is usually one that connects two or more large groups of nodes with the node itself in–between [14]. Centrality scores are normalized to the unit interval of [0, 1]. Marker size is proportional to number of times the keyword appeared between 1990 and 2016.
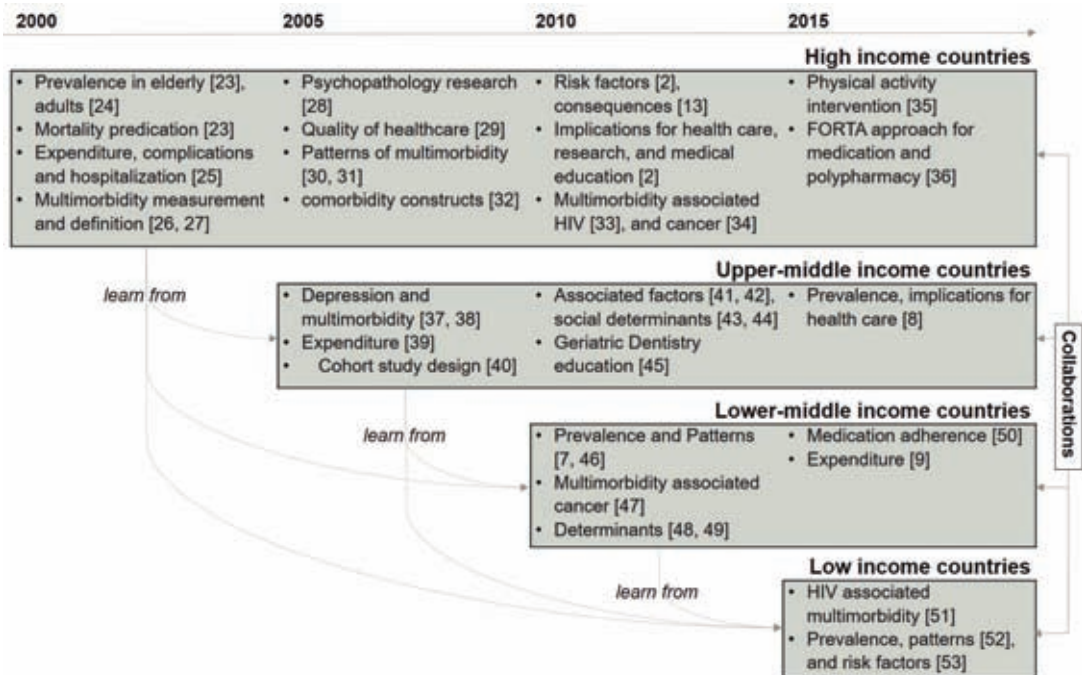


**Figure 5.** Featured research topics to illustrate the knowledge gaps and potential collaboration among countries, 2010–2016.

**tary Document**). Featured research topics in **Figure 5** were based on the top cited publications from each income group in each year: high–income countries [2,13,23–36], upper–middle income countries [8,37–45], lower-middle income countries [7,9,46–50], and low–income countries [51–53].

Most of the research topics evolution was similar among high and low income countries over time, especially in the initial stage when investigation began in this research area. It can be seen from the chart that HICs have contributed more knowledge than LMICs. If we take an epidemiology study as an example, HICs have published studies on "how to define and measure multimorbidity". This research can potentially be used by other income group countries and tailored to fit their own contexts and populations. Other examples such as "multimorbidity associated HIV and cancer", "physical activity intervention", and "approaches for medication and polypharmacy" that had been investigated by HICs have only just emerged as a research topic in other countries.

As the figure shows, although collaborations have existed, such as in the FINE study (Finland, Italy, Netherlands) [23], and WHO's Study on global Aging and adult health (SAGE) (China, Ghana, India, Mexico, Russia and South Africa) [9], these collaborations occurred within the same income groups. There were no collaborations between LMICs and HICs, however, potential collaborations between HICs and LMICs are possible.

## DISCUSSION

According to the best of our knowledge, this is the first study to evaluate the knowledge gaps and the potential for collaborations on multimorbidity between LMICs and HICs. Although it is well recognized that multimorbidity is a neglected research topic, such as in clinical guidelines and in randomized controlled trails (RCTs) [54–59], two of our findings and one implication are largely new.

First, compared with single conditions (diabetes, hypertension, depression, and COPD), there is a mismatch between the high prevalence of multimorbidity and its research outputs at the global level. This finding was also identified by Fortin and co–workers in the Canadian population among people aged 55 to 74 years [11]. Research conducted by the Emerging Risk Factors Collaboration [60] examined 689 300 participants from 91 cohorts and concluded that increasing numbers of chronic conditions within individuals are multiplicatively associated with increased mortality risk. Facing this huge disease burden, there is only a limited evidence base on which to inform policy and practice for these urgent health care needed individuals [61].

Second, research knowledge on multimorbidity from LMICs is comparatively limited compared with HICs (5% vs 95%), whereas nearly 80% of NCD related deaths occurred in LMICs. However, during the past 5 years, the number of publications originating from LMICs has grown substantially. Most publications were from upper–middle income countries, especially Brazil and China. On further analysis, we found that economic status and life expectancy played important roles in this gap, with higher economic status and longer life expectancy positively associated with higher annual publication outputs and the median year of first publication. One large study from Scotland found that the onset of multimorbidity occurred 10–15 years earlier in people living in the most deprived areas compared with the most affluent [2]. This finding coincides with two interesting statistics from our study: (1) onset of the median year of first publication occurred 15 years later in the LMICs compared with HICs, and (2) the life expectancy at the median year of first publication in LMICs was 7.9 years lower than in HICs. The potential implications from these findings are that: people from lower socioeconomic settings are more vulnerable to multimorbidity; and multiple chronic conditions is especially debilitating in LMICs, where they are facing the double burden of communicable and non–communicable diseases where dealing with premature, infectious diseases and single conditions are already great challenges.

Higher income is associated with greater longevity, with differences in life expectancy across income groups increasing [62]. With life expectancy increasing over the world, especially in LMICs, it is estimated that 80% of older people will be living in LMICs by 2050. This leads to questions of whether we have accumulated enough knowledge at a pace that can meet this challenge, especially in LMICs, and what more can we do based on the latest knowledge.

Despite the paucity of studies indicating the lack of research capacity and funding, LMICs may benefit from the theoretical and practical experience of HICs in multimorbidity research and implementation. However, tremendous national and international effort is needed to address the knowledge gaps between

countries and provide better evidence to inform medical and public health decisions needs. The barriers to implementation of knowledge and experience generated from HICs needs to be evaluated, with the purpose to develop better availability and affordability in multimorbidity control and prevention strategies and measures. Take integrated care as an example; although it can create efficiency gains and improve health outcomes [63], it may only apply to HICs with good health systems. For LMICs, challenges from capacity building, better quality services, and a stronger evidence base will be required for implementing integration of care [3,64], but this is feasible as demonstrated by some operational models and approaches, such as the WHO 25×25 strategy (a target of a 25% relative reduction in NCD mortality by 2025) and the Integrated Management of Adult and Adolescent Illness (IMAI) [65,66].

Our findings demonstrate significant gaps in multimorbidity research between HICs and LMICs with limited knowledge of etiology, epidemiology, patterns, progression, risk factors and efficacy and cost–effectiveness of different interventions [64,67]. Knowledge on polypharmacy is lacking, as most of the evidence generated from RCTs is of limited value to guide decisions about medication use by patients with multiple chronic diseases as the possible drug–to–drug, drug–to–disease, and disease–to–disease interactions remain unexamined [5].

### Limitations

Several limitations are associated with our comprehensive bibliometric study. A linguistic bias may exist with the restriction to publications in English language journals. Second, in order to perform a high quality bibliometric analysis, we only searched the Web of Science database, which doesn't include non–SCI journals, such as the *Journal of Comorbidity,* where there may be many multimorbidity relevant publications. In addition, we have not provided a detailed analysis of the research topics, such as the prevalence and disease burden of multimorbidity in each country or income group. In order to move the research agenda forward, we suggest topic specific systematic reviews which cover more databases, a secondary analysis of data at the global level, and primary longitudinal cohort studies are needed.

## CONCLUSION

This study confirms substantial knowledge gaps in multimorbidity research and between HICs and LMICs countries, research agenda and inputs needed to move research forward worldwide, especially for and in LMICs. There is a possibility that LMICs can learn from and collaborate with HICs in this area.

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PAPERS

# Epidemiology of ocular trauma in children requiring hospital admission: a 16–year retrospective cohort study

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**Background** To study the epidemiology of ocular trauma requiring hospital admission in children under 18 years in age.

**Methods** This retrospective cohort study included pediatric patients with ocular injuries at the Ophthalmology Department of the Clinical Hospital Centre, Split, Croatia, from 2000 to 2015, classified according to the Birmingham Eye Trauma Terminology.

**Results** There were 353 children hospitalized, 82% of boys (mean age 11 years) and 18% of girls (mean age 10 years). The majority of traumas occurred in the outside environment (70%, n = 249), followed by occurrences at home (17%, n = 60), and at a school/nursery (8%, n = 28). Final visual acuity was 6/18 or better in 286 (96%) patients with closed globe injury and in 26 (49%) patients with open globe injury. Severe impairment of vision was found in 12 (4.4%) patients in the closed globe injury group and 26 (49%) patients in the open globe injury group. A statistically significant difference was found between final visual acuity and initial visual acuity in all patients ($\chi^2 = 12.8$; $P < 0.001$).

**Conclusion** The majority of pediatric eye injuries are happening in the outside environment and are preventable. Implementation of well–established safety precautions would greatly reduce this source of visual disability in children.

Ocular trauma is a significant problem throughout the world and, in addition to resultant ocular disability, it also has psychological and social effects on the patient. Approximately 1.6 million people worldwide are blind due to ocular trauma, 2.3 million people have bilateral low vision due to trauma and 19 million have unilateral vision loss [1,2]. Eye trauma constitutes 7% of all bodily injuries and 10–15% of all eye diseases [3].

In the United States, eye trauma is the leading cause of noncongenital unilateral blindness in individuals younger than 20 years of age. The American Academy of Pediatrics (AAP) reported that 66% of all ocular injuries occur in individuals 16 years of age or younger, with the highest frequency occurring between 9 and 11 years of age [4–6]. Most ocular injuries occur in boys, as due to their more aggressive nature, they tend to spend more time playing outdoors and tend to play risky games more frequently than girls. The male–to–female ratio in published studies varies from 3:1 to 5.5:1 [5–7]. Most studies have shown no statistically significant difference between affected eyes [8].

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Various studies have reported that children account for 12.5–33.7% of all admissions for eye injury. Trauma is clearly one of the most important preventable causes of childhood blindness [9]. The frequency of hospitalization due to ocular trauma differs between developed and developing countries; for example, the rate is 8 per 100 000 people in Scotland and 33 per 100 000 in Guiana [10].

The standardized classification of eye trauma is useful for ophthalmologists and provides the means for simple and enhanced communication regarding particular patient features [11].

Kuhn et al. [12] developed a prognostic model, the ocular trauma score (OTS), to predict the visual outcome of patients in all age groups after open globe and closed globe ocular injuries. They analyzed more than 2500 eye injuries from the United States Eye Injury Registry and the Hungarian Eye Injury Registry and evaluated more than 100 variables with the goal of identifying specific predictors. In the calculation of OTS, a numerical value is assigned to the following six variables: initial visual acuity (VA), globe rupture, endophthalmitis, perforating injury, retinal detachment, and relative afferent pupil defect (RAPD). The scores are then divided into five categories that provide the probabilities of attaining a range of VAs after injury.

Numerous studies have evaluated various aspects of ocular trauma. The purpose of this study was to analyze epidemiology of all eye injuries in children who required admission to the Ophthalmology Department of the University of Split Hospital Centre, Croatia, from 2000 to 2015.

## METHODS

Medical records of all patients aged 18 years or younger who sustained serious eye injuries requiring admission to the Ophthalmology Department at University of Split Hospital Centre between 2000 and 2015 were reviewed. Ethics committee of University of Split Hospital Centre, Split, Croatia, approved the study to be reported. All study procedures adhered to the recommendations of the Declaration of Helsinki.

University of Split Hospital Centre is the only referral hospital for the population of the Split–Dalmatia County (south Croatia). The population of the province as determined in the 2011 census was 455 242. The number of children in the province was 107 316, which consisted of 54 768 boys and 52 548 girls. The distributions of age, gender and socioeconomic status of children in this county were comparable to those of the entire Croatian population.

The study included 353 children treated acutely in the hospital. The following data were recorded for each patient: age, sex, date of injury, site of incident, cause of injury (accidental self–inflicted injury vs injury by another person), visual acuity, diagnosis, associated injuries and treatment.

The injuries were classified according to Birmingham Eye Trauma Terminology (BETT) [13] as the following: closed eye globe injuries and open eye globe injuries (penetration, perforation, intraocular foreign body injury and rupture).

The data were collected, entered and processed using the statistical package SPSS version 15 (SPSS Inc., Chicago, IL, USA). The results were interpreted using a significance level of $P < 0.05$. The $\chi^2$ test, McNemar test, Kruskal-Wallis test and Mann-Whitney U test were used in the analysis.

**Table 1.** Eye injuries in children according to the type of injuries and duration of hospitalization

| Type of injury | No of children (%) | Duration of hospital admission in days — median (min–max) |
|---|---|---|
| Closed globe: | | |
| Contusion | 279 (79) | 7.2 (5–8) |
| Lamellar laceration | 20 (5.7) | 9.3 (8–11) |
| Open globe: | | |
| Penetration | 48 (13.6) | 9.1 (6–12) |
| IOFB* | 2 (0.57) | 10.9 (9–13) |
| Perforation | 2 (0.57) | 11.1 (10–13) |
| Rupture | 2 (0.57) | 11.1 (10–13) |

IOFB – intraocular foreign body

## RESULTS

A total of 353 children with eye injuries were admitted to the clinic during the 16–year study period; there were 290 (82%) boys and 63 (18%) girls, yielding a male–to–female ratio of 5:1. Assessing and treatment of eye injuries and indications of hospital admission by algorithms that we developed for managing of eye trauma in our Department are presented in **Figure 1** and **Figure 2**. The mean age at admission was 11 years among boys and 10 years among girls. The right eye was involved in 174 (49%) cases, and the left eye was involved in 177 (50%) cases. Binocular injury was found in 1 child (0.2%). There was no statistically significant difference between injuries of the right eye and the left eye according to age ($\chi^2 = 2.33$; $P = 0.506$). In average duration of hospitalization was 9.8 days with median of 5 to 13 days (**Table 1**).
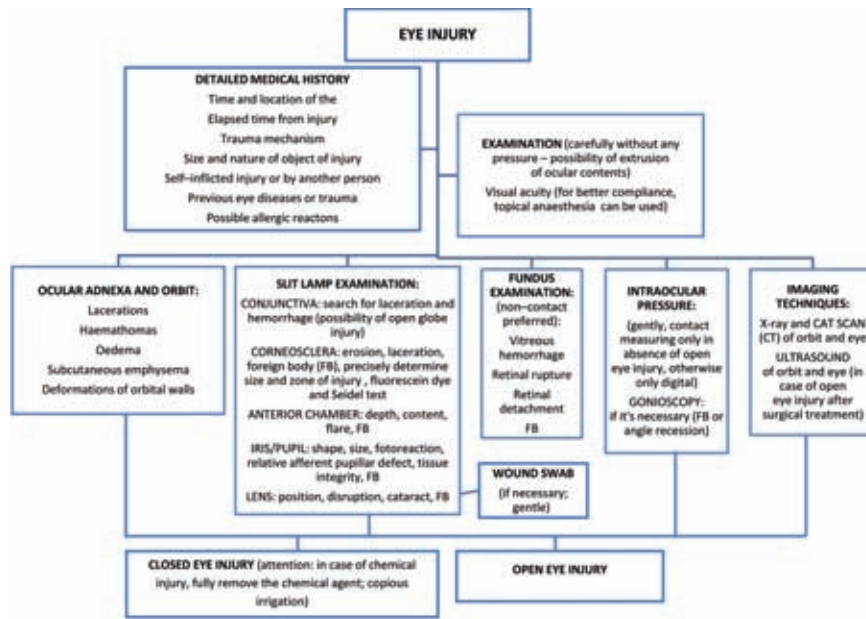
**Figure 1.** Standard operative procedures for managing eye injuries at the Department of Ophthalmology, University of Split Hospital Centre (Ivna Pleština Borjan).
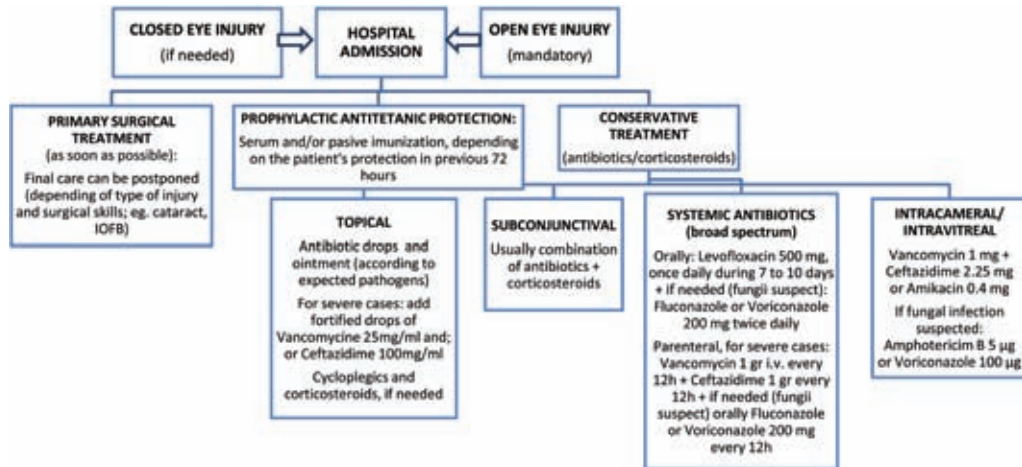


**Figure 2.** Standard operative procedures for hospital admission of eye injuries at the Department of Ophthalmology, University of Split Hospital Centre (Ivna Pleština Borjan).

**Table 2.** Age and gender of children with eye injuries

| Age (years) | Total (n = 53) (%) | Male (n = 290) (82%) | Female (n = 63) (18%) |
|---|---|---|---|
| 0–4 | 30 (8.5) | 27 (9.3) | 3 (4.8) |
| 5–9 | 119 (33.7) | 97 (33.5) | 22 (34.9) |
| 10–14 | 137 (38.8) | 105 (36.2) | 32 (50.8) |
| 15–18 | 67 (19) | 61 (21) | 6 (9.5) |

**Table 3.** Cumulative incidence of children with eye injuries/100 000, from 2000 to 2015

| Age (years) | Total (95% CI) | Boys (95% CI) | Girls (95% CI) | P–value* |
|---|---|---|---|---|
| 0–4 | 120 (80–170) | 220 (150–320) | 30 (10–80) | <0.001 |
| 5–9 | 490 (410–590) | 780 (640–950) | 190 (130–290) | <0.001 |
| 10–14 | 480 (410–570) | 720 (590–870) | 230 (160–320) | <0.001 |
| 15–18 | 220 (170–280) | 400 (310–510) | 40 (20–90) | <0.001 |

CI – confidence interval

*$\chi^2$ test.

The injured children were divided into the following four age groups: 0–4 years (infants and preschool), 5–9 years of age, 10–14 years (elementary school), and 15–18 years (high school). The largest number of injuries (39%) occurred among children aged 10–14 years, followed by those aged 5–9 years (34%), and those aged 15–18 years (19%); the fewest injuries occurred among children aged 0–4 years (8.5%) (**Table 2**).

The cumulative incidence of eye injuries among boys was 530/100 000, and among girls 120/100 000 (**Table 3**). The cumulative incidence of eye injuries among boys was 4.4 times higher than that among girls.

Compared to girls, the cumulative incidence of eye injuries among boys was 7 times higher among children age 0–4 years ($\chi^2 = 16.3$, $P < 0.001$), 4 times higher among

**Table 4.** Number of children (%) with eye injuries according to season

| Season | Total (%) (n = 353) | P–value* |
|--------|---------------------|----------|
| Winter | 86 (24.4) | 0.035 |
| Spring | 100 (28.3) | 0.035 |
| Summer | 106 (30.0) | |
| Autumn | 61 (17.0) | |

*$\chi^2$ test.

**Table 5.** Number of children and age – median according to site of injury

| Site of injury | Total P–value* n (%) | Age – median P–value† (min–max) |
|----------------|----------------------|----------------------------------|
| Home | 60 (17)‡ | 8 (2–17)‡ |
| School/nursery | 28 (8) | 12 (3–17) |
| Outside home/school/nursery | 249 (70) | 11 (2–18) |
| Traffic | 2 (1) | |
| Sport | 14 (4) | 12 (10–18) |

*$\chi^2$ test.
†Kruskal–Wallis test.
‡$P < 0.001$.

**Table 6.** Number of children (%) with eye injury according to age in relation to person who caused an injury

| Age (years) | Total n (%) | Self–inflicted injury n (%) | Injured by other person n (%) | P–value* |
|-------------|-------------|------------------------------|--------------------------------|----------|
| 0–4 | 30 (8.5) | 13 (12) | 17 (7) | 0.307 |
| 5–9 | 119 (33.7) | 39 (35) | 79 (33) | |
| 10–14 | 137 (38.8) | 37 (33) | 100 (42) | |
| 15–18 | 67 (19) | 23 (20) | 44 (18) | |

*$\chi^2$ test.

**Table 7.** Age and types of injuries in children with eye injuries

| Type of injury | No of children (%) | Age – median (min–max) | P–value* |
|----------------|--------------------|------------------------|----------|
| Closed globe: | | 11 (2–18) | 0.03 |
| Contusion | 279 (79) | | |
| Lamellar laceration | 20 (5.7) | | |
| Open globe: | | 9 (2–17) | |
| Penetration | 48 (13.6) | | |
| IOFB | 2 (0.57) | | |
| Perforation | 2 (0.57) | | |
| Rupture | 2 (0.57) | | |

IOFB – intraocular foreign body
*Mann–Whitney U test.

**Table 8.** Number of children (%) with eye injury according to visual acuity in relation to the type of eye injury (closed globe–open globe) at hospitalization

| | Type of injury | | |
|---|---|---|---|
| Initial visual acuity | Closed globe | Open globe | Total |
| Normal (0.9–1.0) | 86 (28.9) | 4 (7.6) | 90 |
| Mildly impaired (0.3–0.8) | 122 (41) | 9 (17) | 131 |
| Poor (0.02–0.25) | | | |
| Moderate (0.125–0.25) | 24 (8) | 4 (7.6) | 28 |
| Serious (0.05–0.1) | 19 (6.4) | 7 (13.3) | 26 |
| Deep (0.02–0.04) | 26 (8.7) | 8 (15.1) | 34 |
| Semi–blindness (light perception to 0.01) | 20 (38) | 20 (38) | 40 |
| Blindness (no light perception) | 1 (0.3) | 0 | 1 |
| Total | n = 299 (85) | n = 54 (15) | n = 353 |

children age 5–9 years ($\chi^2 = 42$, $P < 0.001$), 3 times higher among children age 10–14 years ($\chi^2 = 36$, $P < 0.001$) and 10 times among children age 15–18 years ($\chi^2 = 41$, $P < 0.001$). In all age groups, boys had higher incidence of eye injuries compared to girls.

The majority of injuries occurred during spring and summer (**Table 4**). Compared to autumn, there were 1.6 times more eye injuries during spring and 1.8 times more eye injuries during summer ($\chi^2 = 13.6$; $P = 0.035$).

The majority of traumas occurred in the outside environment (outside of the home, school or nursery) (70%, n = 249), followed by at home (17%, n = 60), at school/nursery (8%, n = 28), at a sporting area (4%, n = 14) and in traffic (1%, n = 2) (**Table 5**).

Children were 9 times more likely to be injured in the outside environment compared to school and nursery, and they were 4 times more likely to be injured in the outside environment than in the home ($\chi^2 = 412$; $P < 0.001$). Our study showed a statistically significant difference in the age of children according to the site of injury ($\chi^2 = 25.1$; $P < 0.001$); the median age of children injured at home was 4 years lower than that of children injured in school (Z = 3.15, $P = 0.02$), 3 years lower than that of children injured outside the home (Z = 4.4, $P < 0.001$), and 4 years lower than that of children who were injured during sports (Z = 3.8, $P < 0.001$) (**Table 5**).

There were 112 (32%) children with accidental self–inflicted injury, and their median age was 10 years (range: 2–18), while 239 (68%) children who were injured by another person, and their median age was 11 years (range: 2–18).

Significant difference between the age of children with accidental self–inflicted injury and those injured by another person was not observed ($\chi^2 = 1.02$; $P = 0.307$) (**Table 6**).

With regard to the type of injury, there were 299 (85%) closed eye injuries and 54 (15%) open eye injuries. The median age of children with closed injuries was 2 years higher than the median age of children with open eye injuries (Z = 2.98, $P = 0.03$) (**Table 7**).

Initial visual acuity was normal or mildly impaired (better than 0.3) in 208 (70%) patients with closed globe and 13 (25%) patients with open globe injury (**Table 8**).

Final visual acuity was greater than or equal to 0.3 in 286 (96%) patients with closed globe in-

juries and 26 (49%) patients with open globe injuries. Severe vision impairment (worse than 0.3) was found in 12 (4.4%) patients with closed globe injuries and 26 (49%) patients with open globe injuries (**Table 9**).

Overall improvement of visual acuity of all patients at the end of the treatment was significantly higher compared to initial visual acuity ($\chi^2 = 12.8$; $P < 0.001$). Compared to initial visual acuity, visual acuity improved in 86% of patients and remained the same in 14% of patients; no patient experienced deteriorated visual acuity (**Table 10**).

**Table 9.** Number of children (%) with eye injury according to final visual acuity in relation to initial visual acuity at release from hospital

| Final visual acuity | Type of Injury | | |
|---|---|---|---|
| | Closed globe | Open globe | Total |
| Normal (0.9–1.0) | 239 (80) | 9 (17) | 248 |
| Mildly impaired (0.3–0.8) | 47 (16) | 17 (32) | 64 |
| Poor (0.02–0.25) | | | |
| Moderate (0.125–0.25) | 2 (0.7) | 6 (11.3) | 8 |
| Serious (0.05–0.1) | 6 (2) | 7 (13.2) | 13 |
| Deep (0.02–0.04) | 2 (1) | 5 (9.4) | 7 |
| Semi–blindness (light perception to 0.01) | 1 (0.33) | 8 (15.1) | 9 |
| Blindness (no light perception) | 1 (0.33) | 0 | 1 |
| Total | n = 299 (85) | n = 54 (15) | n = 353 |

**Table 10.** Number of children according to visual acuity after the treatment in relation to initial visual acuity

| Visual acuity – final | Visual acuity – initial | | | | | |
|---|---|---|---|---|---|---|
| | Normal | Mildly impaired | Poor moderate | Poor serious | Poor deep | Semi–blindness |
| | n = 90 | n = 131 | n = 28 | n = 26 | n = 34 | n = 40 |
| Normal | 90 | 108 | 14 | 15 | 14 | 7 |
| Mildly impaired | | 23 | 12 | 5 | 13 | 10 |
| Poor moderate | | | 2 | 2 | 3 | 1 |
| Poor serious | | | | 4 | 1 | 8 |
| Poor deep | | | | | 3 | 5 |
| Semi–blindness | | | | | | 9 |
| Improvement; n (%) | | 108 (92) | 26 (93) | 22 (85) | 31 (91) | 31 (77) |

## DISCUSSION

Ocular injuries are the most common cause of acquired uniocular blindness in children. Pediatric ocular injuries differ from those of adults in many ways. Ocular trauma in children is mainly accidental and has an age–specific pattern [14].

In this study, pediatric ocular trauma occurred 4.5 times more often in boys than in girls. Boys are usually more susceptible to ocular damage due to the nature of their activities and presumed less supervision by their families, similar to results from other studies [1,4,6,10,14]. In our study, the highest incidence of eye injuries occurred among children age 10 to 14 years, which is also similar to studies from other settings [1,4,15–17].

In contrast to the above findings, Al–Bdour and Azab reported the highest incidence of injuries among children aged 6 to 10 years. Children in this age group are relatively immature and exposed to varying surroundings that make them more vulnerable to injuries [6,14].

Both eyes were affected equally. Bilateral ocular injuries were observed only in 1 patient. This is in accordance with most other studies, where ocular trauma plays a minor role in bilateral blindness compared to its major role in unilateral blindness [6,14].

The majority of injuries occurred during spring and summer, which is similar to results reported elsewhere [18]. The summer vacation months accounted for a disproportionate number of eye injuries received throughout the year. The summer offers children the opportunity to spend more time outside and to have more freedom to play with potentially dangerous objects. Furthermore, the lack of school during the summer months may adversely affect the time children are supervised by adults.

The present study showed that ocular injury occurred most commonly in the outside environment, with the home as a second most common site; this is consistent with observations similar to results reported elsewhere [16]. It speaks in favor of possible lack of adult supervision while children play outside. A study conducted by Aghadoost et al. showed that most injuries happened at home [10]. A study in North Jordan showed that eye injuries occurring during sports and play were the most common [6]. In Canada, eye injuries occurred at a number of locations, with the majority occurring at homes, followed by schools and other residences [18].

Our study showed a statistically significant difference between the age of children according to the site of injury. Children injured at home were approximately 4 years younger than children injured at school and during sports and approximately 3 years younger than those injured outside the home. These results were expected because younger children spend more time at home.

In our study, more than two–thirds of patients were injured by another person, and this did not differ by age group. In other studies, most eye injuries were reported as being unintentional, though there were instances in which the injury happened during a physical altercation [18].

With respect to the BETT classification in our study, closed globe injury occurred five and a half times more frequently than open globe injury, and this is similar to results reported elsewhere [19]. We showed that children with open eye injuries were 2 years younger than children with closed eye injuries. The average age of children was 11 years among those with closed globe injuries and 9 years among those with open globe injuries. We considered that young children are more prone to open globe injuries due to their natural desire to explore, their lack of fear of danger and their limited ability to avoid danger. Jandeck et al. showed that the average age of children with open globe injuries was 8.7 years, which is similar to our results [20]. The standardized classification of eye trauma is useful for ophthalmologists and provides the means for simple and enhanced communication about particular patient features [11].

Initial visual acuity was normal or mildly impaired in 70% of patients with closed globe injuries and 25% of patients with open globe injuries. Decreased visual acuity occurred more in open globe injuries and with ruptured globes. Final visual acuity was normal or mildly impaired in 96% of patients with closed globe injury group and 49% of patients with open globe injuries. Severe vision impairment was found in 4.4% of patients with closed globe injuries and 49% of patients with open globe injuries. Among those with open globe injuries, penetrating injuries were the most common. Penetrating injuries, in general, carry a poorer prognosis, and they are more likely to require surgery and result in long–term visual impairment.

We found a statistically significant difference between final and initial visual acuity. Good visual acuity at presentation and early primary repair were important factors for better final visual outcome. Compared to blunt injuries, penetrating injuries generally resulted in poorer visual outcomes. Posterior segment involvement adversely affects visual results [14,20,21].

Although our study covers a relatively long time period of 16 years, the retrospective nature is an acknowledged weakness of this study.

In conclusion, severe ocular trauma in children that requires hospitalization is mainly accidental and has an age–specific pattern. In general, children are more susceptible to eye injuries due to their immature motor skills, limited common sense and natural curiosity. A safe environment should be maintained for children. The majority of eye injuries in children are preventable, which reflects the importance of health education, adult supervision and application of appropriate measures to reduce the incidence and severity of trauma.

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# Prevalence and associated risk factors of violence against conflict–affected female adolescents: a multi–country, cross–sectional study

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**Background** Over half of displaced civilians in humanitarian emergencies are children, and these settings pose unique threats to children's safety with long–lasting consequences. Our study broadens the limited evidence on violence against adolescent girls in emergencies by estimating prevalence and predictors of violence among adolescent girls aged 13–14 in South Kivu, Democratic Republic of the Congo (DRC), and aged 13–19 in refugee camps in the Benishangul–Gumuz region of Ethiopia.

**Methods** Survey data were collected from a sample of 1296 adolescent girls using Computer–Assisted Personal Interview and Audio Computer–Assisted Self–Interview programming. Predictors of violence were modeled using multivariable logistic regression.

**Results** The majority of adolescent girls (51.62%) reported experiencing at least one form of violence victimization in the previous 12 months: 31.78% reported being hit or beaten, 36.79% reported being screamed at loudly or aggressively, and 26.67% experienced unwanted sexual touching, forced sex, and/or sexual coercion. Across both countries, ever having a boyfriend and living with an intimate partner were strong predictors of violence. Fewer years of education completed in DRC, and young age in Ethiopia, were also associated with reported victimization.

**Conclusions** Prevalence of violence against adolescent girls is high in these two conflict–affected contexts. Findings indicate a need for programs targeting younger populations, broader efforts to address different forms of victimization, and increased recognition of intimate partners and caregivers as perpetrators of violence in conflict–affected settings.

Violence against women and girls is a global epidemic that affects one in three women and one in four girls under the age of 18 [1,2]. Worldwide, females are at highest risk for violence during adolescence, and violence is the second leading cause of death for adolescent girls aged 10–19 [3,4]. Risks of victimization are amplified by both gender and age: societies that support male dominance and restricted roles of females are associated with greater levels of violence against women, and adolescents have less access to services due to their age [5,6]. Physical, emotional, and sexual violence victimization have been associated with negative health consequences that include increased risk of HIV infection, unintended pregnancy, alcohol and substance abuse, depression, post–traumatic stress disorder, and suicide [7–10].

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A number of predictors of violence against women and girls have been identified from developed and developing contexts, largely from studies of intimate partner violence [11,12]. These predictors may best be understood within an ecological framework, which posits that there is no single factor that causes such violence, but that violence is a function of many factors that interact at different levels of the "social ecology" [13]. Indeed, studies have found that demographic predictors of physical, emotional, and sexual violence victimization include factors at the societal level, such as unequal access to wage employment; at the communal level, such as norms that support gender inequity; at the interpersonal level, such as living with a single parent and lower socio–economic status; and at the individual level, such as female gender, lower educational attainment, and younger age [14–19]. Previous studies have also found behavioral risks such as engagement in a relationship that includes sexual intercourse and greater number of romantic partners [10,20]. Additionally, female violence victimization in childhood and adolescence consistently predicts later physical and sexual victimization [21,22].

Humanitarian emergencies pose unique threats to safety, as they may alter family structure, reduce access to basic rights such as health care and education, and increase engagement in risky behaviors. Humanitarian emergencies have resulted in an estimated 59.5 million displaced persons, half of whom are children [23]. Previous research suggests that rates of physical and sexual violence may increase during periods of conflict and that such violence is associated with adverse health outcomes in conflict–affected children [24–29]. Adolescent girls have been shown to be particularly vulnerable to victimization, yet, until recently, have been often overlooked in these contexts [25].

There is limited understanding of both prevalence and predictors of violence against conflict–affected adolescent girls. To date, studies that examine violence in conflicts (eg, communities where at least two armed groups have fought) have focused primarily on the health–related *consequences* of violence exposure and on females over the age of 15 [24,30–32]. Large multi–country initiatives have been instrumental in building the evidence base on violence against girls in developing countries, but these initiatives rarely examine conflicts and do not include younger adolescents [33,34]. Understanding predictors of violence in such settings is critical to developing effective strategies to prevent violence against adolescent girls.

We analyzed data from a baseline sample of displaced, conflict–affected adolescent girls in DRC and Ethiopia to assess the prevalence and related risk factors of physical, emotional, and sexual violence.

## METHODS

Eastern DRC has been in a state of constant conflict since 1996 and houses approximately 2.7 million internally displaced persons [35]. Ethiopia has been a primary destination for refugees fleeing protracted conflicts in Sudan and South Sudan, and as of September 2015, the area of Benishangul–Gumuz hosts an estimated 11 174 South Sudanese refugees [36].

This article draws on data from a cross–sectional survey of violence and related risk factors for internally displaced and refugee adolescent girls between May–October 2015 in 14 sites across South Kivu, DRC, and in 3 refugee camps in Benishangul–Gumuz, Ethiopia. The survey was undertaken to obtain baseline information on girls' experiences of violence prior to the implementation of an adolescent life skills and safe space program run by the International Rescue Committee in both countries [37]. In the DRC, adolescent girls were excluded from the survey if they were outside of the 10–14 age range, or lacked verbal proficiency in Swahili or Mashi. In Ethiopia, adolescent girls were excluded if they were outside the 13–19 age range, or lacked verbal proficiency in Funj, Regarig, Ingessana Kulelek, or Maban. Language exclusion was based on the selected languages spoken by most girls in the research settings and on language limitations of the data collectors (in the case of Ethiopia). Age exclusion was determined at country level based on age groups being targeted for programming. In both countries, participants with significant cognitive impairments or physical disabilities that would prevent independent completion of the questionnaire were excluded for ethical reasons.

Survey questionnaires that allowed for comparability were field–tested and used in both countries. In the DRC, a confidential survey, taking approximately one hour, was administered by data collectors matched to participants by gender and language. Less sensitive questions were administered using Computer–Assisted Personal Interview (CAPI), in which interviewers asked questions verbally and recorded responses on a tablet. Adolescent girls answered more sensitive questions on violence and sexual health using Audio Computer–Assisted Self–Interview (ACASI) programming, which allowed participants to listen to the

questions and responses through headphones, and independently select responses. Girls aged 10–12 completed a modified survey, with questions deemed appropriate by community interlocutors and approved by local and Western ethics bodies; these girls were excluded from our analysis, as the modified survey excluded some of the predictors of interest. In Ethiopia, the entire survey was administered using ACASI, and there were no differences in survey administration based on age. CAPI was not used in Ethiopia because enrollment criteria included non–written languages. A detailed description of recruitment and enrollment methods can be found elsewhere [37].

One thousand two hundred and ninety–six adolescent girls aged 13–19 were included in our analysis. The sample includes girls in "early adolescence", defined as age 10–14, and in "late adolescence", defined as age 15–19 [38]. Based on an assumption of 15% prevalence of sexual violence and inclusion of up to 8 predictors in the model, a sample size of 170 would be needed both to determine prevalence and analyze a robust model, suggesting our sample in each country is sufficiently powered for this analysis.

### Ethics approval

All study procedures were approved by the Columbia University Institutional Review Board (IRB) and by in–country local bodies: the Ministry of Gender in DRC and the Administration for Refugee and Returnee Affairs in Ethiopia. Procedures undertaken to ensure confidentiality and mitigate the potential for harm included extensive training on ethics and consent, private spaces for interviews, use of ACASI for sensitive questions on violence victimization, and standardized debriefs that provided information about available psychosocial support services. Further details of our ethical protocols are detailed in our protocol paper [37].

### Analysis

Independent variables were selected for analysis based on known risk factors in non–humanitarian contexts and formative research on vulnerability in both countries. Variables were selected to include factors at the individual, relational, and communal levels of Michau et al's adapted ecological model [13]. Independent variables included age, educational attainment, presence of biological parents in the home, living with an intimate partner, working without payment in the last 12 months, marital status, and ever having a boyfriend.

Outcome variables were chosen to include different forms of violence victimization, and included binary questions on physical, emotional, and sexual violence occurring in the last 12 months, adapted from ICAST and VACS questionnaires [34,39]. Physical violence was defined as being hit or beaten. Emotional violence was operationalized as being screamed at loudly or aggressively. Sexual violence was operationalized as experiencing unwilling (forced) sex, unwanted sexual touching, or verbal coercion (using influence or authority to threaten or pressure respondent to have sex). Independent relationships to violence outcomes were assessed using chi–square and Fisher exact tests, where appropriate. Models were analyzed using multivariable logistic regression, separated by country. All analyses were completed using STATA 13.1 (StataCorp LP, College Station, USA).

## RESULTS

### Sample demographics

The sample included 1296 subjects aged 13–14 in DRC (N = 377) and aged 13–19 in Ethiopia (N = 919) (**Figure 1**). Mean age was 13.53 (standard deviation (SD) 0.50) years in DRC, and 14.61 (SD 1.51) years in Ethiopia. In DRC, 82.2% of participants had ever attended school, and in Ethiopia, 69.3% had ever attended. On average, participants had completed 4.37 (SD 2.26) years of school in DRC and 2.81 (SD 1.93) years in Ethiopia. In DRC, the most frequently reported reason for non–enrollment in school was financial difficulty in paying for school or associated costs (92.0%), while domestic responsibilities were the most frequent reason for non–enrollment in Ethiopia (27.6%). Marriage or pregnancy was reported as a greater barrier to school attendance in Ethiopia (16.3%) than in DRC (0.0%).

The vast majority of participants reported living with at least one biological parent in both settings (**Table 1**). Of those who provided information on marital status, 23.1% in DRC and 32.6% in Ethiopia reported being either married or living with someone as if married. Adolescent girls who were aged 18 or above were not significantly more likely to be married or living with someone as if married than adolescents
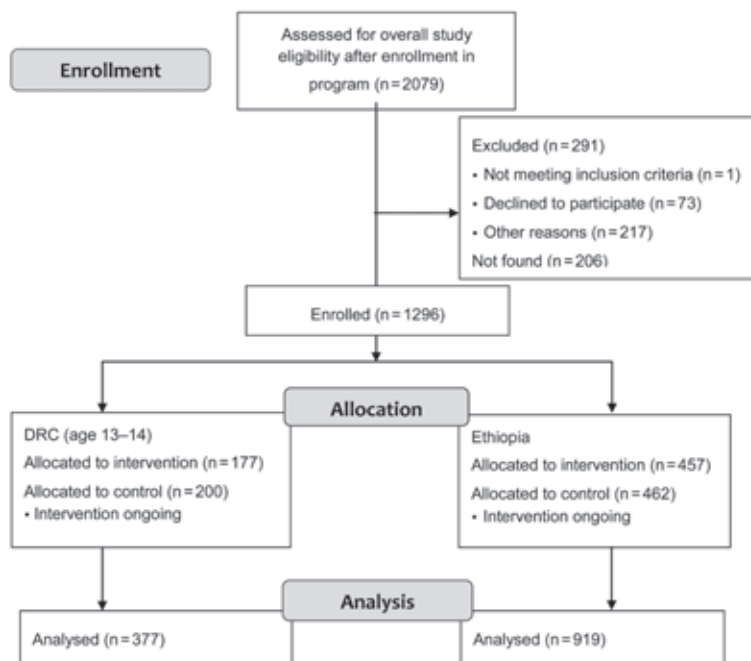
**Figure 1.** Participant flow diagram.

**Table 1.** Demographic characteristics

| | DRC (N = 377) | | ETHIOPIA (N = 919) | |
|---|---|---|---|---|
| | No. | % | No. | % |
| **Marital status:** | (N=350) | | (N=826) | |
| Unmarried | 263 | 75.14 | 527 | 63.80 |
| Married and living with partner | 46 | 13.14 | 149 | 18.04 |
| Married and not living with partner | 25 | 7.14 | 97 | 11.74 |
| Living with partner as if married | 16 | 4.57 | 53 | 6.42 |
| Family structure: | (N=377) | | (N=880) | |
| Living with both parents | 230 | 61.01 | 395 | 44.89 |
| Living with mother only | 104 | 27.59 | 240 | 27.27 |
| Living with father only | 12 | 3.18 | 173 | 19.66 |
| Living with neither parent | 31 | 8.22 | 72 | 8.18 |
| Education: | (N=377) | | (N=890) | |
| Ever attended school | 310 | 82.23 | 637 | 71.57 |
| Enrolled in school in last school year | 160 | 51.61 | 502 | 81.76 |
| Work outside the home: | (N=377) | | (N=919) | |
| Worked without pay in the last 12 months | 53 | 14.06 | 846 | 92.06 |

DRC – Democratic Republic of the Congo

aged 13–17 ($P=0.136$). Approximately 17.7% of participants in DRC, and 24.5% in Ethiopia, reported living with an intimate partner. 20.7% (n=78) of respondents in DRC, and 30.6% in Ethiopia, reported ever having a boyfriend.

## Prevalence of violence

Approximately half of the adolescent girls in our sample (54.4% in DRC, 50.5% in Ethiopia) reported experiencing at least one form of violence victimization in the previous 12 months. Of those who reported experiencing at least one form of violence, 48.3% in DRC and 49.1% in Ethiopia reported poly–victimization. As shown in **Table 2**, the most frequently reported form of violence in the last 12 months across both countries was emotional abuse. Younger adolescent girls (aged 13–14) in Ethiopia reported experiencing significantly more physical (odds ratio (OR)=1.37, $P=0.037$) and emotional violence (OR=1.44, $P=0.012$) compared with older girls (aged 15-19).

**Table 2.** Prevalence of phyposical, emotional, and sexual violence

| | DRC | | ETHIOPIA | |
|---|---|---|---|---|
| | No. | % | No. | % |
| **Physical violence:** | | (N = 355) | | (N = 850) |
| Beaten or hit in last 12 months | 124 | 34.93 | 259 | 30.47 |
| Emotional abuse: | | (N = 346) | | (N = 839) |
| Screamed at loudly or aggressively in last 12 months | 133 | 38.44 | 303 | 36.11 |
| Sexual abuse: | | (N = 337) | | (N = 821) |
| Ever experienced forced sex | 71 | 21.07 | 148 | 17.87 |
| | | (N = 369) | | (N = 914) |
| Experienced forced sex in last 12 months | 58 | 15.72 | 128 | 14.00 |
| | | (N = 349) | | (N = 839) |
| Ever experienced unwanted sexual touching | 69 | 19.77 | 201 | 23.96 |
| | | (N = 345) | | (N = 828) |
| Experienced unwanted sexual touching in last 12 months | 38 | 11.01 | 108 | 13.04 |
| | | (N = 350) | | (N = 824) |
| Ever experienced threats or verbal coercion | 62 | 17.71 | 251 | 30.46 |
| | | (N = 345) | | (N = 808) |
| Experienced threats or verbal coercion in last 12 months | 30 | 8.70 | 96 | 11.88 |

DRC – Democratic Republic of the Congo

Approximately one–fourth of adolescent girls reported at least one type of sexual violence victimization within the previous 12 months (25.5% in DRC, 27.2% in Ethiopia). Forced sex was the most frequently reported form of sexual violence (**Table 2**). Again, younger girls (aged 13–14) in Ethiopia were 2.09 times more likely than older adolescents (aged 15–19) to report unwanted sexual touching (95% CI 1.37–3.20, $P = 0.001$), and 1.77 times more likely to report forced sex (95% CI 1.20–2.61, $P = 0.004$) in the previous 12 months.

The vast majority of adolescent girls reported that their intimate partners (boyfriends or husbands) and/or other family members (parents, caregivers or other relatives) were perpetrators of violence. Intimate partners were the most frequently reported perpetrator of violence for nearly all forms of violence in both countries, followed closely by caregivers or relatives (**Table 3**). In DRC, less than 10% of adolescent girls who reported physical, verbal, or sexual abuse reported that perpetrators were members of an armed group and/or officials with authority in the community. In Ethiopia, closer to 15% of adolescent girls reported members of an armed group and/or officials as perpetrators of physical, emotional, and sexual abuse (**Table 3**).

## Predictors of violence

Because the participants in DRC and Ethiopia are known to have different demographic characteristics (mean age, ethnic group, legal status in country of residence), hypothesized predictors were first assessed for independent relationships to outcomes in the DRC and Ethiopia populations. To obtain a parsimonious model, predictors that were too closely related to other predictors were excluded from the model. Age, family structure, educational attainment, presence of biological parents in the home, living with a romantic partner, working without pay in the last 12 months, and ever having a boyfriend, were independently associated with violence outcomes in DRC and Ethiopia, and placed into an adjusted model to examine against each violence outcome in each country. The odds ratio, standard error, and 95% confidence interval for each model are shown in **Table 4** (DRC) and **Table 5** (Ethiopia).

In examining physical violence in our adjusted models, adolescent girls in both countries who had ever had a boyfriend were significantly more likely to disclose physical violence in the previous 12 months than those who had never had a boyfriend (DRC adjusted OR (aOR) = 2.96, $P < 0.001$; Ethiopia aOR = 4.50, $P < 0.001$). In DRC alone, each additional year of school completed was associated with 0.90 lower odds of victimization ($P = 0.028$). In Ethiopia, adolescent girls living with their father had 2.12 greater odds of disclosing physical violence in the previous 12 months, compared to those living with both biological parents ($P = 0.001$). Further, each additional year of age was associated with reduced odds of physical violence in Ethiopia (aOR = 0.88, $P = 0.038$).

For emotional abuse, adolescent girls in both countries who had ever had a boyfriend had greater odds of reporting exposure to loud and aggressive screaming in the previous 12 months compared with those

**Table 3.** Perpetrators of physical, emotional, and sexual violence

|  | DRC | | ETHIOPIA | |
|---|---|---|---|---|
|  | No. | % | No. | % |
| **Physical violence:** | (N = 124) | | (N = 259) | |
| Boyfriend or husband | 37 | 29.84 | 105 | 40.54 |
| Parent, caregiver or other relative | 58 | 46.77 | 68 | 26.25 |
| Friend or neighbor | 18 | 14.52 | 33 | 12.74 |
| Member of an armed group | 1 | 0.81 | 14 | 5.41 |
| Official | 2 | 1.61 | 20 | 7.72 |
| Other | 8 | 6.45 | 28 | 10.81 |
| Verbal abuse – loud or aggressive screaming: | (N = 133) | | (N = 303) | |
| Boyfriend or husband | 40 | 30.08 | 97 | 32.01 |
| Parent, caregiver or other relative | 69 | 51.88 | 117 | 38.61 |
| Friend or neighbor | 10 | 7.52 | 49 | 16.17 |
| Member of an armed group | 2 | 1.50 | 16 | 5.28 |
| Official | 6 | 4.51 | 16 | 5.28 |
| Other | 8 | 6.02 | 22 | 7.26 |
| Unwanted sexual touching: | (N = 69) | | (N = 201) | |
| Boyfriend or husband | 38 | 55.07 | 86 | 42.79 |
| Parent, caregiver or other relative | 18 | 26.09 | 58 | 28.86 |
| Friend or neighbor | 10 | 14.49 | 17 | 8.46 |
| Member of an armed group | 0 | 0.00 | 13 | 6.47 |
| Official | 0 | 0.00 | 16 | 7.96 |
| Other | 3 | 4.35 | 19 | 9.45 |
| Coerced sex: | (N = 62) | | (N = 251) | |
| Boyfriend or husband | 31 | 50.00 | 93 | 37.05 |
| Parent, caregiver or other relative | 14 | 22.58 | 61 | 24.30 |
| Friend or neighbor | 11 | 17.74 | 41 | 16.33 |
| Member of an armed group | 2 | 3.23 | 22 | 8.76 |
| Official | 1 | 1.61 | 19 | 7.57 |
| Other | 5 | 8.06 | 26 | 10.36 |

**Table 4.** Prediction of adolescent-reported violence victimization in adjusted model, Democratic Republic of the Congo*

| PREDICTOR | PHYSICAL VIOLENCE aOR [95% CI] | EMOTIONAL VIOLENCE aOR [95% CI] | ANY FORM OF SEXUAL VIOLENCE aOR [95% CI] | FORCED SEX aOR [95% CI] | UNWANTED SEXUAL TOUCHING aOR [95% CI] | COERCED SEX aOR [95% CI] |
|---|---|---|---|---|---|---|
| Age | 0.684 [0.42,1.12] | 0.826 [0.51,1.35] | 0.818 [0.45, 1.48] | 0.521 [0.26, 1.02] | 1.085 [0.51, 2.31] | 0.948 [0.42, 2.13] |
| Living with biological parents | | | | | | |
| Living with mother only | 1.522 [0.87, 2.66] | 0.964 [0.56, 1.67] | 1.158 [0.59, 2.28] | 1.383 [0.64, 2.98] | 0.714 [0.28, 1.79] | 1.544 [0.65, 3.69] |
| Living with father only | 2.224 [0.55, 8.93] | 1.56 [0.39, 6.18] | 1.318 [0.24, 7.24] | 1.155 [0.13, 10.66] | 1.277 [0.14, 11.31] | 1.687 [0.19, 14.96] |
| Living with neither parent | 1.308 [0.53, 3.24] | 2.514 [1.01, 6.26]† | [0.31, 2.72] 0.918 | 0.939 [0.28, 3.13] | 0.839 [0.21, 3.32] | 0.302 [0.04, 2.50] |
| Years of school completed | 0.897 [0.81, 0.99]† | 0.948 [0.86, 1.04] | 0.899 [0.80, 1.01] | 0.851 [0.74,0.98]† | 1.005 [0.87, 1.16] | 0.998 [0.85, 1.17] |
| Living with intimate partner | 1.418 [0.75, 2.67] | 0.84 [0.43, 1.62] | 2.899 [1.43, 5.88]† | 2.696 [1.28, 5.69]† | 2.105 [0.90, 4.90] | 3.582 [1.50, 8.56]‡ |
| Worked without pay, last 12 months | 1.126 [0.55, 2.31] | 0.986 [0.49, 1.98] | 2.058 [0.91, 4.65] | 0.892 [0.33, 2.40] | 0.972 [0.33, 2.83] | 1.772 [0.63, 4.98] |
| Ever had a boyfriend | 2.963 [1.69, 5.20]§ | 2.891 [1.64, 5.09]§ | 6.368 [3.43, 11.82]§ | 8.657 [4.40, 17.03]§ | 4.099 [1.90, 8.85]§ | 2.323 [0.99, 5.44] |
| Observations | 313 | 308 | 300 | 320 | 310 | 304 |

aOR – adjusted odds ratio, CI – confidence interval

*95% confidence intervals in brackets.

†$P < 0.05$.

‡$P < 0.01$.

§$P < 0.001$.

**Table 5.** Prediction of adolescent-reported violence victimization in adjusted model, Ethiopia*

| PREDICTOR | PHYSICAL VIOLENCE aOR [95% CI] | EMOTIONAL VIOLENCE aOR [95% CI] | ANY FORM OF SEXUAL VIOLENCE aOR [95% CI] | FORCED SEX aOR [95% CI] | UNWANTED SEXUAL TOUCHING aOR [95% CI] | COERCED SEX aOR [95% CI] |
|---|---|---|---|---|---|---|
| Age | 0.881 [0.78, 0.99]† | 0.856 [0.77, 0.96]‡ | 0.902 [0.80, 1.02] | 0.835 [0.71, 0.98]† | 0.843 [0.72, 0.99]† | 0.99 [0.85, 1.16] |
| Living with biological parents | | | | | | |
| Living with mother only | 1.051 [0.68, 1.63] | 1.44 [0.97, 2.14] | 1.216 [0.77, 1.91] | 1.41 [0.82, 2.43] | 1.013 [0.59, 1.75] | 1.401 [0.79, 2.48] |
| Living with father only | 2.115 [1.35, 3.32]‡ | 1.419 [0.93, 2.17] | 2.008 [1.25, 3.22]‡ | 2.502 [1.46, 4.28]§ | 1.438 [0.83, 2.50] | 1.477 [0.80, 2.74] |
| Living with neither parent | 1.829 [0.93, 3.59] | 1.125 [0.58, 2.16] | 0.849 [0.37, 1.96] | 0.443 [0.13, 1.54] | 0.553 [0.18, 1.68] | 1.046 [0.37, 2.95] |
| Years of school completed | 0.946 [0.86, 1.04] | 1.034 [0.95, 1.12] | 0.927 [0.84, 1.02] | 0.986 [0.88, 1.10] | 0.948 [0.84, 1.07] | 0.879 [0.77, 1.00] |
| Living with intimate partner | 0.752 [0.49, 1.15] | 1.149 [0.78, 1.69] | 1.830 [1.20, 2.79]‡ | 1.28 [0.78, 2.11] | 1.355 [0.82, 2.24] | 1.443 [0.85, 2.45] |
| Worked without pay, last 12 months | 2.324 [0.83, 6.49] | 2.788 [1.11, 7.00]† | 2.848 [0.80, 10.09] | 2.339 [0.52, 10.45] | 4.394 [0.57, 33.60] | 1.00 [1.00, 1.00] |
| Ever had a boyfriend | 4.504 [3.16, 6.41]§ | 2.784 [1.99, 3.89]§ | 4.655 [3.21, 6.76]§ | 4.577 [2.94, 7.13]§ | 4.295 [2.74, 6.74]§ | 4.153 [2.57, 6.70]§ |
| Observations | 697 | 690 | 663 | 723 | 692 | 630 |

aOR – adjusted odds ratio, CI – confidence interval

*95% confidence intervals in brackets.

†*P*<0.05.

‡*P*<0.01.

§*P*<0.001.

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who had never had a boyfriend (DRC aOR=2.89, *P*<0.001; Ethiopia aOR=2.78, *P*<0.001). In DRC, living with neither parent was marginally associated with greater odds of victimization, compared to living with both parents (aOR=2.51, *P*=0.048). In Ethiopia, each additional year of age was associated with a 0.86 reduced odds in reported exposure to loud and aggressive screaming (*P*=0.006). Additionally, working without payment during the previous 12 months was associated with 2.79 greater odds in reported exposure to loud and aggressive screaming in Ethiopia (*P*=0.029).

Sexual violence was examined in relation to experiencing unwanted sexual touching, experiencing forced sex, or experiencing coerced sex through influence, authority, threats or pressure in the previous 12 months. Living with an intimate partner was associated with higher odds of experiencing any form of sexual violence in the previous 12 months in both countries, compared to not living with an intimate partner (DRC aOR=2.90, *P*=0.003; Ethiopia aOR=1.83, *P*=0.005). Adolescent girls who had ever had a boyfriend also reported higher odds of experiencing any form of sexual violence in both countries, compared to those who had not had a boyfriend (DRC aOR=6.37, *P*<0.001; Ethiopia aOR=4.66, *P*<0.001). In Ethiopia, adolescent girls who reported living with their father had 2.01 times higher odds of experiencing any form of sexual violence than adolescents who were living with both biological parents (*P*=0.004).

Having had a boyfriend was significantly associated with forced sex in both countries, when adjusting for other variables (see **Table 4** and **Table 5**). In DRC, living with an intimate partner was associated with 2.70 higher odds of forced sex (*P*=0.009). Further, each additional year of school completed was also associated with 0.85 lower odds of forced sex (*P*=0.022), and each additional year of age was marginally associated with 0.52 lower odds of forced sex (*P*=0.059). In Ethiopia, each increased year of age was associated with 0.84 lower odds of forced sex (*P*=0.027). Adolescent girls in Ethiopia who reported living with their father were 2.50 times more likely to report forced sex in the previous 12 months than adolescents living with both parents (*P*=0.001).

Having had a boyfriend was similarly associated with greater odds of unwanted sexual touching victimization in the previous 12 months in both countries, compared with adolescent girls who reported never having had a boyfriend (DRC aOR=4.10, *P*<0.001; Ethiopia aOR=4.30, *P*<0.001). In Ethiopia, increased age was associated with lower odds of reported unwanted sexual touching (aOR=0.84, *P*=0.037).

Finally, experiencing coerced sex through influence, authority, threats or pressure in the previous 12 months was associated with living with an intimate partner in DRC (aOR=3.58, *P*=0.004), and ever hav-

ing a boyfriend in Ethiopia (aOR=4.15, $P<0.001$). Ever having a boyfriend was also marginally associated with coerced sex in DRC (aOR=2.32, $P=0.052$). Each additional year of completed education was marginally associated with lower odds of coerced sex in Ethiopia (aOR=0.88, $P=0.059$).

## DISCUSSION

The prevalence of physical, emotional, and/or sexual violence victimization among adolescent girls (51.62%) is similar to the regional prevalence of past–year violence estimated from census data of girls and boys aged 2–14 (50%) and 15–17 (51%) in Africa [33].

Our study broadens the limited evidence base on predictors of violence against conflict–affected adolescent girls. The fact that early age was associated with increased odds of physical, emotional, and most measured forms of sexual violence in Ethiopia is concerning, especially in a sample that interviewed girls in early adolescence. We also found a significant association between years of education completed and violence victimization among displaced girls aged 13–14 in the DRC, when adjusting for other factors [12]. Although age and educational attainment are commonly considered to be risk factors for victimization in our contexts, our findings demonstrate that the relationship between these variables and victimization may not be consistent across conflict–affected populations in the East Africa region.

Caregivers and other family members tended to perpetrate much of the reported violence against adolescent girls. Similarly, ever having a boyfriend was the most consistent predictor of sexual violence, even when adjusting for risk factors known to be associated with violence in other contexts. These findings suggest that engagement in intimate relationships may be *the* primary risk factor for violence victimization among adolescents aged 13–19 in conflict settings.

Importantly, predictors of different forms of sexual violence were not uniform, suggesting that adolescent girls' vulnerability to victimization differs across forms of sexual violence and contexts. While living with an intimate partner was associated with coerced and forced sex in DRC for example, it was not significantly associated with unwanted sexual touching in DRC, or with any of the three forms of sexual violence in Ethiopia.

Finally, our findings indicate that living only with one's father is a predictor for both physical and sexual violence in Ethiopia, but not DRC. While high–income countries have also documented increased risk of victimization for girls living with a single parent, the majority of single parents in developed contexts are mothers [14,15]. In our study settings, the particular pathways through which increased vulnerability occurs are unclear, but the absence of the mother in the home increased the vulnerability of adolescent girls in Ethiopia. These findings suggest contextual differences in household makeup that should be further explored.

Taken together, our results have important implications for gender–based violence prevention efforts in conflict settings. Increased risk of violence among younger adolescents indicates that prevention efforts must target younger populations, who may be at increased risk of victimization.

Our findings contradict narratives suggesting that girls are most at risk of violence at the hands of strangers or military personnel in conflict settings [24]. These findings also call into question local narratives positing that early marriage is "protective" in conflict and helps keep girls safe from violence, or preserves a family's "honor" [40,41]. Considering the evidence from our study and others on intimate partners as primary perpetrators of violence, even in humanitarian emergencies [42], prevention programming should focus on explicitly acknowledging the presence of intimate partner relationships, even in more culturally conservative settings. Our findings suggest that humanitarian programming may need to include intimate partner violence prevention strategies for adolescent girls, and work with adult community members to understand how some practices intended to "protect" girls, such as early marriage, may put girls at a greater risk for violence.

Caregivers were also identified as primary perpetrators, which supports existing calls to target key adults in adolescent girls' lives, such as caregivers and other relatives, and to support positive parenting strategies and communication with adolescent girls [43,44]. Such parenting programs should address the additional vulnerabilities that girls may experience in conflict settings. While further research is warranted, our findings suggest that male caregivers should in particular be targeted for primary prevention efforts in conflict settings.

Finally, our study has implications for efforts to document violence against adolescent girls in humanitarian settings. Considering that more than 30% of adolescent girls in our study had not attended school in the previous year, researchers should use school–based sampling methodologies with caution.

Limitations of this study include the fact that single indicators were employed to measure physical and emotional violence, and potentially relevant predictors were not included in the survey such as length of displacement, previous exposure to war–related violence, alcohol consumption or drug use, and caregiver exposure to violence. Although interview methodologies were informed by constraints of the languages of participants, it is possible that use of different methodologies (both CAPI and ACASI in DRC, and solely ACASI in Ethiopia) may have contributed to some differences in predictors identified in the two contexts examined. To account for limitations imposed by the cross–sectional survey design, we restricted independent variables to relationships for which temporality could be reasonably inferred. For example, information on adolescents' self–esteem was excluded from our model because researchers could not determine temporality of self–esteem and reported violence. Finally, the study is limited to adolescent girls and caregivers who self–selected to join the life skills program. To increase awareness of the program, recruitment efforts included community sensitization to the program, which were conducted throughout the villages in South Kivu and camps in Ethiopia. Even so, those adolescents who may be most marginalized and who lack the access and social capital to join the program were likely underrepresented in this study.

## CONCLUSION

Globally, females are at highest risk for violence during adolescence, and humanitarian emergencies may exacerbate these vulnerabilities. Persistent gaps in knowledge of violence victimization have, to date, limited the humanitarian community's ability to appropriately respond to and prevent violence against adolescent girls in these contexts. Our study sheds light on prevalence and predictors of violence for conflict–affected adolescents aged 13–19 in two contexts, and offers important evidence for targeted programming and policy response for emergency actors, as well as guidance for other researchers working in these settings.

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# Risk factors for *Clostridium difficile* infections – an overview of the evidence base and challenges in data synthesis

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**Background** Recognition of a broad spectrum of disease and development of *Clostridium difficile* infection (CDI) and recurrent CDI (rCDI) in populations previously considered to be at low risk has renewed attention on differences in the risk profile of patients. In the absence of primary prevention for CDI and limited treatment options, it is important to achieve a deep understanding of the multiple factors that influence the risk of developing CDI and rCDI.

**Methods** We conducted a review of systematic reviews and meta–analyses on risk factors for CDI and rCDI published between 1990 and October 2016.

**Results** 22 systematic reviews assessing risk factors for CDI (n = 19) and rCDI (n = 6) were included. Meta–analyses were conducted in 17 of the systematic reviews. Over 40 risk factors have been associated with CDI and rCDI and can be classified into three categories: pharmacological risk factors, host–related risk factors, and clinical characteristics or interventions. Most systematic reviews and meta–analyses have focused on antibiotic use (n = 8 for CDI, 3 for rCDI), proton pump inhibitors (n = 8 for CDI, 4 for rCDI), and histamine 2 receptor antagonists (n = 4 for CDI) and chronic kidney disease (n = 4 for rCDI). However, other risk factors have been assessed. We discuss the state of the evidence, methods, and challenges for data synthesis.

**Conclusion** Several studies, synthesized in different systematic review, provide valuable insights into the role of different risk factors for CDI. Meta–analytic evidence of association has been reported for factors such as antibiotics, gastric acid suppressants, non–selective NSAID, and some co–morbidities. However, despite statistical significance, issues of high heterogeneity, bias and confounding remain to be addressed effectively to improve overall risk estimates. Large, prospective primary studies on risk factors for CDI with standardised case definitions and stratified analyses are required to develop more accurate and robust estimates of risk effects that can inform targeted–CDI clinical management procedures, prevention, and research.

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*Clostridium difficile* infection (CDI) is considered an urgent public health threat [1]. In 2011, a total of 453 000 incident CDI cases were estimated in the USA alone, with an additional 83 000 first recurrences (rCDI) and 29 300 deaths [2]. In Europe, where rates of CDI among inpatients range from 0.7 to 28.7 per 10 000 patient bed–days, at least 40 000 CDI cases are

thought to be missed every year through lack of clinical suspicion and inadequate laboratory testing [3]. Endemic CDI and outbreaks have been reported from all world regions, including Asia, Western Pacific, Latin America, and Africa [4–13]. By increasing the length of hospital stay, in addition to the extra costs of diagnosis, treatment, and in some cases surgery or fatal outcomes, CDI places a large economic burden on health care finances and patients [14]. It is estimated that the total annual hospital management of CDI infection in the US alone is US$ 6.3 billion [15].

Recognition of a broad spectrum of disease and development of CDI in populations previously considered to be at low risk has renewed attention on differences in the risk profile of patients. A substantial proportion of CDI cases, between 20 to 30%, are now considered to be community–associated [16] and at least 25% of incident CDI cases will suffer at least a relapse or first recurrence (rCDI) within 30 days of treatment [17]. In the absence of primary prevention for CDI and limited treatment options, it is important to achieve a deep understanding of the multiple factors that influence the risk of developing CDI and rCDI. Commonly reported risk factors include advanced age, co–morbidities, use of antibiotics, proton pump inhibitors (PPIs), histamine–2 receptor antagonists (H2RA) and exposure to health care settings. Other risk factors have also implicated include obesity [18–20], non–steroidal anti–inflammatory drugs (NSAID) [21,22], vitamin D [23], and the role of host genetics in acquiring CDI [24]. We examined systematic reviews and meta–analyses on risk factors for CDI to provide an overview of the state of the evidence and discuss some of the challenges for epidemiological data synthesis for CDI and rCDI.

## METHODS

We searched the following databases: MEDLINE and EMBASE (Ovid); CINAHL; Cochrane database; and Global Health Library. Our eligibility criteria are detailed in **Box 1** and search terms used for each database are available in Table S1 in **Online Supplementary Document.**

## RESULTS

We found that multiple systematic reviews had assessed the same risk factors. Furthermore, meta–analyses provided different estimates of association for similar factors. Thus, we focus our review on the conclusions of the publications rather than numerical risk estimates. **Table 1** provides a summary of the risk factors identified through our review, classified into three main groups. All, but one, of the primary studies in these systematic reviews were conducted in industrialised countries of North America, Europe, and Western Pacific region.

### Pharmacological agents

#### Antibiotics

CDI has traditionally been regarded as a complication of antimicrobial therapy, particularly broad–spectrum antibiotics that can disrupt the gut flora in hospitalised patients [40]. Several systematic reviews, with or without meta–analyses, have evaluated the role of different antibiotics by class or generation. The first meta–analysis to quantify the risk, published in 1998 [25], found a strong and statistically significant

**Box 1.** Inclusion and exclusion criteria

> **Inclusion:**
> - Systematic reviews with or without meta–analysis examining risk factors for CDI or recurrent episodes in all age groups
> - Published between 1990 to October 2016
> - Published in English
>
> **Exclusion:**
> - Systematic reviews and meta–analyses that focused on mortality, health care costs or treatment, or colonization by *C. difficile*
> - Narrative reviews or those with methods not clearly described
> - Randomised controlled trials (RCTs); Observational studies (cohort and case control studies); laboratory experiments and in–vitro studies

**Table 1.** Examples of systematic reviews and meta–analyses on risk factors for *Clostridium difficile* infection (CDI)

| Risk factor | CDI | Recurrent CDI |
|---|---|---|
| | Number of systematic reviews [ref] | |
| **Pharmacological risk factors:** | | |
| Any use of antibiotics (broad and specific) | 8 [21,25-31] | 3 [32-34] |
| Any use of proton pump inhibitors | 8 [21,25-31] | 4 [32,33,35,36] |
| Any use of histamine 2 receptor antagonists | 4 [21,36-38] | |
| Anti–ulcer medications (not specific) | 2 [25,37] | 1 [34] |
| Non–steroidal anti–inflammatory drug | 2 [21,22] | |
| Aspirin | 1 [21] | |
| Corticosteroids | 1 [21] | |
| Use of opiate during the last episode of CDI | | 1 [32] |
| **Host–related risk factors:** | | |
| Age: ≥65 years | 2 [21,31] | 3 [32-34] |
| Age: additional year or decade | 1 [25] | 2 [32,33] |
| Chronic kidney disease | 2 [21,39] | 4 [32-34,39] |
| Diabetes mellitus | 1 [21] | 1 [32] |
| Lymphoma or leukaemia | 1 [21,31] | |
| Solid cancer or malignancy | 1 [21,31] | |
| Severity of co–morbidity | 1 [25] | |
| Inflammatory bowel disease | 1 [21] | |
| Congestive heart disease | 1 [21] | |
| Chronic obstructive pulmonary disease | 1 [21] | |
| Peptic ulcer | 1 [21] | |
| Diverticular disease | 1 [21] | |
| Gastroesophageal reflux disease | 1 [21] | |
| Chronic obstructive pulmonary disease | 1 [21] | |
| Low mean concentration of 25 hydroxyvitamin D | 1 [23] | |
| Female sex | | 1 [34] |
| Previous diagnosis of CDI | | 1 [32] |
| Additional points Charlson scale | | 1 [32] |
| **Clinical interventions or characteristics:** | | |
| Duration of hospitalization | 1 [25] | 1 [32] |
| Nasogastric tube feeding | 2 [25,31] | 1 [33] |
| Stay in intensive treatment unit | 1 [25] | |
| Non–surgical GI procedure | 1 [25] | |
| Vomiting | | 1 [32] |
| Previous GI hospitalization | | 1 [32] |
| History of surgery | | 1 [32] |
| Leucocytes >20 cells/hpf | | 1 [32] |
| High faecal interleukin–8 | | 1 [32] |
| Previous gastrointestinal procedure | | 1 [32] |
| Low day–3 IgM anti–toxin A | | 1 [32] |
| Serum albumin <2.5g/dL | | 1 [32] |
| Hyponatremia | | 1 [32] |
| Lymphopenia | | 1 [32] |
| Colonization with vancomycin–resistant enterococci | | 1 [32] |

GI – gastrointestinal, hpf – high power field

association between antibiotic use and CDI; the risk of CDI was found to be 6 times higher on average compared to individuals not on antimicrobial therapy. Clindamycin, cephalosporins, and fluoroquinolones were and remain associated with the greatest risk of CDI [21,26–28]. Continued use of CDI high–risk antibiotics during follow–up has also been associated with a statistically significant increase in the risk of rCDI [33]. Consequently, antibiotic stewardship programmes are widely recommended for the prevention of CDI and there is substantial interest in recommendations for which antibiotics should be targeted [41].

As several antibiotics have been associated with CDI and rCDI, it is important to consider a number of issues before targeting specific antibiotics over others as means of prevention. Meta–analyses have found substantial heterogeneity in the studies for most antibiotic classes and generations, limiting the ability to

draw conclusions about the risk estimates for specific drugs. Furthermore, there are difficulties in addressing the sources of heterogeneity, as these are wide–ranging: significant pharmacological differences even within generations [41], potential antibiotic selection pressure for particular *C. difficile* strains, such as fluoroquinolones and NAP1/B1/027 [41], increased use of other antimicrobials with unknown effect on CDI [42], and differences in local or national guidelines for antibiotic prescribing. Since much of the literature on risk factors for CDI is based on observational studies, the risk estimates from meta–analyses are both confounded as well as biased.

Interesting findings have emerged from recent meta–analytical approaches estimating the association between antibiotics and CDI in different settings. Differences in strengths of association have been found once data for antibiotics are disaggregated by setting or world region. In the hospital setting, as compared to non–diarrheal controls, clindamycin, cephalosporins, carbapenems, fluoroquinolones and trimethoprim/sulphonamides were associated with at least a 2 times an increased risk of CDI, although confidence intervals for pooled estimates among antibiotic classes overlapped [28]. In the community, these antibiotics were associated with a higher risk for CDI – between 8 to 20 times the risk for clindamycin [21,26,27] and 3 to 5 times for cephalosporins and quinolones, but definition of controls groups varied [21]. Macrolides were associated with a 2– to 3–fold higher and statistically significant risk for community–associated CDI but not for hospital–associated CDI [21,26,27]. Non–significant risks have been reported for tetracycline in either setting [21,26–28]. Aminoglycosides have not been found to be significantly associated with CDI in the health care setting [28], but no evidence were available for community–associated CDI. A greater strength of association between exposure to antibiotics and community–associated CDI in the USA as compared to Europe [21]. Furthermore, stronger associations observed between specific antibiotics and community–associated CDI could be due to less confounding effects inherent to studies within hospitals [43]. Limitations notwithstanding, differing estimates of risk for similar antibiotics for hospital or community–associated CDI underscores the importance of a robust evidence–base for the development of relevant antimicrobial prescribing practices for CDI.

### Gastric acid suppressors

Acid related upper–gastrointestinal disorders including peptic ulcer disease and gastro–esophageal reflux disease are now mainly treated with PPIs and H2RAs [37,44,45]. Although PPIs are generally thought to have a good safety profile, systematic reviews and meta–analyses suggest otherwise, with an overall significant association between the use of PPIs and CDI [21,35–37,44–47] and rCDI [32,33,35,36]. A statistically significant association between the use of H2RAs and CDI has also been reported in meta–analyses [21,36–38]. Limited evidence on the risk posed by the continuous use of H2RAs on rCDI, or on the relative risk of H2RAs vs PPIs for CDI prevents conclusions from being drawn [36,37]. As for much of the evidence on risk factors for CDI, results are largely from observational studies and, thus, despite the extent of the literature and the plausibility of these findings, confounders such as polypharmacy and comorbidities may still play a role and causality cannot be established. It is important to note that varying strengths of association have been reported in primary studies, reinforcing the need for careful interpretation of meta–estimates. For instance, the association between PPIs and CDI remains significant when stratified by antibiotic use among CDI cases (>80% vs £80%) [46] and by study design (case–control studies vs cohort studies) [36,44,46]. However, heterogeneity (defined as >50% or $P < 0.005$) was observed in all subgroup analyses [36,37,44,46], even when unadjusted vs adjusted risk estimates from primary studies were analyzed separately [36]. Similar to antibiotics, regional prescribing practices have the potential to impact meta–estimates. A greater strength of association between exposure to PPIs and community–associated CDI was observed in studies from Europe as compared to the USA.

### Other drugs

Discrepancies have been reported for the use of NSAIDs as a factor influencing the risk of CDI. The use of aspirin was not significantly associated with CDI in the community but corticosteroids were, as reported in one meta–analysis [21]. However, the use of non–selective NSAID (excluding COX–2 inhibitors) was associated with CDI [22]. Understanding the differences between risk estimates and CDI case definition by setting are extremely important for the accurate assessment of the relevance of study findings.

## Host–related risk factors

### Age

The well–known role of increased age as a risk factor for incident CDI and rCDI has largely been assessed using two criteria: per additional year or decade, or age ≥65 years [31–34]. The incidence of *C. difficile* hospitalisations among patients ≥65 years increased most sharply among this age group in Finland in the

early 2000s [48]. In 2011, rates of CDI were 4–fold higher than among adults aged 45–65 and 13–fold higher as compared to those aged 18–44 in the USA [2]. Furthermore, older age has been associated with an increased risk of CDI with the virulent strain BI/NAP1/027 [31] as well as rCDI [33,34].

Age is a common confounder for which estimates are adjusted in primary studies assessing risk factors for CDI [27,28]. There is great value in having age–stratified estimates of risk, and these have been provided in several meta–analyses. For instance, the risk of CDI in the community associated with antimicrobial exposure was approximately 2–fold higher among older adults (≥65 years of age) as compared with children and younger adults [21]. Furthermore, the risk estimate for the use of NSAIDs was significant based on studies with study populations with mean age of 50 or older, but not significant among those with younger age [22]. Similarly, the risk posed by PPI was more pronounced among adults than in the elderly (≥65 years of age) or children [21]. Analytical approaches to elucidate how the risk of CDI differs among populations are important to better differentiate among populations at risk and the development of targeted recommendations.

### Comorbidities

The association between CDI and selected comorbidities has also been explored systematically. A systematic review highlighted an increased risk of community–associated CDI cases among patients with inflammatory bowel disease, diabetes, leukemia or lymphoma, renal failure, and solid cancer [21], among a wide range of other comorbidities that have been implicated. Although other study populations are likely to be susceptible, such meta–analytical approaches add to the evidence base by pointing toward specific conditions that may require further attention in the clinical setting and in research studies.

Although there is evidence that lower 25–hydroxyvitamin D (25(OH)D) status increases susceptibility to infectious diseases, the evidence is insufficient to establish an association with CDI. A recent assessment of studies evaluating the role of low 25(OH)D and CDI suggested a significant association with rCDI. However, considering that these were based on three studies only, no differences can be observed between outcomes of CDI in hospital or community settings.

## Clinical characteristics and interventions

The association between CDI and exposure to health care settings is well recognized. However, the risk posed by different interventions remains poorly understood as the available evidence is potentially confounded by other in–patient associated characteristics. A longer hospital stay is strongly associated with exposure to *C. difficile* spores and the likelihood of colonization [25,49]. However, results regarding the length of stay as a determinant for CDI from primary studies have not been consistent. For instance, patients who developed CDI were hospitalised 2–4 times longer [50], while no differences in hospital stay between CDI patients and non–CDI patients have also been observed [51]. Similarly, one study showed a strong association between CDI and length of hospital stay and ICU stay in univariate analysis but a weak association with a wider 95% confidence interval (CI) was reported in the multivariate analysis [52]. The risk of CDI has been shown to be greater in individuals undergoing invasive procedures, such as abdominal surgery, nasogastric tube placement, mechanical ventilation, all of which are associated with prolonged hospitalization [53,54]. A meta–estimate for the association between CDI or rCDI was not identified for most of the clinical interventions in systematic reviews (**Table 1**). The risk of nasogastric tube feeding and rCDI was estimated in one meta–analysis from data in 3 primary studies and found to be not significantly associated [33].

Despite difficulties in developing a rigid clinical prediction rule for CDI or rCDI, prognostic factors that correlate with poor outcome have been differentiated and informed guidance [55]. Key factors include age, treatment with systemic antibiotics, leucocyte count, albumin, and temperature at time of diagnosis. Furthermore, 5 types of CDI patient groups have been differentiated, based on severity of disease. This classification is important for clinical management and for research.

## DISCUSSION

### Implications of challenges in data synthesis for prevention of CDI and further research

There are two major public health goals in relation to CDI prevention. First, it is important to reduce the total number of cases. Second, it is essential to prevent a poor or fatal outcome of those with severe pre-

sentation. The availability of new therapeutic and preventive measures such as immunoglobulin, faecal transplant, and vaccines could help reduce CDI morbidity, mortality and costs. For these strategies to be effective and properly targeted to high–risk patients, evidence on risk factors is necessary.

Varying definitions and reporting levels in primary studies are common issues that challenge or preclude meta–analytical synthesis of the evidence, particularly, the case definition of CDI. In available studies, criteria for the definition can range from hospitalisation records of *C. difficile*, on its own or combined with prescription of oral vancomycin, clinical diarrhea, to laboratory confirmation of CDI, with or without presence of pseudomembranous colitis. An essential first step in the assessment of risk factors for CDI is that future studies adhere to recommended surveillance case definitions for CDI [56] and that efforts are made to support case ascertainment with adequate diagnostic tests [3]. This will not only minimise misclassification bias of asymptomatic patients but also allow for further analytical differentiation of incident CDI and recurrent cases occurring in the community or in the hospital setting. Early detection of severe cases and targeted management, such as early surgical consultation with CDI patients, is essential to prevent poor or fatal outcomes.

CDI data collated by different setting of acquisition have the potential to enable targeted advances in the development of preventive and treatment options. For instance, both probiotics and fidaxomicin have been proposed for the prevention of rCDI among patients at "high risk" of recurrence. Similarly, faecal transplantation methods are also now available for treating rCDI [57]. Better quality data are required to make official recommendations on the use of probiotics [58] and the high cost of fidaxomicin poses restrictions for a cost–effective use if those at high risk cannot be correctly identified [59]. Prevention through vaccination is a promising perspective that could tackle CDI primary infections [60]. More evidence is also required to develop prescribing recommendations of pharmacological agents (with the potential to disrupt the gut flora, such as PPIs and H2RA) in the community that would result in a reduction of the risk of CDI.

Another common limitation in the assessment of risk factors for CDI is that data are from observational studies. Given that this will likely remain unchanged, special attention and consensus on potential confounders and selection of comparator groups are needed in the study design or analysis stages. Evidence–base guidance requires data on risk factors to identify patient characteristics that correlate positively with the severity of disease. Bias is likely to be introduced if study populations are not representative of all potential cases by restricting the pool of CDI cases to those patients with recent antibiotic exposure or controls to those with antibiotic–associated or hospital–acquired, toxin–negative diarrhea.

Age, sex, concomitant medication, and comorbidities are often common confounders adjusted for in primary analyses [33], but data on risk factors for CDI requires further considerations. It is important that parameters on the duration and dosage of drugs associated with a risk of CDI, including antibiotics, PPIs, H2RA, and even NSAIDs, are reported clearly to enable subgroup analyses and their consideration in multivariate analyses in primary studies. Studies and meta–analyses have not been able to account for these factors adequately, thus more research is needed. Features of research that would strengthen the evidence base include matched control groups (particularly by age, gender, and location) as well as an examination of duration and number of drug doses (antibiotics and other drugs). A full assessment of adherence to drug treatments, particularly in the community, is difficult to achieve and its effects minimised as much as possible in both the study design and analysis (eg, using dispensed drugs data rather than prescribed). The importance of a nuanced approach to better understand the role of antibiotics and development of CDI was demonstrated in a recent study, which found a dose–dependent association of cumulative exposure (in terms of doses) and temporal effect (within 6 months prior to diagnosis) of antibiotics use and community–associated CDI [61].

Finally, the vast majority of primary studies aimed at estimating risk factors influencing CDI are conducted in industrialised countries, where prevention is currently focused on judicious antibiotic use. The burden of CDI in developing countries where overuse of antibiotic is also prevalent [62] remains poorly described and the capacity to detect and report its incidence needs is limited [63]. This represents a large knowledge gap in CDI epidemiology. The paucity of evidence on CDI incidence and strength of association of different risk factors is worrisome in view of the potential wide–spread of hyper–virulent strains of *C. difficile* as seen for BI/NAP1/027 [16]. Additional, well–designed studies and standardised surveillance methods [64] that integrate clinical and epidemiological data are required in these settings to assess the role of multiple in–hospital and community factors –which may differ from high–resource settings – that can have an impact on CDI or rCDI.

## CONCLUSION

Several studies provide valuable insights into the role of different risk factors for CDI and meta–analytic evidence of association has been reported for putative factors. However, despite statistical significance, issues of high heterogeneity, bias and confounding remain to be addressed effectively to improve overall risk estimates. Further, given the evolving epidemiology of *C. difficile* world–wide, there is a particular interest in achieving a better understanding of the role of the various factors leading to CDI in the hospital vs the community setting. Thus, there would be great value in large, prospective primary studies on risk factors for CDI with standardised case definitions and stratified analyses to develop more accurate estimates of risk effects that can inform targeted–CDI clinical management procedures, prevention, and research.

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PAPERS

# Gender bias in careseeking practices in 57 low– and middle–income countries

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**Background** Preventive and curative medical interventions can reduce child mortality. It is important to assess whether there is gender bias in access to these interventions, which can lead to preferential treatment of children of a given sex.

**Methods** Data from Demographic and Health Surveys carried out in 57 low– and middle–income countries were used. The outcome variable was a composite careseeking indicator, which represents the proportion of children with common childhood symptoms or illnesses (diarrhea, fever, or suspected pneumonia) who were taken to an appropriate provider. Results were stratified by sex at the national level and within each wealth quintile. Ecological analyses were carried out to assess if sex ratios varied by world region, religion, national income and its distribution, and gender inequality indices. Linear multilevel regression models were used to estimate time trends in careseeking by sex between 1994 and 2014.

**Findings** Eight out of 57 countries showed significant differences in careseeking; in six countries, girls were less likely to receive care (Colombia, Egypt, India, Liberia, Senegal and Yemen). Seven countries had significant interactions between sex and wealth quintile, but the patterns varied from country to country. In the ecological analyses, lower careseeking for girls tended to be more common in countries with higher income concentration ($P = 0.039$) and higher Muslim population ($P = 0.006$). Coverage increased for both sexes; 0.95 percent points (pp) a year among girls (32.9% to 51.9%), and 0.91 pp (34.8% to 52.9%) among boys.

**Conclusion** The overall frequency of careseeking is similar for girls and boys, but not in all countries, where there is evidence of gender bias. A gender perspective should be an integral part of monitoring, accountability and programming. Countries where bias is present need renewed attention by national and international initiatives, in order to ensure that girls receive adequate care and protection.

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Disaggregation of child health statistics by sex is important in order to identify gender bias in health intervention coverage, and in outcomes such as morbidity, mortality and nutritional status among children under the age of five years. Gender bias is a multidimensional social construct, in which different values are attributed to men and women in a given society, which can lead to preferential treatment of children of a given sex [1,2]; the use of this concept refers to a system of relations including sex, but goes beyond biological differences [3]. The study of gender bias in child health is

affected by the greater biological vulnerability of boys compared to girls; in societies where there is no evidence of discrimination, boys show higher mortality rates than girls [4,5].

Two recent analyses assessed gender bias in the coverage of essential child health interventions in low– and middle–income countries (LMICs) [6,7]. Essential interventions may be classified as preventive (for example, measles vaccination, early initiation of breastfeeding, exclusive breastfeeding from 0–5 months, and use of insecticide treated bednets) or curative (use of antimalarials, careseeking for pneumonia, oral rehydration therapy, etc.) A UNICEF report showed no difference between girls and boys in terms of the seven interventions listed above [6]. There were also no differences in undernutrition (stunting, wasting or underweight). The numbers of countries included in these analyses ranged from 23 to 80 [6]. However, in spite of the lack of gender bias at national level, differences may exist at the subnational level, particularly among disadvantaged groups [8].

A recent systematic review investigated sex differences in hospitalizations for diarrhea, pneumonia and malaria in LMICs, and showed higher admission rates for boys, and higher case–fatality rates for girls [7]. However, hospital admissions are not a good indicator to study gender bias, because admission depends both on severity of the illness – which is likely to be greater for boys – and on careseeking by the caregivers [7]. Comparing careseeking rates among boys and girls for all cases of defined diseases or conditions is likely to be more useful in terms of detecting gender bias. In the same study, the authors analyzed data from 67 Demographic and Health Surveys (DHS) to investigate sex differences in careseeking by type of provider for diarrhea, fever, and pneumonia. Overall, more boys were taken to a health–care facility compared to girls [7].

Careseeking indicators are based on children who presented symptoms for each illness, usually in the two weeks before a survey. In these cases, the number of children is small, which leads to wide confidence intervals for these indicators, and may fail to detect differences between boys and girls as statistically significant due to low power [9].

We attempt to overcome this limitation by measuring sex differences using a composite careseeking indicator for three common childhood illnesses or symptoms. In addition, given the conflicting results of the two above–mentioned analyses, we expand our investigation to also assess whether these differences vary by wealth quintile, and whether sex differences in careseeking are associated with country characteristics such as income, religion and gender inequality indices. By doing so, we test the hypotheses that socioeconomic and related factors may modify the extent of gender bias in careseeking.

## METHODS

We analyzed data from nationally–representative Demographic and Health Surveys (DHS) conducted in low– and middle–income countries. We included all surveys with public–domain datasets available on the DHS website (http://dhsprogram.com/) as of May 2016, which had all the variables required for the analyses.

DHS asks mothers or caretakers of children under five years of age about diarrhea, fever, and symptoms of pneumonia (see Table S1 in **Online Supplementary Document**). We used a composite careseeking indicator; the numerator was the number of children in a survey who were taken to an appropriate health care provider (defined by each country), during recent episodes of diarrhea, fever or suspected pneumonia, and the denominator was the number of children for which such an episode was reported during the two weeks preceding the interview. Pharmacies, shops and traditional practitioners were not considered appropriate providers.

The outcome variable was the proportion of children with symptoms who were taken to an appropriate provider. This was calculated separately for boys and girls in each survey, both at the national level and within each wealth quintile. Wealth indices were calculated for each survey through principal component analysis of household assets and building characteristics [10–12]. The first component resulting from the analysis was divided into quintiles, with Q1 representing the poorest, and Q5 the wealthiest, 20% of all families.

For the descriptive analyses, we selected the most recent survey from each country, from 2005 to 2014. Differences between the sexes in each country were assessed using chi–squared tests. Sex ratios were cal-

culated for each survey by dividing careseeking proportions in girls and in boys, with values below 1.0 indicating gender bias against girls. The 95% confidence intervals for sex ratios were calculated using a jackknife approach based on repeated sub–sampling within the full survey sample. Interactions between wealth quintiles and sex of the child were assessed using Poisson regression with careseeking as the outcome.

Countries with more than one survey were included in the analyses of global time trends in careseeking between 1994 and 2014, using linear multilevel regression models with surveys as level one units and countries as level two units. We fitted separate trends for boys and for girls.

Ecological analyses were carried out with careseeking sex ratios as the outcome, based on the most recent survey for each country. The following explanatory variables were selected: region of the world according to UNICEF classification; religion (predominant and percentage in the population); country income groups; Gross Domestic Product *per capita* in USD; Gini coefficient of income inequality; and three indices related to gender equity (Gender Inequality Index, Gender Development Index, and Global Gender Gap Index) (see Table S2 in **Online Supplementary Document** for full definitions and data sources) [13–20]. Associations between careseeking sex ratios and categorical explanatory variables were analyzed using analysis of variance (ANOVA), and those with continuous explanatory variables using Pearson´s correlation.

All analyses were carried out using Stata version 13.1 (StataCorp LP, College Station, Texas, USA), and considered the complex sampling structure of the surveys and the sampling weights.

## RESULTS

A total of 57 countries had DHS data sets since 2005 with the required variables. The median survey year was 2012. Sample sizes ranged from 1450 (Armenia) to 48 679 (India) children under five years (**Table 1**). The median sample size was 7526 children and the interquartile range was 5054 to 10 935.

Sex ratios for careseeking (girls/boys) ranged from 0.76 (0.68–0.85) in Senegal to 1.11 (0.99–1.24) in Haiti (**Figure 1**). The average value for all countries was 0.97 (0.96–1.00).

Eight countries showed statistical evidence of gender bias. In six of these (Senegal, Yemen, Liberia, Egypt, Colombia and India) girls were less likely to be taken to a provider, with sex ratios ranging from 0.76 to 0.94. In the other two countries, Haiti and Uganda (sex ratios of 1.11 and 1.05, respectively), girls were more likely to receive care. Further results at country level including 95% confidence intervals and p values are shown in **Table 1**.
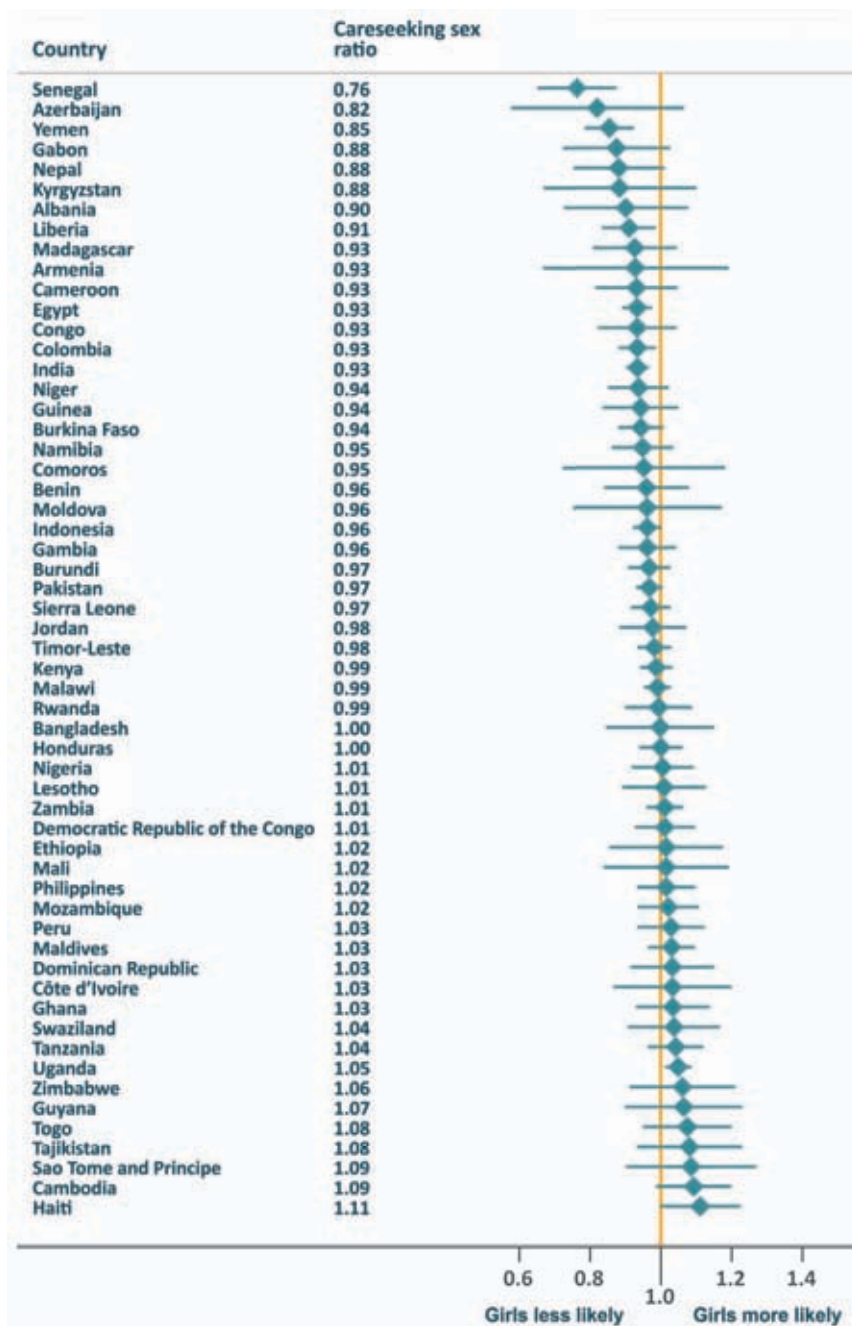


**Figure 1.** Careseeking sex ratios (95% confidence interval), by country.

**Table 1.** Characterization of 57 countries with available DHS surveys post–2005 according to region, income group, sample size and careseeking indicator

| Country | Year | World Region (UNICEF) | Income group (World Bank) | Children under five years (n) | Children with diarrhea, fever or suspect pneumonia (n) | | | Careseeking sex ratio (CI 95%) | P–value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Total | Boys | Girls | | |
| Albania | 2008 | CEE & CIS | Upper middle | 1586 | 267 | 145 | 122 | 0.9 | (0.72–1.07) | 0.292 |
| Armenia | 2010 | CEE & CIS | Lower middle | 1450 | 290 | 153 | 137 | 0.92 | (0.66–1.19) | 0.599 |
| Azerbaijan | 2006 | CEE & CIS | Upper middle | 2196 | 405 | 227 | 178 | 0.82 | (0.57–1.06) | 0.183 |
| Bangladesh | 2014 | South Asia | Low | 7567 | 3089 | 1614 | 1475 | 0.99 | (0.84–1.15) | 0.984 |
| Benin | 2011 | West & Central Africa | Low | 12679 | 1857 | 954 | 903 | 0.96 | (0.83–1.08) | 0.521 |
| Burkina Faso | 2010 | West & Central Africa | Low | 13716 | 4175 | 2143 | 2032 | 0.94 | (0.88–1.00) | 0.099 |
| Burundi | 2010 | Eastern & Southern Africa | Low | 7231 | 3713 | 1864 | 1849 | 0.96 | (0.90–1.02) | 0.302 |
| Cambodia | 2014 | East Asia & Pacific | Low | 6971 | 2248 | 1182 | 1066 | 1.09 | (0.98–1.19) | 0.076 |
| Cameroon | 2011 | West & Central Africa | Lower middle | 10734 | 4443 | 2231 | 2212 | 0.93 | (0.81–1.04) | 0.263 |
| Colombia* | 2010 | LAC | Upper middle | 17443 | 8669 | 4522 | 4147 | 0.93 | (0.88–0.98) | 0.020 |
| Comoros | 2012 | Eastern & Southern Africa | Low | 3022 | 951 | 489 | 462 | 0.95 | (0.72–1.18) | 0.683 |
| Congo (Brazzaville) | 2011 | West & Central Africa | Lower middle | 8857 | 3398 | 1733 | 1665 | 0.93 | (0.82–1.04) | 0.257 |
| Congo D.R. | 2013 | West & Central Africa | Low | 17228 | 7292 | 3657 | 3635 | 1.01 | (0.92–1.09) | 0.781 |
| Cote d'Ivoire | 2011 | West & Central Africa | Lower middle | 7093 | 2453 | 1233 | 1220 | 1.03 | (0.86–1.20) | 0.687 |
| Dominican Republic | 2013 | LAC | Upper middle | 3606 | 1412 | 724 | 688 | 1.03 | (0.91–1.15) | 0.572 |
| Egypt* | 2014 | Middle East & North Africa | Lower middle | 15466 | 5262 | 2867 | 2395 | 0.93 | (0.89–0.97) | 0.004 |
| Ethiopia | 2011 | Eastern & Southern Africa | Low | 10808 | 3161 | 1621 | 1540 | 1.01 | (0.85–1.17) | 0.848 |
| Gabon | 2012 | West & Central Africa | Upper middle | 5747 | 2258 | 1135 | 1123 | 0.87 | (0.72–1.02) | 0.126 |
| Gambia | 2013 | West & Central Africa | Low | 7788 | 2127 | 1112 | 1015 | 0.96 | (0.88–1.04) | 0.370 |
| Ghana | 2014 | West & Central Africa | Lower middle | 5595 | 1396 | 767 | 629 | 1.03 | (0.92–1.13) | 0.513 |
| Guinea | 2012 | West & Central Africa | Low | 6424 | 2547 | 1311 | 1236 | 0.94 | (0.83–1.05) | 0.311 |
| Guyana | 2009 | LAC | Lower middle | 2105 | 600 | 315 | 285 | 1.06 | (0.89–1.23) | 0.427 |
| Haiti* | 2012 | LAC | Low | 6744 | 3650 | 1840 | 1810 | 1.11 | (0.99–1.22) | 0.044 |
| Honduras | 2011 | LAC | Lower middle | 10592 | 4379 | 2335 | 2044 | 1.00 | (0.93–1.06) | 0.978 |
| India* | 2005 | South Asia | Lower middle | 48679 | 11,336 | 6089 | 5247 | 0.93 | (0.90–0.96) | 0.000 |
| Indonesia | 2012 | East Asia & Pacific | Lower middle | 17367 | 7029 | 3787 | 3242 | 0.96 | (0.92–1.00) | 0.068 |
| Jordan | 2012 | Middle East & North Africa | Upper middle | 10128 | 3017 | 1595 | 1422 | 0.97 | (0.88–1.07) | 0.649 |
| Kenya | 2014 | Eastern & Southern Africa | Low | 20093 | 7690 | 3922 | 3768 | 0.98 | (0.94–1.03) | 0.601 |
| Kyrgyzstan | 2012 | CEE & CIS | Low | 4247 | 392 | 200 | 192 | 0.88 | (0.66–1.10) | 0.320 |
| Lesotho | 2009 | Eastern & Southern Africa | Lower middle | 3606 | 1033 | 505 | 528 | 1.00 | (0.89–1.12) | 0.872 |
| Liberia* | 2013 | West & Central Africa | Low | 7058 | 3219 | 1659 | 1560 | 0.91 | (0.83–0.98) | 0.029 |
| Madagascar | 2008 | Eastern & Southern Africa | Low | 11750 | 2029 | 1027 | 1002 | 0.92 | (0.80–1.04) | 0.244 |
| Malawi | 2010 | Eastern & Southern Africa | Low | 18360 | 8227 | 4174 | 4053 | 0.99 | (0.95–1.02) | 0.634 |
| Maldives | 2009 | South Asia | Upper middle | 3761 | 1353 | 689 | 664 | 1.03 | (0.96–1.09) | 0.350 |
| Mali | 2012 | West & Central Africa | Low | 9582 | 1619 | 870 | 749 | 1.01 | (0.83–1.19) | 0.861 |
| Moldova | 2005 | CEE & CIS | Lower middle | 1533 | 368 | 172 | 196 | 0.96 | (0.75–1.17) | 0.723 |
| Mozambique | 2011 | Eastern & Southern Africa | Low | 10291 | 2224 | 1131 | 1093 | 1.02 | (0.93–1.10) | 0.622 |
| Namibia | 2013 | Eastern & Southern Africa | Upper middle | 4818 | 1699 | 855 | 844 | 0.94 | (0.86–1.03) | 0.260 |
| Nepal | 2011 | South Asia | Low | 5054 | 1416 | 793 | 623 | 0.88 | (0.75–1.01) | 0.085 |
| Niger | 2012 | West & Central Africa | Low | 11602 | 2852 | 1418 | 1434 | 0.93 | (0.85–1.02) | 0.165 |
| Nigeria | 2013 | West & Central Africa | Lower middle | 28596 | 5787 | 2965 | 2822 | 1.00 | (0.91–1.09) | 0.897 |
| Pakistan | 2012 | South Asia | Lower middle | 10935 | 5213 | 2750 | 2463 | 0.96 | (0.93–1.00) | 0.095 |
| Peru | 2012 | LAC | Upper middle | 9445 | 3134 | 1617 | 1517 | 1.02 | (0.93–1.12) | 0.543 |
| Philippines | 2013 | East Asia & Pacific | Lower middle | 7012 | 2413 | 1263 | 1150 | 1.01 | (0.93–1.09) | 0.707 |
| Rwanda | 2014 | Eastern & Southern Africa | Low | 7558 | 2190 | 1105 | 1085 | 0.99 | (0.89–1.08) | 0.903 |
| Sao Tome and Principe | 2008 | West & Central Africa | Lower middle | 1851 | 504 | 269 | 235 | 1.08 | (0.90–1.26) | 0.329 |
| Senegal* | 2014 | West & Central Africa | Lower middle | 6526 | 1633 | 865 | 768 | 0.76 | (0.65–0.87) | 0.000 |
| Sierra Leone | 2013 | West & Central Africa | Low | 10618 | 3602 | 1797 | 1805 | 0.97 | (0.91–1.02) | 0.338 |
| Swaziland | 2006 | Eastern & Southern Africa | Lower middle | 2537 | 946 | 524 | 422 | 1.03 | (0.90–1.16) | 0.563 |
| Tajikistan | 2012 | CEE & CIS | Low | 4838 | 922 | 511 | 411 | 1.08 | (0.93–1.22) | 0.265 |
| Tanzania | 2010 | Eastern & Southern Africa | Low | 7526 | 2290 | 1163 | 1127 | 1.04 | (0.96–1.12) | 0.269 |
| Timor–Leste | 2009 | East Asia & Pacific | Lower middle | 9294 | 2661 | 1308 | 1353 | 0.98 | (0.93–1.03) | 0.473 |
| Togo | 2013 | West & Central Africa | Low | 6535 | 2262 | 1155 | 1107 | 1.07 | (0.95–1.20) | 0.221 |
| Uganda* | 2011 | Eastern & Southern Africa | Low | 7355 | 3946 | 2007 | 1939 | 1.04 | (1.01–1.08) | 0.008 |
| Yemen* | 2013 | Middle East & North Africa | Lower middle | 15383 | 7345 | 3875 | 3470 | 0.85 | (0.78–0.92) | 0.000 |
| Zambia | 2013 | Eastern & Southern Africa | Lower middle | 12714 | 4238 | 2139 | 2099 | 1.01 | (0.95–1.06) | 0.656 |
| Zimbabwe | 2010 | Eastern & Southern Africa | Low | 5203 | 1358 | 686 | 672 | 1.06 | (0.91–1.21) | 0.405 |

CI – confidence interval, CEE – Central and Eastern Europe, CIS – Commonwealth of Independent States, LAC – Latin America & the Caribbean
*Countries with significant sex differences in careseeking (P<0.05).
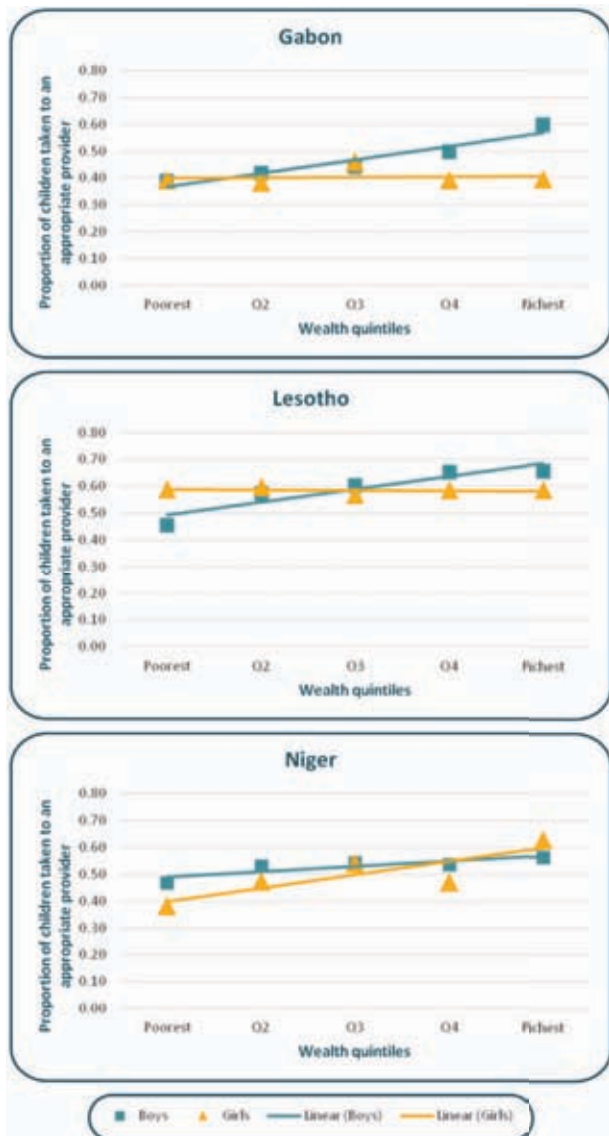
**Figure 2.** Careseeking for common childhood symptoms or illnesses by sex in countries with significant (P<0.05) interactions between child sex and wealth quintile.
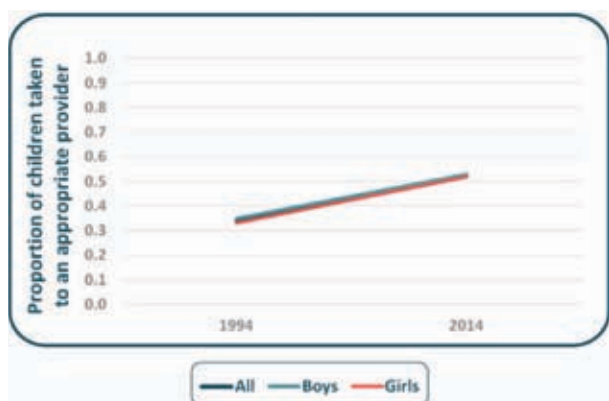


**Figure 3.** Gender differences in child health: evidences from Demographic and Health Surveys. Regression lines for changes in careseeking over time (1994–2014) by sex, for all countries combined.

We also examined interactions between wealth and sex in careseeking coverage. Of the 57 countries, significant interactions (P<0.05) were found in three. In Gabon and Lesotho, higher socioeconomic position was associated with greater careseeking for boys but not for girls; in Niger, the trend was in the opposite direction (**Figure 2**). Another four countries had interactions with p levels between 0.05 and 0.1: Burkina Faso, Congo Brazzaville, Dominican Republic and Senegal. Figure S1 in **Online Supplementary Document** shows that interaction patterns were also inconsistent in these countries.

Time trends analysis showed that global careseeking coverage increased by 0.93 percent point (pp) a year between 1994 and 2014 (from 33.9% to 52.4%) (**Figure 3**). Coverage increased for both sexes (P<0.001): among girls the increase was 0.95 pp a year (32.9% to 51.9%), and among boys, 0.91 pp (34.8% to 52.9%).

Ecological analyses showed a lack of association between the careseeking sex ratio and most explanatory variables (**Table 2** and **Table 3**). There was no evidence of difference between the world regions. However, it should be noted that there are few surveys available for countries in South Asia and in Middle East & North Africa; most surveys are from countries in Eastern & Southern Africa, and in West & Central Africa.

Regarding income levels, most of the countries surveyed are in the low– and lower–middle income groups, and no association was found between the level and careseeking sex ratios (**Table 2**).

There was a negative correlation, which was not statistically significant (P=0.053) between continuous GDP *per capita* and the sex ratio, but not for log GDP per capita (P=0.157).

None of the gender inequality indices were associated with the careseeking sex ratio (**Table 2** and **Table 3**). The Gender Development Index was tested both as a categorical variable, as recommended by its developers, and as a continuous index.

The religion variables were expressed both as categories of the predominant religion in each country (**Table 2**) and as the percent of Christians and Muslims in the population (**Table 3**). In both sets of ecological analyses, Christian religion was associated with improved care for girls, and Muslim religion with preferential careseeking for boys. These associations remained virtually unchanged after adjustment of the religion variables by GDP *per capita* (partial correlation coefficients of –0.351 for percent Muslim and –0.307 for percent Christian). Figure S2 in **Online Supplementary Document** shows the careseeking sex ratios and 95% confidence intervals, for countries ranked according to the percentage of Muslim population.

We opted not to carry out extensive multivariable analyses because several explanatory variables are highly collinear (eg, GDI and income *per capita*, etc.) and because the gender indices also included socioeconomic variables in their construction.

**Table 2.** Ecological analyses of careseeking sex ratio and selected categorical exposure variables at national level

| VARIABLES | CATEGORIES | NUMBER OF COUNTRIES | MEAN | STANDARD DEVIATION | P–VALUE* |
|---|---|---|---|---|---|
| World region | CEE & CIS† | 6 | 0.93 | 0.09 | |
| | East Asia & Pacific | 4 | 1.01 | 0.06 | |
| | Eastern & Southern Africa | 15 | 1.00 | 0.04 | |
| | Latin America & Caribbean | 6 | 1.03 | 0.06 | 0.055 |
| | Middle East & North Africa | 3 | 0.92 | 0.06 | |
| | South Asia | 5 | 0.96 | 0.06 | |
| | West & Central Africa | 18 | 0.97 | 0.08 | |
| Country income group | Low | 28 | 0.98 | 0.07 | |
| | Lower–middle | 20 | 0.98 | 0.06 | 0.398 |
| | Upper–middle | 9 | 0.95 | 0.08 | |
| Gender Development Index groups‡ | 1. High equality | 7 | 0.98 | 0.05 | |
| | 2. Medium to high equality | 3 | 0.96 | 0.07 | |
| | 3. Medium equality | 9 | 0.98 | 0.08 | 0.995 |
| | 4. Medium to low equality | 8 | 0.98 | 0.05 | |
| | 5. Low equality | 28 | 0.98 | 0.07 | |
| Predominant religion | Christian | 35 | 1.00 | 0.05 | |
| | Muslim | 19 | 0.94 | 0.07 | 0.011 |
| | Other | 3 | 0.97 | 0.11 | |

*P–value based on ANOVA.

†CEE & CIS: Central and Eastern Europe and the Commonwealth of Independent States.

‡Gender Development Index groups: Countries are divided into five groups by absolute deviation from gender parity in HDI values. Group 1: countries with high equality in HDI achievements between women and men (absolute deviation of less than 2.5%); Group 2: medium to high equality (absolute deviation of 2.5–5%); Group 3: medium equality (absolute deviation of 5–7.5%); Group 4: medium to low equality (absolute deviation of 7.5–10%); and Group 5: low equality (absolute deviation from gender parity of more than 10%) [20].

**Table 3.** Ecological analyses of careseeking sex ratio and selected continuous exposure variables at national level

| VARIABLES | NUMBER OF COUNTRIES | CORRELATION (95% CI) | P–VALUE* |
|---|---|---|---|
| GDP *per capita* (2012) | 57 | –0.257 (–0.485; 0.003) | 0.053 |
| GDP *per capita* – log (2012) | 57 | –0.190 (–0.429; 0.156) | 0.157 |
| Gini coefficient for income inequality | 46 | 0.306 (0.018; 0.547) | 0.039 |
| Gender Inequality Index (2013) | 50 | 0.074 (–0.208; 0.345) | 0.607 |
| Gender Development Index (2013) | 50 | 0.090 (–0.193; 0.359) | 0.531 |
| Global Gender Gap Index (2014) | 41 | 0.190 (–0.124; 0.470) | 0.231 |
| Muslim (% population) | 57 | –0.361 (–0.568; 0.111) | 0.006 |
| Christian (% population) | 57 | 0.305 (0.049; 0.523) | 0.021 |

CI – confidence interval

*P–value based on Pearson's correlation coefficient.

## DISCUSSION

The analysis of the Demographic and Health Surveys, conducted in low– and middle–income countries, explored the magnitude of gender bias against girls, investigating whether families would be less likely to seek care from appropriate providers for girls with symptoms of fever, diarrhea or pneumonia, compared to boys. We expand upon the existing literature on this topic by calculating a new composite careseeking index encompassing three conditions – diarrhea, fever and suspected pneumonia – and therefore increasing the statistical power relative to earlier analyses in which each condition was treated separately.

We found evidence of gender bias in a limited number of countries. In contrast to the pervasive socio-economic inequalities in careseeking and coverage, gender inequalities in careseeking are modest or even absent in most countries.

A systematic review explored studies on the recognition of signs and symptoms of, and/or careseeking for pneumonia, diarrhea or malaria in low– and middle–income countries. The authors identified seven publications that evaluated careseeking by sex; four which did not find significant differences between girls and boys, two reporting higher prevalence of careseeking for boys (in Burkina Faso and Indonesia),

and one showing higher careseeking for girls, but only for malaria episodes [21]. The mixed results from this review are consistent with our analyses, which do not show a clear pattern of gender bias throughout the world.

At regional levels, we did not identify evidence of gender bias; however, in six countries careseeking was significantly higher for boys, and in two for girls. At the 5% $P$ level, one would expect 1–2 significant pro–boy differences, and another 1–2 pro–girl differences, simply due to chance. We sought interactions between sex and wealth quintiles in careseeking for all 57 countries, but only detected significant interactions (with $P<0.10$) in seven countries, which could have arisen by chance. In addition, interaction patterns were not consistent, sometimes with greater gender gaps in the wealthy, and for other countries with greater gaps among the poor.

The use of a composite careseeking indicator for three common conditions, using data from nationally representative surveys avoid small denominators – a frequent problem in analyses of careseeking – and thus increases statistical power [9]. Nevertheless, in our analyses sample size varied widely between surveys, and countries with the largest surveys such as India, results can be statistically significant even when absolute differences are small.

When comparing our results with the UNICEF analyses on careseeking for separate conditions, we found that three of the six countries we identified as presenting gender bias in the combined careseeking indicator had also been identified as such by UNICEF: Yemen (fever), Egypt (suspected pneumonia) and India (suspected pneumonia and diarrhea) [7]. It is important to highlight that the UNICEF report includes some unofficial health care providers that we did not include (such as shops and traditional practitioners), and that the year of the surveys may not be the same.

We used ecological analyses in an attempt to identify national characteristics associated with gender bias. Surprisingly, we did not detect correlations between careseeking sex ratios and gender inequality indices. A recent study reported a positive association between the Gender Inequality Index with under–five mortality rate for both sexes combined; this association remained after adjustment for GDP per capita, but separate associations with mortality rates for boys and girls were not investigated [22]. The authors speculate that if gender inequality is linked to maternal health, then mortality of boys and girls would be equally affected.

National levels of wealth were not associated with gender bias in careseeking, but bias was more likely in countries with unequal income distributions. We also found that religion was a cultural characteristic that explained part of the variability, with improved careseeking for boys in countries with a higher Muslim population. More research is needed to better understand the effects of religion and culture on careseeking, including whether the ecological association we report here is also found at individual level analyses within a given country, or whether it is due to an ecological fallacy.

Other limitations in the data should be recognized. Differences in careseeking could be due to increased severity of infectious diseases among boys [7], but our results showing similar careseeking rates in most countries suggest that this did not bias the results. Also, information on the incidence of illness and on careseeking patterns is based on maternal recall, which may or may not vary systematically according to child's sex [21].

In addition, a composite index for careseeking does not reflect how different illnesses may be perceived along the spectrum of severity; more detailed analyses might consider only severe cases (such as bloody diarrhea, for example) but this would further reduce the denominator and analyses would only be possible for very large sample sizes.

Lastly, our analyses are limited to the most recent survey per country, so that results on time trends must be interpreted with caution as for some countries the most recent publicly available survey was carried out a decade or more ago, as is the case for India.

## CONCLUSIONS

Our results suggest that, with a few exceptions, the overall frequency of careseeking for common health conditions is similar for boys and girls in most, but not in all countries. Similar results are available for under–five mortality [4,7,23]. Countries where there is evidence of gender bias in careseeking need renewed attention of national and international initiatives, in order to ensure that girls receive adequate care and protection. In addition, more research is needed to understand the reasons behind the different treatment for girls and boys in these circumstances, including a mixture of qualitative and quantitative methods.

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PAPERS

# Integrating palliative care into national health systems in Africa: a multi–country intervention study

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**Background** The WHO is calling for the integration of palliative care in all health care settings globally.

**Methods** A 3.5–year program was implemented in 12 government hospitals, three each in Kenya, Rwanda, Uganda and Zambia. A four–pillared approach of advocacy, staff training, service delivery strengthening and international and regional partnership working was utilized. A baseline assessment was undertaken to ascertain needs, and 27 indicators were agreed to guide and evaluate the intervention. Data were also collected through surveys, interviews and focus groups.

**Results** Palliative care was integrated into all 12 hospital settings to various degrees through concurrent interventions of these four approaches. Overall, 218 advocacy activities were undertaken and 4153 community members attended awareness training. 781 staff were equipped with the skills and resources to cascade palliative care through their hospitals and into the community. Patients identified for palliative care increased by a factor of 2.7. All 12 hospitals had oral morphine available and consumption increased by a factor of 2.4 over two years. Twenty–two UK mentors contributed 750 volunteer days to support colleagues in each hospital transfer knowledge and skills.

**Conclusions** Integration of palliative care within different government health services in Africa can be achieved through agreed interventions being delivered concurrently. These include advocacy at Ministry, Provincial and District level, intensive and wide–ranging training, clinical and support services supported by resources, including essential medicines, and an investment in partnerships between hospital, district and community.

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Globally, over 40 million people currently require palliative care annually [1]. This number will rise with the aging and increasingly multi–morbid population in all regions [2]. Low resource settings account for two–thirds of the global burden of disease [3,4], where 78% of those needing palliative care live, usually presenting with advanced disease [5].

As **Box 1** indicates, the integration of palliative care into health systems in Sub–Saharan Africa (SSA) faces challenges, including poverty, rising communicable and non–communicable diseases, fragile health systems, delayed health–seeking behaviors, poor transport networks, cultural beliefs, conflicts, and lack of access to essential medicines [6,7]. Few African countries have palliative care identified within their national health policies and

**Box 1.** Research in context

Evidence before this study:

- The WHO resolved in 2014 that integration was the only way to ensure universal access to palliative care. The Global Atlas of Palliative Care reveals limited integration and access in Africa.
- The need for palliative care services is strongly recognised within the UN Political Declaration on NCDs. However low resource countries prioritise prevention and cure over palliative care.
- There is little evidence with regard to "best practice" models for integrating palliative care in low resource settings, although several models of specialist palliative care services provide excellent care for a fortunate few.

Added value of this study:

- This palliative care integration initiative was completed after the 2014 WHO resolution, putting us in a unique position to evaluate our programme in the context of the "building blocks" for integration highlighted in this resolution.
- Palliative care can be effectively integrated into different levels of government health systems in sub–Saharan Africa if several interventions are conducted concurrently.
- Advocacy, staff training, mentorship partnerships and improving delivery and supply chain for access to essential palliative care medicines and linkages can enable effective integration of palliative care into generalist healthcare.
- Each setting is unique but core components for integration remain.
- Resource–limited governments can successfully integrate palliative care with preventive and curative care but some funding is required for staff time, training, drugs.
- Utilising mentors from different settings enable mutual learning to take place, including from resource–limited to resource–rich settings.
- The four core intervention approaches utilised in this study should be tested in other national settings.
- This case study is used by the WHO in their guidance on how to integrate palliative care in resource poor countries.

strategies [8]. Only five countries have palliative care integrated in curriculums for health workers [9]. Governments want to provide adequate care for those with life–threatening illnesses, but lack persuasive evidence or funding to effectively deliver palliative care. Centres of palliative care excellence do exist, but their reach is limited, they are often not integrated within the health system and are reliant on external funding [10,11].

Palliative care is on the global health agenda. The WHA resolution of 2014 directed member states to "*integrate evidence–based cost effective and equitable palliative care services in the continuum of care, across all levels of care*" [1]. To achieve Universal Health Coverage, a core component of Sustainable Development Goal (SDG) 3, palliative care is required [12].

A systematic review in 2011 found minimal evidence of effective models of palliative care [13]. An integrated service across all health service levels and settings may be effective in addressing the expanding need [4,14–18]. This paper sets out to provide evidence of impact through a large trial of the integration of palliative care within the health systems of Kenya, Uganda, Rwanda and Zambia.

## METHODS

A 3.5–year program of work jointly led by the University of Edinburgh Global Health Academy, the African Palliative Care Association (APCA) and Makerere University Palliative Care Unit (MPCU) was set up to build integrated models of palliative care provision in 12 hospitals in four countries. The lead partners worked through National Palliative Care Associations (PCA) or the Ministry of Health (MoH). Twelve hospitals, were chosen by the national partners. These included national referral hospitals, regional hospitals and district hospitals. The context of each of the countries is described in **Box 2**.

The program employed a health systems strengthening and capacity building approach, as advocated by the WHO [1,4]. The WHA Resolution called for member states to address the issues of policy, funding, supporting communities, training, supply of essential medicines, control of essential medicines, policy on essential medicines, partnership and the burden of non–communicable diseases [19]. Thus these issues, along with the six building blocks described in the WHO document "Monitoring the Building Blocks

**Box 2.** Context of the intervention

The health systems of the four countries all differ but share characteristics such as low numbers of health workers, and village level health provision operated mainly by Community Health Workers who refer upwards to nurse led health care facilities offering treatment of common diseases, immunization and ante–natal care. They in turn refer to district hospital care through to regional then national tertiary–level referral services. In Uganda, Zambia and Kenya patients could self–refer through the system, but in Rwanda patients were required to pass through each level. In Zambia faith agencies provide an especially significant proportion of health care in addition to the government, in Kenya the devolved structure means health budgets are held at county level. Tertiary and national hospitals are complex, and carry a significant burden of disease but district hospitals offer a closer link with lower level health centers, and greater potential to access the enormous unmet need for palliative care in the community.

of Health Systems" helped to focus a four–pillared multi–layered approach of advocacy, staff capacity, service delivery and partnership, in the integration process (**Table 1**) [20].

An initial baseline was undertaken around each hospital to ascertain the nature and extent of palliative care provision. Twenty–seven key indicators were developed to guide the intervention and act as outcome measures (see Appendix S1 in **Online Supplementary Document**). To build capacity within the existing systems, the 12 hospitals and their community catchment areas were supported to chart their vision for integrated palliative care. Hospitals remained responsible for all staffing costs while the program supported capacity building and training. During the intervention, quantitative and qualitative data were collected through surveys, pre and post training course questionnaires, interviews and focus groups and Most Significant Change methodologies [21]. A detailed final evaluation, utilizing both quantitative and qualitative data collection was undertaken and summarized in this paper and further in depth results will be reported elsewhere.

## RESULTS

Palliative care was integrated into each hospital in different ways. Rapid integration tended to occur where there was pre–existing exposure to palliative care. National level hospitals were slower to achieve integration because of their size and complexity. Results are reported according to the four intervention approaches.

### Pillar 1: advocacy

Advocacy achieved change at community, regional and national levels. Regionally a 'Consensus Statement for Palliative Care Integration into Health Systems in Africa' was adopted at the 2013 APCA hosted African Ministers' meeting, committing to the ongoing integration of palliative care in each country repre-

**Table 1.** The four–pillared multi–layered approach adopted for integrating palliative care in health care

| | |
|---|---|
| **Advocacy** | Supported at three levels – country, hospital and community. A whole system approach was advocated for, including provision of palliative care in policy, access to medications, and inclusion in curricula and services. |
| **Staff capacity** | A critical mass of generalist and specialist staff trained within each hospital network. Training included: |
| | ***Basic training*** to a critical mass of staff of different cadres (supported by clinical placement modeling) |
| | ***Advanced training*** on complex interventions and care strategies, included research and children's palliative care |
| | ***Training of trainers*** to cascade training to others |
| | ***Specialist training*** for the future leaders of palliative care services. Where available, clinicians were sent for Diploma, Degree and Masters training |
| | ***Community training*** raising awareness to community workers within the existing health system |
| **Service delivery** | Development of local policy, standards and protocols, improving and connecting patient pathways, referral systems and supporting frameworks for regular and reliable morphine procurement, provision and prescribing. |
| **Partnership** | Multi–layered partnerships including: |
| | -Partnerships between the lead organisations |
| | -Partnerships with the National Palliative Care Associations and the MOHs |
| | -Partnerships with each hospital |
| | Mentorship hubs – each hospital partnered with a small team of UK mentors who were experienced palliative care professionals, for guidance and support |

sented [22]. Palliative care was included in the national plans of Kenya and Uganda and the National Health Strategic Plan in Zambia and Rwanda [23,24]. In Rwanda, the project directly led to palliative care being included in the Health Management Information System, national non–communicable diseases division planning, and to the adoption of national clinical guidelines disseminated to the hospitals.

Across the 12 hospital sites, 4153 community members attended advocacy awareness training through 73 events. These included sensitization for the hospital community and their referring hospitals and health centers, and training of Community Health Volunteers. Media coverage and community events, including burials and church services, increased coverage with Rwanda reporting 10 000 radio listeners supported by the national cellphone provider. Senior staff participation enhanced advocacy.

## Pillar 2: Building staff capacity through training and mentoring

By the end of the program, national partners were sustainably delivering training. Clinical placement sites were developed in each country providing centers of excellence to model best practice. 781 health professionals were trained in the 12 hospitals and their referring hospitals, of whom 520 also completed clinical placements where staff were mentored by clinical experts at in–country clinical placement sites (some already existing and others strengthened for the program) or the MPCU center of excellence in Uganda where all Rwanda trainees attended. A further 123 were trained as trainers. Additional requests from hospitals for training saw 39 staff trained in children's palliative care, 81 in research skills and 60 in morphine procurement and prescribing (the latter as a national initiative in Rwanda). Training, utilizing a combination of classroom, ward sessions and clinical modeling, extended both depth and breadth of knowledge, establishing a critical mass of trained personnel with knowledge, skills and resources and also changed attitudes and values. Basic and advanced training took place across different cadres (**Table 2**).

Pre and post course questionnaires (immediate post training and six months post training) demonstrated that participants had improved their knowledge and skills, with improved performance and confidence. The final evaluation showed that training led to a step–change in clinical skills, including the ability to identify those requiring palliative care, to discuss with patients, and a better understanding of pain management. A trainee's response of "*Pain is what the patient says it is,*" captured this shift; revealing how this commonly taught concept is becoming embedded in practice. Health workers described how this changed their clinical practice, by allowing patients to take extra doses of analgesia for breakthrough pain "without fear". This included understanding children's pain. A senior nurse explained of her staff:

*"Before they did not attend to children's pain because they didn't imagine they feel the level of pain that they do and they didn't know how to score it. But now they manage pain even in children."* (Nurse, Uganda)

Training created a change in mind set which practitioners considered, a *"life changing"* experience: "*before I thought it (palliative care) was about giving up*" explained one of the nurses from Kenya until she realized that palliation was active care. Training enabled staff to communicate better:

*"Now I have the heart of listening to the patients, talking, counselling and assessing them."* (Nurse, Uganda)

Thirty–six health professionals undertook Palliative Care Diplomas and Degrees which gave staff increased status within their hospitals, and enabled staff to adopt a "whole systems approach" positioning them as palliative care leaders and advocates:

*"The training helped me to approach people in politics, or senior level. Before, the chief county officer would not take my phone calls. They have also recognised us as specialists. Now I am interested in the strategic plan."* (Specialist trainee, Kenya)

**Table 2.** Numbers of health professionals trained

| Training | Total | Cadre | | | |
|---|---|---|---|---|---|
| | | Clinical – officer | Nurse | Doctor | Others |
| Basic training: Introductory training in palliative care | 614 | 43 | 391 | 49 | 131 |
| Advanced training: | | | | | |
| -Research training | 81 | 3 | 36 | 7 | 35 |
| -Children's palliative care | 39 | 1 | 27 | 9 | 2 |
| -Pharmacy training | 34 | 0 | 0 | 0 | 34 |
| Hospital Directors – management | 26 | 0 | 0 | 0 | 26 |
| Training of trainers | 123 | 8 | 83 | 13 | 19 |
| Specialist training; diploma/degree | 36 | 2 | 27 | 4 | 3 |

*"Doctors have recognised that me and the others [specialist trainee colleagues] are experts in some PC areas… people ask us to do counselling, especially."* (Nurse, Zambia)

Training was one component of building staff capacity, the other was on–site mentoring. Mentoring was provided by national partners, lead partners and overseas mentor colleagues. International mentors passed on their expertise through on–the–job training and clinical modeling. As a Kenyan health worker explained, this was essential for consolidating the clinical skills training:

*"KEHPCA [the Kenyan Palliative Care Association, who delivered the training course] gave us the theory, and mentorship gave us the practice."* (Health worker, Kenya)

Palliative care teaching was embedded into pre–service, in–service and postgraduate health worker training institutions. The program successfully supported integration of palliative care into the undergraduate medical curriculum at the University of Zambia (UNZA), School of Medicine and the Faculty of Health Sciences at Moi University, Kenya. A Curriculum Toolkit: *"A practical guide to integrating palliative care into Health Professional Education"* (*http://www.ed.ac.uk/global-health/research/project-profiles/health-systems-strengthening/thet/resources*) was developed at the request of a country partner university, to give practical guidance and resources regarding the integration of palliative care core competencies into curriculums for health care workers.

### Pillar 3: service delivery

Improved outcomes were achieved across three core areas: improved identification of more patients for palliative care, development of management/referral systems, and morphine prescribing.

### Identification of patients for palliative care

Overall, 2.7 times more patients were identified for palliative care, with some hospitals seeing an increase of 13 times and others formally identifying patients for the first time (**Figure 1** and **Table 3**).

Many hospitals adopted a model of a named "link–nurse" in each ward or unit liaising with and supported by a specialist palliative care team. These nurses identified patients in their wards, and managed their care until their complexity required a more specialist input.
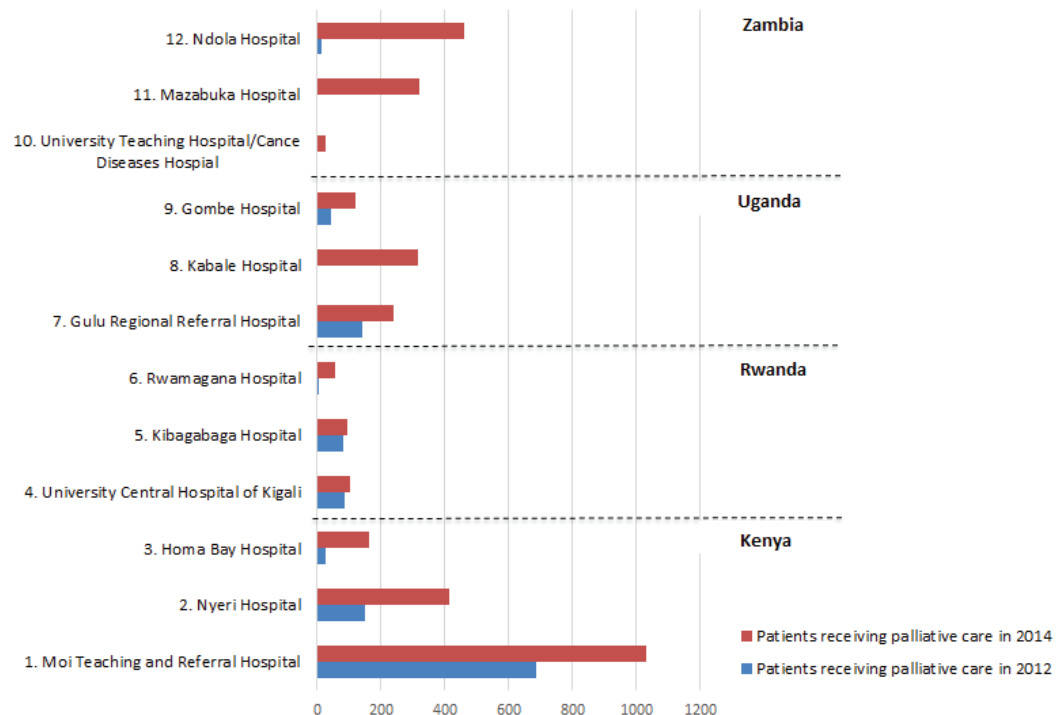


**Figure 1.** Number of patients using the palliative care services at the 12 project hospitals.

**Table 3.** Patients identified for palliative care in the 12 hospitals by the Palliative Care Team

| | PATIENTS IDENTIFIED FOR PALLIATIVE CARE | | |
|---|---|---|---|
| | 2012 | 2014 | Ratio 2014/2012 |
| **Kenya:** | | | |
| 1. MTRH | 687 | 1030 | |
| 2. Nyeri Hospital | 151 | 413 | |
| 3. Homa Bay Hospital | 27 | 163 | |
| *Total Kenya* | 865 | 1606 | 1.85 |
| **Rwanda:** | | | |
| 4. CHUK | 85 | 104 | |
| 5. Kibagabaga Hospital | 80 | 92 | |
| 6. Rwamagana Hospital | 4 | 56 | |
| *Total Rwanda* | 169 | 252 | 1.5 |
| **Uganda:** | | | |
| 7. Gulu Regional Referral Hospital | 140 | 240 | |
| 8. Kabale Hospital | – | 315 | |
| 9. Gombe Hospital | 43 | 121 | |
| *Total Uganda* | 183 | 676 | 3.7 |
| **Zambia:** | | | |
| 10. UTH/CDH | * | 26 | |
| 11. Mazabuka Hospital | * | 319 | |
| 12. Ndola Central Hospital | 11 | 462 | |
| *Total Zambia* | 11 | 807 | 73.3 |
| *Total all countries* | 1228 | 3341 | 2.7 |

*No formal palliative care team on site thus no patients recorded as being identified.

These systems of early identification became core to the integration of palliative care, preventing unnecessary medical interventions and starting discussions between patients, families and clinical staff on patient needs, goals and progress. They also facilitated integration, through development of an extended team and a referral network. One Kenyan health care worker commented:

*"Before I didn't know how to liaise with the PC team. But then they gave us the mandate to be part of them. I could call them when I'm not able to handle some patients. The first time I needed to counsel a patient I called someone [from the core team] to assist me, then I did it myself, and then when someone asked me I did it with her."* (Nutritionist, Kenya)

The researchers advocated for documentation of palliative care needs and services by nurses in case notes to become routine practice, so that patients receive appropriate and documented care. This remained challenging: at the end of the project 75% had information recorded (almost always by doctors) in their clinical records. In Rwanda a more advanced system is being trialled enabling health workers to write limited information in the notes such that there is a management plan within a national level template.

## Clinical management and referrals

All hospitals demonstrated improved policies and professional standards. The program contributed to 35 different strategies, standards, and protocols, including referral documentation, patient registers, assessment forms, clinical and audit protocols, national training materials and policies. Eleven new palliative care clinical protocols were adapted (from MPCU) and adopted as national documents in three countries, with adoption ongoing in the remaining country.

All hospitals developed stronger referral linkages, with central points for receiving and logging referrals. Some had a clear written referrals process. Most had a telephone referral system working alongside. An innovative approach was the establishing of a 24–hour telephone hotline at MTRH, Kenya, advertised on posters throughout the hospital for internal referrals, and given to patients on discharge.

## Morphine prescribing

Six of the 12 hospitals had no oral morphine available initially; all had it by the end. Morphine consumption and consistency of supply increased in all hospitals (**Table 4**). Specific prescribing training and continuing medical education sessions conducted by national partners, trainers, visiting mentors and by staff

**Table 4.** Oral morphine consumption in hospitals

| | Oral morphine consumption (mg) | | Ratio 2014/2012 |
| --- | --- | --- | --- |
| | 2012 | 2014 | |
| Kenya: | | | |
| Moi Teaching and Referral Hospital | 1 560 000 | 3 200 000 | |
| Nyeri Hospital | 40 000 | 220 000 | |
| Homa Bay Hospital | 0 | 66 500 | |
| Kenya total | 1 600 000 | 3 486 500 | 2.2 |
| Rwanda: | | | |
| University Hospital of Kigali | 0 | 77 800 | |
| Kibagabaga Hospital | 0 | 69 690 | |
| Rwamagana Hospital | 0 | 1920* | |
| Rwanda total | 0 | 149 410 | – |
| Uganda: | | | |
| Gulu Regional Referral Hospital | 0 | 198 225 | |
| Kabale Hospital | 36 000 | 336 000 | |
| Gombe Hospital | 39 000 | 118 000 | |
| Uganda total | 75 000 | 652 225 | 8.7 |
| Zambia: | | | |
| University Teaching Hospital/ Cancer Diseases Hospital | 320 000 | 402 230 | |
| Mazabuka Hospital (available from June 13) | 0 | 37 915 | |
| Ndola Central Hospital | 5 200 | 93 340 | |
| Zambia total | 325 200 | 533 485 | 1.6 |
| Total countries | 2 000 200 | 4 821 620 | 2.4 |

of the nascent palliative care teams broke down myths about morphine and empowered staff to prescribe and dispense morphine. A Ugandan nurse described how since the training morphine orders no longer expired on shelves but were prescribed by staff no longer fearful of morphine.

In Rwanda, the program facilitated a national morphine framework meeting which resulted in the first national procurement agreements for morphine. The MoH requested further training for doctors and pharmacists, who then facilitated morphine prescription as a first–choice therapy for unrelenting pain. There was a shift in attitude and understanding in all countries. One doctor explained:

"*As of now, I have taught the group that there should be no pain in any patient. Now we are able to prescribe morphine.*" (Doctor, Kenya)

While managing morphine distribution, legislation and regulation was challenging but innovative strategies emerged:

"*They (pharmacists who have undergone training) could produce it and just give it to the other pharmacists. Or weigh it and send it to the other pharmacies. This would help a great deal – because I have come across patients who do not get morphine at the weekends.*" (Senior Doctor, Kenya).

The most remarkable change reported through the use of morphine was "silence". Health workers in a number of hospitals poignantly said it was the absence of patients crying in pain on wards that spoke most powerfully of palliative care:

"*The staff are starting to understand that patients should not be screaming and crying in hospital!*" (Lead Nurse, Kenya)

Health workers reported that not only patients' physical pain but also holistic pain was addressed and relieved,

"*Initially we didn't know we were supposed to take care of pain for all of a patient's life. As of now, I have taught the group that there should be no pain in any patient.*" (Doctor, Kenya)

"*I learnt about holistic care and finding out about what the patient needs….treating the patient as a person, not a case. Sometimes you feel you hit a brick wall, but PC taught me there is always something we can do.*" (Medical student, Zambia)

Staff were empowered to broach issues of death and dying and challenge cultural beliefs:

*"I understood PC in a holistic manner not just for dying patients but also the chronically ill. I understood that it meant social, spiritual and psychological support. I (myself) went and spoke in churches, and went with a local organisation to do screening and PC awareness at the churches. Right now I have a passion for PC."* (Social Worker, Kenya)

*"At first people used to think perhaps you are cursing the patient to die to break bad news, now we are breaking bad news we realise it is not true."* (Health Worker, Mazabuka)

Senior staff believed that the integration of palliative care empowered patients, allowing them to plan for the future. Staff described how integrated palliative care enhanced the whole care system. They spoke of no longer feeling helpless, because they could do something for patients and engage with families better. Their training helped them outside their work:

*"The training was fantastic – life–changing. Not only in the workplace, but also at home."* (Pharmacist, Kenya)

### Pillar 4: partnership

Partnerships were developed at four levels. Regionally, hospital staff were supported to meet at national and international workshops and conferences on palliative care to present work and participate in specialist training. These included the Kenya and Uganda national palliative care conferences, the African Palliative Care Association conference, the International Multidisciplinary Pain Congress, the University of Edinburgh Global Palliative Care symposium, the International Conference on Advances in Palliative Care, and Pain and Patient Symptom Management.

At national level national partners, who were the lynchpin of project delivery and the main link between the steering group and the local hospitals, received advocacy training and funding both within national associations and within the government systems. In three countries the National Associations were a valuable asset to hospitals. In Rwanda the Ministry of Health took on the support role delivered by other country national associations At hospital level staff worked with local stakeholders, community volunteer workers, their referring hospitals and clinics. International mentors partnered with hospitals and national associations. Mentorship was delivered at different levels: 22 mentors from the UK visited hospitals, providing 621 on–site mentorship days and 145 days distance support; south–to–south mentorship was provided by the MPCU team and by National Associations and palliative care coordinators. Mentorship allowed staff to see new ways to use existing resources, while exchange visits to other facilities to see clinical practice stimulated quality improvement ideas. UK mentors spoke of reciprocal learning. For example, the major role of the family in the SSA context, the need for innovation in resource–constrained settings, and the impact of total integration into community hospitals, all provided models which mentors felt could influence UK care.

## DISCUSSION

The program helped establish systems of integrated care in 12 test sites across four countries. Multi–level advocacy raised the profile of palliative care and resulted in inclusion of palliative care in national plans, clinical guidelines, and health information systems. Training, modeling and mentoring established a workforce of generalist clinicians practising integrated palliative care. Morphine was more effectively procured and utilized in all hospitals and was often used as a step 2 medication in low dose (in keeping with common practice in Africa for a 2 Step approach). Systems to identify need and improve coverage and referral were created. Ownership of the program by each hospital and district health service bred success.

Narrative [11] and systematic reviews [13] have assessed the current degree of integration of palliative care in SSA [25]. This project went beyond mapping and model description into implementing integrated palliative care into national health systems [20]. We found that while weak health systems impede integration, integration can result in a stronger system as staff trained to provide palliative care are more motivated and provide holistic care, and greater staff, patient and family communication. National associations can have a key role and this was different in each of the 4 countries with particular impact from stable and well integrated associations. However there were challenges with funding and local politics. Government leadership and ownership of palliative care is essential.

The training program emphasized delivering outcomes rather than course content. This was achieved through mentors and local trainers prioritising embedding knowledge and skills into ongoing practice and supporting clinical placements. Negative beliefs about morphine, beliefs that curses are real causes

of disease, and complex beliefs in the power of traditional medicine frequently existed [26]. These potential barriers were addressed and incorporated into training and sensitization talks with a wide range of staff, including mortuary attendants, and reception staff in the outpatient departments.

Identifying which patients might benefit from palliative care was a key and challenging component of training. We drew on two recent literature reviews [27,28], APCA guidance documents, a census study from Mulago Hospital, Uganda, and an evaluation of the MPCU model of link nurses to inform the scale up within the program [15,17,18]. Creating confidence in staff in all wards to identify patients who would benefit from palliative care greatly increased access. After staff training, patients received many aspects of palliative care support in the wards, and not necessarily referred to specialist palliative care services. Thus the number of patients receiving palliative care was probably under–documented. A previous study at Mulago Hospital Uganda has suggested that 75% of palliative care patients can have their care provided by trained ward teams without specialist referral [17]. Issues of quality and ongoing support pathways of care require further study.

It is more challenging to train and support generalists than to extend specialist palliative care through outreach work [11,29]. Integrated care has resulted in increased morphine prescription in faith–based hospitals in SSA [30]. We have importantly demonstrated this is also possible in government hospitals if Ministries of Health are committed to achieving integrated care, even with minimal resources.

Resource constraints in SSA mean that financing of palliative care is contentious. External financing for PC has been substantial but integrated sustainable national financing has been more difficult to establish [31]. This program significantly contributes to the financing debate for palliative care by effecting a low–cost integration of care into national systems and into national health plans so that funding can be identified [32]. One setting, Kibagabaga, showed significant cost savings by early pain control and shortening admissions [33]. This program suggests that advocacy and also national commitment to act are needed, alongside modest funding allocated within national and district health budgets.

### Strengths and limitations

This program was set up as a multi–country intervention to test integration strategies for palliative care in different locations and sizes of facilities. We did not have a control arm. We recognize that no change happens in isolation and the changes that this program brought about must be interpreted in the context of the dynamic health systems of each country. We did not collect health–related quality of life information directly from patients. We state the need to view the impact of this program in the context of the overall developments within each country, and to assess long–term outcomes.

### Implications

No one model of palliative care service provision fits every setting [25]. Innovations that embed palliative care values and integrate palliative care as part of good clinical practice within all specialties, cadres, and for all staff and for all diseases are indicated. The World Health Assembly resolution called for the Director General to "*encourage research on models of palliative care that are effective in low and middle–income countries, taking into consideration good practice*" [1]. This paper is one of the first programmes to report on integrating services in different hospitals in different countries in SSA. It provides a blueprint for integrated care provision throughout Africa. Specific recommendations which directly responds to the WHA Resolution are listed in **Table 5**.

## CONCLUSIONS

Multi–level advocacy can facilitate country improved access to palliative care. Health systems need a convergence of national policies and regulations for promoting palliative care, continuous staff training and support and reliable procurement, availability, and access to, and use of, palliative care drugs in all areas all of which require long term funding. The concurrent advocacy, training, and improvements in service delivery and drug availability over the three years of this project did make a difference in the four countries studied. Further monitoring of the longer term benefits is required.

Good quality palliative care requires early detection of patients: long distances to health care facilities deters uptake, so engagement of all staff, clear referral pathways, and reliable links between community and hospital are needed. The approach to advanced life limiting illness and pain that is flexible, responsive,

facilitative and creative can make a huge difference for patients, for providers and for communities. The WHO published in 2016 a practical manual on how to plan and implement palliative care services, integrated into existing health–care services, at national or subnational level. It contains some specific examples from this study and much useful guidance to make integration a reality in resource poor settings. (WHO 2016) (**Box 1**).

Each of the 12 participating hospitals exists as part of a referral system and activities were implemented across this wider system. A list of the participating hospitals is shown in **Table 6**.

**Table 5.** Recommendations

| Governance and leadership | Ministries of Health (MoH) need to integrate palliative care services in country policies, strategic plans and budgets. Ministries should drive this integration with a nominated person responsible for national palliative care who can work with all the stakeholders, including national associations and the various external donors and other development partners who frequently deliver standalone palliative care services. |
|---|---|
| Service delivery | Patients with palliative care needs are found throughout all levels of the health care system. Therefore care should be integrated into each level (tertiary, secondary and primary levels) and across all life–threatening illnesses, with good referral networks for continuity of care. Clear service delivery protocols should be in place. Palliative care interventions should be based on the needs of patients and their families and not limited by disease or health care setting. |
| Human Resources | A critical mass of staff should be trained to understand and deliver a palliative care approach in all settings. Senior hospital staff should be included for effective integration. Both ongoing mentorship and modeling of palliative care are important to ensure the sustainability of services and enable the necessary behavior change in clinicians. The MoH should also ensure strategic deployment of palliative care trained staff with palliative care being incorporated into deployment planning, job descriptions, and training programmes. |
| Finances | This program showed that it is possible to integrate palliative care by utilizing existing staff and procurement systems. The main financial implications elate extra staff hours, staff capacity building for PC, mentorship and supervision all of which need to addressed in MoH budgets. The project also reveals that districts are willing to incorporate palliative care in their budgets once they obtain an understanding of the importance of the service. |
| Medicine, vaccines and technology | The MoH should ensure that palliative care essential medicines are on the country essential medicines list and that the necessary documentation and regulation are in place to make these medicines available and accessible to all who need them over 24 hours. They should also ensure that there is sufficient capacity for prescribing (by encouraging, for example, nurse prescribing) and resilient procurement processes with special attention to oral morphine. |
| Strategic information | The MoH should include palliative care in the Health Management Information Systems, such that all facilities are required and supported to report palliative care interventions. This should be wider than referral to specialist services. National level tools for data collection along with support and supervision will also be needed. The development of an evidence base which is contextual, high quality and value based should be resourced. |

**Table 6.** List of 12 participating hospitals

| County | Level | Hospital | Beds |
|---|---|---|---|
| Kenya | National | Moi Teaching and Referral Hospital (MTRH) | 800 |
| Rwanda | National | Centre Hospitalier Universitaire Kigali (CHUK) | 600 |
| Zambia | National | University Teaching Hospital (UTH) | 1600 |
| Kenya | Regional | Nyeri County Teaching and Referral Hospital | 300 |
| Uganda | Regional | Gulu Regional Referral Hospital | 300 |
| Uganda | Regional | Kabale Regional Referral Hospital | 250 |
| Zambia | Regional | Ndola Central Hospital (NCH) | 800 |
| Kenya | District | Homa Bay Country Referral and Teaching Hospital | 300 |
| Rwanda | District | Rwanangama Hospital | 220 |
| Rwanda | District | Kibagabaga Hospital | 230 |
| Uganda | District | Gombe General Hospital | 100 |
| Zambia | District | Mazabuka District Hospital | 160 |

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## RESEARCH THEME 7: HEALTH TRANSITIONS IN CHINA

*(continued on the inside)*