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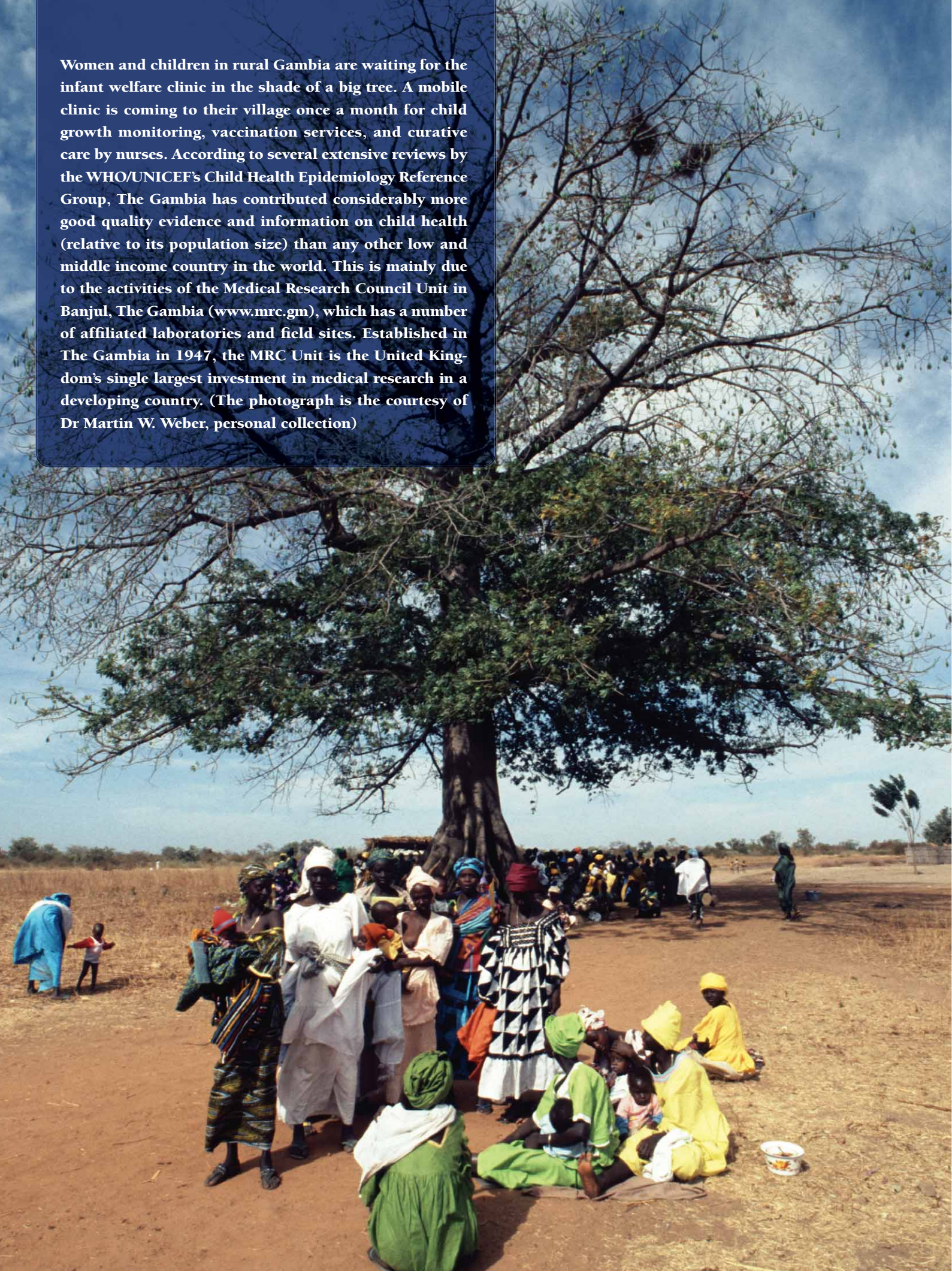

Women and children in rural Gambia are waiting for the infant welfare clinic in the shade of a big tree. A mobile clinic is coming to their village once a month for child growth monitoring, vaccination services, and curative care by nurses. According to several extensive reviews by the WHO/UNICEF's Child Health Epidemiology Reference Group, The Gambia has contributed considerably more good quality evidence and information on child health (relative to its population size) than any other low and middle income country in the world. This is mainly due to the activities of the Medical Research Council Unit in Banjul, The Gambia (www.mrc.gm), which has a number of affiliated laboratories and field sites. Established in The Gambia in 1947, the MRC Unit is the United Kingdom's single largest investment in medical research in a developing country. (The photograph is the courtesy of Dr Martin W. Weber, personal collection)

Journal of Global Health: The Mission Statement

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Photo: courtesy of Dr Martin Willi Weber, personal collection

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* will publish 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 will be dedicated to a specific theme, which will be introduced in the editorial and in one or more viewpoints and related articles. The news section will bring 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 will 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 will 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*

EDITORIAL

Developing biobanks in developing countries

Igor Rudan, Ana Marušić, Harry Campbell

We call for the development of human biobanks in developing countries and describe several examples from low income countries which are already building their own biobanks. Developing human biobanks in developing countries requires strengthening of the research capacity to use the new technologies, as well as a shift in research investment priorities in order to reduce the inequity in international research that currently exists. A responsible approach from low-income countries to ethical issues will be another pre-requisite to the success of the 'hypothesis-free' research that will target the needs of the world's poor.

The sequencing of the human genome, completed and reported a decade ago, increased the potential of what could be described as a 'data-driven' or 'hypothesis-free' approach to biomedical research (1,2). The rise of powerful new technologies for high-throughput analysis of human genetic material resulted in an avalanche of genome-wide association studies (GWAS), which currently contribute to an unprecedented progress in assigning 'biomedical' functions to human genes (3). With massively increased capacity for studying human genetic material, which grew by several orders of magnitude over the past decade, while falling dramatically in price (4,5), we can now measure human genetic make-up more precisely than other human traits or environmental exposures that were traditionally studied in biomedical research – such as dietary habits, blood pressure or biochemical studies of the levels of proteins in the blood (4). Thus far, companies such as Illumina and Affymetrix have managed to provide tools in a form of chip-based technology, which are helping to understand common human genetic variation. Soon it will be possible to sequence the entire human genome, letter-by-letter, at a price under US$ 5000 (€ 3575), and the key limit to further biomedical discoveries may be imposed by the limited capacity of contemporary computers to handle this massive amount of information (5).

In addition to this progress, great advances were made in the high-throughput analysis of so-called '*-omics*' traits – thousands of circulating molecules and metabolites that were jointly named the 'metabolome', 'proteome', 'lipidome', or 'glycome' (6–8). An explosion of information that can now be collected and analysed for each individual led to the development of large 'human biobanks', the largest of which are catalogued by the Public Population Project in Genomics (or P3G) (9). These are repositories of human DNA material and plasma samples collected from large number of individuals and stored anonymously along with other information on their lifestyle, diet, anthropometric and physiological measurements, genealogies and psychological well-being. These biobanks all have several things in common. Firstly, they share the principle of adherence to rigorous ethical principles for recruiting participants and for using and handling the collected information. Secondly, they are very large and store information on many (tens of) thousands of individuals. Thirdly, they provide researchers with an opportunity to maximise the research and clinical and public health translation potential from the new high-throughput research technologies, which require such biobanks to generate important new health knowledge.

Biomedical research that relies on the application of high-throughput technologies in human biobanks can be described as 'data driven', 'hypothesis-free' science. Traditionally, the advancement of science relied on the accumulated, existing knowledge, which was then used by the researchers to generate and test further hypotheses, thus advancing their field further. This alternate paradigm of biomedical research that relies on human biobanks is not dependent on 'a priori' hypotheses, because it can simply apply rigorous statistical methods to search for apparent associations between thousands or millions of variables that were measured simultaneously in a very large sample of participants, using exceptionally precise (and increasingly inexpensive)

The diseases that are currently being studied by the wealthy nations would have been almost entirely 'invisible' to selection pressures. This may be one of the reasons why the results of genome-wide association studies have not yet found strong genetic effects that could be easily translatable into clinical practice and commercialized.

measurement tools, while correcting for and discarding false positive results expected due to multiple testing (10).

What is so appealing about this 'hypothesis-free science'? Firstly, it is virtually free of human bias, opinion, or imbalanced interpretation. It is typically based on extremely accurate measurements, often using very large sample sizes generated through international collaboration of many centres that applied the same measurement methods and a common analysis plan, so that the results are directly comparable, relatively free from bias and confounding and not subject to sampling variations due to small sample sizes. Many recent successes of this 'hypothesis free' approach have also exposed that the science of the 20th century – where many small research groups were working in isolation from each other, using small sample sizes and publishing their results independently of each other – was much more likely to report false positive results (11). It was quite an embarrassment to the field to realize that the vast majority (more than 95%) of the reported results on associations between genes and human traits and diseases in the period before 2007, when the rise of genome-wide association studies begun, were not replicable in much larger and better designed studies (11). Secondly, and equally importantly – 'hypothesis-free' studies do not depend on previous knowledge, thus allowing large leaps forward in scientific discovery, and unexpected and exciting new breakthroughs in understanding (12). However, there is still an important place for hypothesis-driven experiments in following up these findings to understand their full significance in terms of improved knowledge of underlying pathophysiological mechanisms or their health impact if translated into clinical guidelines or public health action.

However, the current state of 'hypothesis free' science that relies on human biobanks is not free from concern. A quick look at the biobanks listed in the P3G observatory shows that nearly all of them have been developed to address the health problems relevant to the minority of people living in wealthy countries, mostly the complex chronic non-communicable diseases of late onset. This reflects the disease burden in these countries and also the potential for research commercialization to address these problems. Ten years after the human genome has been sequenced there are still hardly any biobanks in low and middle income countries. Even among those that exist, only a few seem to address the problems of the poor, which contribute to the majority of global burden of disease. A recent study showed that that nearly all the progress made by the powerful new high-throughput research technologies was currently confined to wealthy countries and their health needs (13).

The human genome has been shaped through continuing struggle of humanity to survive among many other species and in challenging environmental conditions. The strongest effect of human genes should therefore be expected to ensure successful conception and intrauterine growth and development, safe and full-term delivery and resistance to infectious diseases of childhood and early adulthood. These were historically the main selective pressures that could significantly shape the human genome. They are also still the main contributors to the burden of disease in many developing countries today, but they have not yet been the main focus of interest of human biobanks. The diseases that are currently being studied by the wealthy nations would have been almost entirely 'invisible' to selection pressures. This may be one of the reasons why the results of genome-wide association studies have not yet found strong genetic effects that could be easily translatable into clinical practice and commercialized (14). Because of this, some opinion leaders are beginning to question this approach (14,15).

We believe that research into health problems of low income countries and the poor may be a better placed endeavour for human biobanks, and it may result in more obvious successes. Some experts have already proposed this, too, based on other considerations, such as needs, feasibility and equity (16–18). We call for the development of human biobanks in developing countries, and praise several examples from low income countries which are already building their own biobanks (19,20). However, this will require strengthening of the research capacity in many low-income countries to enable them to use the new technologies. It will also require a shift in research investment priorities in order to reduce the inequity in international research that currently exists. Finally, a responsible approach from low-income countries to ethical issues will be another pre-requisite to the success of the 'hypothesis-free' research that will target the needs of the world's poor. We explore this topic in the viewpoint (21) and two research articles in this issue of the Journal (22,23).

We believe that research into health problems of low income countries and the poor may be a better placed endeavour for human biobanks, and it may result in more obvious successes.

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Africa

Vaccine contributes to dramatic reduction in meningitis in 3 African nations

Though Burkina-Faso, Mali and Niger form part of a belt across Africa traditionally associated with high rates of meningitis, statistics show that this year the rates of meningitis A are the lowest ever recorded during an epidemic season. This is the result of the successful introduction of a new vaccine MenAfriVac™. Nearly 20 million people were vaccinated in a massive immunization campaign in these three countries. New analyses published in the journal *Health Affairs* shows that introducing this vaccine in seven highly endemic African countries could save as much as US$ 300 million (€ 210 million) over a decade and prevent about 1 million cases of disease. To bridge the funding gap of US$ 475 million (€ 332 million) for scaling up the programme, the GAVI Alliance has contributed US$ 100 million (€ 70 million) for the campaigns in Cameroon, Chad and Nigeria. Even though the vaccine is highly affordable at less than US$ 0.50 (€ 0.35) per dose, the significant funding gap needs to be closed if the vaccine is to be rolled out in all 25 countries of the meningitis belt by 2016.

Investing in child health: promises of most African governments are not being kept

A report by the African Child Policy Forum that ranks the performance of 52 African governments on the basis of their spending in the key sectors that affect child welfare reveals that most countries allocated only between 4% and 6% of their national budget to health in 2008. This is well below their commitment to a target of 15%. The survey indicates that the governments of Tanzania, Mozambique, and Niger are the most committed in terms of using available resources for the wellbeing of children. Sudan ranks at the bottom, along with Guinea-Bissau, Eritrea, Burundi, Democratic Republic of Congo, Comoros, Sierra Leone, Angola and the Central African Republic. The report suggests they were ranked unfavourably because of low levels of their investments in sectors benefiting children. A declining trend of their allocations over the years and their relatively high military expenditure also contributed to low rankings.

African Development Bank estimates that one in three Africans is now middle class

A recent report by the African Development Bank indicates that one in three Africans is now middle class. This rising group of consumers is expected to rival those of China and India. Record numbers of people in Africa own houses and cars, use mobile phones and the internet and send their children to private schools and foreign universities. The growth rate of the middle class over the past 30 years was about 3.1%, which is slightly faster than that of the total population. Tunisia, Morocco and Egypt had proportionately the largest middle classes in Africa, while Liberia, Burundi and Rwanda had the smallest. The African middle classes are more likely to have jobs with regular salaries or to own small businesses. They tend not to rely entirely on public health services and often seek more expensive medical care. The middle classes tend to have fewer children and spend more on their nutrition and schooling. However, the report also notes that poverty remains deeply entrenched, with more than half of Africa's population living on less than US$ 2 (€ 1.4) a day.

Africa Progress Panel: private sector is increasingly important for continents' development

A report by the Africa Progress Panel indicates that public-private partnerships (PPPs) for development "are among the most promising, and potentially most effective" options for African growth, and that the private sector was playing an "increasingly important" role. "We have come to the conclusion that all actors (governments, private sector, civil society and international community) can do more to facilitate the spread of successful partnership models across countries and sectors – and that doing so is in their own self-interest," says the report. However, the authors warned that too many companies were not adhering to the UN Global Compact when seeking to invest in the continent. Global Compact is a set of voluntary guiding principles aimed at businesses seeking to work in developing countries. The report also emphasizes that PPPs are not a "panacea for all of Africa's problems." Good governance and strong political leadership are the most important ingredients in African success. International donors also need to fulfil their financial commitments to the continent.

Can mobile phones improve health across Africa?

Countries across sub-Saharan Africa are increasingly turning to cell phones to provide better health care to their population. The help sometimes comes in a form of a reminder text message to pick up a fresh batch of anti-HIV drugs in South Africa. On other occasions a dedicated network provides free voice calls or texts for consultations amongst physicians in Ghana. mHealth is revolutionizing medical practice in Africa and the value of the mHealth sector is estimated to up to US$ 60 billion, with mHealth companies on the rise. A recent report by the World Health Organization's Global Observatory for eHealth indicates that in Africa, mobile penetration exceeds infrastructure development – including paved roads, and access to electricity and the internet.

Asia

Gates Foundation and Abu Dhabi crown prince plan immunization partnership in Asia

The Bill and Melinda Gates Foundation has announced a partnership with Sheikh Mohammed bin Zayed, Crown Prince of Abu Dhabi, through which they would be funding the immunization of about 40 million children in Afghanistan and Pakistan against deadly diseases such as polio, diphtheria, tetanus, whooping cough, pneumonia and hepatitis B. Bill Gates and Sheikh Mohammed bin Zayed have each pledged US$ 50 million (€ 46 million) towards the cause. The Gates Foundation has previously worked with UAE. In 2009 the two parties agreed to jointly fund Dubai Cares, a charity that works to improve the health and education of children in certain countries in the developing world.

Midwives improve survival rates of mothers and infants in Afghanistan

Afghanistan has the one of the highest maternal and infant mortality rates in the world. It is estimates that approximately one of every 60 women dies giving birth, and 129 infants out of every 1000 die in their first year of life. However, this trend appears to be changing. The country's infant mortality rate has been decreasing by an estimated 22% since 2003, thanks in part to better midwifery. As a result of multi-donor support-including from USAID, the European Commission, the World Bank, and the GAVI Alliance – the number of midwives in Afghanistan has increased from 467 in 2002 to more than 2500 in 2010. Though it appears there has been progress, the country's health gains will be better appreciated when the USAID-supported Afghanistan Mortality Survey now underway is completed in summer 2011. The survey report will provide data on the magnitude of maternal mortality, the main causes of death, risk factors, and barriers that affect women's access to care.

Pakistan launches immunization drive against polio, targets 32 million children

The incidence rate of infective poliomyelitis has risen by 65% in Pakistan, partly as a consequence of floods in the summer of 2010 and conflicts in the north-west. The tribal belt has become a safe haven for the polio virus as vaccination has become impossible in many areas. Fighters have reportedly killed health workers and conservative tribal leaders have denounced the vaccine as "a part of a western conspiracy against their children." Last year the tribal belt accounted for half of all infections in Pakistan. Worried now that the disease will spill into other polio-free parts of the country, the authorities in Pakistan launched an emergency drive to immunize 32 million children under the age of five against polio. This plan, supported by a US$ 65 (€ 42 billion) million grant from the Bill and Melinda Gates Foundation, should see armed police and paramilitary soldiers protecting teams of vaccinators in the most dangerous areas.

Shortage of antiretroviral drugs in Myanmar and strategy for treating AIDS cases

While Myanmar's AIDS crisis is not yet of the scale that some of the African countries are facing, the country lags far behind in its ability to deal with the spread of the epidemic. It is estimated that around 242 000 people (about 1% of the adult population) are infected with HIV, with as many as 120 000 currently needing antiretroviral treatment. But drugs are only available for 20 000 patients. The shortages mean that only those with a CD4 count of less than 200 will be considered eligible to receive antiretroviral medications from the aid organisations distributing these drugs. This strategy appears to be backfiring as the immune systems in these patients have completely collapsed, making them an easy target for tuberculosis and other infections.

Infant deaths prompted Japan to suspend, then clear two childhood vaccines

Earlier this year Japan's Health Ministry halted the use of Pfizer's Prevenar and Sanofi's ActHIB following the deaths of several children aged between 6 months and 2 years. Up to 6 children died shortly after receiving the vaccines, but no direct relationship could be established. Similar events have been reported sporadically from other countries in the recent past. In February 2010 three infants died after receiving Prevenar, but Dutch health authorities later said that they could not find any causal association between Prevenar and the deaths in vaccine recipients. Pfizer Inc. and Sanofi-Aventis SA said in March 2011 that Japanese health authorities cleared the way for the companies to resume sales of the two widely used childhood vaccines, whose use had been temporarily suspended amid safety concerns. A panel of medical experts soon concluded that the child deaths weren't connected to the vaccines.

Australia and Western Pacific

The toll of Australia's floods

The flooding that inundated much of south and central Queensland in January 2011 is the worst to hit Australia in half a century. It was triggered by unusually heavy monsoon rains just before Christmas and was fed by much higher-than-normal rainfall ever since. More than 200 000 people were affected and the flood resulted in financial damages of more than US$ 20 billion (€ 14 billion). More than half of the country's wheat crop was damaged, leading to 45% increase in global grain prices. The Australian parliament has approved the government's plan to raise US$ 1.8 billion in floods tax to help rebuild the damaged infrastructure.

Australia pledges additional US$ 140 million to global vaccination roll-out

At the GAVI Alliance conference in London in June 2011, Australia pledged to commit US$ 200 million (€ 139 million, i.e. an extra US$ 140 million (€ 97 million), during the next two years to support a vaccination program to help fight infant mortality in the world's poorest countries. This commitment comes at a time when GAVI was worried about facing a substantial shortfall in its funding needs. The move makes Australia the sixth largest contributor to GAVI in direct funding. The donation will help support introduction of a rotavirus vaccination programme in African and Asian countries and will help vaccinate an extra 7.1 million children globally.

Rotavirus vaccination proves consistently effective throughout the world

New data which were published in *Journal of Pediatrics and Child Health* in May 2011, and which prominently involve Australia, indicate that in the years 2007 and 2008 hospitalisations for rotavirus gastroenteritis declined by 75%. This dramatic fall comes after vaccine introduction, and it is expressed in comparison to the mean annual hospitalisations during six years prior to vaccine introduction (i.e., during the period between 2001 and 2006). The greatest decline was seen in those younger than 12 months (93%), but the reduction occurred consistently across all age groups. The reduction was even recorded among children who were not eligible for immunisation, suggesting an effect on herd immunity. Similar effects have been shown in studies conducted in other countries (United States, El Salvador, Belgium), where hospitalizations and clinic visits for rotavirus diarrhoea have declined substantially. The decline typically ranges from 60% to over 90%.

New family planning initiatives supported by AusAID

Data released by the Australian government have shown an intention to spend around 20 million Australian dollars in 2010 and 2011 on family planning activities in developing countries. The aid program should support improved health outcomes for women. Health programs would target women in Indonesia, Papua New Guinea, Bangladesh, Pakistan, Cambodia, Solomon Islands, Afghanistan, East Timor and Nepal. The aid program will also be supported by UNFPA, International Planned Parenthood Federation, UNICEF and the GAVI Alliance. The key activities will include family planning information and education, establishing safe birth sites, and supplying and distributing contraceptives.

Australian Medical Association records the first fatal diphtheria case in nearly two decades

A 22-year-old Brisbane woman died in hospital in April 2011 after contracting diphtheria from a friend who had

returned from overseas. This caused both surprise and concern in the medical community in Australia, because the disease is virtually unheard of there. Experts believe that the woman wasn't immunized. Queensland Health said it last confirmed a case of diphtheria in the state in 1993. The vice president of the Australian Medical Association, Steve Hambleton, said he had never heard of a case in Australia during his work as a health professional. The vaccination coverage for diphtheria in Australia is more than 90%.

China

China reveals its foreign aid policy plans

In April 2011, the Chinese government published its first report – referred to as the "white paper" – on foreign aid. The report claims that China's foreign aid to Africa was motivated by solidarity. China's budgeted foreign aid grew steadily (by nearly 30% a year) between 2004 and 2009, with more than 40% of this funding spent on grants. The report does not provide more detailed information on aid flows, though. It has been suggested in some media that Beijing withheld details of its foreign assistance programme to prevent domestic criticism. Despite its remarkable growth, China is still home to the world's second largest population of poor people, with more than 200 million still living on less than US$ 1.25 (€ 0.9) per day.

China increases its spending on health

China plans to increase its health spending by 16.3% in 2011, to approximately US$ 26 billion (€ 18 billion) in total. The government will increase its funding for basic health services to 25 yuan (US$ 3.8, € 2.6) per capita, which is a 67% increase from last year. Health insurance subsidies are also expected to grow from US$ 18.2 (120 yuan, € 12.6) to US$ 30.4 (200 yuan, € 21.1) per person. This increase in health spending is a major part of China's plan to create affordable universal access to medical treatment, hospital care and pharmaceuticals. By lowering health-related costs, the government also hopes to drive domestic consumption. Increasing the capacity of health facilities and health-insurance coverage in rural China is also a part of the funding target.

Disability care volunteers to double in China by 2015

The China Disabled Persons' Federation (CDPF) reported that the government hopes to double the number of active disability care volunteers in China by the year of 2015. This is the latest effort to aid disabled people over the next five years. China currently has about 83 million disabled people. Only a minority of them have access to 'one-on-one' aid services, which are provided by up to 5.3 million registered volunteers throughout China. The authorities will aim to gradually recruit a further 5 million volunteers to aid disabled people and assist them in leading a valuable and dignified life. Lu Shiming, the vice chairman of the CDPF, stated that the country has made much progress in providing social security for the disabled.

China set to ban smoking in public places

China is set to ban smoking in public places including restaurants, bars and buses. Previously, China had only banned it in hospitals. The new regulations came into effect on the first day of May 2011, as announced by the Chinese Ministry of Health. The new regulations also ban cigarette vending machines in public areas and call for health education programmes to warn about the dangers of smoking. China has more than 300 million smokers – almost a quarter of its population. It is thought that smoking-related illnesses kill more than 1 million people every year. The measures of enforcement and the punishment for breaking the rules have yet to be announced in the new regulations. Smoking is still permitted in workplaces.

China launches orphan welfare database

In March 2011 China launched a nation-wide database to compile information on orphans and ensure welfare services. It will record data on the country's estimated 712 000 orphans, including basic identification details and photographs. This should provide precise statistics on orphans across the country. According to the Ministry of Civil Affairs, the database is especially designed to ensure the timely payment of basic living expenses for orphans and to monitor the distribution of living allowances paid to orphans, in order to maintain accuracy and fairness in welfare coverage.

Europe

Lethal *Escherichia coli* strain's outbreak concerns experts

The last week of May 2011 saw the outbreak of a toxic strain of *Escherichia coli* bacteria, which has so far left more than 2000 people ill and claimed at least 17 lives across Western Europe and the United States of America. Experts believe that the outbreak, which has its origin in Germany, may be caused by the deadliest *E. coli* strain ever recorded. Though the exact source of the illness still remains poorly understood, it was generally felt that eating contaminated vegetables and salads may have resulted in the infection. None of the currently available antibiotics were effective against this strain. Some US experts expressed the opinion that antibiotics should not even be used to treat this particular infection.

Large peaks in measles cases across Europe

There has been a tenfold rise in measles cases this year in England and Wales. The data released by the Health Protection Agency (HPA) revealed 334 confirmed cases of measles for the period January to April 2011, compared with 33 in the same period last year. The highest number of cases was recorded among under-25 year olds who were not vaccinated. Other European countries like France, Spain, Former Yugoslav Republic of Macedonia, Serbia and Turkey have also seen a similar sharp increase in measles cases, with France being the worst hit of them all. This information has triggered concerted efforts by health agencies across Europe to improve measles vaccination rates.

United Kingdom will commit an extra 814 million pounds to buying vaccines for the poor

Despite a weak economy and cuts in public spending, the UK Prime Minister David Cameron pledged GBP 814 million (US$ 1303 million, € 906 million) at a GAVI Alliance conference in London in June 2011 to help vaccinate children around the world. The purchased vaccines will protect children against preventable infectious diseases, such as pneumonia. This move will see UK's total contribution increased to GBP 1.5 billion pounds, which makes it the GAVI Alliance's largest donor. Britain's total contribution is now about five times larger than the amount pledged by the United States, more than 30 times higher than Germany's € 49 million (GBP 44 million, US$ 70 million), and almost 50 times larger than Spain's donation. According to GAVI, this investment could help save the lives of four million children over the next four years.

Russia spent US$ 472 million on foreign aid in 2010

Russia has reportedly spent US$ 472 million (€ 328 million) in 2010 on foreign aid. This reinforced the position of the large country as an important aid donor, rather than a recipient. Of this, more than US$ 80 million (€ 56 million) was spent on improving health care in developing countries. The Russian government is considering setting up its own aid agency in a bid to increase its influence in the developing world. Some analysts think that the intention behind the move is to match the growing influence of Brazil and South Africa in the developing world. Russia has admitted that a more consistent policy on international development would help strengthen its international position. It is also expected to spur Russia's domestic development by promoting trade and economic cooperation with countries that receive Russian aid.

Growing number of European academic institutions focused on global health

A new organisation – the European Academic Global Health Alliance (EAGHA) – brought together a large number of academic institutions in Europe whose activities address the broad scope of global health. It was launched in early 2011. Its main aims are to create a forum for European academic institutions interested in global health, exchange views and ideas, develop a European voice on global health issues, influence relevant policies and bring together international health, tropical medicine and public health institutions. EAGHA has already attracted 36 member institutions from 19 countries, and will be hosted by the Association of Schools of Public Health in the European Region (ASPHER) in Brussels. It has also developed partnerships with institutions in more than 50 low and middle income countries

India

Indian economy is growing, but its children are still under-nourished

A study by Harvard School of Public Health (HSPH) revealed that India's impressive economic growth has not led to a reduction in under-nutrition among its children. The study analysed economic and children's growth patterns from data based on the National Family Health Surveys on 77 326 Indian children in the periods 1992–1993, 1998–1999 and 2005–2006. Under-nutrition was worst in the poor and populous states like Bihar, Madhya Pradesh and Uttar Pradesh, in comparison to the north-eastern and southern states. While the researchers found the prevalence of under-nutrition slightly decreasing during the study period, the decline did not correspond to the increase in economic growth. The authors concluded that India is not on track for achieving the target for Millennium Development Goal (MDG) of reducing child mortality.

Rotavirus vaccines launched in India

In March 2011, MSD (a fully owned subsidiary of Merck & Co.) launched the rotavirus vaccine – RotaTeq – in India. RotaTeq is a pentavalent rotavirus vaccine that helps in preventing rotavirus associated gastroenteritis, estimated to be associated with about 39% of all diarrhoea-related hospital admissions in India among children aged less than five years. Since this vaccine was priced beyond the reach of the common people, there was considerable interest in the products being developed by local Indian companies. One of the manufacturers, Bharat Biotech, has announced that it plans to sell Rotavac, India's first indigenously developed Rotavirus vaccine, to global public markets at a price of US$ 1 (€ 0.7) per dose. The company is not just targeting Indian markets: they are well positioned to manufacture and supply the vaccine to national immunization programmes across the world.

All Indian newborns will get hepatitis B vaccine

The World Health Organization estimates that there are over 40 million Hepatitis B surface antigen (HBsAg) carriers in India and that every year over 100 000 Indians die from illnesses related to HBV infection. It is estimated that of the 25 million infants born in India every year, over 1 million run the lifetime risk of developing chronic hepatitis B virus (HBV) infection. In November 2010, the Indian Ministry of Health decided to introduce hepatitis B vaccination for all newborns as part of the national immunization programme (NIP) from April 2011. Hitherto, hepatitis B vaccination (initiated as a pilot in the year 2002 with GAVI Alliance support), was only being carried out in 10 states with relatively better child health indicators. Now, as a result of this far-reaching decision, all newborns in India will be immunised after birth and then at six, 10 and 14 weeks.

A potential anti-tuberculosis agent is fished out of the sea

From a coral reef off Rameswaram in South India, Indian scientists have isolated Transitmycin, a novel antibiotic that could fight tuberculosis and HIV better than most drugs available today. Unlike many of the present anti-tuberculosis drugs, transitmycin acts on dormant bacilli, which are a reservoir of infection. Doctors also found this compound to be active against HIV (subtypes B and C). While the project has so far cost US$ 50 000 (€ 34 699), it may take another US$ 700 million (€ 486 million) to develop the drug. Scientists estimate that it would take another 10 years before the drug reaches the market, but are hopeful that this could be an entirely novel and important medicine.

Two thirds of India's population could be middle class within 15 years

A report by Asian Development Bank indicates that nearly 70% of India's population could be middle class within 15 years if the country's economy continues to show sustained growth. If Asian middle class consumers can substitute for those in advanced economies, the Asian countries will gradually become major exporters to each other, without excessive reliance on the consumer markets of Europe or North America. The Indian economy, Asia's third-largest, has steadily been growing above 8% annually and it has contributed significantly to rising prosperity. The report says that Asia's rise will be led by China, India, Indonesia, Japan, South Korea, Malaysia and Thailand. By 2050, those seven economies alone should account for 45% of global GDP, and this may be a conservative estimate.

The Americas

United States will provide US$ 450 million for vaccines to save 4 million children's lives

At the GAVI conference in London, the United States government pledged to commit US$ 450 million (€ 312 million) over the next three years to the Alliance. The funding will provide vaccines for more than 250 million children, preventing 4 million premature childhood deaths and a large amount of suffering from diseases like pneumonia and diarrhoea. Although this is much lower than the funds committed by some other countries, USAID chief Raj Shah said: "In this fiscal climate, a multi-year pledge is an extremely difficult commitment to make. But we have made tough reallocations across our portfolio in order to make that commitment because only a multi-year pledge will ensure the highest possible return for every taxpayer dollar."

Stephen Harper moves to Geneva to keep track of US$ 40 billion fund for women's health

In January 2011, the Canadian Prime Minister Stephen Harper co-chaired a meeting of a United Nations' commission in Geneva. The task of the commission will be keeping track of how US$ 40 billion (€ 28 billion) is being spent on improving the health of women and children in poor nations.

Re-introduction of controversial US bill would hurt world's poorest women

Republicans in the US House of Representatives are pushing to re-introduce a law that would not only hurt women's health and reproductive rights in the developing world, but also affect some of the poorest and most vulnerable women in the United States. The bill includes cutting funding to the 'Title X' family-planning program, which would affect low-income families' access to contraception and sexual health services in the United States. In an international context, the bill seeks to re-impose the 'global gag' rule which strips international non-governmental organizations of all funding if they convey any information about abortion, along with other aspects of family planning, such as contraception and HIV/AIDS prevention, to the communities which they serve.

Prevention of cholera deaths in Haiti

In the absence of new interventions, it is estimated that the number of Cholera cases in Haiti may rise up to 800 000 this year, resulting in more than 11 000 deaths. These estimates, published in *The Lancet* in May 2011, are substantially higher than those generated by UN agencies. The authors point out that with an extremely weak sanitary infrastructure and a favourable environment for indefinite persistence, cholera is likely to remain a threat in Haiti for many years. They conclude that a combination of three approaches (access to safe drinking water, provision of vaccines, and improved case management using oral rehydration and antibiotics) are needed to have a beneficial effect in a post-disaster situation.

More than 100 cholera cases recorded in Venezuela

In January 2011, Venezuela reported 111 cases of cholera. It is thought that these cases became infected after consuming contaminated food at a wedding in the Dominican Republic. Lobsters bought from a town adjoining cholera-stricken Haiti have been identified as the likely source of infection. Before this, the last reported case of cholera in Venezuela was recorded more than 10 years ago. The fear of cholera has lead to the deportation of Haitian immigrants since the beginning of the year. The Dominican Republic has acknowledged only one cholera death since the outbreak began in Haiti.

The Bill and Melinda Gates Foundation

Bill Gates calls for prioritizing vaccines at the 64th World Health Assembly

Bill Gates addressed government leaders at the recent World Health Assembly, which is the highest-level decision-making body of the World Health Organization. He called upon them to increase funding support for global vaccine roll-out, also stressing their accountability in providing the large benefits of vaccination to every child. He also called for this support to be shown at the GAVI Alliance pledging meeting in London in June 2011. Vaccines remain the most cost-effective interventions in averting the deadly burden of childhood infections; in recent years, Bill Gates has assumed a role of the most prominent advocate who ensured that vaccines were given proper attention and funding support. The most recent estimates show that the GAVI Alliance's vaccination roll-out has resulted in several millions of child deaths prevented over the past decade.

Bill Gates calls for polio eradication, United Kingdom responds positively

In early 2011, Bill Gates called the global health community for a final push, which should see polio eradicated. This crippling disease is hardly remembered in wealthy countries, but there are still areas of the world where the vaccine has not reached children and where pockets of disease persist. Bill Gates launched his call in a Manhattan town house that was once a property of possibly the most highly profiled victim of this disease – Franklin D. Roosevelt. The push to eradicate polio can be dated back to 1985, and the Bill and Melinda Gates Foundation started their large investments towards this goal in 2005. The Foundation's donations have changed the context and they have now emerged as the key donor – having invested up to US$ 1.3 billion (€ 0.9 billion). British Prime Minister David Cameron has responded positively, announcing that the United Kingdom would double its contributions to polio eradication.

Smallpox eradication pioneer expresses scepticism over Gates' polio goal

Donald Henderson is an acclaimed pioneer of smallpox eradication. Having heard Bill Gates' call for polio eradication, he expressed some scepticism over the feasibility of this goal. As reported by the Financial Times, Donald Henderson said that polio eradication had "...become more of a 'movement' than a public health initiative capable of being examined by objective judgment." In his opinion, polio may not be "susceptible" to eradication in the same way as other infectious diseases have been in the past. He sees the future of the fight against polio in cheaper, but sustained control programmes with regular annual immunisations, which should minimize the devastating effects of polio over time.

Gates Foundation announces winners of Grand Challenges Exploration grants, launches Round 7

The Bill & Melinda Gates Foundation have been praised for their remarkable grant-awarding scheme. They provide US$ 100 000 (€ 69 407) to each of the large number of recipients who propose to start-up innovative research with potential to improve lives in poor countries. This unique funding scheme, called "Grand Challenges Exploration" (GCE), offers a total of US$ 100 million (€ 69 million) to the awardees. It has been designed to encourage innovation and enable creative researchers worldwide to test genuinely novel ideas that could address persistent global health issues in an effective way. A total of 88 new winners were announced after Round 6 of these grants had been closed. The Foundation has been accepting proposals for Round 7 of the scheme up until late May 2011. The new calls focus yet again on research areas where unconventional thinking is needed. The topics in Round 7 included creating ways to accelerate, sustain and monitor polio eradication; creating the next generation of sanitation technologies; creating low-cost cell phone-based solutions for improved uptake and coverage of childhood vaccinations; designing new approaches to cure HIV infection; exploring nutrition for healthy growth of infants and children; and applying synthetic biology to global health challenges.

WHO's programme for research and training in tropical diseases wins the 2011 Gates Award

This year's Gates Award for Global Health has been given to the Special Programme for Research and Training in

Tropical Diseases (TDR). This programme, hosted and co-financed by the headquarters of the World Health Organization in Geneva, has also been funded by UNICEF, UNDP and the World Bank. One of the world's largest public health prizes was awarded to programme Director Robert Ridley at a ceremony in Washington, USA. Over the past 36 years, the programme has attracted researchers from all over the world who worked with TDR to find improved health solutions for people in poor countries, resulting in major progress against many infectious diseases of the poor.

The GAVI Alliance
(formerly The Global Alliance for Vaccines and Immunisation)

GAVI raises US$ 4.3 billion, exceeds targets and meets its financial needs until 2015

The global vaccine charity – Global Alliance for Vaccines and Immunisation (GAVI) – held a donor summit in London on June 13th in a bid to overcome its financial shortfall and secure its financial needs for the next several years. International donors eventually pledged US$ 4.3 billion (€ 3 billion), which will be used to vaccinate nearly 250 million children against the leading causes of child deaths such as pneumonia and diarrhoea. The donors which were critical for this success, which far exceeded gloomy expectations, were the governments of the United Kingdom, Norway and the Bill & Melinda Gates Foundation. The United Kingdom pledged US$ 1.34 billion (€ 0.9 billion), the Gates Foundation promised US$ 1 billion (€ 0.7 billion) and Norway offered US$ 677 million (€ 463 million). This should allow GAVI to carry out all its immunization plans through 2015.

Ten years of GAVI Alliance – Progress Report 2010

Earlier this year GAVI has marked 10 years of its operations. It has also appointed a new Chief Executive Officer (CEO), Seth Berkley, who has been a founder and CEO of the International AIDS Vaccine Initiative. His strong track record as a global vaccines advocate has been praised and his appointment widely welcomed. GAVI has also issued its progress report for the year 2010. Some of the highlights include an estimate of more than 5 million future child deaths that have been prevented through GAVI activities. GAVI also estimated that more than 288 million additional children had been immunised with support from GAVI and its partners. Recently, GAVI are increasingly focusing on vaccines that could prevent childhood pneumonia and diarrhoea – the leading killers. It is hoped that this could contribute to preventing further 4 million deaths by 2015.

Large pharmaceutical companies finally reduce the prices of vaccines for the poor

In June 2011, leading pharmaceutical companies that produce vaccines against childhood infections announced that they will reduce the costs of their products for the poorest countries by a truly substantial amount. GlaxoSmithKline (GSK), Merck, Johnson & Johnson and Sanofi-Aventis have all agreed to cut prices through the international vaccine alliance, GAVI. This welcome move comes after years of pressure and calls on these companies to consider this reduction in order to enable life-saving vaccines to reach the low resource settings, where child deaths from the preventable infectious diseases tend to cluster. The vaccines included in this strategic decision by the companies will protect against diarrhoea (i.e., rotavirus) and human papillomavirus. A pentavalent vaccine which prevents diphtheria, tetanus, pertussis, hepatitis B, and *Haemophilus influenzae* type b will also be offered at a dramatically reduced price. GlaxoSmithKline will supply developing countries with its vaccine against rotavirus at a 95 per cent discount to the western market price.

Non-governmental organizations unhappy with appointment of a drug company to GAVI board

Although the GAVI Alliance continues to make remarkable progress towards immunizing children world-wide and preventing diseases and deaths, it is not free of critics. There are several non-governmental organizations (NGOs) which continue to stress that GAVI serves well the interests of large pharmaceutical companies, too, and that it has not done enough to improve the value for the money which GAVI donors are currently paying for the life-saving vaccines. They demand to see the prices of those vaccines low-

ered substantially. Earlier this year a Dutch pharmaceutical company Crucell (recently acquired by Johnson & Johnson) has been appointed to the board of the GAVI Alliance, which again sparked NGO's "... concerns over conflicts of interest and demands for tougher competition to reduce prices," according to the Financial Times. This is because nearly 60% of Crucell's revenues in 2010 were coming from sales of its pentavalent vaccine to GAVI.

GAVI strengthened by the former CEO of MTV networks

The Global Alliance for Vaccines and Immunisation (GAVI) has announced that Bill Roedy, who was the key developer of the MTV Networks, has agreed to join the GAVI network and assist their advocacy for immunisation world-wide. Bill Roedy, former CEO of the MTV, will become the first GAVI Envoy. This unexpected appointment underscores the importance of the public perception of the value of immunization. The recent scare over (apparently unfounded) reports that some vaccines may be linked to autism in children has revealed how quickly the behaviour of the general public changes under the influence of media reports, regardless of their accuracy. Mr Roedy is expected to raise awareness about the importance of vaccines, especially in fighting the main killers of children globally – such as pneumonia and diarrhoea.

The World Bank

Shifting the funding for global health from vertical to horizontal

As recently discussed in the *New England Journal of Medicine*, health systems researchers have long debated whether health care is better organized 'vertically' or 'horizontally'. Vertical funding usually refers to supporting one (or a few) specific diseases, while horizontal funding can affect many diseases at the same time, through supporting health care systems. Examples of vertical interventions in global health are e.g. smallpox and polio immunization programmes. Horizontal approaches include e.g. support to primary care, as advocated by the World Health Organization's 1978 Alma Ata Declaration, or sector-wide approaches to promoting health care reform, supported by the World Bank. The US President's Emergency Plan for AIDS Relief (PEPFAR) and the Global Fund to Fight AIDS, Tuberculosis, and Malaria are further examples of disease-specific funding initiatives. Although many theoretical models predict larger benefits from horizontally structured support, there are very few such programs in place. In the world of global health today, it is much easier to get donors enthusiastic about the more specific, vertical programs.

Innovative health financing – the role of Advance Market Commitment

According to Wikipedia, an 'advance market commitment' (AMC) is "...a binding contract, typically offered by a government or other financial entity, used to guarantee a viable market if a vaccine or other medicine is successfully developed. As a result of such a commitment, the market for vaccines or drugs for neglected diseases would be comparable in size and certainty to the market for medicines for rich countries. This would enable biotech and pharmaceutical companies to invest in the development of new vaccines to tackle the world's most pressing health problems, such as pneumonia, diarrheal disease, HIV/AIDS and malaria, in the normal course of their business decisions." An editorial in *Lancet Infectious Diseases* recently described how the roll-out of the GAVI initiative is helping to provide poor countries with low-cost pneumococcal vaccines: "The recent launch of pneumococcal vaccination in Nicaragua under AMC has shown that innovative approaches to health financing can benefit both global health and pharmaceutical companies."

Center for Global Development publishes an analysis of the future of development finance

In a recently published 'Working Paper 250', posted online by the Center for Global Development (which conducts independent research and develops practical ideas for global prosperity), it has been stressed that development finance is currently "at a turning point." The report mentions a "triple revolution of goals, actors and tools." The report predicts that "...as much of Asia grows its way out of poverty, aid will increasingly be focused on Africa and on countries plagued by instability, or with governments unable to meet the basic needs of their populations." Also, the share of development finance directed to tackling global public goods – like climate change, conflict prevention, and public health – is likely to expand substantially. The authors predict that the responsibility for addressing global challenges will increasingly be borne by coalitions that cut

across States, the private sector and civil society. It sees the role of multilaterals (such as WHO, GAVI, Global Fund, UNICEF, UNAIDS and the World Bank) as focussed on providing a coordinated mechanism/platform for delivering common objectives.

World Bank identifies five poor African states as potential "Growth Poles"

Africa is lagging behind the rest of the world in most economic and health indicators. However, this presents the continent with a remarkable opportunity for growth and development over the coming decades, at the rate which could hardly be expected anywhere else, according to the World Bank. Its new strategy for the continent aims to leverage growing South-South investments, which have recently been initiated by the growing low and middle income economies like China, India, Brazil and South Africa. The World Bank would like to ensure more inclusive development. To foster this development strategy, the World Bank suggested five poor states as 'Growth Poles' of the new Africa. These poles are being planned in Madagascar, Cameroon, Mozambique, The Gambia and the Democratic Republic of Congo.

Pakistan seeks financial aid from the World Bank to purchase polio vaccine

The government of Pakistan has been reported to request an emergency financial package worth US$ 41 million (€ 28 million) from the World Bank to purchase oral polio vaccine. The move should support its polio eradication initiative. The financial package should be awarded by the International Development Association of the World Bank. This assistance to the government of Pakistan is given under the third project since the year 2003, enabling it to procure OPV as part of the larger global campaign. The aid should help Pakistan to meet this year's vaccine requirements in support of the National Emergency Action Plan 2011 for polio eradication in the country.

United Nations (UN)

High-level UN meetings to focus on burden of non-communicable diseases

In January 2011, Ban Ki-moon called on the world's business leaders to help address the risk factors which underlie the most prevalent non-communicable diseases (NCDs). Health ministers from many countries met under the auspices of the United Nations in late April 2011 to adopt tougher measures against non-communicable diseases. These measures include preventive approaches, such as the promotion of healthy lifestyles and encouraging a multi-sectoral approach to prevention and treatment of NCDs. NCDs, principally heart disease, stroke, cancer, diabetes, and chronic respiratory diseases, have recently emerged as the leading cause of morbidity and mortality not only in high-income countries, but also in low and middle income countries. The UN High-Level Meeting (UN HLM) on NCDs in September 2011 will present global leaders with an opportunity to develop a coordinated global response to NCDs.

General Assembly appoints Ban Ki-moon to second term as UN Secretary-General

On 21st June 2011 the United Nations General Assembly agreed to appoint Ban Ki-moon to a second consecutive term as the Secretary-General of the Organization. Under the resolution, which was adopted by acclamation, his second term will run until the end of 2016. He is the eighth person to serve as UN chief and has been in office since January 2007. Following the re-appointment, Ban Ki-moon told the Assembly that he was "proud and humbled to accept it." He also said that the UN had "laid a firm foundation for the future" on a number of issues since he assumed office, including climate change, nuclear disarmament, education, sustainable development and global health.

WHO highlights the growing burden of non-communicable diseases

In April 2011, the World Health Organization reported that chronic illnesses of late onset (such as cancer, heart disease and diabetes) now cause more deaths than all other diseases combined. WHO, the United Nations' health body, issued a global report on non-communicable diseases (NCDs). NCDs have reached epidemic proportions and pose a much greater threat world-wide than infectious diseases. They caused about 63% of the 57 million deaths recorded globally in 2008. Nearly 80% of these deaths were in low and middle income countries. Furthermore, NCDs are also projected to rise further in the coming decades, especially in rapidly growing middle income countries. Cost effective in-

terventions, such as reducing risk factors, early detection and timely treatment, will become critical in tackling the problem. However, the capacity of many low and middle income countries to implement those interventions is poor.

United Nations are increasingly harnessing the power of social media

The United Nations Department of Public Information (DPI) is increasingly using social media and the internet to disseminate the work of the United Nations, according to UN News. In April 2011, Kiyo Akasaka, Under-Secretary-General for Communications and Public Information, told the opening of the latest session of the UN's Committee on Information that the recent popular uprisings across North Africa and the Middle East illustrated the power and reach of social media tools. Furthermore, in an effort to encourage individuals to help feed tens of thousands of hungry children across the world, the United Nations World Food Programme (WFP) has created a social media platform through which people can make donations to the agency.

Tracking the progress towards UN's Millennium Development Goals

Each year the World Health Organization presents a report summarizing the state of health in its 193 member countries. Part of the report usually focuses on tracking the progress towards the UN's Millennium Development Goals (MDGs). These goals, set in 2000 by consensus of all member states, aimed to ensure political commitment to accelerating global progress in health and development. This year's report shows continuing overall progress, but there are still regions where little or no improvement has been made. Child mortality in some countries in sub-Saharan Africa is now higher than it was in 1990, while the fourth MDG demands a reduction by two-thirds between 1990 and 2015. In parallel, the World Bank estimated that two-thirds of developing countries are either on track, or very close, to meeting key targets for tackling extreme poverty and hunger.

UN AIDS

UN Secretary General calls world leaders to end AIDS by 2020

Ban Ki-moon used the three-day UN's summit on AIDS in June 2011 to call upon world leaders to end AIDS by 2020. He said: "That is our goal – zero new infections, zero stigma and zero AIDS-related deaths." The meeting in New York marked the 30th anniversary of the discovery of human immunodeficiency virus (HIV). According to UN's estimates, some 34 million people have AIDS, but up to 50% do not know that they have the disease. More than 9 million people still do not get antiretroviral treatment, and about 1.8 million people die from AIDS each year. Ban Ki-moon stressed that new infections have dropped by 20% since 2001, when the world leaders first organized and developed plans to control the pandemic. The meeting was attended by 30 presidents and heads of government, and African leaders spoke of the desperate need for more financial support to fight the disease in their nations.

UN AIDS summit aims to cover 15 million sufferers with medical treatment

A UN AIDS summit this year has set a target of more than doubling the global coverage of life-saving AIDS treatment. The concrete target is to provide 15 million AIDS patients with antiretroviral treatment by 2015. Over the past three decades, the number of cases increased from a small group of young homosexual men in Los Angeles to 34 million men, women and children globally, who are estimated to be living with HIV today. It is hoped that, within the next decade or two, this trend can be reversed and AIDS stopped through a combination of high coverage of antiretroviral drugs and the development of a vaccine that will prevent the disease.

Cheaper antiretroviral drugs will be offered to 70 of the world's poorest countries

Although cocktails of AIDS drugs which once cost more than US$ 10 000 (€ 6905) per year in wealthy countries are now available in poor countries for less than US$ 200 (€ 138), many patients still receive drugs which were developed decades ago and can have very serious side effects. The World Health Organization now recommends combinations containing tenofovir because they have fewer side effects and show less risk of development of resistance by the virus. The current price of one such combination is US$ 159 (€ 110), which is down from about US$ 400 (€ 278) three years ago. The lower prices of these drugs will be offered by eight Indian pharmaceutical companies. They were negotiated by the Clinton Health Access Initiative, with support

from British foreign aid and the Bill and Melinda Gates Foundation. The funding which will guarantee the initial payments, and which is crucial to getting the Indian suppliers to increase the production of these drugs, will come from Unitaid. Unitaid is an independent agency founded at the United Nations, which collects several agreed taxes which were set up to finance global health programs.

Babies who escape mother-to-child HIV transmission are at increased risk of other diseases

According to a study published by *JAMA*, babies who manage to escape mother-to-child HIV transmission still face up to a four times greater risk of dying in the first year of life. The main reason is thought to be a greater susceptibility to infectious disease. Researchers examined some 100 mothers and babies in South Africa and compared antibody levels among children who were born infected with HIV to children who escaped HIV. Those who did not get HIV showed lower levels of antibodies to whooping cough, tetanus and *Pneumococcus* infections. All those infections are vaccine-preventable, but vaccines are not always available to these children. Births of HIV-positive babies have dropped dramatically in the past decade due to use of medications that mothers can take during pregnancy to prevent transmission.

China reports large successes in AIDS mortality reduction

Government scientists in China have reported that AIDS mortality in the country has decreased by nearly two-thirds since free antiretroviral drugs were introduced in 2002. It is estimated that the coverage by AIDS drugs among those who need it in China has reached about 63%, while it was practically non-existent in 2002. Consequently, a 64% drop in mortality (measured per 100 'person-years') is reported: from 39.3 in 2002 to 14.2 in 2009. The study, which was led by China's national Center for control and prevention of AIDS and other sexually transmitted diseases, was published by *Lancet Infectious Diseases*. The number of infected people in China has reached nearly 750 000, but in a population of 1.3 billion the prevalence is still less than 1 in 1000 population. Of those infected, it is estimated that more than 300 000 have been tested and more than 80 000 are being treated. China begins treatment when a patient's CD4 cell count (which is a measure of immune system strength) drops below 350 per cubic millimetre. The government's experts are now debating whether to start treatment as soon as a patient tests positive for HIV. This strategy, also known as 'treatment as prevention', can reduce the risk of new infections by up to 96%, because it protects sexual partners.

UNICEF

UNICEF's 'State of world's children' report for 2011 focused on adolescents

The key theme of UNICEF's 'State of world's children' (SOWC) report for the year 2011 is investing in adolescence to break cycles of poverty and inequity. Today, young people throughout the world face the problems of economic turmoil, climate change, environmental degradation, urbanisation, migration and the rising costs of healthcare. Strong investments during the last two decades have resulted in large progress in the health and welfare of young children, but there have been fewer gains in areas critically affecting adolescents. Anthony Lake, UNICEF Executive Director, said that "...adolescence is a pivot point – an opportunity to consolidate the gains we have made in early childhood or risk seeing those gains wiped out." In the report, UNICEF says investment is needed to improve data collection to increase the understanding of adolescents' problems; invest in education and training to help adolescents lift themselves out of poverty; expand opportunities for youth to participate and voice their opinion; promote laws, policies and programmes that protect the rights of adolescents; and prevent poverty and inequity.

UNICEF's initiative to promote transparency in vaccine pricing

Many stakeholders in the global health community have been expressing concern in recent years that large pharmaceutical companies are using the global health funding drive to generate huge profits on life-saving vaccines. They argued that vaccines against life-threatening childhood infections should be made available for the poor at much reduced prices, and profits reduced. UNICEF launched an initiative recently to improve transparency by making vaccine prices available on its website. For the first time, UNICEF publicly listed the prices it pays individual drug manufacturers for vaccines. It is hoped that this move will lead to a more competitive market and lower prices, while the donors will also be assured that UNICEF and GAVI are getting reasonable prices. UNICEF has traditionally been one

of the largest buyers of children's vaccines and this move should ensure that vaccine supply is sustainable and affordable. UNICEF's partners in immunisation, such as GAVI Alliance, welcomed this positive development.

UNICEF carries out yellow-fever immunization, supports restoring education in Côte d'Ivoire

Although the country has been facing political uncertainties and concerning unrests in aftermath to the 2010 presidential elections, UNICEF carried out immunization against yellow fever among nearly 1 million people in this troubled country. This move was conducted in four health districts with UNICEF's support as a result of 25 reported deaths from the disease since November 2010. UNICEF's Officer-in-Charge for Côte d'Ivoire, Sylvie Dossou, expressed gratitude to the GAVI Alliance for providing the yellow-fever vaccines, and to the World Health Organization for their partnership with UNICEF in carrying out this critically important campaign. In addition, UNICEF assisted more than 1 million children to return to school after months of disruption to the country's education system, caused by the political and security crisis in the country.

Online consultation process launched to set standards for child-friendly businesses

Together with Save the Children and UN Global Compact, UNICEF has launched an online consultation process. The aim is to invite businesses and civil society to take an active role in developing a global standard of business principles pertaining to children's rights. An online consultation process should enable representatives of the private sector and civil society to shape the Children's Rights and Business Principles, setting the standard for child-friendly businesses everywhere. A series of follow-up meetings and global consultations is planned. The first meeting will take place in London, and it is hoped that it will attract leading business and civil society representatives.

On the 21st annual Day of the African Child, UNICEF reminds governments to protect children

A very large number of children in Africa still experience violence, exploitation and abuse – many of them on a daily basis. This problem is particularly troublesome among children who live and work on the streets of Africa. Recently, on the occasion of the 21st annual Day of the African Child, UNICEF called on African governments to strengthen support systems which can provide a more protective environment in families and communities to keep children safe. The main approach is to strengthen families through the provision of basic social, health and education services.

World Health Organization (WHO)

World Health Organization undergoes a major reform

The last World Health Assembly – the highest-level decision-making body at the World Health Organization (WHO) – has supported proposed reforms which could bring the most substantial changes to the agency in more than six decades of its history. The reforms are clearly needed at WHO. Only a decade ago, it was the only important agency focused on global health issues. Today, it is struggling to maintain its relevance amidst the surge of sharply focused, well managed, innovative, and better funded big new players, such as The Global Fund, the GAVI Alliance and the Bill & Melinda Gates Foundation. Global health issues have attracted an unprecedented interest among the donors over the past decade, but WHO has not seen much of these funds. In fact, WHO reported a US$ 300 million (€ 209 billion) deficit in 2010. The reforms at WHO will see the agency slashing its next budget by nearly US$ 1 billion (€ 0.7 billion) and cut hundreds of jobs at the Geneva headquarters and elsewhere at regional offices. The agency's Director General, Margaret Chan, explained these cuts as being due to financial problems among rich donor nations and the exchange rate for the weak U.S. dollar. Addressing the annual assembly, she also said WHO was clear of suspicion of pharmaceutical industry influence on the management of the H1N1 pandemic, and that innovative fi-

nancing mechanisms from the GAVI Alliance had helped to introduce new vaccines against childhood pneumonia and diarrhoea to developing countries.

WHO: fighting for relevance in the new world of global health

After long consultations with WHO member states on its funding support, Director-General Margaret Chan called the WHO overstretched and unable to respond with sufficient speed and efficiency to many global health problems. More than six decades ago, the United Nations (UN) granted the WHO extensive normative powers which established this agency as the only relevant authority on international health globally. However, several modern initiatives, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria, the GAVI Alliance (formerly the Global Alliance for Vaccines and Immunisation), US President's Emergency Plan for AIDS Relief (PEPFAR) and well-funded donor agencies (such as the Bill & Melinda Gates Foundation) established themselves as the new leaders in their respective fields of interest. These agencies do not suffer from constraints which often interfere with WHO's efficiency. Now, WHO is facing a financial crisis, at a time when funding support for global health issues has never been greater. Many donors question the WHO's actual performance, find the new initiatives a better and safer investment, and worry about the WHO's vision, efficiency and focus. The existing funding support for WHO largely targets its extra-budgetary activities, while there seems to be little enthusiasm for supporting the WHO's core budget, which is under the tight political control of its leaders.

An attempt by the WHO to explore the issue of fake medicines will require more time

Fake drugs, or counterfeit medicines, are beginning to pose an increasingly serious threat to global public health. It is estimated that up to 15% of all medicines that are being sold worldwide are fake. This problem has attracted attention at the World Health Assembly in 2010. The member states requested WHO to establish an intergovernmental working group on counterfeit medicines which will decide WHO's role in tackling this problem. According to the journal *The Lancet*, although this intergovernmental group was required to make specific recommendations to this year's 64th World Health Assembly in May 2011, they only met once (in February 2011) and agreed that they needed more time.

WHO's careful warning on mobile phone link to brain cancer

In June 2011, the World Health Organisation issued a statement which was quickly disseminated through the global media. The agency warned that there was some evidence linking use of mobile phones to brain cancer. But this warning was worded very carefully, and rightly so. Most human diseases are hugely multi-factorial and caused by an interaction of many risk factors and their interplay with the genetic susceptibility of the host. Because of this, contributions of individual risk factors to an overall burden of disease in the population are typically rather small, albeit real. Because of this general property of most human diseases, it is wise not to overplay the role of individual risk factors, such as mobile phone use, when reporting these disease associations to the media. The story could have potentially been very damaging to the thriving mobile phone industry, but a well-balanced warning from the WHO will be unlikely to cause such damage.

WHO to address innovative financing of research and development for the poor

The WHO has established a Consultative Expert Working Group on Research and Development: financing and coordination (CEWG). The group met in April 2011 to define their mandate and work plan. One of the main tasks of this group will be to assess proposals for innovative financing of research and development which should serve the needs of the people in low resource settings. CEWG launched a call for proposals and ideas for innovative financing, which will be posted on the CEWG website. CEWG plans to analyse the proposals and submit its report to the World Health Assembly in 2012.

Environment

Study reveals global hotspots of climate change and food insecurity

A project by the CGIAR Research Program on Climate Change, Agriculture and Food Security (CCAFS) was set out to identify hotspots of climate change and food insecurity. They reported nine climate change indicators which included decline in the length of the growing period for crops, long periods of high temperature and increase in rain intensity. When these were combined, Southern Africa emerged as highly exposed, followed by the regions of northeast Brazil, Mexico, Pakistan, India and Afghanistan. This analysis means that millions of people already living in poverty are to be challenged further, with hotter and more variable weather, which will pose a threat to crop yields and livestock.

Strange mass death events affecting animal species are being reported worldwide

Since the middle of 2010, the world media have been reporting a series of rather strange events involving the mass death of different animal species. Birds and fish were predominantly involved. The events seem to be isolated from each other, but they have received a significant attention from the media and internet bloggers. The academics are still uncertain on how to explain these rare events. There is a growing list of proposed factors and explanations, but very little certainty over the true causes. Some believe that these mass death events are truly alarming, because they might indicate an early warning about the disturbances in Earth's natural cycle, which could possibly be related to the global climate change. Among suspected or proposed causes, the media suggested new infectious diseases, earthquakes or mass collisions and stress caused by fireworks.

Australia experiences some of the worst floods in living memory

A high intensity rainfall in January 2011 caused major flooding across much of the western and central parts of the state of Victoria, Australia. Although the true extent of the damage is nearly impossible to assess, a rough estimate predicted a loss in revenues from Australia's GDP of nearly 30 billion Australian dollars. The floods damaged a large portion of Australia's coal mines and cotton fields, along with many other natural resources. The events follow the 2010 weather pattern of La Niña, which brings wetter conditions to eastern Australia. It has been reported that last year's La Niña was the strongest since 1973.

A book suggests links between climate change, health and political stability

Dan Ferber and Paul Epstein are the authors of the new book: Changing Planet, Changing Health: How the Climate Crisis Threatens Our Health and What We Can Do About It (University of California Press, April 2011). According to the authors, climate change threatens more than our environment. Steadily rising temperatures have already led to the spread of infectious diseases – such as malaria in Kenya, Lyme disease in Maine, and cholera. It is also thought to contribute to food shortages and malnutrition. An unstable climate can even fuel political and social unrest – for which they see an example in the recent revolts in the Middle East and North Africa.

A report points to high corruption levels in countries most affected by climate change

The watchdog group Transparency International (TI) has released a report entitled Global Corruption: Climate Change, based on contributions from more than 50 experts. According to this report none of the countries most affected by climate change (mainly in Africa and South Asia) scored higher than 3.5 in a corruption scale, with 0 being extremely corrupt and 10 being very transparent. They stated that corruption risks are high because of the complexity, uncertainty and novelty around many climate issues and mechanisms to fight climate change need to be strengthened and made more transparent to reduce increasing risks of corruption.

Demography

More than a billion residents of India to get unique twelve digit identification numbers

'Aadhar', a project to provide unique twelve digit identification numbers (UID) to all residents of India, was initiated in January 2009. Apart from providing identity, the UID will enable better delivery of services and effective governance. In becoming a single source of identity verification, it could enable the easier roll-out of wide number of services such as bank accounts, passports, driving licences and many others. It is hoped that proof of identity and greater financial inclusion could lay the basis for checking fraud and corruption, avoiding duplication and targeting intended beneficiaries in a range of welfare programs. The first set of Aadhar cards were handed over by the Indian Prime Minister in September 2010 and it is expected that in the next five years all 1.2 billion Indian residents will have an Aadhar card.

Hundreds of millions keep moving to urban areas in China

One of the main strategic focuses of China's economic plan for the next decade is the idea of urbanisation. In the past 20 years, more than 200 million people have moved from villages to bigger cities, which is the most extensive process of urbanisation the world has ever seen. According to some estimates, urbanisation will continue to grow, with as many as 300 million people moving to cities over the next couple of decades. The country's leaders hope that urbanisation will transform hundreds of million of Chinese into consumers. At the same time, the movements to cities should help maintain high investment rates.

New census exposes gender imbalance in India

India's 2011 census shows a serious decline in the number of girls under the age of seven, with the female/male ratio dropping from 0.98 (in 1961) to 0.92 (in 2011). This represents the most striking gender imbalance seen since the Indian independence. Although the proportion of women in the Indian population is steadily growing (mainly due to factors such as longer life expectancy), India's ratio of young girls to boys is one of the most unbalanced in the world. Some researchers explained this by neglect of very young female children and possibly the increased availability of antenatal screening for gender. Activists interested in this issue claim that the current level of imbalance suggests that up to eight million female foetuses may have been aborted in the past decade in India.

One-child policy in China may be revised in urban areas

China's one-child policy, which was introduced in 1979, was a major demographic policy decision launched at the beginning of China's economic reforms. In 2007, Chinese authorities assessed that the policy had prevented about 400 million births. The policy has been revised in the rural and minority areas of China where, if the first child of a family was a girl, the family is allowed to have a second child. On March 6 this year, during the annual Chinese People's Political Consultative Conference and the National People's Congress, further revisions have been proposed. Experts have suggested that since the aging population problem has become increasingly prominent, and with the growing sex-ratio imbalance, a revision of one-child policy should also be considered in urban areas, starting from 2015.

U.N. Reports steady rise of refugees

According to the New York Times, The United Nations refugee agency reported that 43.7 million people around the globe are displaced from their homes by conflict or persecution. The number is the highest reported in the past 15 years. In addition, 80% of all refugees in the world are being sheltered in the world's poorest countries, which cannot continue to withstand this large burden on their own. The UN's refugee agency, based in Paris, France, suggested in its 2010 Global Trends report that Pakistan, Iran and Syria were the world's biggest hosts of refugees, sheltering about three million people. Among the wealthy countries, Germany has the largest refugee population (about 600 000 people). António Guterres, the United Nations high commissioner for refugees, said that "Fears about supposed floods of refugees in industrialized countries are being vastly overblown or mistakenly conflated with issues of migration, with... poorer countries (being) left having to pick up the burden." He urged industrialized nations to address this worrying imbalance by increasing the number of people they accept.

Economy

South Africa becomes the fifth member of the 'BRIC club'

According to the Guardian, Jacob Zuma, South Africa's president, had succeeded in gaining an invitation to join the BRIC (now BRICS) club of Brazil, Russia, India and China in their third summit on China's Hainan Island in April 2011. With the United States and Europe still trying to overcome the 2008 financial crisis, these five large, populous and fast growing economies are trying to challenge the world's traditional councils of power. Recently, after the announcement that the French Finance Minister Christine Lagarde will be the likely new head of the International Monetary Fund (IMF), the BRICS club stated that the choice of managing director should not be based on nationality alone, but also on competence.

G8 leaders off track on their Gleneagles commitments

In the G8 summit in Gleneagles two years ago, the leaders of the eight richest countries agreed to double their annual aid to poor nations to US$ 50 billion (€ 58 billion) per year, with half of that money going to the world's poorest countries in Africa. But during the recent G8 summit in Heiligendamm, it was clear that the rich world was well off track to deliver on their Gleneagles commitments. A report by Oxfam suggested that, if present trends were to continue, the G8 would miss its target by about US$ 30 billion (€ 21 billion).

One thousand economists join the call on G20 to accept 'Robin Hood' (Tobin) tax

The Robin Hood tax is a package of financial transaction taxes. It was proposed by a campaigning group, largely composed of civil society non-governmental organizations. Campaigners have suggested the tax could be implemented globally, regionally or unilaterally by individual nations. Conceptually similar to the Tobin tax (which was proposed on foreign currency exchange only), it could be imposed on the purchase and sale of stocks, bonds, commodities, unit trusts, mutual funds, and derivatives such as futures and options. Recently, a thousand economists from 53 countries have written to G20 finance ministers asking them to apply the 'Robin Hood tax' on transactions in financial markets. The idea is to levy a very small charge (around 0.05%) and use the money raised from this charge to maintain rich nations' commitments to the developing world. One of the main objections to this tax from the speculators is that since there are millions of trades every minute in global financial markets it will be unworkable to calculate the tax. However, this argument is rather unconvincing, since share transactions are already being taxed.

Brazil seeks a role in Africa through friendly approach towards local workforce

According to Reuters, Brazil seeks a different approach in Africa from that already practiced by China. At building sites from Angola to Zambia, teams of Chinese workers often do the work instead of Africans. Wherever local African residents are employed, there have been reports that Chinese may be treating them rather roughly. But engineering groups from Brazil, such as Odebrecht (recently contracted to fix Liberia's railway), decided to employ locals and to treat them well. Odebrecht and other Brazilian companies want to distinguish themselves from companies from other emerging powers and to find a sustainable role in Africa through an approach which is friendly to the locals.

India announces plans to invest in Africa

The 2nd Africa – India Forum Summit was held this year in the Ethiopian capital, Addis Ababa. During the opening session of the summit, Indian Prime Minister Manmohan Singh announced that India will offer to Africa a record US$ 5 billion (€ 3.4 billion) loan grant for the next three years to help the continent achieve its development goals. India has also offered an additional US$ 700 million (€ 482 million) for the establishment of new institutions and training programs in Africa and US$ 300 million (€ 207 million) support for the new Ethiopia – Djibouti railway line project. The Indian Prime Minister also suggested the establishment of several clusters including an India – Africa Food Processing Cluster and an India – Africa Institute of Agriculture and Rural Development. He finally proposed the creation of an India – Africa Virtual University, which will provide 10 000 new scholarships for African students.

Energy

Germany moves towards closing its nuclear power plants by 2021

A committee appointed by Chancellor Angela Merkel proposed that Germany should close all of its nuclear power plants by 2021. Nuclear energy currently meets nearly a quarter of Germany's electricity needs, according to the Energy Ministry. The rest comes from coal supplies (42%), renewable sources like wind and solar energy (17%) and natural gas (14%). Interestingly, not even Japan, where a major nuclear scare occurred in March following an earthquake and tsunami, plans to abandon its reliance on nuclear power. Japan currently derives 30% of its electricity from nuclear power plants. Germany's move away from nuclear energy, which partly reflects the strong influence of environmentalist groups in this country, is being closely watched by other European governments. Contrary to Germany, many nations in Central and Eastern Europe plan to develop or expand nuclear power production.

IPCC projects that renewable sources could provide 77% of world's energy by 2050

The experts from UN's Intergovernmental Panel on Climate Change (IPCC) said that renewable sources could provide a majority of the world's energy supplies by 2050 in their recent report. However, this projection is conditional on global governments' dramatic increase of financial and political support for technologies such as wind and solar power. The report also stressed that the availability of renewable sources, like the wind and the sun, was virtually unlimited and could provide up to 77% of the world's energy needs within the next 40 years. The report also pointed that all renewable sources used today, such as wind, solar, geothermal, hydropower, bioenergy and ocean energy, currently accounted for only about 13% of global energy supply. To scale this up to three quarters, large investments by governments and the private sector would be needed, amounting to US$ 5.1 trillion (€ 3.5 trillion) through 2020 and nearly US$ 7.2 trillion (€ 5 trillion) between 2021 and 2030.

Bright prospects for wind power scale-up in the United States

Wind power is one of the fastest-growing sources of energy around the world. It is popular because it is abundant and clean, providing communities with their local source of electricity. In the United States, which has passed Germany and become the country producing the most wind power, the Department of Energy estimated that wind power could account for 20% of the nation's electricity supply by 2030. Despite a prolonged recession and restricted credit markets, the wind power industry grew very strongly in the United States in 2009, adding 39% more capacity in comparison to a year earlier. The country is now very close to meeting 2% of its electricity needs from wind turbines. The American Wind Energy Association said the growth of wind power was helped by the federal stimulus package. The package extended a tax credit and provided other investment incentives for the industry.

Winners of the annual Goldman Prizes announced

The annual Goldman Prizes, presented at a ceremony in San Francisco Opera House to six recipients this year, are awarded to activists who challenge those in power while either enhancing, or defending the environment. Each winner receives a stipend of US$ 150 000 (€ 103 305) stipend. The Goldman juries have been particularly prone to awarding those whose activities involve considerable risks. As an example, Wangari Maathai, the Kenyan founder of the Greenbelt Movement, has spurred the planting of tens of millions of trees across Africa. He won a Nobel Prize in 2004 – which was 13 years after receiving a Goldman Prize. This year's winners include Ursula Sladek from Schönau, Germany, who created a small local power company, EWS, that rivalled the previous provider and which now provides electricity from renewable energy sources to her entire town and 110 000 other customers across Germany. Other recipients range from a Zimbabwe-based conservationist who worked to save the endangered black rhino, to a Texas man who fought refinery pollution in Port Arthur.

Germany's energy company among many to back out of India

Enercon of Germany is one of the world's biggest makers of wind turbines. Recently, they announced a loss of its entire Indian subsidiary with annual sales of more than US$ 566 million (€ 390 million) after a dispute with a local partner and an encounter with Mumbai law enforcement authorities. They also claim that they have lost control of its patents in India, and fear that technology could be appropriated by their competitors in this big and growing market. The case has caused diplomatic tensions and clouded the image of India in Germany as a desirable investment market. Enercon is among many foreign companies and

investors which have started to grow weary of the country's widespread corruption, weak infrastructure and government limits on foreign investment in certain industries. Because of this and similar experiences, direct investment in India by foreign companies and investors fell by more than 31% in 2010, in comparison with the previous year.

Peace and Human Rights

United Nations declare internet access a basic human right

The UN declared that internet access should now be considered a human right. The Special Report states that the Internet is one of the most powerful instruments of the 21st century, because it helps increasing transparency, accessing information and facilitating active citizen participation in building democratic societies. However, given that access to basic necessities such as electricity remains difficult in many developing countries, the report states that universal access to the internet for all individuals worldwide cannot be achieved instantly, but it stretches the obligation for all countries to promote or facilitate the right to freedom of expression and the means necessary to exercise this, including the internet.

UN reports on serious human rights breaches in more than 50 countries

A report, presented in early June 2011 to the UN Human Rights Council (UNHRC), documented serious violations of human rights in more than 50 countries. According to the UNHRC, some clear examples of these violations were the killings of demonstrators in Syria, Yemen and some other Arab countries. In addition, the report contains new evidence on alleged atrocities committed in the final stages of Sri Lanka's civil war. The report concluded that there is a great need for transparent independent investigations into the human rights violations that have taken place in more than 50 countries.

India and Pakistan agree to keep pushing for peace over Kashmir

According to the Associated Press, India's foreign secretary and the next Ambassador to the United States, Nirupama Rao, said in June 2011 that her country would remain concerned about the threat of terrorism, but is committed to peace talks with Pakistan. Those talks have stalled since the 2008 terrorist attacks in Mumbai. Her comments came following a two-day gathering of the delegations of the two nations in Islamabad. The two countries, both with nuclear weapons, held their first formal talks on the disputed region of Kashmir since the Mumbai attacks. They have already fought three wars since their independence in 1947, two of them over Kashmir, which both nations claim in its entirety. The attacks in Mumbai left between 100 and 200 people dead and they have been blamed on Pakistani militants, who are suspected of building paramilitary forces and developing strongholds in Kashmir. Pakistan has denied that any state institutions were involved in any way with the attacks on Mumbai. The home secretaries met in New Delhi in March 2011 and agreed to set up a terrorism hotline and to cooperate on the Mumbai attack investigation, while the secretaries for commerce from both sides met in April 2011.

US to pull out from Afghanistan, Europeans to follow swiftly

The President of the United States, Barack Obama, announced in June 2011 that a phased pullout of troops from Afghanistan will be set in motion, seeking to end this costly engagement. He currently plans to withdraw 10000 troops by the end of 2011 and a further 23000 by the end of the summer 2012. His announcement won immediate support from France's President Nicolas Sarkozy, who promised to follow swiftly. After nearly a decade of fighting in Afghanistan, Obama's withdrawal plan was welcomed by NATO allies. A number of other European nations which have contributed troops to the military operation against the Afghan Taliban insurgency said they would also initiate phased reductions. This mission has burdened state budgets and has been entirely against public opinion across much of Europe.

US commission to watch over human rights in clinical trials

The United States Presidential Commission is a special commission, set up by President Barack Obama in 2009, which considers how best to protect the human rights of people who take part in clinical trials. This Commission was set up after the discovery that the US Public Health Service had conducted unethical research in Guatemala from 1946 to 1948, in which nearly 700 people were deliberately infected with syphilis and other sexually transmitted diseases. The trials were trying to show that penicillin could be used immediately after sex to prevent infection. Although an unethical experiment like the Guatemala trial is thought to be considerably less likely today, transparency, strict regulations and clearer guidelines are still necessary.

Food, Water and Sanitation

Rising food prices could threaten economic growth in Asia

In April 2011, the Asian Development Bank released a report in which it stated that sharp rises in food prices are a threat to economic growth in Asia. The bank made a gloomy prediction that this trend could soon push millions of people into extreme poverty. Food prices in Asia have increased at an average of about 10% in the first half of 2011, which could force more than 60 million people below the poverty income threshold of US$ 1.3 (€ 0.9) per person a day. Changyong Rhee, the chief economist of the bank, reminded that "...Asia is (still) home to two-thirds of the world's poor." Economic growth in China and India is blamed for pushing up prices, while the region's population density and uneven income distribution make the lower social classes especially vulnerable to food prices growth. The poor in Asia typically spend nearly two-thirds of their income on food alone. The rise in prices of food and fuel leave Asia's consumers with less income for other goods, while inflation could also prompt central banks to further raise interest rates. These factors would all work together to slow down economic growth.

European Commission marks World Water Day by launching a new funding mechanism

The focus of World Water Day 2011, which is celebrated on 22 March each year, is 'Water for cities – responding to the urban challenge'. The European Commission marked this day by announcing the launch of a pooling mechanism in the framework of the African, Caribbean, Pacific and European Union (ACP – EU) water facilities. Under this mechanism, the European Commission will provide 40 million Euros for grants from the European Development Fund (EDF) with further loans from the EU multilateral and bilateral finance institutions. The scheme is expected to finance projects for access to water and sanitation services in African, Caribbean and Pacific countries. In most of the industrialized countries, nearly everyone has access to abundant supplies of safe and clean drinking water. However, in most low and middle income countries it is still not advisable to drink water from the tap.

Sanitation Millennium Development Goal is badly off track

Despite all the progress in human development, 2.6 billion people, or about 40% of the total World's population, still do not have access to proper sanitation. It is estimated that each year 1.5 million children of pre-school age die of diarrhoea caused by unsanitary conditions and poor hygiene. The UN's Millennium Development Goal on expanding access to water and sanitation services by 2015 is very likely to be missed. Donors have increasingly avoided funding projects relevant to water and sanitation, and focused on health and education-related initiatives instead, according to research by the World Bank and Water Aid. The Guardian reports that women and girls will be among the hardest hit by this failure, quoting the World Bank's report released in May 2011. Water Aid is also due to publish its new report this year, showing that water and sanitation programs accounted for about 8% of global financial aid in 1990, while between 2007 and 2009 they accounted for just over 5%. Julia Bucknall, the World Bank's water chief, said that issues such as sanitation simply do not seem to be as attractive to donors as some other areas, particularly tackling specific diseases.

A community-led approach to sanitation for low resource settings

Community-led total sanitation (CLTS) is gaining increasing attention as the Millennium Development Goal on sanitation is being missed. The traditional approach to hygiene has been education and subsidy. But in rural areas of low and middle income countries there have been many failed programmes, with toilets not being used or put to other purposes, or dismantled and materials used for other purposes. The cost of these failed development programmes runs into billions of dollars. CLTS does not use any standard design, hardware subsidy, teaching or any special measures. Communities are mobilised into analysing their own sanitation and waste behaviour, making their own participatory defecation and social maps, inspecting the areas of open defecation and analysing pathways to the mouth. The CLTS approach was pioneered in Bangladesh in 2000 by Kamal Kar, a development consultant from India. Since then he has been joined by many others to promote it, including Plan International, UNICEF, the Water and Sanitation Programme of the World Bank and Water Aid. The approach has now been adopted in more than 40 countries. It is usually driven by passionate champions, as many become committed once they experience the enhancement of their community's human wellbeing. For women and girls it has helped to promote menstrual hygiene, self-respect, and the bodily wellbeing brought about by being able to defecate during daylight and in private.

Fears over contamination of Japanese food exports

The United States' Food and Drug Administration blocked imports from Japan's radiation zone. It announced that it would avoid milk, vegetables and fruit from areas near the tsunami-smashed nuclear plant because of contamination fears. Other nations may follow with formal bans, while some private importers have stopped any shipments from Japan. Earlier, Japan had reported that above-safety radiation levels had been discovered in 11 types of vegetables from the area, in addition to milk and water. But the officials insisted that there was no danger to humans, and urged the world not to over-react. Tokyo authorities said water at a purification plant for the Japanese capital, with 13 million residents, had 210 becquerels of radioactive iodine, which was more than twice the level of safety for infants.

Science and Technology

Malaria vaccine trials move to Phase III with next generation vaccine already planned

It has been estimated that malaria still kills up to 800 000 people each year. GlaxoSmithKline and the PATH Malaria Vaccine Initiative recently started Phase III clinical trials on a developmental vaccine against malaria after Phase II testing proved effective. In the experiments completed in previous stages, the incidence of malaria was decreased by 53%. The potential to reduce episodes further was even larger if infants and young children were primarily targeted. Reuters reported further that even as the world's first malaria vaccine moves closer to the market, GSK, PATH and Crucell have joined forces to test a next-generation vaccine against malaria. The new vaccine will be an amended version of the currently tested GSK vaccine. It will try to add an engineered common cold virus developed by Crucell to 'prime' the immune system to get a stronger response.

Scientific publishers controversially tried to deprive poor countries from free access to journals

Lack of access to knowledge is widely accepted to be one of the main limitations to human development. In 2002, the World Health Organization launched the Health Inter-Network Access to Research Initiative (HINARI) project. Within this initiative, 137 publishers have provided content from 7000 journals free to local non-profit institutions in 105 eligible countries. Kimberly Parker, WHO's HINARI programme manager, stated that 400 new journals were added to the network in 2010 alone. HINARI offers the opportunity of access to knowledge for the most resource-poor countries in the world. However, this programme seemed to be falling apart at one point during 2011, because big publishers began to withdraw from the scheme. Their decision has caused much debate and controversy. The HINARI program has recently been reviewed and an agreement seems to have been reached, in which publishers would continue to provide access until at least 2015.

Researchers test needle-free, inhalable vaccine against measles

Sustained high vaccination coverage is critical to preventing deaths from measles. Despite the availability of a vaccine and its very high level of implementation globally, measles remains an important killer of children worldwide. The areas under most danger are deprived, less-developed regions where vaccination coverage is limited. A team of researchers, led by scientists from the Johns Hopkins Bloomberg School of Public Health and the University of Colorado, developed and successfully tested a dry powder containing live-attenuated measles vaccine that can be inhaled. The novel vaccine against measles was studied in rhesus macaques, and the results were published in January 2011 in the journal *PNAS*.

The growing case for 'open science' and online raw data sharing

The value of routinely sharing the results of all clinical trials would be immense. Meta-analyses of the raw data from many clinical trials would have a potential to provide definitive answers on the effects of health interventions. The increasing use of electronic medical records in an anonymised format could provide high quality pharmacovigilance at unprecedented scale. However, a regime of open access to scientific data also poses many problematic questions. Because of the importance and timeliness of the issues, the UK's Royal Society has established a Working Group to explore these questions, issues and challenges in great depth and to make recommendations about how they might be addressed. The Working Group is currently seeking evidence from scientists and from the public alike.

China looking forward to becoming the new world leader in science and technology

Chinese Premier Wen Jiabao said in May 2011 that China "must develop powerful strength in science and technology and foster a large number of talented individuals in order to 'gain the upper hand' in international competition." Addressing a plenary session of the National Congress of the China Association for Science and Technology (CAST), he stressed that the future of China relies on science and technology. He also said that China should improve the quality, performance and competitiveness of traditional industries through scientific and technological progress, suggesting that China should develop its own basic research and frontier research. The premier pledged that the government will provide long-term, stable financial assistance for basic and frontier research and set up a number of research centres, which will be based at high-level national research institutions and research-centred universities. He concluded that China should also gradually reform the systems of management, decision-making, appraisal, and personnel in the field of science and technology, so as to form a modern system in this sector that fits the country's socialist market economy. He also pledged to firmly carry out the national strategy on intellectual rights, by stepping up efforts to protect them.

A health policy and systems approach to addressing the growing burden of noncommunicable diseases in China

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Over the past two decades, China has undergone a socio-economic transition unprecedented in human history in terms of its scale and the speed of change (1,2). It is estimated that, while three quarters of the Chinese population lived in rural areas until 1990, almost half were living in cities by 2009 (3). The effect of the one-child policy introduced in 1979 has produced new generations of Chinese children who did not need to share resources with siblings and represent their parents' sole investment in terms of care, education and mentorship (4,5). This transition period also marked massive government investment in infrastructure, including health investments in access and treatment for all strata of the Chinese population.

China's socio-economic transition will inevitably lead to changes in the health burden of its population, where the fall in maternal and child health burden will soon be replaced by a chronic non-communicable diseases (NCDs) burden in both urban and rural areas.

My colleagues and I recently documented the dramatic decline in child mortality yielded by these investments, and showed that China has achieved Millennium Development Goal 4 (reduction in child mortality by 2/3 by 2015) nine years ahead of schedule (6). This achievement is all the more significant when one considers the size of China's population, and the relative performance of other low and middle income countries (7). In population health terms, one of the most remarkable outcomes of China's extensive transition has been the decrease in maternal and child health problems (8,9).

China's socio-economic transition will inevitably lead to changes in the health burden of its population, where the fall in maternal and child health burden will soon be replaced by a chronic non-communicable diseases (NCDs) burden in both urban and rural areas. The increase in the burden of non-communicable diseases will be driven by three key factors: (i) a demographic shift marked by an ageing population; (ii) a change from rural to urban ways of life, marked by sedentary lifestyle, high-energy food consumption, increased use of personal transportation, a change in work style, and exposure to outdoor air pollution, and alcohol and tobacco use; (iii) improved access to care and health-seeking behaviour of people in both urban and rural areas (10–11). These factors are already contributing to a rising epidemic of obesity, type 2 diabetes, cardiovascular diseases, degenerative diseases of musculoskeletal system, road traffic accidents, cancers of multiple sites, asthma, depression, dementia and other neuropsychiatric conditions (12–16). Without appropriate inventions, the problem is likely to worsen.

These massive changes and shifts in China's health burden merit a re-thinking of the future development and structural needs of the Chinese health system. Costs are likely to grow exponentially over the next two decades because of the interaction between an aging population, increased ex-

posures to the key environmental and lifestyle risk factors, and changing patterns of care-seeking and healthcare expectations. China will soon face millions of cases of diseases such as Alzheimer, and up to a 4-fold increase in the number of new cases of type 2 diabetes, strokes, road traffic accidents and certain types of cancer. China's health system is currently not structured to efficiently address the management of such a large and growing chronic disease burden. This problem will first become apparent in the fast-growing urban areas, where the majority of Chinese will live, and where population aging and risk factor exposures for NCDs are most immediate.

The most cost-effective strategy for dealing with this growing problem will be to use a combination of strong preventive measures with a strong primary health care system to address the majority of health demands. This would help alleviate the congestion of the hospital services in urban areas, which represent a reasonably strong secondary health care service that must not become over-burdened. Preventive activities will reduce exposure to the main risk factors for chronic non-communicable diseases, and delay or avert a sizeable portion of the burden. This requires a strong public health network in urban areas, and a significant government investment to support the programs. Currently there are small, usually isolated preventive efforts, but the size of the problem will require a co-ordinated set of preventive programmes at the national level, which would be implemented in a standardized way in all urban areas.

China currently does not have a system of doctor-maintained, primary care practices comparable to those in the West. At present, in many rural areas, primary health care is carried out by village doctors with relatively low level (Technical College) training which provides them with a licence to treat and prescribe drugs for common illnesses (17). Incentives for medical graduates to work at this basic level of health care are low and few choose this career path. In urban areas, primary health care is provided at community health centres by nurses and medical and/or public health doctors with basic university degrees (18). However, consultation at these clinics for hospital or specialists referrals is not compulsory. Unlike many western health systems, doctors in these clinics do not have an exclusive power of referral to secondary health care. In spite of reforms to the urban primary health care systems, community health clinic positions do not attract the best of medical graduates due to lower salaries, and a lack of prestige and career opportunities.

Patient confidence in the performance of primary care clinics is low, and many prefer to seek treatment in hospitals (19). This has led to long queues in public hospitals, congested with patients better treated in a primary care facility. This will become unsustainable as the NCDs burden increases demand for care. Not enough is being done to develop a stronger primary health care system, which would attract patients away from secondary care hospitals as the point of entry into the health system.

It is widely acknowledged that NCDs can be effectively managed through prevention and primary health care, at a fraction of the cost of hospital care – which is also prone to over-medication and over-treatment. Unless strategies are put in place to reverse the over-reliance on hospitals, the rapidly increasing burden of NCDs will continue to strain the existing health system, and add to the cost of health care, which over time, might interfere with China's economic growth.

> Critical interventions in health system restructuring in China will be needed to improve the cost-effectiveness of the response to the burden of non-communicable diseases in China. Subject to the level of success, China may provide a model for many other low- and middle-income countries which will inevitably face similar problems in future.

I propose that a critical point of intervention in health system restructuring in China, to help address the massive increase in the burden of non-communicable diseases (which will certainly continue over the next two decades), is to:

- Strengthen the network of public health institutes in urban areas, promote them into leading institutions to monitor and evaluate the role of the key risk factors for non-communicable diseases in modern Chinese society;
- Establish sound evidence base on the distribution of common NCDs and their causes for different parts of China and use it for the development of prevention and intervention strategies;
- Implement large-scale national prevention programs that target common chronic non-communicable diseases (eg, cardiovascular diseases, cancer, traffic and workplace accidents) in both urban and rural areas through the network of public health institute. The programs should be based on sound evidence and be monitored and evaluated. Program evaluation should be made available to the public;
- Building upon the National Standards for the Control of Chronic Disease and Prevention set out by the Ministry of Health (China), adopt a holistic approach to prevention that includes strategies to tackle the structural and environmental factors that underlie

the risks of chronic diseases (20). The successful implementation of these programmes will necessarily require sound co-ordination with the local media, regulators, health authorities and other stakeholders;

- Strengthen primary health care networks in rural areas by significant government investment into human resources to improve the number of skilled health workers, and target the training of rural doctors towards active participation in disease prevention and patient support in the disease self-management. Lessons should be learned from on-going studies of payment reform (like capitation) as ways of creating provider incentives;
- Strengthen primary health care networks in urban areas by improving the skills and training of the providers, and creating the necessary incentives for medical practitioners to work and remain at these health centres. This will raise the status of the health centres and make them the point of entry into the health system for all but acute care NCDs patients;
- Undertake ongoing case-mix analyses of patient data from secondary care hospitals to (i) determine optimal, cost-effective care strategies, and (ii) identify which categories of patients should be directed to primary care facilities.
- Trial the introduction of a compulsory specialist referral mechanism with primary care facilities as the gate-keepers.

Photo: courtesy of Dr Kit Yee Chan, personal collection

Appropriately implemented, these recommendations, will improve the cost-effectiveness of the response to the growing problem of NCDs in China. Subject to the level of success, this will become a potential model for many other low- and middle-income countries which will inevitably face similar problems, with a slight time delay.

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A roller-coaster ride: Introduction of pentavalent vaccine in India

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Introduction of *Haemophilus influenzae* type B (HiB) containing pentavalent vaccines (a combination vaccine which protects against five killer diseases- diphtheria, pertussis, tetanus, hepatitis B and *Haemophilus influenzae* type B) in the Universal Immunization Program (UIP) was a far sighted decision taken in 2009 by the Ministry of Health and Family Welfare, Government of India. This decision was based on the recommendations of National Technical Advisory Group on Immunization (NTAGI) and was aimed at reducing the burden of HiB related infections (1). The decision was supported by the GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunizations) and in August 2009 they decided to provide funding worth US$ 165 million to the Government of India to support the introduction of pentavalent vaccine (2). The vaccine was to be introduced in a phased manner. In the first phase, the vaccine would have been rolled-out in 10 states and an estimated 18 million infants were expected to receive the vaccine. The decision of the Indian Government to introduce HiB vaccination into its UIP was hailed internationally by public health practitioners as India constitutes 34% of the birth cohort in GAVI-eligible countries (3) and even in the absence of population-based data, the country is estimated to have the highest number of deaths due to HiB in children under 5 years of age (4).

> Petitioners in High Court cite low disease burden due to Hib and safety concerns as main reasons for opposing the introduction of the vaccine.

However, the plans to introduce the vaccine were stalled following the filing of a Public Interest Litigation (PIL) in the Delhi High Court in December 2010, which questioned rationale for introducing the vaccine as well as its efficacy (5). The petitioners, comprising of a mixed group of medical practitioners including paediatricians, policy advisors to the Government of India, and a former civil servant (who also oppose the introduction of Hepatitis B vaccine into the UIP) claimed inter alia that the NTAGI had based its recommendation without considering data from studies which reveal that the burden of meningitis caused by HiB in Indian children is much lower than in other parts of the world (6, 7). Moreover, the petitioners claimed that recent evidence from countries which have used pentavalent vaccine for several years revealed that there was no real benefit to children (8). They also claimed that the vaccine had been withdrawn from neighbouring Bhutan and Sri Lanka after reports of adverse effects following immunization with the vaccine. The Delhi High court sought a reply from the Indian Council of Medical Research (ICMR), NTAGI and Indian Ministry of Health (9). Under increasing pressure, the government decided to halt the introduction of the vaccine and set up an expert committee to review all the available evidence on the HiB disease burden, assess the need for introducing pentavalent vaccine as a part of UIP and review the possible adverse effects. Although the findings of the expert committee have not been made public, recent reports in the media indicate that the Indian Government plans to introduce the vaccine in two South Indian states (Tamil Nadu and Kerala) in September 2011 (10,11). Amidst all this controversy, it is justified to question if the objections raised by the petitioners were based on sound evidence.

In the absence of surveillance data or good quality community based studies with active ascertainment of cases of invasive HiB disease to base the burden of disease estimate in India, the only option is to use data derived from hospital – based studies with passive case ascertainment and mathematical models based on systematic literature review and vaccine probe studies. Using the latter approach, Watt and colleagues estimated the burden of invasive HiB disease (which includes pneumonia and meningitis) in India in 2000 to be about 2.4 million cases with 72 000 deaths in children aged less than 5 years, which accounted for approximately 4% of all child deaths in India (4). It is well acknowledged that the incidence of pneumonia far exceeds meningitis while the latter has a higher case fatality ratio. In 2008, Rudan and colleagues estimated that in India, 43 million new cases of clinical pneumonia in children under the age of 5 years occur each year and result in 408 000 deaths (12). Using the estimates from the HiB study (4), we estimate that around 215 000 new cases of HiB pneumonia occur yearly in Indian children under the age of 5 years and result in over 61 000 deaths. Thus, studies have consistently projected the burden of HiB disease in India to be significant. The studies cited by the petitioners (7, 13) have serious limitations, making it extremely difficult to generalise the results to the Indian population as a whole – the studies were conducted more than 15 years ago in an area which had, even at that time, less than half the infant mortality rate compared to the Indian average; the investigators only looked at HiB meningitis as an outcome; and have themselves concluded that "these estimates are minimal" (7). However, in the light of the present controversy, it may be worthwhile to conduct a systematic literature review of Indian studies to estimate the burden of HiB related acute bacterial pneumonia and meningitis in India to provide a clearer picture.

The concerns raised regarding the adverse effects of the pentavalent vaccine appear to be unsubstantiated. The World Health Organization had established a panel of international experts to examine the reports of hypotonic-hyporesponsive episodes (HHEs) following administration of the pentavalent vaccine (HHE is a recognized adverse reaction to whole-cell and acellular pertussis-containing vaccines, and to HiB and hepatitis B vaccines). The expert panel concluded that there was no evidence to establish a causal relationship between pentavalent vaccine and any of the deaths reported following its administration (14). It also concluded that "the reporting rate of HHE following the pentavalent vaccine (14.9 cases per 100 000 doses) was found to be well within the reported estimates of HHE following whole-cell pertussis-containing vaccines (21–250 cases per 100 000 doses)." Following this, the Sri Lankan

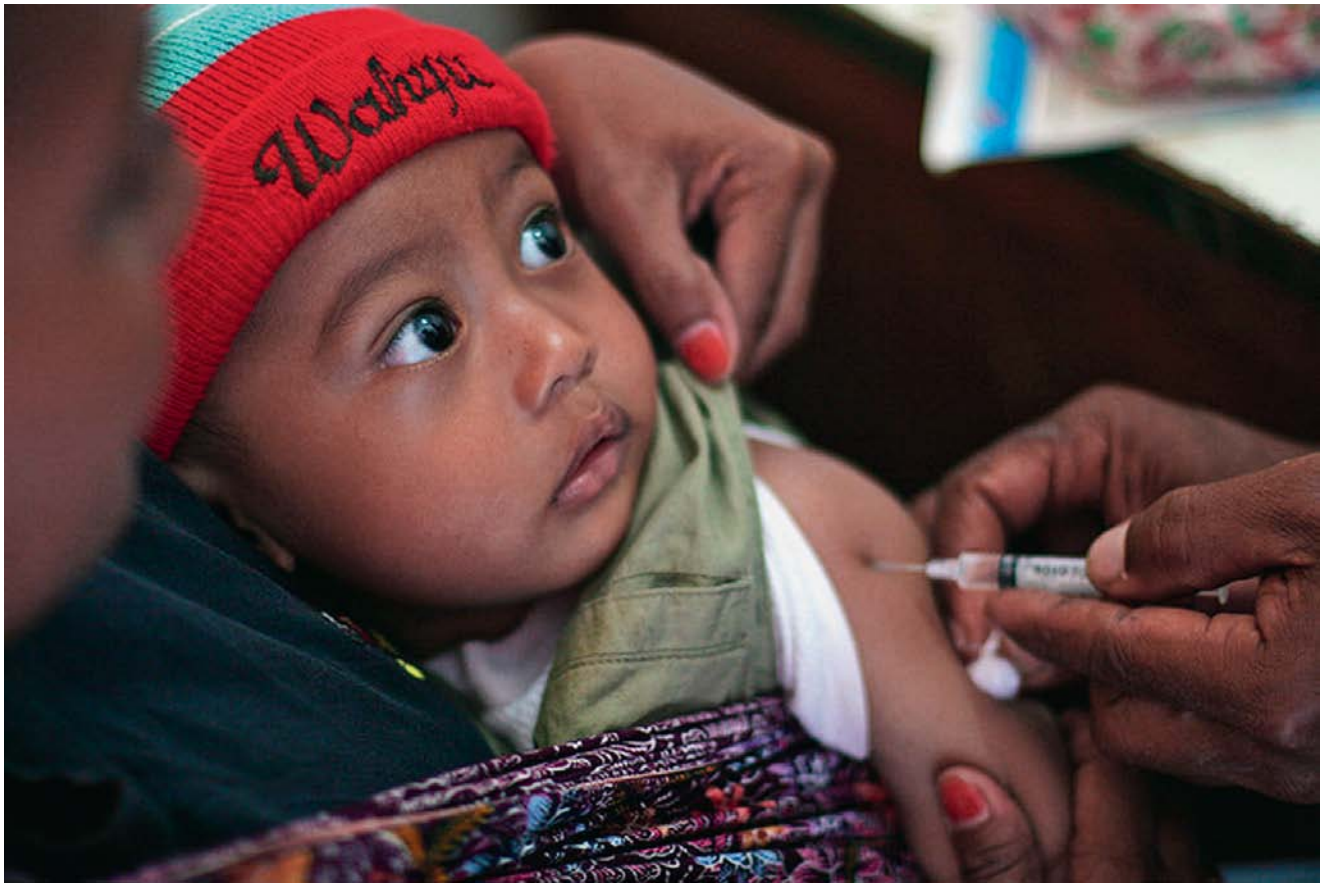


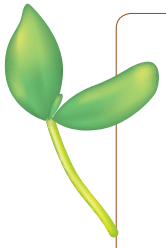
Photo: Courtesy of UNICEF Sverige

government decided to re-introduce the vaccine from September 2009. However, due to shortage of fresh stocks this was only possible in February 2010 (15).

Contrary to the remarks on the lack of beneficial effects of the vaccine, 150 countries across the globe that have already introduced HiB vaccine have reported a dramatic decline in the incidence of invasive HiB disease and death. Morris and colleagues in a systematic review of the effectiveness of HiB vaccine demonstrated that HiB conjugate vaccines were highly effective in reducing the incidence of invasive HiB disease, with similar effectiveness seen across geographical regions and different levels of socioeconomic development. (16) Even in countries which have poor immunization coverage, indirect benefits of the vaccine have been reported due to the herd effect. For instance, data from Gambia have shown the benefits of herd immunity even when vaccine coverage has been below 60% (17). The vaccine should thus be effective in India where UIP coverage is poor. In fact, long before the NTAGI recommended introduction of HiB vaccine into the UIP, the Indian Academy of Pediatrics had called for incorporating the vaccine into the UIP (18).

The Cochrane study which has been cited by the petitioners to show that there is no benefit of a combination vaccine in terms of disease burden reduction and immunogenicity found that no studies reported the primary outcome for the study ie, incidence of disease (8). The authors themselves conclude that "[T]he results of this review should be viewed with caution, mostly as an indication that high quality data are lacking." Moreover, Dutta and colleagues recently carried out a phase-III multicentric trial of the pentavalent vaccine and found that the combination vaccine had a high immunogenicity and was well tolerated (19). In resource-poor settings like India, decisions to use the vaccine are expected to be guided by the cost associated with its introduction. While the concerns regarding the costs are legitimate, recent data suggest that the cost of the vaccine has reduced substantially. At present there are at least five Indian companies manufacturing the vaccine. With one of the Indian manufacturers, the Serum Institute of India, announcing in June 2011 that they plan to sell the vaccine at US$ 1.75 (€ 1.2) per dose, it is expected that the other manufacturers will follow suit (20). In the future the price will reduce even further – as a result of bulk procurement by the Government and competition between the manufacturers. It has already been demonstrated that any price lower than US$ 2 (€ 1.4) per dose is highly cost effective (21).

The concerns regarding the introduction of a new vaccine on an already overwhelmed public health system in India appear to be valid. However, experience from other developing countries suggests that it is feasible despite limited resources (22). Further, it may not be inappropriate to assume that the opportunity offered by the introduction of a new vaccine may provide the desired boost to the health system through refresher trainings to the health workers and generating demand among parents and caregivers and may lead to an improvement in the routine immunization coverage especially in the North Indian states. Hence, while the decision regarding GAVI Alliance's efforts to introduce the pentavalent vaccine in India seems to be centred around debates regarding the associated commercial considerations, it may be prudent to focus more on the long-term benefits of the vaccine and its potential to reduce mortality and morbidity amongst children aged less than 5 years, bringing the country closer to Millennuim Development Goal 4.



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Mega sporting events:

A poisoned chalice or a new dawn for low- and middle-income countries?

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The increasing number of mega sporting events, such as Olympic Games, the World Cup or Commonwealth Games, awarded to low- and middle-income countries is, at first sight, a significant move in the direction of fairness and equity. In 2010, South Africa hosted the football World Cup and India hosted the Commonwealth Games, while Brazil will be hosting the football World Cup in 2014 and the Olympic Games in 2016. In South Africa, during the bidding process and in the lead up to the hosting of the World Cup, there was considerable commentary on the merits and otherwise of South Africa hosting the event, including benefits for the host country in particular and the continent in general. In the case of India, the Commonwealth Games was specifically marketed as an event that would improve 'national prestige' (1). In this brief viewpoint, using South Africa as a case study, I will outline a number of relevant health and economic issues associated with mega sporting events, and suggest that there are no tangible benefits to hosting these events, and that any intangible benefits (such as improving national prestige) are tenuous at best.

> Mega sporting events in South Africa, which has the largest number of HIV-positive people in the world, and India, with 1.8 million deaths of children under 5 each year and 52 million stunted children, raise questions about the effective and, as importantly, the moral imperative of spending billions of dollar to host a sporting event. From a health perspective, selling alcohol and debt tarnishes further the notion of any intangible benefits of mega events to low- and middle-income countries.

One of the central rationales for South Africa bidding to host the football World Cup, which was being voiced to the nation in many different shapes and forms, was the expected poverty relief that would be provided by the event, in the form of employment creation, infrastructure development and tourism and marketing. From the initial euphoria in 2004 when South Africa was awarded the rights to host the mega event, projections of tourist numbers and budget surpluses were significantly tempered in the run up to the event. The selling point for the 2010 World Cup in South Africa centered on government spending on infrastructure development and the expected tourist windfall. Organizers however, had to revise tourist estimates down from an initial 750 000 to between 200 000 and 250 000 (2). Tourism windfalls for mega events are often overstated – during the 2006 World Cup in Germany, despite large numbers of visitors (in line with expectations), hotel occupancy rates during the World Cup actually dropped (3).

It has been shown that while World Cup football is 'extraordinarily' profitable for international football association, FIFA, the economic projections for host countries usually overestimated the benefit and underestimated the cost (4), with some commentators arguing that in other mega sports events, such as the 2012 London Olympics, there is in fact a deliberate misrepresentation of costs and benefits (5). In terms of the misrepresentation of costs the

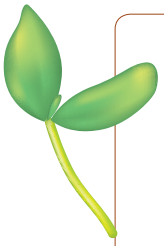
2010 World Cup in South Africa was an extreme example. In 2003, the estimate for the construction of stadiums was projected to be just over 1 billion rand (US$ 130 million, € 92 million), which by 2006 had ballooned to 8.5 billion rand (just over US$ 1 billion, € 0.7 billion) with the final costs likely to far exceed this figure (6). To put the figures in perspective, the cost of the Cape Town stadium was 3 times the entire housing budget for a single South African province in 2010. In the case of India, the initial budget of the Commonwealth Games was US$ 412 million (€ 291 million), with the eventual spend calculated to be in the region of US$ 15 billion (€ 11 billion) (7), while it has been reported that the residents of New Delhi will be paying for the Games in the form of increased prices of land, basic commodities and petrol for the next 25 to 30 years (8). Matheson and Baade (9) have argued that mega events are an even worse investment for low- and middle-income countries than for rich countries, and that net gains are invariably overestimated.

Photo: www.bigphoto.com

Collin and Mackenzie (10) have argued that there is a significant tension between international sport and health promotion when the image projected by FIFA of providing a legacy for health and contributing to societal development is in fact bankrolled by junk food producers and alcohol companies. While FIFA would never countenance the sponsorship of the World Cup by a cigarette company (in 2002, FIFA received an award from the WHO for their tobacco free policy) (11), they appear to have no ethical, economic or health objection to the event being sponsored by a beer company (Budweiser), junk food producers (Coke and McDonalds) or by a company that actively markets debt (Visa). This particular triangle of sponsors is an inappropriate one for countries such as South Africa and India, which are experiencing a health transition with simultaneous epidemics of infectious diseases, non-communicable diseases, as well as high levels of morbidity and mortality associated with alcohol related violence and motor vehicle accidents (12,13). South Africa has the highest rate of fetal alcohol disease in the world, with 7% of the country's mortality rate attributable to alcohol abuse (14). In addition, South Africa has particularly high levels of obesity, with 56% of women being overweight or obese (15). Finally, South Africa's debt levels are notably high (as a consequence of easily accessible credit) with consequent interest levels of 10%.

It is likely that the financial benefits for South Africa or India of hosting mega events will be negligible. It is also probable that hosting the event will not provide poverty relief as articulated in the rationale for hosting the World Cup, but rather it is likely that it will increase inequality both regionally and within cities (4). One of South Africa's major cities (Port Elizabeth) has already begun a process of cutting back on services in order to try and service the debt incurred building a single World Cup stadium. The public relations nightmare that preceded India's hosting of the Commonwealth Games, such as construction delays, bridges collapsing, poor facilities and corruption allegations (7), has surely undermined any benefit of the games for 'national prestige'.

Having said this, South Africa has been described as a miracle nation (16), with the transition from apartheid to a democratic nation being a largely peaceful one. In 1995, South Africa won the rugby World Cup with the then President Nelson Mandela sporting a rugby jersey with the captain's number on it. This moment was seen as a pivotal one in the process of South African nation building and beginning a process of unifying all South Africans. It has been argued that the true benefits of hosting the 2010 World Cup for South Africa were to celebrate African culture and to decrease Afro-pessimism (4). Such intangibles may be important and undoubtedly need to be considered. However, in the case of South Africa (largest number of HIV-positive people in the world) and India (1.8 million deaths of children under 5 each year and 52 million stunted children) (17), questions about the effective and (as importantly) the moral imperative of spending billions of dollar to host a sporting event must be asked. This, together with the questionable association, from a health perspective, with multinationals selling alcohol and debt, tarnishes further the notion of any intangible benefits of mega events to low- and middle-income countries.



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The case for launch of an international DNA-based birth cohort study

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The global health agenda beyond 2015 will inevitably need to broaden its focus from mortality reduction to the social determinants of deaths, growing inequities among children and mothers, and ensuring the sustainability of the progress made against the infectious diseases. New research tools, including technologies that enable high-throughput genetic and '-omics' research, could be deployed for better understanding of the aetiology of maternal and child health problems. The research needed to address those challenges will require conceptually different studies than those used in the past. It should be guided by stringent ethical frameworks related to the emerging collections of biological specimens and other health related information. We will aim to establish an international birth cohort which should assist low- and middle-income countries to use emerging genomic research technologies to address the main problems in maternal and child health, which are still major contributors to the burden of disease globally.

INTRODUCTION

Progress towards the reduction in child mortality target in Millennium Development Goal (MDG) 4 is being made in many low- and middle-income countries (1). This is mainly as a result of notable efforts of national governments and the international community to improve the prevention and treatment of the main causes of child death and to expand access to health care. The exact causes of the sharp declines in child mortality have not been identified definitively but successful countries have significantly increased coverage of basic public health interventions and increased

access to quality health services (1). The 'advanced market commitment' programmes, which are heavily supported by The Gates Foundation, Global Alliance for Vaccines and Immunization and national governments of the developed countries, will try to sustain and enhance the development and implementation of vaccination against major pathogens throughout the developing world (2).

Many low- and middle-income countries are now experiencing a markedly different pattern of early mortality, with more than half of child deaths attributable to causes directly related to birth and very early infections and complications – such as preterm birth complications, birth asphyxia, congenital anomalies, sudden infant death syndrome and accidents (3). At the same time, attention is shifting from not only ensuring survival, but also attaining optimal development. A growing body of evidence suggests that social and environmental influences, especially during pregnancy and in early childhood, can have important long term health and development implications (4). Another important trend that accompanies the epidemiological and demographic transitions is increasing inequities in child health outcomes within countries.

The progress made recently through the application of novel genetic technologies in large population cohorts has also exposed the importance of very large and well-designed studies with adequate power to test study hypotheses. Large multi-centre studies using rigorous statistical approach lead to reproducible and consistent findings.

The global child health agenda for 2015 and beyond will inevitably need to broaden its focus from mortality reduction to also addressing the social determinants of deaths, growing inequities among children and mothers, and ensuring the sustainability of the progress made against the infectious diseases. With continued reduction in child mortality, the focus of international efforts will also need to shift from merely averting deaths to promoting better health, development, social functioning and education of children in the poorest countries and reduce the effects of inequity. The research needed to address those challenges will require conceptually different studies than those used in the past to address infectious causes.

HUMAN GENOME PROJECT AND MEDICAL RESEARCH

The past decade has witnessed remarkable progress in the development of more reliable, replicable and standardized methods that have improved the quality of research in all areas of human health and development. This is true across a wide range of disciplines, from qualitative research and indicators of quality of life or inequity, to cutting-edge basic research. In parallel to global child mortality reduction, we have witnessed a particular revolution in biomedical research which was brought about by the progress in genetic technology as a result of the Human Genome Project (5).

Genome-wide association studies and whole-genome sequencing have led to an unprecedented level of discovery with novel insights into human biology and the genetic determinants of many common and rare human diseases. However, common human diseases of late onset – such as cardiovascular diseases, most types of cancer, or type 2 diabetes, which are typical of the industrialized countries, have a complex aetiology, including large numbers of strong environmental, social and behavioural determinants and non-genetic risk factors. For most traits studied, the contribution of genetic factors associated with those diseases is due to many common genetic variants, each with very small effects (6). More importantly, the research into genetic determinants of common human diseases has been very largely confined to industrialized countries and focused on their health needs, which form a relatively minor part of the global burden of disease (6). Several researchers in the field have expressed concern that genetic research into common diseases of late onset conducted to date has mainly been serving to increase the gap between the health needs of the global poor and the rich (7).

In the past 2 million years of human evolution, diseases of the late onset had little impact on the natural selection processes that shaped the human genome. They occur in a post-reproductive period and are therefore almost invisible to selection. Thus their genetic architecture is likely to be mostly defined by so-called 'neutral evolution'. Diseases and conditions that had a much greater power to shape human genetic make-up – the problems related to birth, early child survival and maternal mortality – are still present in low-income countries. Those are mainly the problems occurring during labour and persisting infectious causes of mortality of children and young people. They have been shaping the human genome through natural selection. Applying new genetic technologies to study the genetic variants protecting from the major causes of maternal and child deaths would likely yield significant insights into pathogenesis of those diseases and mechanisms of evolved host resistance. Moreover, some of these traits are likely to be subject to balancing and shifting selection, and may reveal larger genetic effects.

Another impact of the human genome project was the development of technologies for fast and relatively cheap sequencing of genomes. Currently, a polymerase chain reaction (PCR) test for a specific infectious agent can be developed in the course of few days through re-sequencing of the genome of an infectious agent, as demonstrated by a recent example during the H1N1 ('swine') flu outbreak in 2009.

LARGE-SCALE BIOMEDICAL SCIENCE

The progress made recently through the application of novel genetic technologies in large population cohorts has also exposed the importance of very large and well-designed studies with adequate power to test study hypotheses. Comparison of small candidate gene studies (which were routinely performed in 1990s and in the beginning of 2000s) with large multi-centre collaborative genome-wide association studies (which became very popular from about 2007) shows that conducting many small studies with insufficient power and without the standardized methodology is an inefficient use of resources and leads to inconsistent and false positive reports in an overwhelming majority of cases. Conversely, large multi-centre studies using rigorous statistical approach lead to reproducible and consistent results.

The need for large scale collaborative research programmes is even more important as research turns to the study of the interaction of genes and environment in causing disease (8). This problem is not limited to genetic research. Information on morbidity and mortality from the diseases of the poor, which form the large majority of global burden of disease and death, is often based on data from relatively few studies conducted in different low-income contexts without standardized methods. They often provide very inconsistent estimates that are not comparable. The recent progress made by genome-wide association studies and, more generally, in the field of genetic epidemiology, has highlighted the importance of 'biobanks'. These are large collections of biological material and extensive associated epidemiological data from large population cohorts assembled in a standardized way. They are designed and developed with close attention to quality assurance, so that emerging technologies can be applied to generate high quality reproducible data on very large numbers of well characterised individuals. One of the main reasons why the developing world is not enjoying potential benefits from the application of novel epidemiological and genetic research technologies is because there are very few biobanks and large population cohort studies in low- and middle-income countries available for systematic study (see Campbell et al. (9) and McKinnon et al. (10) in this issue). Such cohorts are becoming a pre-requisite for reliable research into biological, environmental, genetic, behavioural and social determinants of diseases relevant to their population.

THE CASE FOR LAUNCH OF AN INTERNATIONAL DNA-BASED BIRTH COHORT STUDY

The development of a very large dataset ('biobank') that would include or contain directly comparable data on epidemiological, biological and social factors and samples representative of a large number of human populations would allow researchers to study the determinants of diseases which have made major contributions to the global burden of disease, thus reducing the large inequity in research effort on different causes of morbidity and mortality globally. An international biobank would allow researchers in low- and middle-income countries to gain access to emerging research technologies and use them to study diseases that affect their populations. It would also serve to build and enhance the research capacity in developing countries, to create a large collaborating network of interested researchers globally, and to enable comparisons between their results using the same methodology. The results of biomedical research that would be generated from such a biobank would make a substantial contribution to improving the available information on the morbidity, mortality and the main risk factors for the diseases relevant to the developing world and provide the opportunity to study interactions between genes and a wide range of levels of environmental exposures in causing diseases in different contexts (8). The longitudinal nature of the study could provide valuable information on long-term (life-course) effects of biological, environmental, genetic, social and other factors and their interplay in the modern age.

The development of a global birth cohort would hold out the promise of understanding genetic, environmental and social determinants of health, development and survival of pre-school children. It would also enhance our understanding of the interactions of context-specific social, economic and environmental factors and the human genetic make-up. Ultimately, what will start as a cohort of newborns and children will eventually, over the course of the 21st century,

One of the main reasons why low and middle income countries are not enjoying potential benefits from the application of novel epidemiological and genetic research technologies is because there are very few biobanks and large population cohort studies available for systematic study.

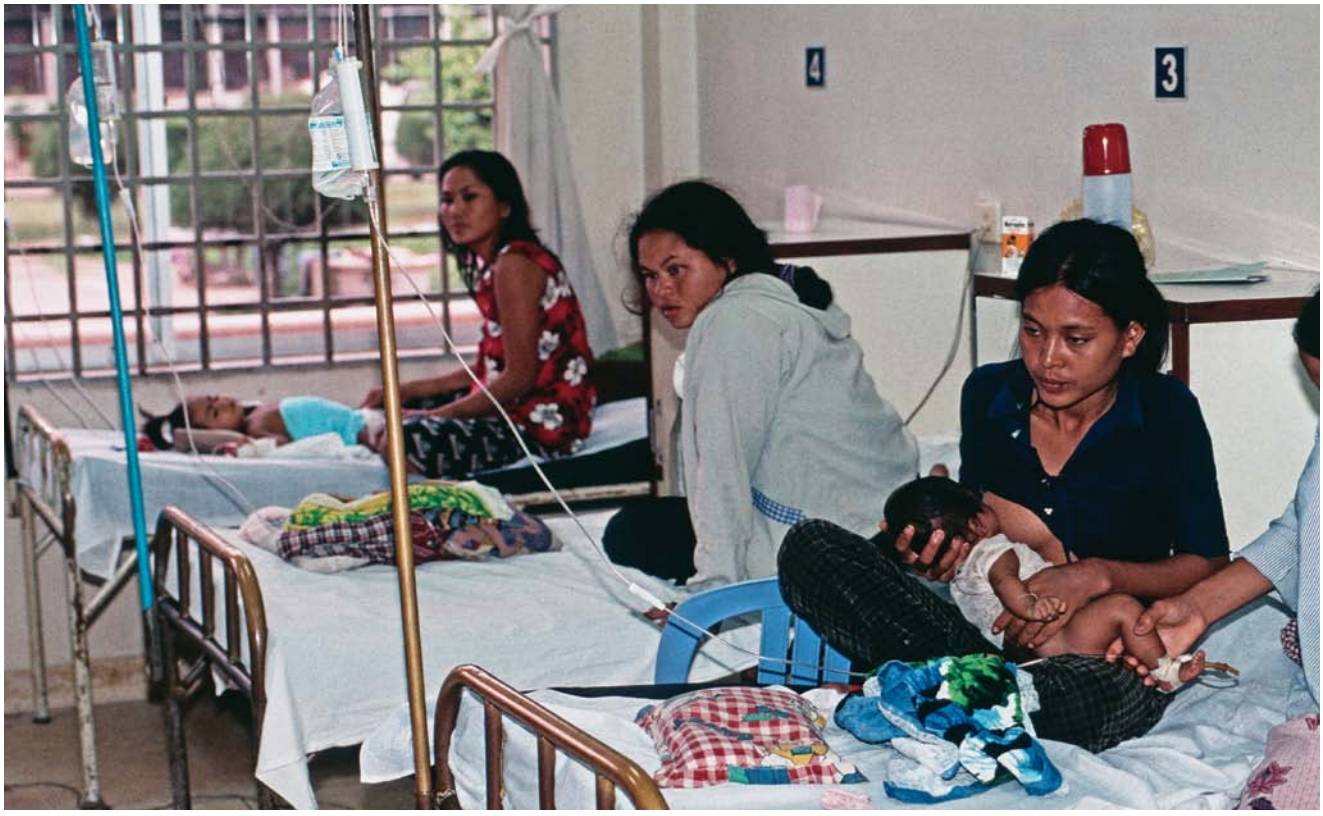


Photo: Courtesy of Dr Martin Willi Weber, personal collection

develop into a longitudinal cohort study of adolescents, and then adults with multiple data points through a time series. This will allow testing many current hypotheses on the causal role of different major risk factors – social, environmental, behavioural and genetic – in human disease and provide answers relevant to all human populations, rather than being limited to high-income countries. It would create a reliable information base that could assist in understanding the burden of health problems in mothers and children globally. There would also be a role for this resource to help understand the genetic and other factors that make children prone to poor response or adverse effects of medicines or vaccines. The conduct of this coordinated study in a consistent way across many sites from low- and middle-income countries, starting with several 'core' sites and expanding through addition of other sites interested in following the same methodological approach, and including up to 1 million newborns, would maximise the power to address many high priority research and health care system questions. Results would also be generalisable globally, rather than confined to specific ethnic, social or economic groups. Through parallel recruitment and involvement of mothers, it would serve to integrate research into interlinked maternal and child health problems.

Building up an all-inclusive international biobank based on best research practice would, over time, develop into a resource that could serve the research needs of many diverse groups of researchers from developed and developing countries alike. The principle that would underlie this cohort is adherence to the highest ethical standards, which have now been developed through the setting up of large biobanks in developed countries, and also the principles of open access to anonymised data (consistent with adherence to ethical principles and local approvals) to interested researchers with legitimate research ideas. This is in line with the emerging 'open science' framework, which enabled open discussion and reanalysis of existing data. Stringent adherence to the highest ethical standards needs to be emphasized throughout each study as one of the goals of the larger project. The development of an international biobank would involve the human and technological capacity of developing countries to work on this project and to assist in building their research capacity and competitiveness.

In many countries there will be a strong sensitivity towards allowing foreign institutions to access genetic material. Most poor countries will rightly fear that any commercial interests from this type of research will only benefit rich countries. Some of them already have laws in place which restrict sending any biological materials outside their borders, particularly those that may have commercial implications. This is why planning an international birth cohort based on DNA will require developing of local capacity. Local researchers will need to be trained to obtain biological materials in the same way across many field sites, store them properly, and generate data locally, while the analysis of the data could then be standardized and centralized. Pre-

serving commercial interests from any patents and sharing them fairly with all the participants from low and middle income countries will represent an important challenge.

WHY IS THE TIME RIGHT?

We need a vision beyond the MDG4 timeframe of 2015. It is time to move beyond focusing on simply averting child deaths and to start planning for this resource. We now have standard operating procedures developed specifically for setting up biobanks and validated genetic technologies and analytical methods for replicable and reliable genetic analyses (11,12). We also have standard ethics principles that are applicable to biobanks and large experience in setting up biobanks in high-income countries (13). Greatly improved communication globally, through internet and mobile phones, and cheaper international travel, has enabled a new kind of research. It is based on massive collaborations of scientists, big projects and large sample sizes, and it generates more reliable results. We propose that globalization of the lifestyle, industry, and many other segments of human activity should be followed by globalization of research into human health and development. There is increasingly a technological capacity in developing countries that could support this kind of vision. For example, several large international organizations, multilateral agencies and even donor foundations have both the legitimacy and organisational infrastructure to provide parallel access to many field sites in low-income countries. They also represent a well-known 'brands' in the international community that could ensure wide participation and commitment from all those taking part in this study. Some organizations and agencies maintain programmes of regular and repeated contacts with a high proportion of children in low resource settings, which could provide a highly cost-efficient framework for recruitment and longitudinal follow up throughout early childhood.

In addition, the incredibly fast progress in development of supporting genetic research technologies, which led to many recent genetic breakthroughs through genome-wide association studies, is beginning to make this vision increasingly realistic. In fact, technological advances are now the main driver of the research progress. It can already be assumed that the appropriate research technologies will become affordable in several years to perform large-scale whole-genome sequencing projects. The costs of genotyping and sequencing of the human genome have been falling rapidly since the year 2000 – from about US$ 3 billion (€ 2.1 billion), which was spent to sequence the first human genome, to only about US$ 4000 (€ 2800) in early 2011 (14–15). The time required to sequence the entire human genome has also fallen from 11 years to only a few hours (14–15).

We need to anticipate the possibility of affordable mass-sequencing several years from now. With this vision, the remaining time would be well spent developing and assembling the datasets from many countries and designing studies which will be the most informative, assuming the availability of genomic information (16).

WHAT SHOULD BE THE STUDY DESIGN OF *GENERATION 2015*?

The study sample should be large and represent many of the world's populations. In each country, a local academic expert in paediatrics/neonatology or obstetrics would be identified and would be responsible for obtaining ethics approval from the nationally relevant body to conduct the study. This person should also be a key / committed member of the study team and should own and drive the process at the country level.

The study would typically involve one large urban teaching hospital and 3–4 health facilities in less developed and rural regions. In each country, a proportional number of newborns and mothers would be recruited to achieve a global sample size of up to 1 million newborns and as many of their mothers and fathers. A sample size of this magnitude is required to ensure sufficient number of cases with different social, economic, behavioural, health and development outcomes in different contexts for an adequate, globally representative study. Each pregnant woman would be informed about the goals of the study and she would be asked to give informed consent for herself and the newborn. In some countries, the signature of the father will also be required. At birth, a baseline questionnaire with the basic information would be filled out for each mother and child, and a blood sample would be obtained from each participant. Any complications during birth would be recorded, as well as the basic anthropometric, clinical and psychomotor assessment of the child.

RESEARCH OUTCOMES AND BENEFITS OF *GENERATION 2015*

Likely short term research outcomes of *Generation 2015* for children would be:

- Description of the morbidity and mortality associated with major child diseases, preterm birth and pregnancy complications;
- Description of normal and abnormal growth and development; and of health and disease from foetal life until early adulthood;
- Identification of biological, environmental, genetic, and social risk factors and their interactions for major child diseases and pregnancy complications

in different contexts (including those associated with low birth weight, preterm birth and congenital anomalies; eclampsia, antepartum haemorrhage, placental abruption, thromboembolism and postpartum sepsis);
- Identification of biological, environmental, genetic, and social determinants of host resistance against the major neonatal and childhood infections (such as neonatal sepsis, pneumonia, diarrhoea) and determinants of immune system development;
- Identification of biological, environmental, genetic, and social determinants of malnutrition and stunting (including micronutrient deficiencies);
- Identification of biological, environmental, genetic, and social determinants of child development (including motor, behavioural, cognitive and psychomotor development);
- Understanding of genetic and environmental determinants of host-pathogen interactions, carriage of microorganisms, immune response to vaccination, and antibiotic resistance.
- Linking the whole genome studies to similar studies that are starting on global pathogens (17).

For mothers, short term research outcome could include:
- Description of the mortality and morbidity associated with the major maternal diseases and pregnancy complications;
- Identification of biological, environmental, genetic, and social risk factors for these conditions and their complications (including eclampsia, placenta previa, lactation duration, postpartum haemorrhage, twinning, obstructed delivery, and puerperal sepsis) in different contexts.

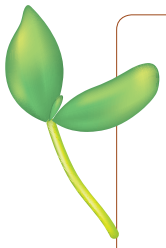
Research outcome for participating countries could be:
- Training of local staff and development of local research capacity, establishing local biobanks and international competitiveness in biobanking;
- Possibility to participate in research at a high international level through large collaborations and to compare its capacity and progress in maternal and child health research with other countries.

Finally, likely indirect research opportunities afforded by *Generation 2015* would be:
- Identification of genes, gene-environment and gene-social interactions;
- Identification of biomarkers for birth related and early childhood disease outcomes or adverse events;
- Establishing global standards for the frequency of gene variants in different populations;
- Defining the content of a genotyping array containing the major disease associated variants across all global population groups;
- Studying the effects of urbanization on genetic structure of populations and impact of admixture on disease traits;
- Studying of the migrations of historical human populations;
- Looking for 'signatures' of natural selection in the genome.

WHAT IS THE PROPOSED STRATEGY OF DEVELOPMENT OF GENERATION 2015?

In the first phase, several 'core sites' would be chosen in low- and middle-income countries, in which the approach would be piloted. The sites would fall in one of two categories: 1) they would be set up in each one of the BRICS countries – Brazil, Russia, India, China and South Africa – i.e., the five very large and rapidly developing economies. Those five countries are front-runners among the developing nations and their economic potential and research capacity are both on a remarkable increase. These countries should have most interest in, and ability to, harbour study sites in which DNA-based birth cohorts could be developed, as a logical next step necessary to acquire competitiveness in genomic research at an international level; 2) they would be set up in several rare sites in low-income countries in which high-quality research was being conducted for many years, and study populations are used to research of effectiveness of different interventions. These study sites were set up by driven individuals from low-income countries, frequently through bilateral collaboration with a western institution. Because of randomized controlled trials that are being conducted at such sites, the studies have availability of 'cold chains' required for vaccine delivery, appropriate ethics approvals, and a motivated team of researchers and study populations. They represent rare and relatively unique sites where a proper DNA-based biobank could be set up.

The pilot studies in those several selected sites would improve our knowledge and understanding of the challenges with developing biobanks in low- and middle-income countries. We would aim to develop standardized study protocols based on those early experiences, and then invite groups from many more low- and middle-income countries to join this Generation 2015 with their data collections assembled in a standardized way. Through this 'snowballing' development, we would hope to achieve sufficiently large numbers to develop a true international DNA-based birth cohort, which would allow studying of genetic determinants of health and disease in children across the world, but also try to document the effects of inequity and socioeconomic differences on children's biology and development potential.



The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.

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PAPERS

Systematic review of birth cohort studies in Africa

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Aim In sub-Saharan Africa, unacceptably high rates of mortality amongst women and children continue to persist. The emergence of research employing new genomic technologies is advancing knowledge on cause of disease. This review aims to identify birth cohort studies conducted in sub-Saharan Africa and to consider their suitability as a platform to support genetic epidemiological studies.

Methods A systematic literature review was conducted to identify birth cohort studies in sub-Saharan Africa across the following databases: MEDLINE, EMBASE, AFRO and OPENsigle. A total of 8110 papers were retrieved. Application of inclusion/exclusion criteria retained only 189 papers, of which 71 met minimum quality criteria and were retained for full text analysis.

Results The search revealed 28 birth cohorts: 14 of which collected biological data, 10 collected blood samples and only one study collected DNA for storage. These studies face many methodological challenges: notably, high rates of attrition and lack of funding for several rounds of study follow up. Population-based 'biobanks' have emerged as a major approach to harness genomic technologies in health research and yet the sub-Saharan African region still awaits large scale birth cohort biobanks collecting DNA and associated health and lifestyle data.

Conclusion Investment in this field, together with related endeavours to foster and develop research capacity for these studies, may lead to an improved understanding of the determinants of intrauterine growth and development, birth outcomes such as prematurity and low birth weight, the links between maternal and infant health, survival of infectious diseases in the first years of life, and response to vaccines and antibiotic treatment.

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The last two decades have seen a dramatic rise in research output in longitudinal birth cohort studies (**Figure 1**) (1). Several large quality birth cohort studies have been conducted, and are still ongoing, in high income countries (2–11). These studies provide useful insight into the developmental, social and environmental exposures that interact in determining disease risk (4–6) and they have led to many notable discoveries (7–9).

In recent years, large 'biobank' studies have emerged as the most successful way of harnessing new genomic technologies, with the aim of providing resources for the future investigation of the separate and combined effects of genetic, environmental and lifestyle factors underlying multifaceted human diseases (10). The value of combining epidemiological and genomic data by using large scale cohort study design is growing in recognition and studies recruiting more than 500 000 participants are already established or underway. These studies, such as the UK Biobank (11), have focussed mainly on studying the major common diseases of public health importance, amongst adults in the developed world.

Many diseases of the poor, which represent the greatest health burden in terms of global mortality, have largely been neglected from this field of research. In 2008 there were an estimated 8.8 million child deaths; 5.97 million (68%) were caused by infectious diseases and nearly half (4.20 million) of the deaths occurred in Africa (12). Global child mortality has fallen since 1990, yet the targets outlined in the Millennium Development Goals to reduce this by two thirds before 2015, are not being met by many countries (13). In sub-Saharan African (SSA) countries, maternal complications of pregnancy and communicable diseases of women and children are still major public health concerns, with an unacceptably high burden of mortality (2,12,13).

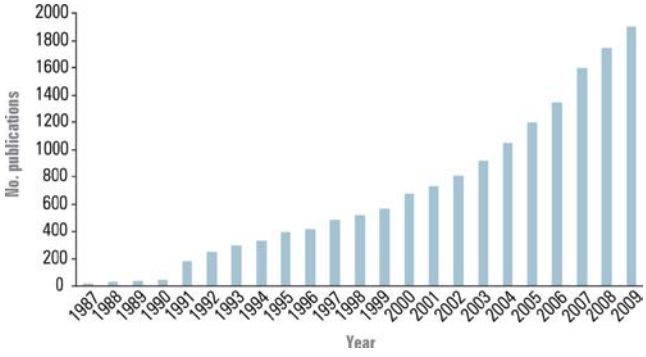


Figure 1 Number of publications resulting from a search of the ISI *Web of Science* database for any article containing the term 'birth cohort study' in the past 20 years; no language or other restrictions.

A study by Moran et al (14), at the Institute for International Health in Sydney, observed a marked discrepancy between funding for research and development relative to disease burden. This mismatch (with very low research investment relative to disease burden) was most notable for bacterial pneumonia and diarrhoea which account for 18% and 15% of global child deaths respectively, most of these death's being concentrated in several large developing countries in SSA and South East Asia (12). In addition to this, the transferability of research findings on determinants of disease from high-income countries to SSA may be limited. For example, between African and European studies different distributions of genetic polymorphism have been found which determine genetic susceptibility to both communicable disease (eg, malaria, HIV, tuberculosis) and non-communicable disease (eg, breast and prostate cancer) (15). Birth cohort studies conducted in high income countries fail to represent the conditions in poverty stricken areas of the world and there is a clear need for broader geographical representation in this area of research.

The aims of this review were 3-fold:

1. to provide a systematic review of birth cohort studies from SSA and discuss some important characteristics of these studies (population size, length of study, and follow up frequency);
2. to examine the methodology of and the data collected from birth cohort studies in SSA;
3. to offer recommendations on the feasibility and sustainability of support for this area of research based on the findings of this review and in the context of the existing literature.

METHODS

Search strategy

After initial scoping exercises and input from a librarian to provide MeSH headings and keywords pertinent to this study, a systematic search was conducted across the following databases (Figure 2):

1) via OVID: Medline (1950 onwards) on 30 July 2010 and Embase (1980 onwards) on 19 August 2010, using the strategy outlined in **Table 1**;
2) via the Global Health Library Regional Index: AFRO on 22 August 2010, using 'cohort' as a keyword;
3) search of grey literature: via OpenSIGLE on 22 August 2010, using 'birth' and 'cohort' as keywords.

An informal search of Google Scholar produced no additional results.

Reference lists of finally selected papers were hand searched for further studies.

The aim of this search was to identify all birth cohort studies and not necessarily all publications relating to each study.

Inclusion/exclusion criteria

We defined a birth cohort study as a study collecting data from a group of people born at a similar time, by active (medical examinations etc) and/or passive (hospital records, etc.) surveillance, with follow up over a variable period of time (months to decades) (**Table 2**). Initial inclusion

Table 1 Search strategy for Medline and Embase*

Birth cohort	OR	Longitudinal studies
1. (birth* adj3 cohort*).ti,ab. 2. (pregnan* adj3 cohort*).ti,ab. 3. famil* cohort*.ti,ab. 4. (birth* adj3 longitudinal).ti,ab.		5. Longitudinal Studies/ 6. cohort* survey*.ti,ab. 7. panel stud*.ti,ab. 8. panel survey*.ti,ab.
AND		
Developing countries		
1. exp Developing Countries/ 2. africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or tunisia/ or "africa south of the sahara"/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/ or "antigua and barbuda"/ or cuba/ or dominica/ or dominican republic/ or grenada/ or guadeloupe/ or haiti/ or jamaica/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or central america/ or belize/ or costa rica/ or el salvador/ or guatemala/ or honduras/ or nicaragua/ or panama/ or panama canal zone/ or mexico/ or argentina/ or bolivia/ or brazil/ or chile/ or colombia/ or ecuador/ or guyana/ or paraguay/ or peru/ or suriname/ or uruguay/ or venezuela/ or asia, central/ or kazakhstan/ or kyrgyzstan/ or tajikistan/ or turkmenistan/ or uzbekistan/ or cambodia/ or east timor/ or indonesia/ or laos/ or malaysia/ or myanmar/ or philippines/ or thailand/ or vietnam/ or asia, western/ or bangladesh/ or bhutan/ or india/ or sikkim/ or afghanistan/ or iran/ or iraq/ or jordan/ or lebanon/ or syria/ or turkey/ or yemen/ or nepal/ or pakistan/ or sri lanka/ or exp china/ or korea/ or "democratic people's republic of korea"/ or "republic of korea"/ or mongolia/ or albania/ or lithuania/ or bosnia-herzegovina/ or bulgaria/ or byelarus/ or "macedonia (republic)"/ or moldova/ or montenegro/ or romania/ or russia/ or serbia/ or ukraine/ or yugoslavia/ or exp transcaucasia/ or armenia/ or azerbaijan/ or "georgia (republic)"/ or comoros/ or madagascar/ or mauritius/ or seychelles/ or fiji/ or papua new guinea/ or vanuatu/ or palau/ or samoa/ or tonga/ 10. low income countr*.tw. 11. middle income countr*.tw. 12. (low adj2 middle income countr*).tw.		

*Within each box all terms were combined with Boolean operator OR. Developing countries were those defined by the World Bank list of economies (July 2010) as low- or middle-income.

criteria were sensitive but not specific, so that we could retrieve longitudinal studies which, whilst not necessarily meeting strict definitions of birth cohort studies, are useful in providing an overview of the characteristics of studies collecting longitudinal data in infancy/childhood in SSA. For more specific birth cohort analysis, strict criteria were applied to studies in a follow-up to the initial assessment. Studies that met the criteria were retained for full text analysis in order to focus further on quantitative and qualitative aspects of data collection.

Table 2 Inclusion and exclusion criteria for assessing the studies relevant to birth cohorts in sub-Saharan Africa

Inclusion criteria	Exclusion criteria
Stage 1	**Stage 1**
• birth cohort/ longitudinal cohort or cross sectional study of longitudinal population or qualitative review of birth cohort. • low and middle income countries • reporting primary results or insight to methodology or meta-analysis of studies	• enrolment at >10 years of age • primarily a pregnancy study limited to birth weight follow up
Stage 2	**Stage 2 –Quality criteria**
• country in WHO South Saharan African Region	• minimum of 12 months of follow up • minimum cohort size of 500 • less than 60 months of age at induction

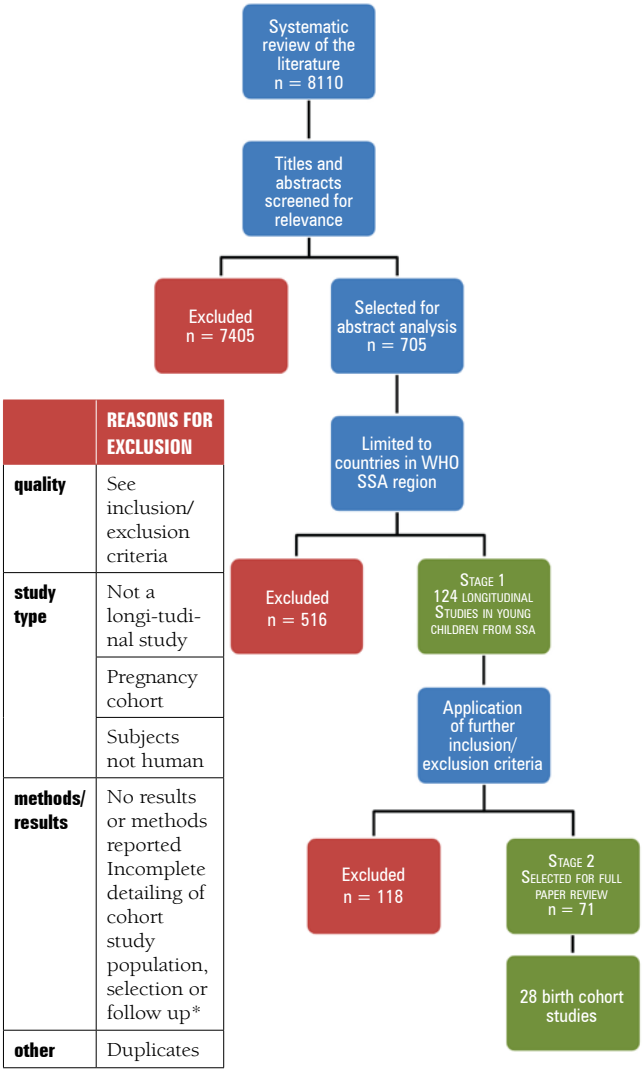


Figure 2 Summary of the literature search.

Data extraction

Studies included in Stage 1 were extracted to an Excel file and analysed by abstract alone. This exercise aimed to provide background perspective of longitudinal studies in SSA rather than provide comprehensive data extraction. Studies included for full paper review (Stage 2) were assessed in full and the data obtained was intended to be comprehensive.

Both qualitative and quantitative data were assessed. Studies were assessed by categories that included, but were not limited to, biological samples (such as blood, DNA and urine); anthropometric data; cognitive, psychological and other developmental indicators; socioeconomic data; methodological challenges; and attrition.

RESULTS

Abstract analysis of 189 papers produced data from 124 longitudinal cohort studies (**Table 3** and **Figure 3**) meeting Stage 1 criteria. Abstracts were analysed for basic study characteristics (**Table 3**).

Study characteristics – Stage 1

Study size: The study sizes ranged from 30 to 11,342 participants. 79 of the studies recruited 1000 or less participants and only 27 studies recruited more than 1000 at induction. 59 recruited less than the quality criteria (500 participants) suggested in this study.

Follow up: 53 studies began data collection either in the antenatal period or at birth. The follow up period of participants ranged from 3 months to 20 years. The 'Birth To Twenty' study in South Africa is the longest running, has followed the initial cohort for 20 years and is still ongoing. The majority of the studies (n = 63), however, followed the cohort for 2 years or less.

Frequency: Frequency of follow up ranged from daily to two-yearly. Most abstracts did not report data on follow up frequency and full text analysis was needed.

Methods: 48 studies were identified that followed a specific population. The large majority of studies identified for setting were conducted in the community.

Study characteristics – Stage 2

The study characteristics of the full paper reviews are found in **Table 4**. Analysis of 71 full text publications produced data for 28 separate birth cohort studies. All further results relate to these 28 studies.

Study size: Of the 28 studies retained for full paper analysis, the median number of participants at induction is 1272, ranging from 571 to 11 342.

Table 3 Characteristics of 124 birth cohort studies in Sub-Saharan Africa (SSA)

Characteristics		No. of studies
Size of study*	0–500	49
	501–1000	22
	1001–1500	6
	1501–2000	6
	2001–2500	4
	>2500	11
	Not reported†	26
Maximum age at enrolment (months)	Antenatal-birth	53
	0–12	14
	13–24	5
	25–36	5
	37–48	3
	49–60	12
	>60	10
	Not reported†	22
Duration of follow up (months)	0–24	64
	25–48	13
	49–72	7
	73–96	1
	96–120	3
	>120	5
	Not reported†	31
Follow up frequency (months)	Daily	1
	Weekly	5
	Monthly	13
	2–6 monthly	17
	>6 monthly	15
	Not reported†	74
Setting	Community based	46
	Facility based	7
	Not reported†	71
Specific population	Born to HIV+ mother	19
	Malaria endemic area	9
	Malnourished/ underweight	6
	Intervention population	2
	Not specific	76
	Other	12

* Sometimes varied between publications.
† Details not presented in abstract.

Follow up: Median follow up was 24 months, ranging from 12 to 216 months. Median frequency of follow up was bi-monthly, ranging from bi-weekly to five annualy.

Age at induction: The mean age of study participants at induction was 17 months.

Biological measurements

Blood: Ten of the studies collected blood from study participants (**Table 5**). A number of these ten studies also took other blood samples, including: maternal blood (n = 8), cord blood (n = 5), placental blood (n = 3) and blood smears

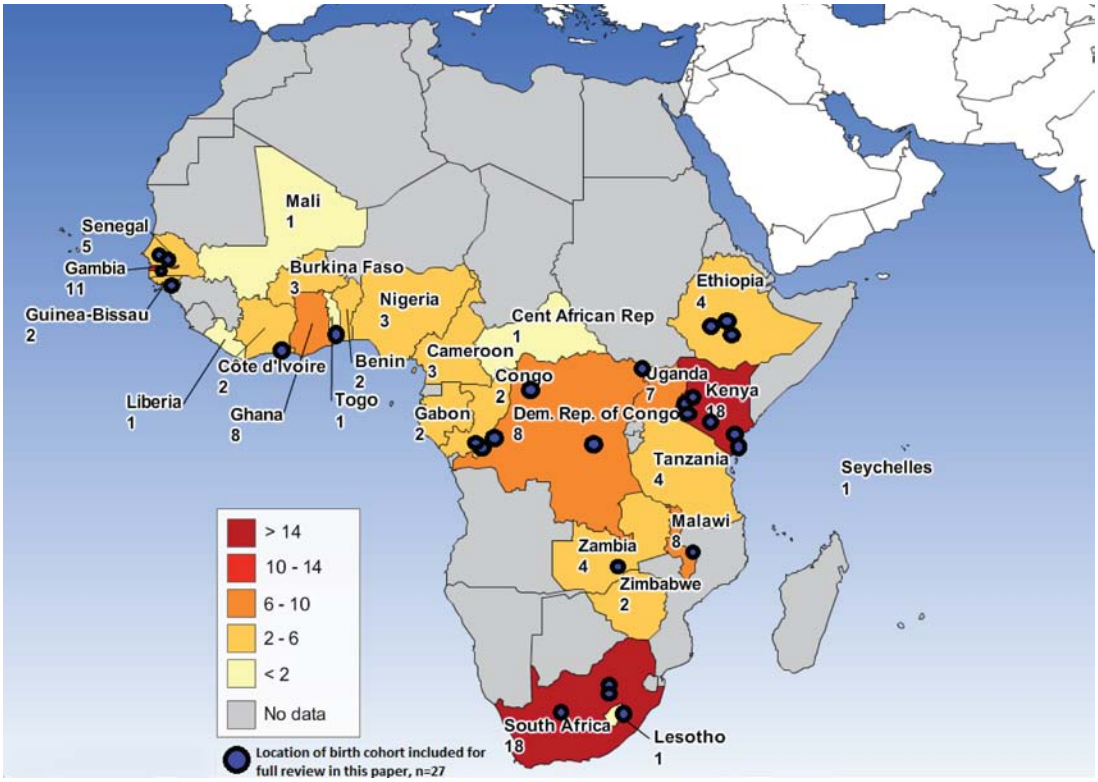


Figure 3 Number of birth cohort studies in Sub-Sahran Africa (SSA) by country. Coloured boxes refer number of studies in each country (out of 124 birth cohorts). Blue spots relate to the specific locations of the 28 cohorts which met full quality criteria. One paper was not presented due to multiple locations of study site.

(n = 5). Analysis of samples varied. The most common tests performed on samples were ELISA and Western blot for HIV status and Giemsa stain for malaria.

DNA: most of the longitudinal studies in SSA did not take DNA samples. Five studies collected DNA: 3 were to assess HIV status, 1 to detect malaria and only 1 stored DNA. The 'Birth to Twenty' study in South Africa began DNA collection in 2005 and currently has samples for 2200 participants.

Other biological samples

Very few other biological samples were taken by studies. Thirteen of the 28 studies collected no biological data at all.

Anthropometry: 18 studies detailed methods of anthropometric measurements. The World Health Organisation/ National Centre for Health Statistics were the most commonly used growth references.

Other data: Only one study measured psychological variables. Measurement of nutrition, cognitive development, socio-economic status and psychological variables most frequently used questionnaire based data collection.

Loss to follow up

Attrition in SSA birth cohorts, measured from induction to last follow up, has a median of 28% ranging from 0% to 72.9%. Attrition rates were as follows: 0 to 10% attrition in 4 studies, 11–20% in 1 study, 21–30% in 4 studies, 31–40% in 3 studies and more than 40% in 4 studies. Twelve studies did not clearly report loss to follow up.

Problems reported by studies leading to high rates of attrition included: high infant mortality rates, family relocation, refusal to participate, maternal death, wave attrition (not present for one follow up, but return for the next) and failure of researchers to retrace study individuals.

Efforts to promote successful follow up included: providing participants with incentives – eg, 'Birth To Twenty' provided participants with basic mobile phones to aid contact; the Asembo bay cohort study provided free health clinics for all participants and a gift pack containing baby care items was given to mothers (this reduced attrition from 18.9% in 1992 to 7.7% in 1994). The Asembo Bay study also provided free medications, immunizations, and transportation to and from the study clinic, which contributed to a rate of loss to follow-up of only 4 percent over the first 18 months of follow up.

Table 4 Characteristics of studies included for analysis

Reference	Country	Location	Year	Type of cohort study	Cohort size at enrolment	Maximum age at enrolment (months)	Follow up (months)	Follow up frequency	Attrition* (%)
Carme 1984; Guillo du Bodan 1984	Congo	Linzolo	1984†	retrospective	1003	birth	60	‡	‡
Carme 1992; Carme 1994	Congo	Linzolo	1981	retrospective	2424	birth	24	twice	‡
Adjorlolo-Johnson 1994	Cote d'Ivoire	Abidjan	1990	prospective	619	birth		3 monthly	4.4
Greenberg 1991	Democratic Republic of Congo	Kinshasa	1986	prospective	587	9	18	‡	4
Hauspie 1989	Democratic Republic of Congo	‡	1977	prospective	4030	48	48	‡	‡
Van Lerberghe 1986	Democratic Republic of Congo	Kasongo	1974	prospective	4273	60	12	‡	26
Ryder 1994a; Ryder 1994b	Democratic Republic of Congo	Kinshasa	1986	prospective	1091	birth	36	monthly	‡
Alemu 1996; Asefa 1996; Asefa 1998; Lesaffre 1999	Ethiopia	Jimma	1992	prospective	1563	birth	12	2 monthly	14
Byass 2008	Ethiopia	Butajira	1987	prospective	1884	birth	216	monthly/ quarterly	‡
Lindtjorn 1992	Ethiopia	Dubluk/ Elka	1989	prospective	828	60	24	2 weekly	‡
Kristensen I 2000	Guinea-Bissau	‡	1990	prospective	8752	birth	20	‡	0†
Fegan 2007	Kenya	‡	2004	prospective	3500	59	24	yearly	‡
Malhotra 2009	Kenya	‡	2002	prospective	586	birth	36	6 monthly	34
McElroy 1999; McElroy 2000; McElroy 2001	Kenya	Asembo bay	1992	prospective	942§	birth	48	2 weekly	28
Nokes 2004; Ochola 2009	Kenya	Kilifi	2002	prospective	635	birth	12	monthly	10
Oomen 1979	Kenya	Machakos	1974	prospective	568	60	22	monthly	32
ter Kuile 2003; van Eijk 2002	Kenya	Kisumu	1996	prospective	661	0	12	monthly	46
Cohen 1976	Lesotho	‡	1969	cohort/ cross sectional	1317	60	60	‡	‡
Maleta 2003	Malawi	Lungwena	1995	prospective	767	0	36	monthly	72.9
Chilongozi 2008	Malawi, Tanzania, Zambia	‡	2001	prospective	2383	0	12	2 monthly	44
Elguero 2005	Senegal	‡	1989	analysis of two birth cohorts	11342	0	24	‡	‡
Simondon 1998	Senegal	Niakhar	1983	mixed retro-spective/ prospective	1650	60	120	twice	46.8
Kristensen 2006	South Africa	Soweto	2000	prospective	571	0	12	2 weekly	21
Reid 1990	South Africa	Prieska	1932	retrospective	1227	0 /birth record	48	twice	32.5
Adair 2009; Ellison 2000; Griffiths 2008; Heerden 2010; Jones 2008; MacKeown 2000; MacKeown 2003 MacKeown 2007; Martorell 2010; Naicker 2010; Norris 2009; Pedro 2008; Richter 1995; Richter 2006; Richter 2007; Sabet 2009; Sheppard 2009; Steyn 2000; Steyn 2006; Thandrayen 2009; Vidulich 2006; Whati 2005; van Yach 1991	South Africa	Johannesburg (Soweto)	1990	prospective	3273	antenatal period (mother) and birth	ongoing	yearly	28§
Rayco-Solon 2004	The Gambia	West Kiang	1950	retrospective	3981	0	death/ oct 97	yearly	‡
Vella 1993; Vella 1994	Uganda	Arua	1987	prospective	1072	60	24	‡	‡
McDowell 1982	Zambia	‡	1970	prospective	1342	0	60	6 monthly	‡

PC = prospective cohort, RC = retrospective cohort

*Attrition at last recorded study of initial cohort. Attrition varied by study outcome.

†Publication year.

‡Data not reported.

§ Reporting of study size varies (1570, 942 and 833); 942 reported in first paper, so this value taken.

Table 5 An overview of the studies that collected biological samples

Reference	Blood sample						Sample analysis	Frequency of sampling	
	Maternal blood	Cord blood	Placental blood	Offspring blood	Plasma/ serum	Blood smear		Fixed	Ongoing
Adjorlolo-Johnson 1994	Y	N	N	Y	serum	N	ELISA, western blot, synthetic peptide tests, flow cytometry, cell counts.	–	–
Greenberg 1991	Y	Y	N	Y	–	Y	Screen for HIV-1 antibodies by ELISA, confirmed by Western blot. Cord-blood from 64 randomly selected seropositive infants.	12 and 18 months of age	–
Ryder 1994a; Ryder 1994b	Y	N	N	Y	serum	N	ELISA, western blot.	–	–
Malhotra 2009	Y	Y	Y	Y	Y	Y	Immunoglobulims, antibodies, filter for Wuchereria bancrofti microfilariae, Hb levels (HemoCue). Antigens, mitogens and recombinant cytokines.	Birth	Six monthly
McElroy 1999; McElroy 2000; McElroy 2001	Y	Y	Y	Y	plasma	Y	Hb levels: "hemocue", Microscopy: giemsa	Birth	Monthly (finger prick) Two weekly (blood film)
Nokes 2004; Ochola 2009	N	Y	N	Y	–	N	ELISA	Birth	Three monthly
ter Kuile 2003; van Eijk 2002	Y	N	Y	Y	–	Y	Finger prick for HIV test, malaria smear, Haemocue for hb, serostrip HIV-1/2 and Capillus HIV1-HIV2 tests	Pre-inclusion (maternal blood), pregnancy, 1 month post partum	–
Chilongozi 2008	Y	N	N	Y	–	N	Syphilis screen, ELISA or western blot test, complete blood count, CD4 cell count, plasma viral load.	–	–
Adair 2009; Ellison 2000; Griffiths 2008; Heerden 2010; Jones 2008; MacKeown 2000; MacKeown 2003; MacKeown 2007; Martorell 2010; Naicker 2010; Norris 2009; Pedro 2008; Richter 1995; Richter 2006; Richter 2007; Sabet 2009; Sheppard 2009; Steyn 2000; Steyn 2006; Thandrayen 2009; Vidulich 2006; Whati 2005; van Yach 1991	Y	Y	N	Y	–	–	Non fasting sample- lipids. Lead, glucose, insulin, cotinine, HIV status, vit D and bone turnover markers.	Birth, 5 years, 13 years and 14 years.	
Rayco-Solon 2004	N	N	N	Y	–	Y			
TOTAL	8	5	3	10		5			

Y – yes, N – no

Other factors contributing to successful follow up included modern communication systems, close and frequent contact with all study sites for standardisation, short periods between phases of data collection and detailed contact information stored in computerised systems. These measures, however, were not appropriate or feasible for the majority of the studies reviewed.

DISCUSSION

This review examined birth cohort studies in SSA – their methodologies and the challenges they face – in light of the absence of biobank studies in this region and with a view to making recommendations about future plans for this area of research. The study clearly shows that, although a number of efforts do exist, they evolved in their local settings and they weren't planned or organized in any systematic way. Also, they very rarely (if ever) collect and store DNA material and frozen plasma for further genetic and biochemical studies.

Study limitations

Attempts to overcome publication bias were made by searching for unpublished literature via OpenSIGLE (System for Information on Grey Literature in Europe) an open access source of bibliographical references of reports and other grey literature produced in Europe until 2005. It is, however, possible that some sources of grey literature were missed. Only two papers were retrieved in French, and none in Portuguese, despite the large Francophone and Lusophone populations in Africa. Although no language restrictions were applied, it may suggest the design of the search criteria was not optimised to retrieving these studies.

Due to the longitudinal nature of cohort studies large numbers of papers are produced, over long periods of time,

from multiple rounds of study follow up. It is, as a result, challenging to capture the most updated description of an individual study. Efforts were made to group papers by study, both by hand (matching authors, years and sample sizes) and citation mapping, in order to identify the most recent description of any particular study and to capture all the data across the spread of publications arising from a single cohort. It is, however, possible that the current status of a study was not identified. Study characteristics are often reported differently between publications as cohort studies continue to develop over time in their methods and study sub-populations. It is possible that the conclusions of this study about the lack of good biological data collection reflect unreported data or failure to capture data, rather than a genuine lack of samples. Writing to authors may have helped to indentify the most comprehensive and current descriptions of birth cohort studies.

Study quality

Comparability across birth cohort reviews is complicated by the different definitions of birth cohort studies. The definition is generally recognised as the longitudinal follow up of a group of people born at, or around, the same time. The descriptive elements considered important in this review include the study size at enrolment, the age of study participants at enrolment, the duration of follow up and the frequency of these follow ups. This review identified a subgroup of twenty eight studies that met strict criteria (minimum enrolment of 500 or more study participants with at least 12 months of follow up and enrolment at less than 60 months of age) with a view to identifying studies suitable for biobank data collection for the purposes of studying important causes of child health and development.

This review demonstrated, first, that the majority of birth cohort studies researched a specific sub-population rather than representative population samples eg, assessing HIV related outcomes in offspring of HIV positive mothers. Second, the SSA birth cohorts are largely restricted to small sample sizes with short periods of active follow up, with sample sizes varying from 571 to 11342. Only two birth cohort studies were identified with study sizes greater than 5000. The 'Birth to Twenty' study in South Africa began following an unselected population of 3275 mothers and their children in 1990 and is still ongoing today. It is the best example of a large scale, long term birth cohort in SSA. However, it is of relatively small scale when compared to similar birth cohort studies in developed countries such as Avon Longitudinal study of Parents and Children (ALSPAC) which studied 13971 births at induction (2). Typical genome wide association study sizes comprise several thousand, or even tens of thousands, of individuals. Recommended sample sizes for gene-environment interaction studies are of the order of twenty thousand participants with a specific outcome of interest (16). Small sample sizes of the African studies identified in this review are unlikely to provide a secure basis upon which to study the genetic and environmental influences of health and development outcomes in pregnancy and early childhood.

Second, the large majority of studies followed the cohort for less than two years, an insufficient amount of time on which to draw conclusions relating to the long term influence of developmental factors on future child, adolescent and adult health.

Third, the large majority of studies followed the cohort for less than two years, an insufficient amount of time on which to draw conclusions relating to the long term influence of developmental factors on future child, adolescent and adult health.

Finally, there is no single coordinated definition of a birth cohort and measurements vary greatly between different studies. It is, therefore, difficult to combine study results or conduct meta-analyses of data due to inherent differences in birth cohort study design and measurement methods. Efforts have been made to bring together data from the largest low and middle income country birth cohorts as part of the work of the Consortium of Health Orientated Research in Transitioning Societies (COHORTS), but this initiative does not include the creation of a large biological resource (17). The five largest prospective birth cohorts with sample sizes of 2000 or more newborns and at least 15 years of follow up were included in this initiative and the data sets of these studies pooled. Some of the challenges identified by the COHORTS group included differences in variable definitions and measurement techniques; different ages for which data are available; and different time periods captured by each study. These differences between the studies resulted in restriction of their analyses to only those variables which were collected consistently across the cohorts. These limitations also apply to the SSA studies identified in this review.

Biological data

Human genomic studies have revolutionized our understanding of disease and rapid progress has been made in high income countries with completion of the human genome project, emergence of genome wide association studies and the prospect of whole genome sequencing and pharmacogenomics (18,19).

Africa, where all human populations originated, is the most genetically diverse region in the world. To date, the relative risks (or odds ratios) for complex diseases associated with genetic loci – studied mainly in high-income countries – have been small (1.5 or less) (20). People of African origin display shorter linkage disequilibrium (LD) blocks, allowing for more precise mapping of loci associated with disease risk and the potential to discover disease causing variants

which may previously have been masked by large LD blocks in European populations (21,22). Genetic factors do not account for chronic disease susceptibility alone, rather they interact with environmental exposures to determine disease risk (23). Africa's genetic diversity, combined with its environmental diversity, unique life exposures and natural selection pressures presents many exciting possibilities for genetic research.

This review serves to highlight the lack of systematically collected birth cohort data on genetic, environmental and lifestyle factors underlying child health and development problems of SSA. Only one of the birth cohorts identified took DNA samples to establish a DNA bank, and this contained only 2 200 individuals. The majority of DNA samples taken by studies were one-off measurements for diagnostic assessment of HIV or malaria status. The 473 GWA articles contained in the National Human Genome Research Institute catalogue were assigned weight according to country of origin in a study by Rosenburg et al. (24). These comparative weightings showed that the contribution of sub-Saharan African countries to genome wide association studies, even when all SSA country inputs are combined (0.34), is insignificant compared to those of high income countries (eg, 205.5 in USA, 68.15 in UK and 37.02 in Germany).

Overall, 13 of the 28 studies collected no biological samples of any sort reflecting either a primary interest in alternative data collection, or a simple lack of resources, manpower and laboratory facilities to do so.

The same technologies which are being used in developed world biobanks have the potential to generate new knowledge about communicable diseases amongst mothers and children in Africa. However, a gaping divide exists in clinical and genomic research capacity between SSA and higher income countries (21). DNA based studies require stringent quality criteria for complex processing and storage of samples, access to laboratories which are equipped with state-of-the-art facilities and run by well trained staff (22). The complexity of undertaking these studies could, however, foster local capacity building and drive innovation for new research opportunities and development in SSA.

Genome-based studies in developing countries present important ethical considerations (25). Valid consent must be obtained in a way that ensures an informed and voluntary choice can be made by study participants, regardless of their level of education and literacy. Protecting the privacy of study participants is an essential consideration as GWA studies have the potential to reveal stigmatising information about an individual or population which may be used for harm (26). Due to the lack of large scale genotyping facilities in most sub-Saharan African countries, samples may require storage and export for processing in high income countries (27). It is essential that a balance is struck between protection of study participant's privacy and the need for data sharing and release in research (28). Strict guidelines on sample handling and destruction are often required limiting the ability for secondary analysis and reuse of archived samples (29). Obtaining ethical approval for genomic research in developing countries is understandably a complex and challenging process. However, these challenges can be successfully met as the experience in malaria research has shown (25).

Challenges of longitudinal studies in low-income countries

Longitudinal studies pose unique methodological challenges to researchers. In birth cohorts two types of sample loss are reported: initial non-enrolment and attrition on follow up. Both have the potential to cause systematic bias in collection and interpretation of results. In the developing world, failure to trace individuals is reported as the most common cause of attrition (30). Lack of infrastructure, administrative centres, national databases and aids such as widespread patient identifiers in SSA pose a challenge to data collectors. High rates of migration also pose a challenge to longitudinal studies especially as the more educated, urban section of a cohort may be more likely to migrate, potentially resulting in a sample no longer representative of the original population from which it was taken.

Efforts to overcome attrition have included providing participants with incentives to continue with the study, however, there is a risk of subsequently conditioning the cohort such that they are no longer representative of the normal population. Other studies have used national census information, army enlistment days and systematic searching of all homes in the study area to retrace study participants.

Despite the methodological challenges faced by longitudinal cohorts in the developing world they are achievable and studies such as the Pelotas birth cohort in Brazil are testament to this (31). The study which began in 1982, measuring over 4000 variables for 5914 study participants, is one of the largest and longest running birth cohorts in the developing world and is still ongoing today. Household sampling, army enlistment and the low emigration rate in Pelotas limited attrition and follow up in 2005 retraced 77% of the original cohort.

Funding

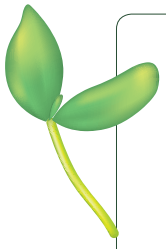
Most birth cohort studies report difficulty in attracting funding for initiating studies and then supporting multiple rounds of follow up. There is a particular need for multiple sources of funding if birth cohort studies are to collect biological samples for biobank data. The UK Biobank, a cohort of 500 000 people with a baseline assessment and 8 year

follow up is projected to cost US$ 104 million (€ 72.5 million) (32). The UK Biobank was funded by Wellcome Trust (the UK's largest independent medical research charity), the Medical Research Council, the Department of Health, the Scottish Government, British Heart Foundation, the Northwest Regional Development Agency and others.

One study estimated that the cost of setting up a ten year study similar to the UK Biobank in SSA with additional exposure measurements, intervention trials and research capacity building – would cost anywhere between, US$ 23.7 million (€ 16.5 million) for a cohort of 150 000 people across three countries or US$ 2.56 billion (€ 1.8 billion) for a cohort of 400 000 people across four countries (33). The cost per person per year for the UK Biobank estimate to US$ 26 (€ 18) compared to US$ 14–644 (€ 9.8–449) for a large scale SSA study. Such investments are substantial. They will, however, have a long term effect by revolutionizing the infrastructure, training and future development of academic and clinical research in SSA, and may subsequently stimulate economic development.

CONCLUSION

This review identified a larger number of relevant studies from 28 sites in Africa (34–91). Only one birth cohort study which systematically collected DNA samples and related health data was identified but this was of a small scale. Investment in research training, infrastructure and pilot studies alongside the creation of ethical frameworks, quality assessment and locating long term sources of funding are just a few of the initial challenges that need to be addressed to establish and then ensure the sustainability of such biobanks in SSA. Governments and not-for-profit agencies have made large investments towards funding biobanks in high-income countries. We suggest that it is now time they turned their resources towards investing in the research capacity of SSA, and in doing so, investing in the future of mothers and children upon whom a large burden of avoidable mortality is centred.



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Systematic review of birth cohort studies in South East Asia and Eastern Mediterranean regions

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Background Few longitudinal studies of children have taken place in the developing world, despite child mortality being concentrated there. This review summarises the methodologies and main outcomes of longitudinal studies of pre-school children (0 to 59 months) in the World Health Organization's South East Asia (SEA) and Eastern Mediterranean (EM) Regions.

Methods A systematic search of literature using pre-defined criteria revealed 7863 papers. After application of quality criteria, 120 studies were selected for analysis.

Results The search revealed 83 studies in the SEA region and 37 in the EM region, of which 92 were community-based and 8 facility-based. Objectives were diverse but topics included growth (n = 49 studies), mortality (n = 28), nutrition (n = 24), and infectious diseases (n = 33). Only 12 studies focused on non-communicable diseases. Duration ranged from 7 to 384 months. Measurements included anthropometric (n = 56 studies), socioeconomic (n = 50) and biological sampling (n = 25), but only one study was DNA-based.

Conclusion Biobanks have emerged as the most successful approach to generating knowledge about disease causes and mechanisms. Little of this is possible to undertake in the in SEA or EM regions, however. Further longitudinal studies of young children with DNA sampling should be set up to better understand determinants of diseases in low-income countries.

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Very few longitudinal studies of children have been conducted in the developing world, despite the global burden of child morbidity and mortality being centred there (1,2). A history of birth cohort studies in the UK has outlined the important determinants of individual well-being and established these studies as invaluable in planning services (3–7). Examining genetic and environmental determinants of child health and disease is fundamental in reducing child mortality, to achieve the Millennium Development Goal 4 – "to reduce child mortality by two thirds by 2015" (8), Health determinants in low and middle-income countries are somewhat different to those studied in the UK and developed world, however. The most taxing diseases in the developing world are those that affect mothers and children and continue to cause high morbidity and mortality (9). Infections

are still of greatest concern (including acute respiratory infections, diarrhoea, malaria, HIV/AIDS, tuberculosis and maternal tetanus), followed by neonatal issues (including birth asphyxia or preterm birth) (2,9,10). Further birth cohort studies may better establish the determinants of such diseases and inform health expenditures. Understanding the epidemiology of those diseases has important policy implications. There has been some concern within the scientific community for example, toward the movements against a HiB-vaccine programme in India (11).

A birth cohort study with genetic samples could considerably advance the understanding of the influence of genetics and epigenetics on disease burden, particularly in developing countries. This is because the natural selection imposed by infectious diseases through child mortality has been shaping the human genome for hundreds of thousands of years (12). Large biobanks have emerged as the most successful way of harnessing the new health research technologies available and generating new knowledge about disease causes and mechanisms. Moreover, storage of samples may enable testing of future hypotheses, although the screening of biobanks for research purposes does not need to be hypothesis-driven, and the whole of the genome may be screened in search for genetic associations. There has been a surge in global interest towards birth cohort studies in recent years, as shown by the trend in global publications (**Figure 1**). It is essential however that this interest be directed toward those in greatest need in the future, thus reducing inequalities in global health research.

The aims of the present paper were:

1. to produce a systematic review of birth cohort studies from the World Health Organisation's South East Asia (SEA) and Eastern Mediterranean (EM) regions;
2. to examine the methodology, data collected from, and strengths / weaknesses of these studies and
3. to offer recommendations on the feasibility and sustainability of this area of research based on the findings of this review and in the context of the current literature.

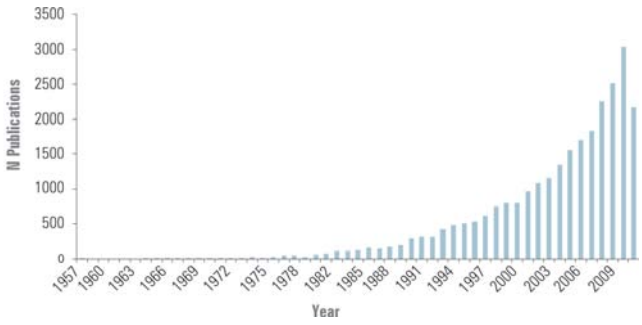
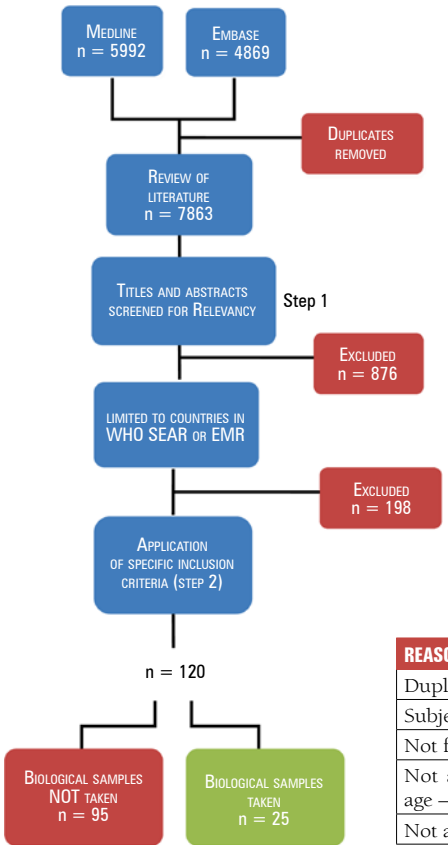


Figure 1 Global number of publications per year when 'birth* cohort*' was used as a search term in ISI Web of Knowledge database on 27 September 2010; no language or other restrictions.



REASONS FOR EXCLUSION
Duplicate
Subjects not human
Not from EMR / SEA
Not a child study (start age – 60 months)
Not a longitudinal study

Figure 2 Summary of the literature search. SEAR – South East Asian Region, EMR – Eastern Mediterranean Region of the World Health Organisation (WHO).

METHODS

Search strategy

An initial scoping exercise was conducted to identify key words and MeSH headings, and the final search terms agreed with a librarian. Systematic searches were run across the following electronic databases via Ovid (**Figure 1**): Medline (1950-onwards) on 30 July 2010 and Embase (1980-onwards) on 7 July 2010.

Specific countries were those identified by the World Bank list of economies (July 2011) as being lower or middle income countries. There were no additional limitations placed on publication date, type or language.

Inclusion and exclusion criteria

All titles, abstracts, then full papers were screened for relevance.

Data extraction

Data were extracted from abstracts and entered into Microsoft Excel sheets. Where more than one paper refered to a single study, the first chronologically published paper

Table 1 Search strategy for Medline and Embase*

Birth Cohort / Longitudinal Study
1. Longitudinal Studies/
2. (birth* adj3 longitudinal).ti,ab.
3. (birth* adj3 cohort*).ti,ab.
4. (pregnan* adj3 cohort*).ti,ab.
5. famil* cohort*.ti,ab.
6. cohort* survey*.ti,ab.
7. panel stud*.ti,ab.
8. panel survey*.ti,ab.
AND
Developing Country
1. Developing Countries/
2. low income countr*.tw.
3. middle income countr*.tw.
4. (low adj2 middle income countr*).tw.
5. africa/ or africa, northern/ or algeria/ or egypt/ or libya/ or morocco/ or tunisia/ or "africa south of the sahara"/ or africa, central/ or cameroon/ or central african republic/ or chad/ or congo/ or "democratic republic of the congo"/ or equatorial guinea/ or gabon/ or africa, eastern/ or burundi/ or djibouti/ or eritrea/ or ethiopia/ or kenya/ or rwanda/ or somalia/ or sudan/ or tanzania/ or uganda/ or africa, southern/ or angola/ or botswana/ or lesotho/ or malawi/ or mozambique/ or namibia/ or south africa/ or swaziland/ or zambia/ or zimbabwe/ or africa, western/ or benin/ or burkina faso/ or cape verde/ or cote d'ivoire/ or gambia/ or ghana/ or guinea/ or guinea-bissau/ or liberia/ or mali/ or mauritania/ or niger/ or nigeria/ or senegal/ or sierra leone/ or togo/ or "antigua and barbuda"/ or cuba/ or dominica/ or dominican republic/ or grenada/ or guadeloupe/ or haiti/ or jamaica/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or central america/ or belize/ or costa rica/ or el salvador/ or guatemala/ or honduras/ or nicaragua/ or panama/ or panama canal zone/ or mexico/ or argentina/ or bolivia/ or brazil/ or chile/ or colombia/ or ecuador/ or guyana/ or paraguay/ or peru/ or suriname/ or uruguay/ or venezuela/ or asia, central/ or kazakhstan/ or kyrgyzstan/ or tajikistan/ or turkmenistan/ or uzbekistan/ or cambodia/ or east timor/ or indonesia/ or laos/ or malaysia/ or myanmar/ or philippines/ or thailand/ or vietnam/ or asia, western/ or bangladesh/ or bhutan/ or india/ or sikkim/ or afghanistan/ or iran/ or iraq/ or jordan/ or lebanon/ or syria/ or turkey/ or yemen/ or nepal/ or pakistan/ or sri lanka/ or exp china/ or exp japan/ or korea/ or "democratic people's republic of korea"/ or "republic of korea"/ or mongolia/ or albania/ or lithuania/ or bosnia-herzegovina/ or bulgaria/ or byelarus/ or "macedonia (republic)"/ or moldova/ or montenegro/ or romania/ or russia/ or serbia/ or ukraine/ or yugoslavia/ or exp transcaucasia/ or armenia/ or azerbaijan/ or "georgia (republic)"/ or comoros/ or madagascar/ or mauritius/ or seychelles/ or fiji/ or papua new guinea/ or vanuatu/ or palau/ or samoa/ or tonga/

*Within a box, all terms were combined with Boolean operator OR.

Table 2 Inclusion steps

Inclusion criteria	Exclusion criteria
Stage 1 – Titles	**Stage 1**
• Primary data OR methods from a birth cohort study / child longitudinal study (including cross sectional data) • Meta-analysis of several birth cohort / child longitudinal studies	• Not from a developing country (12)
Stage 2 – Abstracts and Full Papers	**Stage 2**
• Country in WHO South East Asian or Eastern Mediterranean regions.	• Start age < 60 months.

was entered into the database and any additional data from other paper(s) inputed into relevant cells. Noted study characteristics include: country, city/state, urban/rural, year of start, recruitment strategy, start number, start age, proportion of population, specific population characteristics, measurements and observations, measurement frequency, family inclusion, end age, duration, attrition, study aims, funding.

Data analysis

Measurements were categorized into anthropometric, socioeconomic, and biological samples / measurements. Study aims and/or outcomes were characterised into topics. These included infectious diseases (respiratory tract infections (RTIs), diarrhoea, other), non-communicable diseases, nutrition, growth, socioeconomic factors, and mortality. Some studies were relevant to ≥1 topic. To provide an overview of studies, data types were counted. Where possible, summations and calculations were done with Excel formulae to minimise human error. A specialist programme (StatPlanet MapMaker, developed by Frank van Cappelle, 2011; http://www.sacmeq.org/statplanet) was used to display the geographical spread of studies.

RESULTS

Study characteristics

We analyzed 120 studies. There were only a small number of papers being published each year on birth cohort studies in the SEA or EM regions (with a maximum of 10 in total) and little change in trend in the past 20 years (**Figure 3**). In total, there were more than twice the number of studies in the SEA region (n = 83) compared to the EM region (n = 37) and these are most concentrated in India and Bangladesh and in Pakistan, respectively (**Figure 4**).

An overview of studies (**Table 3, Supplementary Web Table 1**) revealed large diversity in their methodologies.

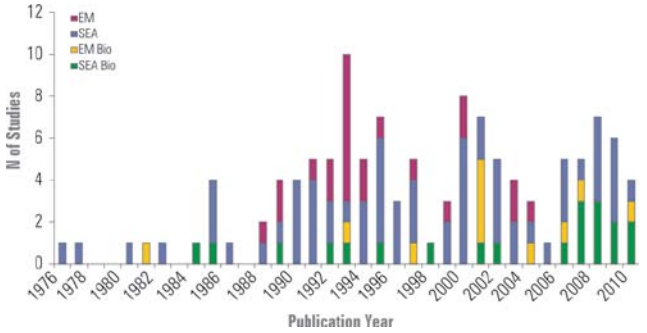


Figure 3 Number of studies published each year (n = 120). EM – Eastern Mediterranean, SEA – South East Asia, Bio – countries in the region taking biological samples (Bio).

The number of children enrolled ranged from 22 (13) to 5 711 337 (14). The latter were recruited retrospectively in Korea using nationally linked birth and death certificates, but made no active measurements. The largest prospective study was a cohort of 3729 in rural Bangladesh followed from birth for 36 months to examine the effect of birth spacing on mortality (15). In most studies (58), subjects were <3 months of age at the start, with many studies recruiting mothers during pregnancy. A number of the studies presented recruited older children (**Table 3, Supplementary Web Table 1**). Studies tended to be of short duration (12–24 months), but at least three of them followed up their subjects for >60 months. The Mysore Parthenon cohort (16), in which maternal serum folate, B12 and homocysteine concentrations were measured during pregnancy and child cognition (measured at 9 years) was a positive example. An even better established cohort is a New-Delhi cohort contacted at mean 32 years, with birth weight and adult glucose metabolism examined (17). Most studies tended to record socioeconomic measurements. These included parental age, education and occupation, and often indicators of household wealth (including monthly income, land size, possession of animals, and pos-

Table 3 Characteristics of all studies in South East Asia (SEA) and Eastern Mediterranean (EM) regions (n = 120)

Characteristic		WHO SEA	WHO EMR	EMR or SEA (% of 120)
Year	Pre 1980	1	1	2 (1.7)
	1980–1989	9	5	14 (11.7)
	1990–1999	31	16	47 (39.2)
	2000–2010	42	15	57 (47.5)
Number of subjects at start	< 100	4	2	6 (4.2)
	100–499	25	6	31 (25.8)
	500–999	13	5	18 (15.0)
	≥ 1000	22	11	33 (27.5)
	No data*	19	13	32 (26.7)
Max age at start (months)	<0	5	24	29 (24.2)
	0–3	28	1	29 (24.2)
	3–6	0	0	0 (0.0)
	6–12	1	0	1 (0.0)
	12–59	14	1	15 (12.5)
	No data*	35	11	46 (38.3)
Duration of follow up (months)	<12	1	0	1 (0.8)
	12– 24	16	13	29 (24.2)
	25–60	15	3	18 (15.0)
	>60	3	0	3 (2.5)
	No data*	48	21	69 (57.5)
Measurements / Samples (≥1 possible per study)	Anthropometric	40	16	56 (46.7)
	Socioeconomic	28	22	50 (41.7)
	Biological	17	8	25 (20.8)
	DNA	0	1	1 (0.0)
Family included*	Yes	11	7	18 (15.0)
	No	40	13	53 (44.2)
	No data*	32	17	49 (40.8)
Setting	Community-based	65	27	92 (76.6)
	Facility-based	5	3	8 (6.6)
	No data	13	7	20 (16.7)
Topic (≥1 possible per study)	Growth	31	18	49 (40.8)
	Nutrition	21	3	24 (20.0)
	Infectious diseases	24	9	33 (27.5)
	Non-communicable diseases	6	6	12 (10.0)
	Socioeconomic effects	13	7	20 (16.7)
	Mortality	25	3	28 (23.3)

*Some papers did not include data searched for. Moreover, some full papers (n=22) were not obtained and details not presented in abstract.

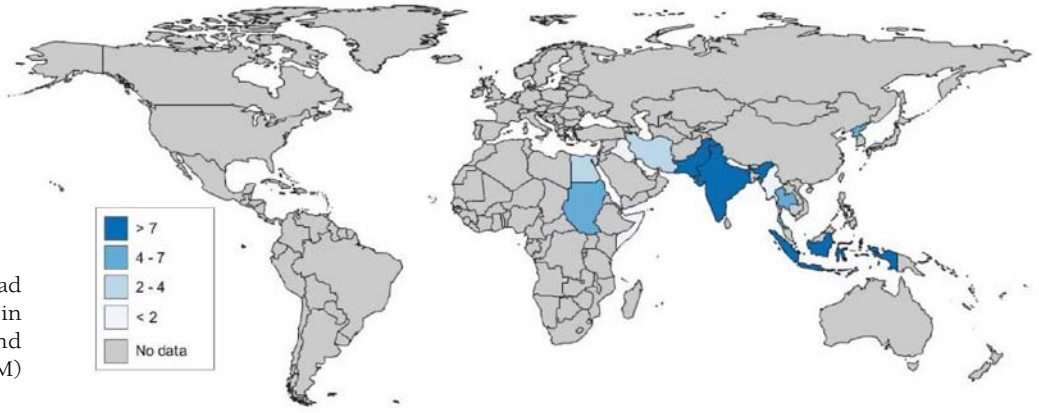


Figure 4 Geographical spread of all birth cohort studies in South East Asia (SEA) and Eastern Mediterranean (EM) regions (n = 120).

session of transportation). Living circumstances (number of rooms: family size ratio, water supply, proximity of latrine) were also measured occasionally. Other observations commonly made in retained studies included family size and spacing and nutrition practices (prelactal feeds, exclusivity of breastfeeding, specific supplements given). Finally, exposures (eg, specific occupational hazards, household cigarettes or fuel-burning), utilisation of health services and mental health were also noted. There were only 25 studies taking biological samples (**Figure 5**) and their characteristics are presented in **Tables 4–5**.

Biological sampling

We found a total of 25 studies in this region which took and stored biological samples (9 of them conducted in India, 6 in Bangladesh and 3 in Pakistan) (**Figure 5**). Their characteristics are shown in **Table 4**. The samples collected in a total of fifteen studies that stored blood samples are shown in **Table 5**.

DISCUSSION

A review of birth cohort studies in the SEA and EM regions has identified some positive examples of research. There is a distinct lack of studies addressing infectious diseases however, especially respiratory tract infections (RTI). Diarrhoea and RTI are a major cause of child morbidity and yet these topics receive little proportionate funding in research (18). Furthermore, biobanking has emerged as the most efficient way of studying the mechanisms of major diseases. However, there was only a single study from the SEA and EM regions in which DNA has been stored, in contrast to the numerous studies in the developed world benefitting from the Human Genome Project (19). A new birth cohort study and biobank in the SEA or EM regions would require significant planning, but such research must be directed to these areas of high child mortality in order to ensure future equity in health research.

In addition to infections, the incidence of non-communicable diseases such as cardiovascular disease, diabetes, cancers, cognitive defects and mental illness, are also increasing in low and middle-income countries (2,10). Thus, the developed world faces a dual burden of communicable and non-communicable disease. The diseases of adulthood have known associations with risk factors in earlier life. A life-course perspective of health determinants is now well outlined with understanding being drawn from previous longitudinal studies. Data from the UK NCDS study (3) for example outlined the association between maternal smoking and low birth weight (20). Risk factors even for the same non-communicable diseases are likely to differ somewhat between developed and developing countries. Therefore, any future birth cohort studies in the developing world would be more informative than those in the developed world.

Environmental exposures may differ in addition to different cultural manifestations. Breastfeeding, for example, is more prevalent in affluent members of developed countries in contrast to an association with poor socioeconomic status in low-income countries (21). Breastfeeding in the developed world is linked to obesity; however this may be socially patterned with high income (21). Comparative trends between countries with thus the removal of confounding factors may lead to a better understanding of causality of disease. Furthermore, the influence of the environment on child development has been better explored with new technologies made available by the Human Genome Project (22). Following the association of maternal smoking with low birth weight as outlined in the NCDS study (3), specific polymorphisms and their associations with maternal smoking, birth weight and adult cardiovascular disease have been examined (23).

Figure 5 Geographical spread of birth cohort studies in the Eastern Mediterranean (EM) and South East Asia (SEA) regions taking biological samples (n = 25).

Table 4 Studies in South East Asia (SEA) and Eastern Mediterranean (EM) regions taking biological samples (n = 25)

Ref.	Author	Country	Location	Publication year	Study type	Number subjects enrolled (attrition %)	Max age at enrolment (months)	Duration of follow up (months)	Frequency of follow up
58	Bhuiyan et al.	Bangladesh	Dhaka	2009	prospective	238 (25.9)	0	24	Monthly
34	Rousham et al.	Bangladesh	Jalampur	1998	prospective	117 (4.9)	59	12	0, 2, 4, 6, 8, 12 months
61	Black et al.	Bangladesh	Matlab	1984	prospective	197 (–*)	48	12	Every second day
129	Raqib et al.	Bangladesh	Matlab	2007	retrospective	132 (0)	0	60	0, 60 months
35	Hasan et al.	Bangladesh	Mirzapur	2006	prospective	252 (3.2)	0	24	Twice weekly
77	Granat et al.	Bangladesh	Svar	2007	prospective	99 (3.0)	0	24	Fortnightly
55	Bhan et al.	India	Anapur-Palla	1989	prospective	452 (0)	35	13	Weekly
17	Fall et al.	India	Dehli	2008	retrospective	1492 (0)	0	384	6 monthly
76	Gladstone et al.	India	Haryana	2007	prospective	281 (7.3)	10	20	Weekly
119	Mathur et al.	India	Hyderabad	1985	prospective	721 (–*)	59	12	*
63	Broor et al.	India	Mysore	2010	cross-sectional	663 (19.2)	<0	120	Annually till 5 years, 6 months thereafter
146	Yajnik et al.	India	Pune	1995	retrospective	379 (–*)	0	48	*
68	Coles et al.	India	Tamilnadu	2001	prospective	539 (13.9)	0	6	2 monthly
51	Banerjee et al.	India	Vellore	2006	prospective	452 (–*)	0	36	Twice weekly
126	Raghupathy et al.	India	Vellore	2010	retrospective	2218 (13.8)	0	336	0, 3 months, every 6 months until 14 years, mean 336 months
100	Khin-Maung-U et al.	Myanmar	Intakaw	1990	prospective	75 (0)	59	6	Monthly
148	Burke et al.	Thailand	Bangkok	1988	retrospective	218† (–*)	48	8	Daily
132	Ruangkan-Chanasetr et al.	Thailand	Bangkok	2002	prospective	84 (–*)	0	72	Twice yearly till 2 years, 6 years
149	Bassily et al.	Egypt	Alexandria	1999	prospective	169 (–*)	<0	18	At 8, 18 months
98	Kelishadi et al.	Iran	Isfahan	2007	prospective	442 (0)	0	0, samples stored for future	At birth, 72h
13	Amin-Zak et al.	Iraq	Baghdad	1981	retrospective	32 (0)	12	66	At 18, 42, 66 months
99	Khalil et al.	Pakistan	Lahore	1991	prospective	1476 (–*)	0	24	*
115	Lone et al.	Pakistan	Lahore	2004	prospective	629 (–*)	<0	1	At 1 month
142	Tikmani et al.	Pakistan	Karachi	2010	prospective	1690 (–*)	0	2	Weekly
88	Ibrahim et al.	Sudan	Khartoum	2006	prospective	205 (16.1)	0	24	6 monthly

*Not stated.
†Branch (aged 4 years) of a larger study (aged 4 – 16 years).

Table 5 An overview of studies taking blood samples

Reference	Blood sample			Analysis	Frequency
	Subject	Cord	Maternal		
58	Y	Y	N	ELISA – ABO & Rh group; Anti-H Pylori iga and igg. (Samples stored at –70 °C)	Every 3 months
34	Y (fingerprick)	N	N	Serum albumin, IgA, alpha-1-antichymotripsinogen	Every 2 months
61	Y	N	N	T-cell telomere length, CD3 concentration, plasma interleukin 7 concentration; serum stored at at –70°C and PBMCs stored for DNA.	Once (60.8 ± 3.2 months)
17	Y	N	N	Serum glucose, lipids, insulin (fasting and afte oral load)	Once (25–32 years)
63	N	N	Y	Hb, B12, folate, homocysteine	Once (30 ± 2 weeks gestation)
146	Y	N	N	Glucose (0, 30 minutes after oral load)	Once (48 months)
126	Y	N	N	Fasting glucose, fastinginsulin	Once (mean 28 years)
148	Y	N	N	Anti-dengue antibodies – haemagluttinin inhibition methods	At 0 and 8 months
132	Y	N	N	Serum lead	Biannually
149	Y	N	Y	Maternal anti-H. Pylori IgG in 3rd trimester; subject anti-H. Pylori (Pylori-stat ELISA)	3rd trimester, At 7–9 and 18 months
98	N	Y	N	Triglyceride, LDL-c, HDL-c, apo-A, apoB, Lpa; frozen plasma sample stored	Once (birth) (stored for future study)
13	N	N	Y	Mercury	At 0–18 months
115	N	N	Y	Hb	Once (3rd trimester)
142	Y	N	N	bilirubin	If jaundiced (assessed weekly)
88	Y (heel prick)	Y	N	ELISA and immunofluorescence for measles IgG	At 6, 12, 24 months
Total = 15	11	3	4		

Y – yes, N – no

Limitations

The search for studies was systematic, explicit and designed to have high sensitivity. The databases searched are extensive and thus it is unlikely that any studies of interest were missed. In the future, however, further databases could be searched, including IndMed and the Global Health Library. More studies may also be found by screening the cited papers. Due to the small number of studies, no further quality criteria were set, such as minimum number of subjects or minimum duration. This ensured a valid overview. Application of further exclusion criteria could highlight higher quality studies for analysis. Moreover, no distinction was made in this review between prospective and retrospective studies (with individually linked data from cohort at <60 months). Detailed analysis of only prospective studies may better inform the methodological considerations of a future prospective birth cohort study. In addition, analysis of more variables could be useful. Frequency of measurements, although documented for individual studies, was not compared accross studies for example. One author (24) noted that more frequent anthropometric measurements resulted in faster recognition of reduced growth in infants such that therapeutic interventions (eg, food supplements) could be directed to individuals more quickly but that it resulted in more false reports of reduced growth at younger ages. Moreover, attrition data was noted for individual studies but no comparison made between studies, including for example between geographic areas (rural vs. urban), setting (community-based vs. facility-based), start number, study duration, measurement types. Again, this may be informative when planning a new study. Finally, whilst the end date of studies was noted where possible, there was often no indication in papers as to whether or not the cohort may be followed up later.

Study quality and comparison to international birth cohort studies

A comparison with birth cohorts in other low-income regions (including Sub-Saharan Africa) would be interesting, as well as to cohorts in middle-income (25,26) and developed countries. The cohorts examined in the SEA and EM regions are generally of a far smaller start number than those in the developed world. The National Child Development Study (3), British Cohort Study (4) and Millennium Cohort Study (5) for example initially recruited 16 634, 17 287 and 18 818 babies, respectively. Studies in the SEA and EM region are also generally of shorter duration than such studies. Finally, only a single study stored DNA from index children for later analysis, and no studies took genetic material from family members. By contrast, for example, the Avon Longitudinal Study of Parents and Children (ALSPAC) in the UK included 10 000 mothers and children for with consent for genetic sample storage and future analysis. Cohorts in middle-income countries, however, including the Pelotas study (25,26) and Birth-to-Twenty (27) recruited a large number of children for genetic analysis, providing a positive example.

Funding

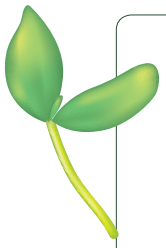
Few studies have detailed their source of funding, and this should be further examined. Other publications, however have described the main sources of funding in health research (18) including governments, NGOs and private organisations.

Recommendations for future cohort studies

Considerable planning would be needed before a birth cohort study is undertaken in SEA or EM regions. A series of papers have been published detailing the steps towards a 2012 British Birth Cohort (28,29) and this review highlights some of the considerations of a study in the SEA or EM regions. Clear aims and objectives should be agreed in order to facilitate direction and efficient methodology. Data may be used to test future hypotheses, and so as much information should be gathered as concisely as possible. The Aberdeen cohort (30) has been criticised for having no information on smoking in households, despite making detailed social observations, since this was before the association between maternal smoking and low birth weight had been established (31). The study must be feasible for staff, as well as not too invasive to subjects. Studies should be sensitive to local cultures, with adversities to certain measurements considered (32). Moreover, consent for future analysis of measurements should be obtained from subjects and family (33). In some studies (34) fingerprints of parents were used to sign documents where literacy rates were low.

A large number of examinees should be enroled in the cohort from an early age, so that conclusions can be drawn on the whole lifecourse perspective. Pregnant mothers could be sourced through prenatal services wherever possible, or through door-to-door interviews, aided by a registry of women of child-bearing age (eg, census) if available. Attrition could be minimised by following a population with a low migration rate, since this is a major reason for loss of follow-up. Mothers may also be offered incentive, for example meals at test facility (34) or healthcare for the duration of the study (35). One group described possible bias created by mothers attending facilities only to seek care (34). Moreover, number at follow up could be maximised through efficient planning, for example by utilising scheduled vaccination clinics or at entry to compulsory military service (20,26). Also, care should be taken to avoid recall errors. One study team gave calendars to mothers to record daily symptoms and treatment, thus reducing recall bias (36).

Local capacity must be developed and ensured before executing such a study. Laboratory staff should receive training and local field workers should be recruited. A number of sampling types towards the building of a biobank have been described including blood, saliva, and hair (37). Suitable media and storage should be further considered. The full list of studies retained for analysis in this paper is given at the end of our reference list (38–149), and their description in **Supplementary Web Table 1**. None of the present studies have included DNA from family members. Family members can act as proxies of exposure and can help identify parent-of-origin effects and de novo mutations and can help control for population stratification effects and should be included wherever possible (31).



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PAPERS

Food safety and security: what were favourite topics for research in the last decade?

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The world is faced with the challenge to feed an estimated 9 billion population of the Earth by 2050. To address the scientific evidence for the safety of food, I searched the *Web of Science* bibliographical and citation database for most cited articles from this research area. The topics with greatest impact on the research community, judged by their annual rate of citations during the last decade, were foodborne pathogens and toxins, with emerging genetic studies and new methods of visualising toxins on surfaces. Epidemiological and survey studies demonstrated that there was systematic effort to document, rapidly detect and control epidemic spread of disease and that these measures decreased the threat to food safety in developed countries, but that there is still much room for improvement. Research relevant for developing countries included the potential molecular targets to alleviate accumulation of arsenic in rice. As in other areas of research and life, human factor seems to be the most important one for the safety of food. The five keys to safer food of the WHO – keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials – are thus still very relevant for the developed as much as the developing world.

The safety of food is an important health, social and economical issue. According to the World Health Organization (WHO), foodborne and waterborne diarrhoeal diseases kill an estimated 2.2 million people annually, 1.9 million of them children (1). Unsafe food can be the cause of or contribute to many diseases, from diarrhoea to some cancers, so that food safety, nutrition and food security are among WHO's 13 strategic objectives (1). Food safety also has potential impact on at least 4 of the 8 millennium development goals set by the United Nations for 2015 (2): eradication of extreme poverty and hunger, reduction of child mortality, improvement of maternal health, and ensuring of environmental stability. To ensure safer food for health, WHO also developed training materials called 'Five Keys to Safer Food', promoting simple health measures based on evidence from scientific research for use of food handlers, including customers, in order to decrease the burden of foodborne diseases (3).

Food and its safety has become the topic of globally increasing research efforts, particularly in view of the growth of human population. The inter-

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est of the scientific community in food safety is illustrated by the recent special issue of the *Science* magazine, which explored the potential of science to tackle the challenge of feeding the estimated 9 billion people who will inhabit the Earth by 2050 (4). The topic stirred a heated debate on the printed and electronic pages of the journal (5). The 2011 crisis at a nuclear power plant after the earthquake in Japan and the detection of radioactivity in certain food samples contributed to the concerns about the safety of food from that area (6). Most recent outbreak of a deadly haemolytic-uremic syndrome in Germany, caused by bacterial contamination of vegetable sprouts (7), also drew the attention to food safety. In view of the attention of the scientific community to the topic of food, I was interested in the scientific evidence for its safety. To assess research published on this topic in the last decade, I searched the *Web of Science*, bibliographical database that also uses citations to published research as a measure of impact on research community (8).

METHODS

I performed the search of the *Web of Science* (WoS), the citation database of the Thomson Reuters, formerly the Institute for Science Information (ISI) (8). WoS was chosen as a widely used citation database (9–12), so that the results of the study could be comparable to other citation analyses. The search was performed on 18 March 2011 and included all databases available in WoS (*Science Citation Index Expanded*, *Social Sciences Citation Index* and *Arts and Humanities Citation Index*). The search term was 'food safety', as this term is used by the WHO (3) and the time span was limited to the last 10 years (2001–2010). The search was then refined by selecting 'article' as the document type. The articles with highest citations rates, defined as the number of citations per year after publication (11), were analyzed. WoS tools were used to present the number of articles and their citations, relevant research areas, leading journals, countries, institutions and funding sources.

To get an insight into the possibly most influential articles in the area of food safety, I identified top 10 articles according to their citation intensity, defined as the average number of citations received per year after the publication date. Because of the different times of publication, the total number of citations at a certain time point may not be the best measure of the article's visibility and influence, so the citation intensity was taken as the proxy for the interest of the research community for the research, regardless of the time of its publication (11). Only the most recent studies, particularly those published in 2010 would have disadvantaged by such approach (11).

RESULTS AND DISCUSSION

The search retrieved 11 565 out of 14 417 309 indexed items for the 2001–2010 time span. Out of those, 69.6% were designated as 'articles' (n = 8044) and the rest were 'reviews' (13.1% items) 'proceedings papers' (10.5%), or other types of bibliographical items (**Table 1**). Items classified as 'articles' by WoS should bring results of original research (11), so that further analysis was performed only for this bibliographical item. As the database retrieved articles and/or citations to some items from 2000 and 2011, citation data for individual articles were manually checked and only the relevant post-publications years up to the end of 2010 were included in the analysis. Descriptive data on the total publications (**Table 1** and **Figure 1**) were presented for all retrieved items because it was not possible to separate citations for outlying years.

Time trends in food safety research publications

The number of articles continually increased over time, from 385 in 2001 to 1316 in 2009 and 1307 in 2010 (**Figure 1**). These articles received increasing numbers of citation over the years, from 128 in 2000 to 16 018 in 2010 (**Figure 1**). The number of citations increased more rapidly than the number of published articles, demonstrating the growing interest for and the impact of food safety research. The causes for the increasing trend are not clear, and may include a number of factors, from the increasing number of relevant journals covered by the database; grow-

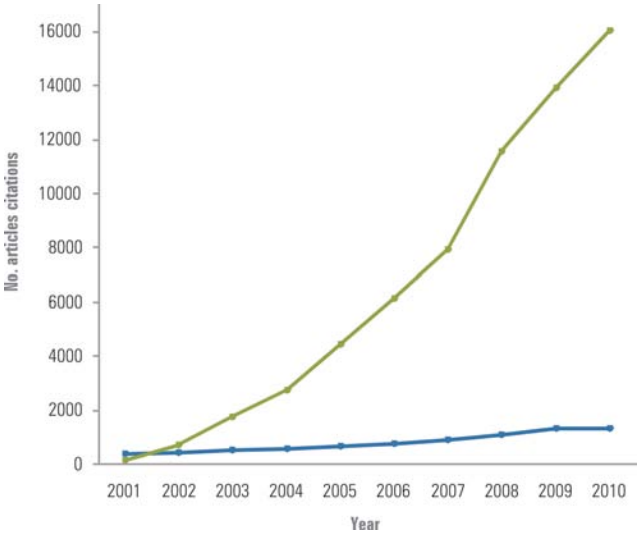


Figure 1 Number of publications about food safety (blue line), classified as 'articles' by the *Web of Science*, and citations to these publications (green line) in 2001–2010.

Table 1 Types of items, areas of research and top 10 countries, funding agencies, institution and journals publishing research on food safety in 2001–2010*

Bibliographical characteristic	No.	%†
Type of item published (n = 11 565):		
Article	8044	69.6
Review	1512	13.1
Proceedings paper	1215	10.5
Editorial material	385	3.3
Meeting abstract	182	1.6
News items	162	1.4
Letter	35	0.3
Book review	16	0.1
Correction	9	0.08
Reprint	3	0.03
Bibliographical item	1	0.01
Software item	1	0.01
Areas of research (articles only, n = 8044):		
Food science & technology	1547	
Biotechnology & applied microbiology	501	
Nutrition & dietetics	473	
Veterinary sciences	368	
Environmental sciences	360	
Public, environmental & occupational health	332	
Microbiology	330	
Agriculture, multidisciplinary	329	
Economics	278	
Chemistry, applied	211	
Countries (articles only):		
USA	3057	38.0
England	545	6.8
Germany	496	6.2
Canada	415	5.2
Italy	390	4.8
France	385	4.8
Spain	369	4.6
Peoples R. of China	355	4.4
Netherlands	347	4.3
Japan	286	3.6
Funding agencies (articles only, n = 8044):		
European Commission or European Union	62	0.8
National Natural Science Foundation of China	34	0.4
National Institutes of Health	30	0.4
Ministry of Agriculture of the Czech Republic	14	0.2
National Science Foundation	12	0.1
United States Department of Agriculture	12	0.1
Funding agencies – continued:		
Ministry of Education, Youth and Sports of the Czech Republic	11	0.1
National Council for Scientific and Technological Development (CNPq), Brazil	9	0.1
Pfizer	9	0.1
Public Health Agency of Canada	6	0.1
Institutions (articles only, n = 8044):		
US Department of Agriculture, Agriculture Research Service	143	1.8
US Department of Agriculture	89	1.1
Wageningen University & Research Centre, The Netherlands	74	0.9
Cornell University, USA	70	0.9
Ohio State University, USA	64	0.8
Michigan State University, USA	63	0.8
Chinese Academy of Sciences	62	0.8
University of Guelph, Canada	60	0.7
University of California Davis, USA	58	0.7
Institut Scientifique de Recherche Agronomique, France	53	0.7
Journals (articles only, n = 8044):		
Journal of Food Protection	336	4.2
Food Control	216	2.7
Food and Chemical Toxicology	193	2.4
International Journal of Food Microbiology	188	2.3
Journal of Agricultural and Food Chemistry	141	1.8
British Food Journal	97	1.2
Journal of Food Science	84	1.0
Regulatory Toxicology and Pharmacology	83	1.0
Annals of Pharmacotherapy	74	0.9
Journal of Applied Microbiology	73	0.9
Languages (articles only, n = 8044):		
English	7481	93.0
German	205	2.5
French	89	1.1
Spanish	51	0.6
Portugese	49	0.6
Chinese	33	0.4
Japanese	33	0.4
Hungarian	28	0.3
Polish	21	0.3
Korean	18	0.2

*Data from *Web of Science* (WoS), search performed 18 March 2011. Categorisation of items is according to WoS.

†Percentages were calculated from total number of published items in 2001–2010 (n = 11 565) for the type of bibliographical item or the total number of articles (n = 8044) for all other items. Percentages for areas of research were not calculated as articles may be assigned to more than 1 area of research.

ing number of researchers in this area; increased interest of funders, both public and commercial; increased collaboration in the field, particularly in globally relevant topics, or improved quality of research which generates more and better (and more publishable) data. While it is difficult to assess factors related to the research community, the journal coverage of the Thompson Reuters' databases increased 22% from 2002 to 2010 (12) and surely contributed to the general increase in publications and their citations.

Most of the published articles were classified into the category of 'Food science & technology', followed by a range of related categories, from 'Biotechnology and applied mi-

crobiology' to 'Chemistry, applied' in the top 10 categories (**Table 1**). Top 10 countries that published most articles in food safety were responsible for 82.6% of all retrieved articles (**Table 1**). Among them the leader was the USA, followed by England, Germany and Canada. The only developing country that made a significant contribution to this area was China, which may reflect the rising concerns in China over food safety, particularly after the 2008 scandal of milk formulas tainted with melamine (13).

Agencies for funding research on food safety were few (**Table 1**). As most of the published articles did not carry statements on funding, it is difficult to make an objective conclusion on the extent of financial support for food safety research and the interpretation is possible only for those articles that carried funding declaration. The top 10 funding agencies provided support for only 199 of the 8044 articles (2.5%) (**Table 1**). Among them, the European Commission or the European Union funded most articles (62 articles), followed by the National Natural Science Foundation of China (34 articles).

The top 10 institutions with most published articles were responsible for 9.1% of all publications (**Table 1**). Among them, 6 were US-based, and non-US based institutions were located in The Netherlands, China, Canada and France (**Table 1**).

There was no dominating journal among the 10 journals with the highest volume of articles on food safety, which published 18.5% of all retrieved articles (**Table 1**). The lead was taken by the *Journal of Food Protection*, which published 336 articles or 4.2% of all retrieved articles. Finally, the dominating language of the publications was English (93.0% of all retrieved articles), followed by German and French (3.6%). All other languages were used by only 3.4% of the retrieved articles.

Most cited publications on food safety

Among the top 10 articles with highest citation intensity there were 3 review articles (14–16) and 7 original research articles (17–23) (**Table 2**).

The review article with the highest citation rate (34 citations per year) was published in the *British Medical Bulletin* in 2003 and addressed the hazards of heavy metal contamination, predominantly lead, cadmium, mercury and arsenic (14). Cadmium exposure comes mainly from re-chargeable nickel-cadmium batteries, which are often thrown away with the regular garbage, as well as from cigarette smoke. Exposure to mercury occurs via food, mainly fish, while there is no evidence so far that amalgam dental fillings contribute to mercury exposure and poisoning. Lead exposure currently comes primarily from emissions of petrol combustion in vehicles, while the lead-based paints and food containers have been abandoned. Finally, food is the most important source of arsenic poisoning for most populations, although drinking water could be a source of long-term exposure to arsenic.

Two other review articles received an average of 16 citations per post-publication year. The paper published in the *International Journal of Food Microbiology* in 2004 covered state of the art research on foodborne viruses (15). Norovirus and hepatitis A virus are highly infectious and lead to wide spread outbreaks of disease because they can persist in food manually handled by an infected food-handler and if such food is not heated or treated in other way after handling. Thus, greatest attention in preventive efforts should be given to good manufacturing practice to avoid introduction of viruses during food handling. The article on the control of *Listeria monocytogenes* (16) in the food-processing environment was published in the *Journal of Food Protection* in 2002, addressing the problem of large outbreaks of scattered cases after a virulent strain got established in the food-processing chain and thus infected multiple food lots over a short period of production. To increase the safety of ready-to-eat foods, there is a need to establish a sampling programme in the production environment, organization and interpretation of collected data and appropriate response to the positive finding of *Listeria* contamination.

The article with the highest citation rate (annual average of 44 citations) among all 8044 retrieved articles was published in *Nature* in 2005 (17), describing the genome sequencing and analysis of *Aspergillus oryzae*, a fungus used in the production of traditional fermented foods and drinks in Japan. The article shows that the genome of this *Aspergillus* species acquired specific expansion of genes for secretory hydrolytic enzymes, amino-acid metabolism and amino-acid/sugar uptake transporters, making it a suitable organism for fermentation.

The article ranked as the 3rd among the 10 top publications came from a collaborative group of researchers in Japan and UK and explored the transporters of arsenite in rice plants (18). The article was published in the *Proceedings of the National Academy of Sciences USA* in 2008 and received an average of 16 citations each year since then. The authors demonstrated that the possible accumulation of carcinogenic arsenite in rice grains, which caused massive poisoning in some Asian countries, was due to two different types of transporters in the rice roots, which are also used for silicone transport. High expression of genes for these two transporters in rice leads to silicone accumulation, which increases yield production, but also increases arsenic accumulation in the grains. The authors suggest that increasing silicone availability in the soil may suppress arsenic accumulation in rice and thus alleviate potential risk of arsenic poisoning.

Table 2 Top 10 articles published in 2000–2009 with highest number of citations intensity, presented as the average number of citations per each year after publication*

Rank	Authors	Title	Bibliographical reference	Cumulative citations	Citations per year
1	Machida M, Asai K, Sano M, et al.	Genome sequencing and analysis of *Aspergillus oryzae*	*Nature* **2005**;438:1157–1161	266	44.3
2	Jarup L	Hazards of heavy metal contamination	*British Medical Bulletin* **2003**;68:167–182	236	33.7
3	Ma JF, Yamaji N, Mitani N, et al.	Transporters of arsenite in rice and their role in arsenic accumulation in rice grain	*Proceedings of the National Academy of Sciences of the USA* **2008**;105:9931–9935	80	26.7
4	Li JF, Huang YF, Ding Y, et al.	Shell-isolated nanoparticle-enhanced Raman spectroscopy	*Nature* **2010**;464:392–395	21	21.0
5	van Boekel MAJS	On the use of the Weibull model to describe thermal inactivation of microbial vegetative cells	*International journal of Food Microbiology* **2002**;74:139–159	145	16.1
6	Koopmans M, Duizer E	Foodborne viruses: an emerging problem	*International Journal of Food Microbiology* **2004**;90:23–41	128	16.0
7	Tompkin RB	Control of *Listeria monocytogenes* in the food-processing environment	*Journal of Food Protection* **2002**;65:709–725	141	15.7
8	Adak GK, Long SM, O'Brien SJ	Trends in indigenous foodborne disease and deaths, England and Wales: 1992 to 2000	*Gut* **2002**;67:832–841	125	15.6
9	Bocio A, Llobet JM, Domingo JL, et al.	Polybrominated diphenyl ethers (PBDEs) in foodstuffs: Human exposure through the diet	*Journal of Agricultural and Food Chemistry* **2003**;51:3191–3195	120	15.0
10	Zhao CW, Ge BL, De Villena J, et al.	Prevalence of *Campylobacter spp.*, *Escherichia coli*, and *Salmonella* serovars in retail chicken, turkey, pork, and beef from the Greater Washington, DC, area	*Applied and Environmental Microbiology* **2001**;67:5431–5436	130	13.0

*Citations were calculated for the years after publication, including the year of publication, up to the end of 2010. The exception was article by Koopmans and Duizer, which had 1 citation in 2003 although the official paper publication was in 2004.

The next most cited article, published in *Nature* in 2010 (19) and receiving 21 citations in the same year, described the new methodology for the non-destructive and ultra-sensitive visualisation of single molecules on surfaces. The formation a monolayer of gold nanoparticles as a 'smart dust' over surfaces allowed the demonstration of pesticide residues on citrus fruits.

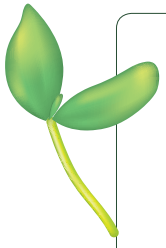
High citation rate was achieved by the article presenting a case study of using a specific kinetic model to describe thermal inactivation of microbial vegetative cells in the food (20). The article was published in the *International Journal of Food Microbiology* in 2002. Based on published studies on thermal inactivation of microbial agents, the author made a theoretical exploration with a new mathematical model to calculate the necessary time and temperature treatment to pasteurize or sterilize foods.

Research articles describing outbreaks of common food poisoning also reached the top list of citation-intense publications. An epidemiological study of trends in indigenous foodborne diseases and deaths in England and Wales in 1992 to 2000 was published in the *Gut* in 2002 (21), and attracted an annual average of 15.6 citations. The authors analyzed routinely available surveillance data, special survey data and hospital episode statistics to estimate the burden and trends of indigenous foodborne disease. Between 1992 and 2000, the burden of indigenous foodborne disease fell by 53%.The most important pathogens were campylobacter, salmonella, *Clostridium perfringens*, verocytotoxin-producing *Escherichia coli* O157 and *Listeria monocytogenes*. In 2000, campylobacter still remained the highest threat, and the control of other pathogens was required to lower the mortality rates. A description of prevalence of *Campylobacter species*, *Escherichia coli* and *Salmonella* serovars in retail meat products from Greater Washington DC area in the USA was published in the *Applied and Environmental Microbiology* in 2001 (22) and received an average of 13 citations annually since its publications. The authors analysed 825 samples of retail raw chicken, turkey, pork and beef meat from supermarkets, and found that retail raw meats were often contaminated with foodborne pathogens. Chicken meat was more contaminated with *Campylobacter* that any other meat (70% of samples in comparison to 14% in turkey and 1.7% in pork and 0.5% in beef). The authors called for the introduction of stricter measures for ensuring food safety, particular the implementation of hazard analysis of critical control points (HACCP), as well as increased consumer education efforts to ensure food safety at home.

Finally, an article on the toxicity of polybrominated diphenyl ethers (PBDE) in foodstuffs also reached high citation rate and was ranked the 9th on the top 10 list, with 15 citations per year since its publication in the *Journal of Agricultural and Food Chemistry* in 2003 (23). PBDE is used as a flame retardant and seems to be present in a number of food samples, mostly in meat products and eggs, with an estimated dietary intake for an adult male of 97 ng/day in an area in Spain.

INSTEAD OF A CONCLUSION

Taking into consideration all limitations of a scientometric analysis of research topics (9–12), the most useful topics in food safety during the last decade, according to their impact in research community, seemed to have been foodborne pathogens and toxins. We have also witnessed the emergence of genetic studies and new sophisticated methodologies for detecting small amounts of toxin residues on surfaces. Epidemiological and survey studies showed that there was a systematic effort to document, rapidly detect and control epidemic spread of disease. Some of these measures decreased the threat to food safety in developed countries, but there is still much room for improvement. Novel areas for improving the safety of food in the developing countries were also opened, such as the study on the potential molecular targets to alleviate accumulation of arsenic in rice. The five keys to safer food of the WHO (3) will remain most relevant for the developed as much as the developing world. As in other areas of research and life, the human factor is the most important one for the safety of food, and cannot be fully replaced by a novel chemical, agricultural or processing technology or gene transfer.



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Competing interests: The author has completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the author) and declares: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

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Quality of maternal healthcare in India: Has the National Rural Health Mission made a difference?

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Despite a five decade old Family Welfare programme, India still continues to contribute almost a quarter of the global estimates of maternal morbidity and mortality. Quality aspects in maternal health care have long been ignored in the Indian public health system. It is only with the launch of the National Rural Health Mission (NRHM) that quality of care has been accorded due recognition at the policy and planning levels of the national health programmes. Using review of available data sources and published literature, this paper aims to examine the scenario of quality of care in maternal health over the last decade and the impact of NRHM initiatives on the same. While NRHM has made efforts to address lacunae associated with quality of maternal care in the public health system, there is much scope for improvement.

The WHO estimates show that out of the 536 000 maternal deaths globally each year, 117 000 (22%) occur in India (1). In addition to these, millions suffer pregnancy related morbidity. According to Global Burden of Disease estimates for 2004, India contributes 21% of the disability adjusted life years (DALYs) lost due to maternal conditions (2). Public health initiatives over the last two to three decades have helped India to improve health indicators such as life expectancy and total fertility rate to a great extent, but some crucial indicators like Maternal Mortality Ratio (MMR) and Infant Mortality Rate (IMR) have stagnated at around 400 per 100 000 live births and 60 per 1000 live births, respectively, in the 1990s (3). Despite a series of national level safe motherhood policies and programmatic initiatives over the past two decades there is little evidence that maternity has become significantly safer in India. The National Rural Health Mission (NRHM) was launched with much fanfare in April 2005 "to provide accessible, affordable and quality health care to the rural sections especially the vulnerable populations" (4). An integral component of NRHM is the safe motherhood intervention in the form of Janani Suraksha Yojana (JSY) for reducing maternal and neo-natal mortality. JSY is a 100% centrally sponsored scheme under the umbrella of NRHM which integrates cash assistance with antenatal care during the pregnancy period, institutional care during delivery and immediate post-partum period in a health centre by establishing a system of coordinated care by field level health worker. Though the scheme has been successful in pushing up the insti-

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tutional delivery rate in some high focus states, the ambitious goals of reducing the MMR from existing ratio of 301 to 100 per 100 000 live births, by 2012 (4) will not be possible if 'quality' aspects are ignored while addressing issues related to equity and access to health care for the Indian population. Addressing the issues of quality in maternal health service delivery is important not just to decrease the MMR and reduce maternal morbidity but also to instill confidence in the public health system amongst end users and thereby increase the demand for institutional deliveries. This alone will ensure that the gains made in the JSY scheme in the last 4 years will lead to the final expected outcome of the NRHM of decreasing maternal mortality and morbidity.

QUALITY OF CARE: THE CONCEPT

The concept of quality of care is complex and multidimensional. The definition of quality of care is highly varied-ranging from excellence (5) to expectations or goals which have been met (6,7) to "degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge" (8). At a population level, quality of care can be defined as "ability to access effective care on an efficient and equitable basis for the optimisation of health benefit/well-being for the whole population" (9). All dimensions of quality of care reduce to two questions. First, can an individual get the care they need when they need it (ie, is the care accessible)? Second, when they get care, is it effective both in terms of clinical effectiveness and interpersonal relationships? This definition of quality of care is appropriate when applied at an individual level. This paper will largely restrict to analysing the quality of care in maternal health at the individual level through an equity lens.

Though India's Health and Family Welfare Programme has been in existence for almost five decades, it is characterised by modest achievement and unfulfilled promise. Information on the services at the provider-client level remains limited, much of the evidence having become available only in the last decade with a good deal being unpublished and inaccessible to those interested in this issue (10).

Access to care

Access to care is a vital but complex element of quality of care since it determines whether a client even gets to the service provider. The available community based evidence suggests that there is considerable variation in the level of outreach visits by the Auxiliary Nurse Midwife (ANM), largely by geographical location, with significantly higher visits in the southern and western than in the north Indian states. In a four state study conducted over a decade ago, 89% and 93% women surveyed in Tamil Nadu and Karnataka reported having been visited by a female paramedical worker in the last three months, compared with 53% and 61% women from Bihar and West Bengal, respectively (11). There were also differentials in access to care between urban and rural areas, if utilization of care is taken as a proxy for access to care. The National Family Health Survey-3 (NFHS-3) conducted during 2005-06 reports that only 62.4% of ever married women respondents living in urban areas reported having received the WHO recommended four antenatal visits compared to 27.7% rural women (12). The District Level Household Survey-3 (DLHS-3) conducted during 2007–2008 (13) indicates an overall improvement in access to maternal care (if three or more ante-natal check ups are taken as proxy) in the post NRHM period, perhaps more for the high focus states (with poor health indicators) than the non high focus states (which hitherto had better health indicators) (**Figure 1**).

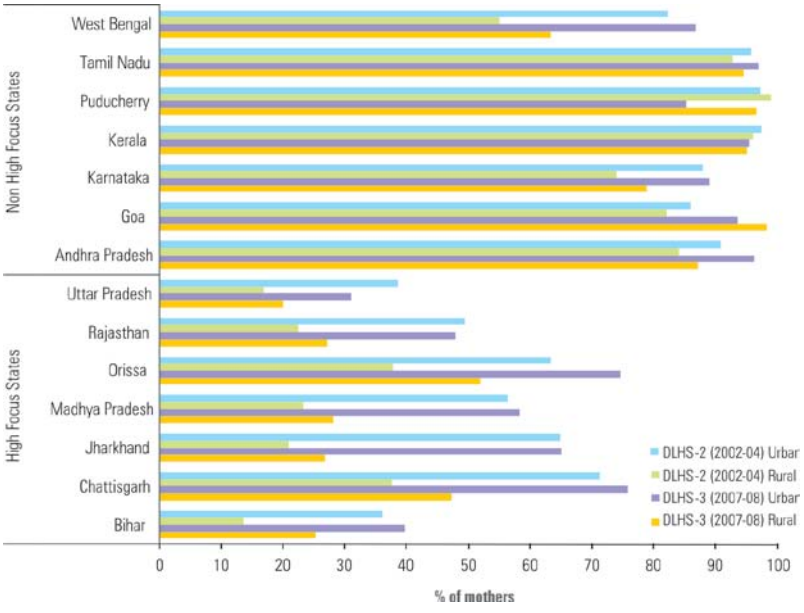

Figure 1 Comparative proportion of mothers who had three or more antenatal check ups during their last pregnancy. (DLHS-3 against DLHS-2). DLHS: District level health survey. High focus states under NRHM were 18 states identified for special attention based on weak public health indicators and/or weak health infrastructure.

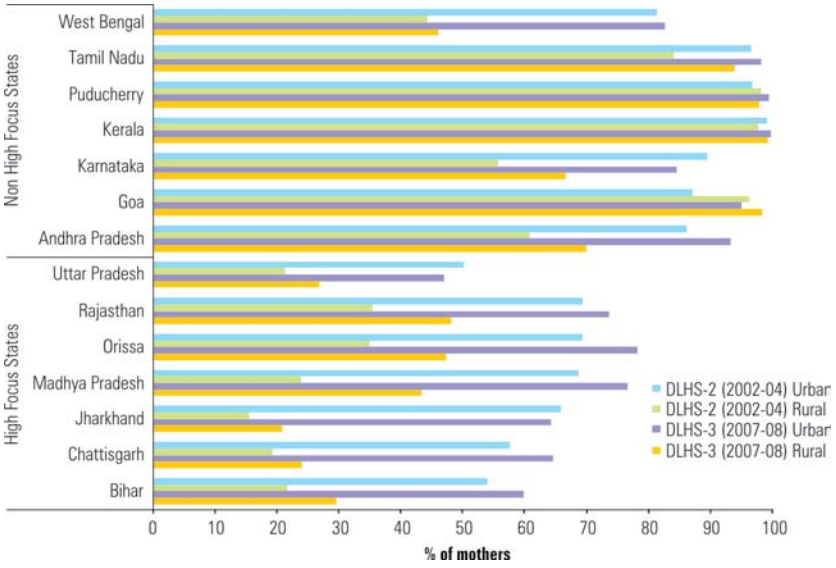

Figure 2 Comparative proportion of mothers who had safe delivery (ie, institutional delivery or home delivery attended by a skilled health personnel like doctor, nurse, LHV, ANM, midwife etc.) during last pregnancy. (DLHS-3 against DLHS-2). DLHS: District level health survey; LHV: Lady health visitor; ANM: Auxiliary nurse midwife. High focus states under NRHM were 18 states identified for special attention based on weak public health indicators and/or weak health infrastructure.

Data over the last three decades reveal that significant differences in frequency of outreach visit exist even within the same geographic region. One study from rural Maharashtra found that respondents residing in villages more remote from those, to which the ANM was assigned, were significantly less likely to have reported a recent visit by a health worker, to have been visited for meaningful lengths of time and to have received other maternal and child health services (14). An earlier study also found a much greater tendency for workers to visit communities and households accessible to main roads (15). NRHM does not appear to have made much of a difference in this regard. In Orissa, JSY beneficiaries had to travel, on average, 15.8 km to reach the ultimate place of delivery (16). Without an efficient referral system, women with complications are referred from facility to facility before they finally reach their place of delivery. This results in loss of precious time and contributes to one of the major delays responsible for maternal mortality. A study conducted in Andhra Pradesh showed that among the 98 women who used hospital facilities nearly sixty percent went to two or more hospitals. One woman had visited as many as nine hospitals and finally died at home (17). According to NFHS-3, more than half the births in India take place at the woman's own home and 9% at parent's home (12). Overall, only 47% of all deliveries are attended by a skilled birth attendant (SBA); 73.4% in urban areas compared to 37.4% in rural areas. The DLHS-3 data reveal that the rural-urban gap for safe deliveries remains wide as ever in the northern Indian states (13) (**Figure 2**).

Investigators in a study conducted at the beginning of the millennium and involving rural and urban women in Maharashtra have listed safety and good quality of care as one of the motivating factors for choosing to give birth at home (18). "In government hospital delivery room is not there. Toilet and water facilities are not there in public health centre properly. So I felt safe to give birth in house," remarked one of the respondents from Pune (18).

The Government of India constituted Common Review Missions (CRMs) under the NRHM to review the implementation of NRHM. The teams constitute of central and state government officials, public health professionals from the academia, public health activists from civil society organizations and representatives from development partners. The teams constituted for the Second Common Review Mission (CRM) (November – December 2008) reported that although there is some improvement in the levels of cleanliness and provision of waiting space for patients in the post 2005 period, cleanliness of toilets was still lacking (19). Assessments carried out on health facilities across India indicate a suboptimal degree of purchases, maintenance and utilization of general medical equipment and a lack of support facilities like 24 hour water and electricity supply (20). This is reinforced by the observations of one of the visiting State teams of the CRM.

"The infrastructure is old and requires repairs. OPD patient load is very high, institutional delivery load is also very high, however the PHC has only 4 beds which require to be augmented, there is no referral transport service available and laboratory services are inadequate" (19).

The findings of the Third Common Review Mission teams to Bihar, Chattisgarh and West Bengal in November 2009 indicate that very little has changed in the one year since the second CRM (21). The team visiting Bihar observed that the "basic utilities (toilet and running water) in the observed facilities were very poor and are not conducive for the women to stay for long after delivery" (22). Thus, insufficient public healthcare infrastructure, unclear account-

ability, and the lack of empathy towards the poor have severely limited the optimal reach of even available maternal health services in the public health system in India.

Postnatal care is one of the most neglected components of maternal care. Data from NFHS-3 reveal that only 42% of women surveyed received postnatal care after their most recent delivery. Births to urban mothers are twice as likely to be followed by a postnatal check-up (66%) compared to their rural counterparts (34%) (12). The findings of DLHS-3 are no different – the rural-urban differential remains as wide as ever in the high-focus states (13) (**Figure 3**). It is thus evident that rural India where about 70% of Indian population resides has less accessibility to good quality care. Even in urban areas, lack of knowledge and awareness about health facilities among the poor, weak linkages between service providers and communities, and the limited role of community negotiating capacities severely impede the demand for healthcare services in these areas (23). Recent evaluation of the JSY in Orissa revealed that that only half of the JSY beneficiaries were given referral slips by Accredited Social Health Activist (ASHA) or other health personnel to help them access delivery services. The same report also notes: "With manifold increase in the institutional deliveries, quality of care has become an issue, for instance, women were discharged on average, 16 hours after normal delivery and there were instances of being discharged even within 3–4 hours after delivery. This is risky to the life of both mother and the newborn and would not serve the purpose of reducing maternal and neonatal mortality"(16).

Even the third CRM report indicates that mothers tend to be in institutions less than a day in most cases and that quality of care needs to improve in a large proportion of the health facilities (24).

Clinical effectiveness

Khan and colleagues in a study from Bihar reported that 41% of the respondents felt that the time the health worker spent with them was very short and only 31% were fully satisfied with the visits they received (25). In another study from Maharashtra, almost two-thirds of the respondents reported that the ANM had spent less than five minutes in her most recent household visit (14). This lack of time spent by the ANM reflected on the lack of clinical effectiveness for those who manage to gain access to the care provided by the public health system. NFHS-3 data indicate that overall, only 15% women receive all recommended types of antenatal care, there being wide disparities between the states (4% in Uttar Pradesh compared to 64% in Kerala) (12). Though the DLHS-3 data indicate an overall improvement in clinical effectiveness of maternal health care (if full ante-natal check up which includes at least three ante-natal visits, one tetanus toxoid injection, 100 tablets of iron-folic acid supplement or its equivalent in syrup is taken as proxy), they appear to suggest that the improvement has been more in the non-high focus states which hitherto had better health indicators(13). In fact, some high focus states (e.g. Uttar Pradesh, Bihar and Jharkhand) appear to have deteriorated in the post-NRHM period (**Figure 4**).

Rani and colleagues have highlighted the north-south differential in a recent study involving secondary analysis of NFHS-2 data from four south Indian states (Andhra Pradesh, Karnataka, Kerala and Tamil Nadu) and four north Indian states (Bihar, Madhya Pradesh, Rajasthan, Uttar Pradesh) (26). The study shows that only 40.3% of the women receiving antenatal care in the north reported having their blood pressure measured during antenatal visit

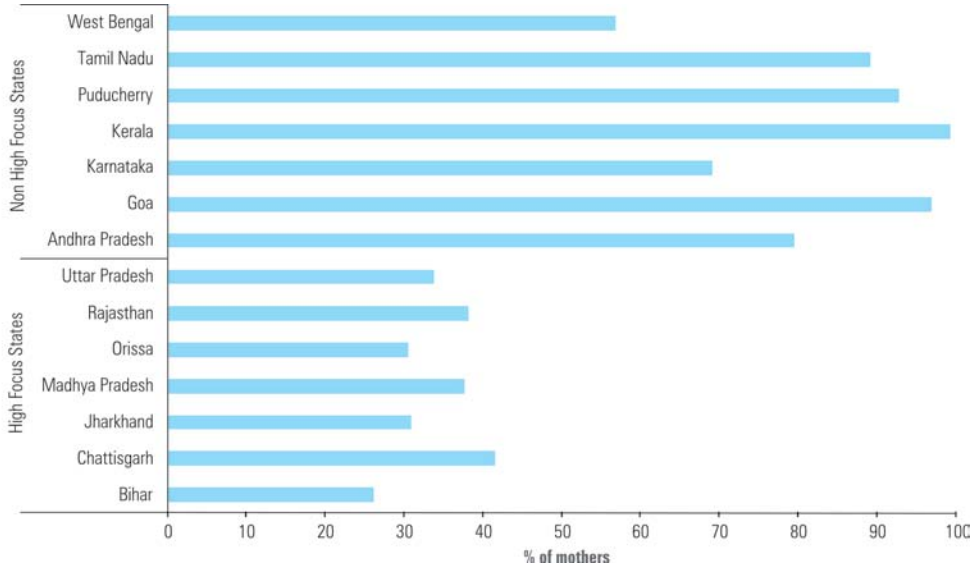

Figure 3 Proportion of mothers who received post natal care within 2 weeks of delivery during their last pregnancy. Data are overall for the state based on DLHS-3 (2007-2008). DLHS, District level health survey. High focus states under NRHM were 18 states identified for special attention based on weak public health indicators and/or weak health infrastructure.

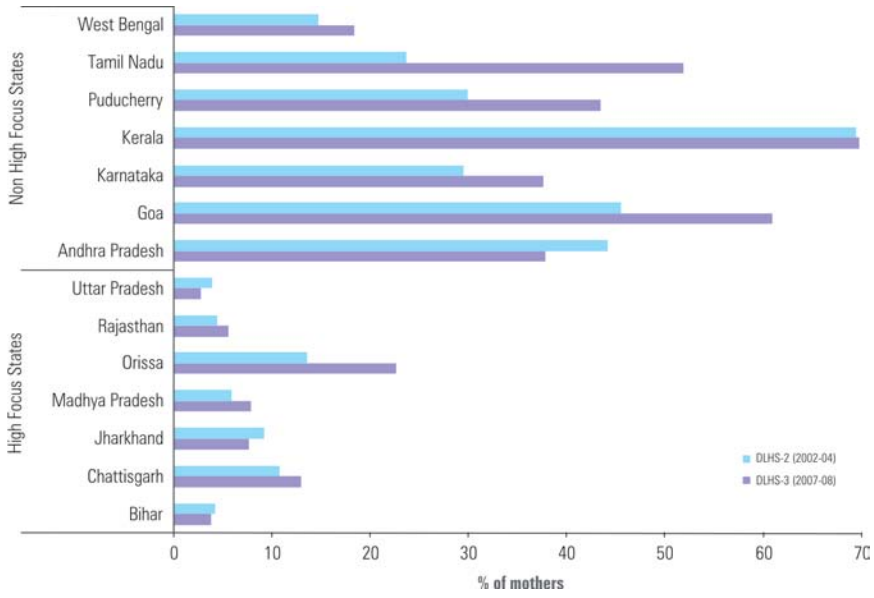

Figure 4 Proportion of mothers who had full antenatal care (at least 3 visits for ANC, one injection of tetanus toxoid and 100 tablets or equivalent thereof of iron and folic acid supplement) during their last pregnancy. Data are overall for the state based on DLHS-3 (2007–2008). ANC: Antenatal care; DLHS: District level health survey. High focus states under NRHM were 18 states identified for special attention based on weak public health indicators and/or weak health infrastructure.

compared to 87.4% in the south. Though the DLHS-3 data indicate that these differentials persist, they present a greater cause for concern (13). In the post NRHM period, the northern Indian states of Bihar, Jharkhand, Madhya Pradesh, Rajasthan and Uttar Praesh have slipped further on this index of quality of care. (**Figure 5**). NFHS-3 reports that while 80–82% of the urban women had their blood pressure measured and weight taken, only 55% of the rural respondents reported having received these basic prerequisites of quality antenatal care (12). DLHS-3 data seem to indicate that the rural- urban differential has only grown wider in the post-NRHM period.

It is important to note that while southern states have made significant progress to address accessibility to good quality of care for antenatal care (ANC), they too fall woefully short of the standards in quality required to bring down maternal mortality. NFHS-3 indicates that 65% of the pregnant women received IFA during ANC which is a seven percentage point increase from NFHS-2. However, the survey also shows that that 59% of the pregnant women were found to be anaemic which is suggestive of poor quality of ANC resulting in poor compliance.

Client – provider inter-personal relationships

Inter-personal relationship between the provider and the client is the key to improved client satisfaction, continued and sustained use of services and thereby better health outcomes. Government health clinics have long been accused of being apathetic and ignorant to client perspectives. It is thus no wonder that clients perceive private sector health services to be superior to that offered by the government program (14). The study on north-south differential cited earlier found that women in both the north and south India reported better quality of interpersonal care in the private sector (26). Births in a private facility are more likely to have a postnatal check-up at 6 weeks (85%) as well as a check-up within four hours of delivery (62%) than births in a public facility (76% and 53%, respectively) (12). Ravindran points out that the clients have a negative impression of government health facilities citing staffs' and nurses' verbal abuse of clients and demands for informal payments even for the most basic health services (27). A focus group study in Uttar Pradesh which documented perceptions among female respondents revealed that staff and medical officers in government institutions are often rude and discourteous to clients (28). Rao narrates the plight of an urban slum dweller in Bangalore who was slapped repeatedly by the nurses in a government hospital because she was too weak to bear down (29). "My mother's house where I had my first born was better," says the respondent. To add insult to the injury the hospital staff refused to hand over her baby until she made informal payments. Once she paid up, she was sent home within 24 hours of delivery without any medicines or postnatal check up.

Quality issues notwithstanding, government clinics continue to be used in large numbers because the costs to the clients are minimal. However, some studies are already revealing new evidences that the poor have also preferred to use the much costlier services provided by the largely unregulated private sector even when they have access to subsidized or free public health care (30). This is inherently regressive and has put a disproportionate burden for health care on poor households. It is not just the poor who face the double burden of poverty and ill-health, the financial burden of ill health can even push the non-poor into poverty.

The teams constituted under the second CRM in their final report re-iterated the need for attention to procedures for registration, patient flow and information through appro-

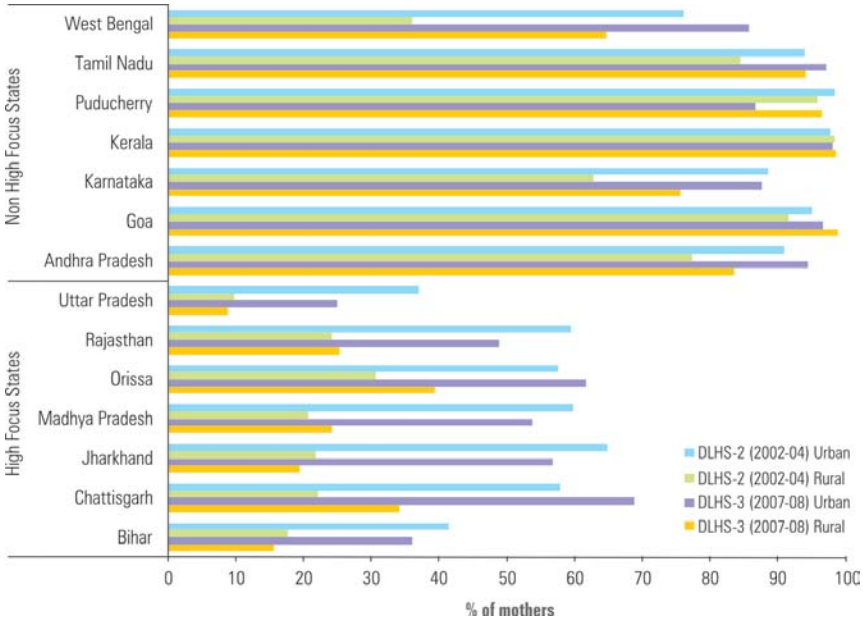

Figure 5 Comparative proportion of mothers who had their blood pressure measured at least once as part of antenatal care during their last pregnancy (DLHS-3 against DLHS-2). DLHS, District level health survey. High focus states under NRHM were 18 states identified for special attention based on weak public health indicators and/or weak health infrastructure.

priate signage, waste disposal and other aspects crucial for a patient friendly facility (19). The shortage of human resources and thereby of the expected services was also noted as an issue of quality. The report of the Third CRM (unpublished) indicates that a positive outcome of the thrust of the changes that the NRHM has brought about in the last 3 years has been on infrastructure strengthening, facility improvement and enabling adequate numbers of human resources- and these measures seemed to have brought about a huge increase in institutional deliveries. It also concludes that even though "[t]he quality of care in the private sector is not necessarily much better than that reported for the public facilities, but because of the push of the system case loads seems to have migrated from the public system to the private system." For example the team constituted under the Third CRM for the state of Gujarat observed that the quality of Chiranjeevi providers (a Public Private Partnership health provider scheme promoted by the State Government) is not necessarily better; however they are supported by a better demand generation involving the government workers at the village level and by a mindset that deems private sector provision better than government provision (31).The report submitted by the team recommends that increased patient load and overcrowding now at public health facilities can be resolved by planned efforts to rationalize patient load (deliveries) by upgrading the primary level services at Primary Health Centres and Subcentres. In general the report of the third CRM observes that lack of respect shown to the patients by the service providers is still a pervasive phenomenon that discourages use of public facilities.

CONCLUSION

It is evident that quality is a more significant predictor of utilization of maternal health care than access. The second CRM report echoes the general finding in the high focus states that, "given the problems of the past, expectations of providers and even of the public had been set at very modest levels. The system is in danger of stabilizing at this low level of expectations and outputs, and even as one appreciates the effort that has gone in to reach this level, there is a need to set the benchmarks higher. There is much more that needs to be done, if the increased patient load and utilization of services was to manifest in increased outcomes" (19).

The report also recommends that improving the quality of care and comfort of stay for the in-patients in the public hospitals especially at the secondary level, through clean toilets, fresh linen, and a friendly environment are steps towards a system of ensuring quality improvement in all public health facilities. One of the major road blocks towards fostering a movement in enforcing quality of care in maternal health services has been the absence of independent advocates for promoting quality of care in this realm within the civil society. The third CRM report lays importance on the use of external assessment and certification of the facilities and for building a policy framework that mandates this.

In summary, although there has been some improvement in the quality of maternal health services in the last decade, India is still a long way off from the standards in most emerging economies leave alone developed countries. Unless the health system is able to ensure good quality care translating into continued and sustained use of maternal health services throughout the country, achievement of MDG-5 goal will likely remain out of reach for a long time.

RECOMMENDATIONS

Though more NRHM has just completed five years of existence, scant data are available on the impact of the mission on quality of care in health facilities. It is imperative that further research is conducted to assess the impact of NRHM on maternal health services and the change it has brought about in client perspectives so that gains from the mission can be consolidated. Community based organisations and consumer groups will need to advocate for quality of care in maternal services by forging collaborations and sharing resources amongst all stakeholders involved in advocating for quality of care in maternal health services. This could be initiated by a pan national organisation which would be able to bring together national and international organisations like the White Ribbon Alliance, UNICEF, WHO, UNFPA and other international donors on a common platform. State Governments will need to establish task forces for enforcing Indian Public Health Standards (IPHS) guidelines at all levels and these should be monitored by an independent body at the centre. State Governments should also set up mechanisms for efficient procurement, management and monitoring of supply chain systems [on the lines of Tamil Nadu Medical Supplies Corporation (TNMSC)] for equipment and drugs for essential maternal health services. Standard treatment guidelines created in consultation with senior medical officials also need to be implemented and monitored. Hospitals need to be certified as women and baby friendly. Multi pronged strategies should also be worked out to improve the quality and efficiency of services being delivered by ASHAs as these will have a major impact on the success of NRHM in general and improvement of maternal health indicators in particular.

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journal of global health

Efficacy and effectiveness of 20 child health interventions in China: Systematic review of Chinese literature

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Aim The research production of the Chinese academics for the past few decades, which is being published in more than nine thousands of Chinese academic periodicals, has recently been digitalized and made available in the public domain. The aim of this study was to systematically identify and assess the evidence from Chinese literature sources on the efficacy and effectiveness of child health interventions in China.

Methods The Chinese National Knowledge Infrastructure databases were searched for the studies with primary data on efficacy or effectiveness of child health interventions in China between 1980 and 2011. The searches of PubMed and the 'Lives Saved Tool (LiST)' evidence base were also performed to identify the counterpart evidence in the English language.

Results Of 32 interventions initially identified in the Chinese literature, 20 interventions sustained the primary information addressing efficacy or effectiveness. Among preventive interventions (14 interventions), most studies were dedicated to complementary feeding (7 studies), kangaroo mother care (7 studies) and syphilis detection and treatment (4 studies). Among treatment interventions (6 interventions), the most frequently studied were zinc for treatment of diarrhoea (11 studies) and newborn resuscitation (9 studies). The evidence on efficacy or effectiveness of the 32 interventions conducted in Chinese children in the Chinese literature was either of comparable quality, or more informative than the available reports on China in the English literature, which rarely contained studies on child health intervention effectiveness exclusively in Chinese population. The included studies reported positive results unanimously, implying a likely publication bias.

Discussion The evidence on the efficacy and effectiveness of child health interventions in China is typically modest in quantity and quality, and implies a notable urban-rural discrepancy in applied health systems research to improve child health interventions and programmes. However, it is clear that considerable research interests and initiatives from both inside and outside the country have been concentrating on implementation, long-term operation, evaluation and further development of child health interventions, especially preventive interventions in China.

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In 2000, the UN defined a set of goals on which a global political consensus was reached – the 'Millennium Development Goals' (1,2). The fourth goal was defined as an ambition to decrease the levels of global child mortality between 1990 and 2015 by two thirds (3). The leading strategies for achieving child mortality reduction were to implement cost-effective interventions in the largest part of the population in low and middle income countries (4–7). These interventions were developed to prevent and treat the leading causes of child mortality, eg, preterm birth complications, birth asphyxia, neonatal infections, pneumonia, congenital abnormalities, diarrhoea, tetanus and HIV/AIDS (5,6). Clearly, there are many possible interventions available, and prioritization of those interventions for implementation among children has become one of the most important health policy goals for the governments, especially in low and middle income countries (8). They are calling for better evidence on the efficacy, effectiveness and cost-effectiveness of each intervention, and also better information on the patterns of child mortality burden in their countries (8). Therefore, understanding the causes of child mortality and the effectiveness of the preventive and treatment interventions has become one of the main interests of the global health community. The 'Child Survival Series' published by *The Lancet* is the earliest and one of the best examples (5,9–12).

The controversy over the true value of many child health interventions still rekindle debates now and then. First, once a few published randomized controlled trials show effectiveness of an intervention, it becomes unethical to scale up the evaluation only to deprive the control arm of apparent benefits. Second, the diversity of study settings and contexts produces enormous confounding and distorts generalization. Third, due to resource constraints, not every study can achieve sufficiently large simple size. Many of them eventually become underpowered, which leads to diverse and often conflicting results. Furthermore, mortality is rarely – if ever – an acceptable outcome of an intervention trial, and the introduction of proxy indicators creates uncertainty over the true effects on mortality and causes ambiguous conclusions. The most recent effort to integrate estimated effectiveness of interventions on child mortality has been published in 2 supplements of the *International Journal of Epidemiology* and *BMC Public Health*, providing the theoretical and methodological background information for the 'Lives Saved Tool (LiST)' (13). LiST is an evidence-based software module that allows prediction of the impact of scaling up different child health interventions at the national, regional and global level. Although this project is designed and performed to produce reasonably conservative estimates, the primary information gap is still an open issue and that new evidence from any proper sources would further refine the estimates.

Table 1 List of 32 interventions chosen for the review*

Preventive interventions
• Antenatal steroids to prevent preterm birth
• Antibiotics for premature rupture of membranes
• Breastfeeding (exclusively for 6 months)
• Calcium supplementation to prevent pre-eclampsia and eclampsia
• Clean delivery practices
• Complementary feeding
• Detection and management of breech births (Caesarean section)
• Folic acid (vitamin B) supplementation
• HiB vaccination to prevent pneumonia
• Insecticide-treated materials
• Intermittent presumptive treatment for malaria in pregnancy
• Kangaroo mother care
• Labour surveillance (including partograph) for early diagnosis of complications
• Measles vaccination
• Nevirapine and replacement feeding (where possible) to prevent HIV transmission
• Newborn temperature management
• Prevention and management of hypothermia
• Syphilis detection and treatment
• Tetanus toxoid (neonatal)
• Vitamin A supplementation
• Water, sanitation, hygiene
• Zinc supplementation
Treatment interventions
• Antibiotics for dysentery
• Antibiotics for neonatal sepsis
• Anti-malarials
• Community-based pneumonia case management, including antibiotics
• Corticosteroids for preterm labour
• Detection and treatment of asymptomatic bacteriuria
• Newborn resuscitation
• Oral rehydration therapy
• Vitamin A
• Zinc for treatment of diarrhoea

*The interventions were chosen based on Lancet's Child Survival Series list of interventions (5) and supplemented with any additional interventions on which at least 1 publication in Chinese literature could be found during the period 1980–2011.

One of the potential sources of this kind is academic literature in the Chinese language. The research production of Chinese academics for the past few decades, which is being published in more than nine thousands of Chinese academic periodicals, has recently been digitalized and made available in the public domain. It has been proven that strategically retrieving and analysing qualified publications in the Chinese literature contributes significant evidence and updates to the understanding and knowledge on various topics in the field of child health epidemiology (14). The aim of this study was to systematically identify and assess the evidence from Chinese literature sources on the efficacy and effectiveness of child health interventions in China.

METHODS

The China National Knowledge Infrastructure (CNKI) databases were searched for the period January 1980 to March 2011. CNKI is the most complete source of academ-

Figure 1 Geographical distribution of 59 retained studies during 1980–2011.

Table 2 The list of 59 retained studies for 20 interventions

Preventive interventions	Key search terms	General search terms	Crude hits	Title hits	Abstract hits	Final hits
Antibiotics for premature rupture of membranes	抗生素; 胎膜早破	效果; 评价; 影响; 作用; 干预	309	26	2	1
Clean delivery practices	科学接生	效果; 评价; 影响; 作用; 干预	30	16	4	1
Complementary feeding	辅食添加; 辅食喂养	效果; 评价; 影响; 作用; 干预	147	23	13	7
Folic acid (vitamin B) supplementation	叶酸; 维生素B;补充	效果; 评价; 影响; 作用; 干预	123	21	12	2
HiB vaccination to prevent pneumonia	HiB疫苗	效果; 评价; 影响; 作用; 干预	124	34	2	1
Kangaroo mother care	袋鼠式护理; 皮肤接触护理	效果; 评价; 影响; 作用; 干预	60	31	15	7
Labour surveillance (including partograph) for early diagnosis of complications	产前检查; 并发症; 早期诊断	效果; 评价; 影响; 作用; 干预	366	27	6	2
Measles vaccination	麻疹疫苗	效果; 评价; 影响; 作用; 干预	68	21	5	2
Nevirapine and replacement feeding (where possible) to prevent HIV transmission	奈韦拉平; 替代喂养; 艾滋病	效果; 评价; 影响; 作用; 干预	156	44	2	1
Newborn temperature management	新生儿; 温度管理	效果; 评价; 影响; 作用; 干预	1	1	1	1
Syphilis detection and treatment	梅毒	效果; 评价; 影响; 作用; 干预	184	12	10	4
Tetanus toxoid (neonatal)	破伤风; 类毒素; 新生儿	效果; 评价; 影响; 作用; 干预	197	9	3	2
Vitamin A supplementation	维生素A; 维他命A	效果; 评价; 影响; 作用; 干预	558	56	10	2
Water, sanitation, hygiene	水与环境卫生(WES)项目	效果; 评价; 影响; 作用; 干预	19	8	2	1
Treatment interventions						
Antibiotics for dysentery	痢疾; 抗生素	效果; 评价; 影响; 作用; 干预	263	5	1	1
Corticosteroids for preterm labour	糖皮质激素; 早产	效果; 评价; 影响; 作用; 干预	231	12	6	1
Newborn resuscitation	新生儿复苏	效果; 评价; 影响; 作用; 干预	969	29	18	11
Oral rehydration therapy	口服补液疗法	效果; 评价; 影响; 作用; 干预	112	15	1	1
Vitamin A	维生素A; 维他命A	效果; 评价; 影响; 作用; 干预	138	28	2	2
Zinc for treatment of diarrhoea	锌; 腹泻; 治疗	效果; 评价; 影响; 作用; 干预	170	39	12	11

ic information in China and represents the Chinese equivalent of PubMed or the Web of Knowledge (15). A systematic search of CNKI was performed to identify clinical and community-based studies with primary data reporting either efficacy or effectiveness of child health interventions relevant to neonates, infants, pre-school children or parents in China. Studies were included if: the total cohort was more than 50 subjects; the study design was prospective; the sample population was exclusively Chinese who lived in China at long-term residency base (16,17).

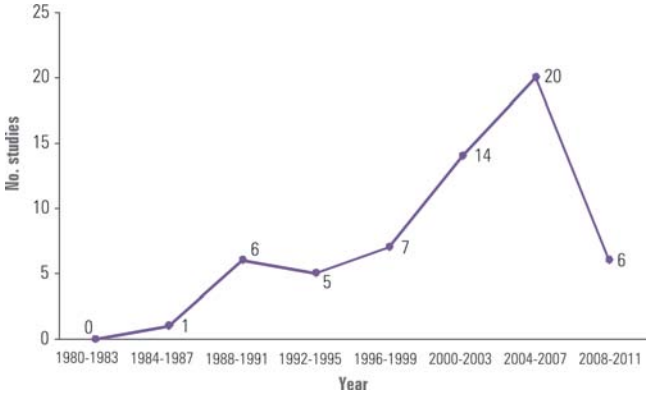

Figure 2 The time trend of 59 retained studies during 1980–2011.

The search terms used were various combinations from a set of terms for 'efficacy' and 'effectiveness' in their Chinese equivalences, i.e. '效果', '评价', '影响', etc. and a set of terms for each intervention in their Chinese equivalences as well, eg, '叶酸', '维生素B', '补充', etc. for 'folic acid (vitamin B) supplementation'. The first step was to search prevention and treatment interventions targeting causes of child death in general (early development- related excluded). As this search strategy aimed to be as inclusive as possible, it resulted in 6476 publications which mentioned 32 interventions (**Table 1**). The first level screening based on titles left 649 studies for further identification as the majority were not relevant at all to the topic of 'efficacy' or 'effec-

Table 3 Three most investigated preventive child health interventions in Chinese literature

Study No	Year	Province	Cohort site	Cohort No.	Sample size (Intervention 1)	Sample size (Intervention 2)	Sample size (Controls)	Outcome	Indicators of the outcome			
									1	2	3	4
• Kangaroo mother care												
1	2009	Zhejiang	Hospital	–	100	–	100	Body temperature management	Temperature recovery speed (hr): I=1.665±1.36, C=6.635±3.838 P<0.05	–	–	–
2	2008–2009	Guangdong	Hospital	–	50	–	50	Venepuncture pain management	Heart rates (/min): I<C, (8–14), P<0.05	Blood oxygen rate (%): I<C, (1–5), P<0.05	–	–
3	2007	Hebei	Hospital	–	80	–	80	Body temperature management	Temperature recovery speed: I=38(<4h), C=18(<4h), P<0.05	–	–	–
4	2007–2008	Guangdong	Hospital	–	30	–	30	Weight gain	Weight gain in the 28th day: I=835g, C=750g, P<0.0005	–	–	–
5	2006–2008	Hunan	Hospital	–	60	–	60	Physiological and behaviour indicators	Heart rates (/min): I=142.4±19.1, C=157.1±24.8, P<0.01	Blood oxygen rate (%): I=91.7±4.6, C=87.9±9.1, P<0.01	–	–
6	2004–2009	Shanxi	Hospital	–	55	–	53	Pain management	Heart rates (/min): I=152.77±15.98, C=162.34±22.02, P<0.05	Blood oxygen rate (%): I=94.03±10.89, C=93.08±10.62, P<0.05	–	–
7	1999–2002	Guangdong	Hospital	–	54	–	50	Prognosis of very LBW	MDI: I=99±12, C=89±10, P<0.01	PDI:, I=91±10 C=83±11, P<0.05	–	–
• Complementary feeding												
1	2007–2008	Guangxi	Community	–	100	–	100	–	Percentage-Nutrition (P0-P100): I>C, P<0.05	–	–	–
2	2006–2008	Jiangsu	Hospital	–	206	–	175	–	Hb (g/L): I=80.74±13.24 C=66.43±12.57, P<0.05	IDA: I=9(4.5%) C=33(19.4)P<0.05	–	–
3	2004	Gansu	Community	–	1000	500	127	–	DQ: I>C, P<0.0001	–	–	–
4	2003	Guangdong	Hospital	–	251	–	237	–	Malnutrition: I=9, C=42, P<0.01	–	–	–
5	2002	Jiangsu	Hospital	–	52	–	52	–	Anaemia(%): I=17.31, C=38.46, P<0.05	–	–	–
6	1997	Liaoning	Hospital	–	107	–	34	–	Standard BW: I=64(87.7), C=21(61.8), P<0.01	–	–	–
7	1994	Sichuan	Hospital	–	45	60	58	–	BW, Height, HC: I>C, P<0.05	–	–	–
• Syphilis detection and treatment												
1	2006–2009	Inner Mongolia	Hospital	–	168	–	32	–	Syphilis(+): 72 children born to Interventions; 19 children born to Controls	–	–	–
2	2005	Guangdong	Community	159 017	–	–	–	–	125(syphilis child cases in theory for 2005) – 4 (syphilis child cases in 2005)	–	–	–
3	2001–2005	Guangdong	Hospital	–	50	–	13	–	Syphilis(+): 8 children born to Interventions; 10 children born to Controls	–	–	–
4	2001–2002	Guangdong	Community	186 517	–	–	–	–	Reduction: 61.90%	–	–	–

I – interventions, C – controls, LBW – low birth weight, MDI – mental developmental index, PDI – psychomotor developmental index, Hb – hemoglobin concentration, IDA – iron deficiency anaemia, DQ – developmental quotient, BW – birth weight, HC – head circumference

tiveness'. The abstract screening then left 136 relevant records for full text retrieving. Eventually, 59 studies (up to 1% of the initial screen) for 20 interventions were retained (**Table 2**). The most common reasons for exclusion were: 1. the total sample cohort was less than 50 subjects, considering that the small sample size might lead to large errors; 2. study design was retrospective, which might cause massive recall bias; 3. the study method was not sufficiently described to understand or interpret the results.

RESULTS

The distribution of the 59 included studies clustered mainly in the eastern and central regions of China (**Figure 1**). The latest classification of Chinese regions based on regional macro-economy development recommended dividing China into the eastern, central and western regions. Of the three macro-regions, Western China suffered the most from economical disadvantages. This also provides insight into a further discrepancy: the retained studies conducted in Eastern and Central China were generally led by major university-affiliated hospitals, which were in control of the key resources, such as the provincially leading research and teaching hubs and/or networks. In Western China, however, the retained studies were mostly conducted through cooperation with international organizations, as the overseas aid programmes. Also, an analysis of the period 1980 to 2011, which separated the included studies into 4-year time-periods by frequency, showed the time trend of a steady increase until the period 2004–2007. This was followed by a sharp drop during the period 2008–2011, to the level of activity observed back in 1992–1995 (**Figure 2**).

All the included studies that evaluated a total of 20 interventions were focused on addressing efficacy or effectiveness as the primary outcome. Among preventive interventions (14 interventions), most studies were dedicated to complementary feeding (7 studies), kangaroo mother care (7 studies) and syphilis detection and treatment (4 studies) (**Table 3**). Among treatment interventions (6 interventions), the most frequently studied were zinc for treatment of diarrhoea (11 studies) and newborn resuscitation (9 studies) (**Table 4**). Within each intervention, the results from individual studies generally supported each other, providing evidence on the positive effects for all interventions. However, several peculiarities need to be noted: for complementary feeding, each study adopted different food formulas and this may be due to the widespread geographic distribution. For Kangaroo mother care, the research interests varied dramatically, which made the targeting outcomes very diverse – including body temperature management, pain management, weigh gain, physiological and behavioural factors, etc. For syphilis detection and treatment, it was notable that one community-based study conducted in Guangdong province and recruiting 186 517 subjects reported an impressive 61.90% reduction rate during a period of two years. For zinc for treatment of diarrhoea, although OER and anti-diarrhoea duration were common indicators, the ingredients and portions of zinc formula adopted in each study were not consistent. Finally, for newborn resuscitation the universal outcome indicators employed in each study were Apgar-5 and Apgar-10, while Apgar-1 and Apgar-7 occasionally reported with other specific outcomes such as mortality, morbidity of asphyxia, pneumonia and infections.

The evidence on efficacy or effectiveness of the 32 interventions conducted in Chinese children in the Chinese literature was either of comparable quality, or more informative than the available reports on China in the English literature (**Table 5**). Although the selected English literature sources showed a substantial and strikingly increasing number of publications on child health interventions during the same period, studies on intervention effectiveness exclusively in Chinese children were very rarely published, and the few rare studies were unlikely to scale-up a systematic analysis or meta-analysis for any of the 32 selected interventions in this paper.

DISCUSSION

This paper represents the very first attempt to systematically investigate the accessibility, quantity and quality of the research production of Chinese academics over the period of the past 30 years on efficacy and effectiveness of child health interventions in China. It is possible that a parallel review and/or the extended systematic review of other digital Chinese-language databases such as Chongqing VIP and Wanfang would have identified slightly more studies. However, the initial searching within the two additional databases did not seem to add any further evidence (my search on February 15, 2011), and this might due to the extremely massive overlap in indexed journals of the three domains (15,18,19). It is very unlikely that substantial omissions could have drawn dramatically different conclusions on quantity assessment from those that this paper offers.

Conducting studies which evaluate interventions generally not only requires substantial financial support and high-level technical expertise, but it is also subject to various vital factors, such as ethical approval, unique local conditions/customs and liaisons with multiple-organizations, to name a few. Usually, a single team of researchers has to invest tremendous efforts to ensure smooth workflow for years to achieve the ultimate outcome, either positive or negative, even possessing sufficient essential resources.

Table 4 Two most investigated treatment child health interventions in Chinese literature

Study No.	Year	Province	Cohort site	Cohort No.	Sample size (Intervention 1)	Sample size (Intervention 2)	Sample size (Controls)	Outcome	Indicators of the outcome			
									1	2	3	4
• Zinc for treatment of diarrhoea												
1	2009	Shandong	Hospital	–	65	–	60	–	OER (%): I=96.92, C=78.33, P<0.05	Anti-diarrhoea duration (days): I= 6±1.05, C=7±1.02, P<0.05	–	–
2	2008–2009	Jiangxi	Hospital	–	90	–	90	–	OER (%): I=90.0, C=60.0, P<0.05	Anti-diarrhoea duration (days): I=3.11±2.41, C=5.32±2.11, P<0.01	–	–
3	2008–2009	Tianjing	Hospital	–	45	–	42	–	OER (%): I=86.3, C=76.2, P<0.05	–	–	–
4	2008–2009	Liaoning	Hospital	–	55	–	55	–	OER (%): I=89.09, C=65.45, P<0.01	–	–	–
5	2007–2009	Shaanxi	Hospital	–	40	–	40	–	OER (%): I=92.5, C=80.0, P<0.05	Anti-diarrhoea duration (days): I=2.81±0.83, C=4.21±1.98, P<0.01	–	–
6	2007–2009	Sichuan	Hospital	–	120	–	120	–	OER (%): I=93.4, C=82.5, P<0.05	–	–	–
7	2007–2009	Jiangxi	Hospital	–	60	–	60	–	OER (%): I=93.4, C=73.2, P<0.01	Anti-diarrhoea duration (hrs): I=48.92±3.02, C=100.23±3.16, P<0.05	–	–
8	2007	Hubei	Hospital	–	55	–	50	–	Anti-diarrhoea duration (hrs): I=43±6, C=49±5, P<0.01	–	–	–
9	2006–2008	Chongqing	Hospital	–	164	–	168	–	OER (%): I=92.07, C=74.41, P<0.01	Anti-diarrhoea duration (days): I=3.11±1.41, C=4.07±2.12, P<0.01	–	–
10	2005–2007	Sichuan	Hospital	–	95	–	91	–	OER (%): I>CP; <0.01	–	–	–
11	2005–2006	Shandong	Hospital	–	124	–	126	–	OER (%): I=98, C=92, P<0.05	–	–	–
• Newborn resuscitation												
1	2003–2006	Shandong	Hospital	–	3050	–	2850	–	Asphyxia (%): I=0.4, C=2.1, P<0.01	–	–	–
2	2002–2005	Qinghai	Hospital	–	682	–	1318	–	Mortality (%): I=15, C=38, P<0.05	–	–	–
3	2001–2006	Hubei	Hospital	–	13905	–	7808	–	Asphyxia (%): I=0.48, C=2.7, P<0.01	–	–	–
4	2000–2003	Henan	Hospital	–	168	–	55	–	Apgar-5: I=8.0±1.0, C=6.3±0.8, P<0.01	Apgar-10: I=9.0±1.1, C=8.0±0.5, P<0.01	–	–
5	1999	Anhui	Hospital	–	143	–	143	–	Apgar-7: I=3.4, C=12.5, P<0.05	Pneumonia (%): I=1.3, C=6.9, P<0.05	Infections (%): I=1.3, C=6.2, P<0.05	–
6	1997–2000	Sichuan	Hospital	–	52	–	56	–	Pneumonia: I=9, C=2, P<0.05	HIE: I=9, C=1, P<0.05	Apgar-5: I=46, C=50, P<0.05	Apgar-10: I=50,C=52 P<0.05
7	1997–1998	Jilin	Hospital	–	2478	–	782	–	Asphyxia (%): I=5.29, C=15.22, P<0.01	–	–	–
8	1993–1997	Shandong	Hospital	–	54	–	63	–	Survival rate (%): I=100, C=90.47, P<0.005	–	–	–
9	1989, 1997	Shaanxi	Hospital	–	1349	–	2414	–	Asphyxia (%): I=2.3, C=4.4, P<0.05	Apgar-1: I=6.1, C=3.7, P<0.01	Apgar-5: I=9.7, C=7.7, P<0.01	–

I – interventions, C – controls, OER – overall effect rate, HIE – hypoxic ischemic encephalopathy

This may explain why, in the global context, the research production on intervention evaluation is relatively scarce and the relevant studies with large sample sizes and robust study designs are extremely valuable.

According to GRADE criteria, the retained studies in the Chinese literature are generally of modest quality (17). Relatively small sample sizes and wide confidence intervals make it unjustified that all retained studies should be expected to show positive effects of the investigated interventions, implying a likely publication bias. This has not ridden the Chinese literature only, as there is a traditional academic and industrial resistance to reporting and pursuing publication of negative effects, especially where the previous evaluation showed benefits. China may consider incorporating the existing national ethics approval system with a mandatory national trail registration system in order to keep all the trails conducted in China well tracked and ensure that the final outcomes are reported and made public.

Despite insufficient information to fully assess the current situation of child health interventions in depth in China, the urban-rural discrepancy in study distribution and funding resources is particularly notable. While the studies in Eastern and Central China were conducted by regional leading institutes as scientific research projects, Western China, the most remote and mountainous region of the country, seems to still be reliant on overseas aid to implement child health interventions. The longstanding urban-rural socio-economical imbalance results in limited academic and industrial ac-

Table 5 The remaining 15 child health interventions with addressed effectiveness in Chinese literature

PREVENTIVE INTERVENTIONS

Study No.	Year	Province	Cohort	Cohort Size	Sample size (Intervention 1)	Sample size (Intervention 2)	Sample size (Intervention 3)	Sample size (Control)	Outcome	Indicators of outcome			
										1	2	3	4
• Folic acid (vitamin B) supplementation													
1	1996–1997	Zhejiang	Hospital	–	2265	–	–	2265	Congenital heart diseases	RR=1.77(95 % CI: 1.082 – 2.466, AR=1.29% ARP=43.63% P<0.01	–	–	–
2	1993–1995	National	Community	–	130142	–	–	117689	NTD	120(NTDs) / 130142 137(NTDs) / 117689, P<0.01	–	–	–
• Tetanus toxoid (neonatal)													
1	1991–1993	Hunan	Community	–	170	–	–	170(self)	–	IU/ml(mothers) increased =0.137–0.008 IU/ml(children) =0.054 P<0.01	–	–	–
2	1986–1987	Ningxia	Community	–	67	–	–	41	–	IU/ml >0.01: 89.55% of children born to Interventions; 14.63% of children born to Controls P<0.01	–	–	–
• Antibiotics for premature rupture of membranes													
1	1992–1997	Henan	Hospital	–	30	–	–	30	–	BW: I=2580g; C=2391g, P<0.01	1 min Apgar ≤ 7: I=4; C=9 P<0.01	Infections: I=5; C=7, P<0.01 Intracranial haemorrhage: I=5; C=5, P<0.01	Death: I=0; C=2, P<0.01
• Labour surveillance (including partograph) for early diagnosis of complications													
1	2006–2008	Zhejiang	Hospital	–	11186	–	–	1066	–	RDS: I=290; C=52, P<0.01	LBW: I=551; C=88, P<0.01	Preterm birth: I=554; C=95 P<0.01	Caesarean section rate: I=68; C=113; P<0.01
2	2006–2007	Shandong	Hospital	–	226	–	–	208	–				
• Clean delivery practices													
1	1991–1993	Heilongjiang	Hospital	–	355	–	–	366	–	Death (Children): I=9; C=5; P<0.01	–	–	–
• Newborn temperature management													
1	2002–2003	Gansu	Hospital	–	715	–	–	1096	–	neonatal scleredema: I=3, C=10, P<0.01	–	–	–
• HiB vaccination to prevent pneumonia													
1	2006	Shanghai	Community	–	372	–	–	305	–	HiB+ (%): I=9.8; C=3.8, P<0.01	–	–	–
• Water, sanitation, hygiene													
1	1996–2000	Gansu	Community	21 villages	–	–	–	–	–	Sanitation per household, population educated, children hygiene behaviour positive change rate are all increased.	–	–	–
• Vitamin A supplementation													
1	2001–2005	Chongqing	Institute	–	64	–	–	61	–	Hb (g/L): I=122.0±7.5, C=120.3±7.87, P<0.001	–	–	–
2	1991–1992	Hebei	Community	–	327	–	–	343	–	Z value: I>C, P<0.01	–	–	–
• Nevirapine and replacement feeding (where possible) to prevent HIV transmission													
1	2005	Yunnan	Community	–	61	61	–	–	–	Reduction: 7.0%	–	–	–
• Measles vaccination													
1	2000–2007	Guizhou	Community	25302	–	–	–	–	–	Morbidity: 26.68 / 100 000 (2002) 3.52 / 100 000 (2003) 0.20 / 100 000 (2007)	–	–	–
2	1991	Hubei	Community	503	–	–	–	–	–	Reduction in 6 years: 59.22%	–	–	–

I – intervention, C – control, RR – risk ratio, AR – attribute ratio, ARP – attribute ratio percentage, RDS – respiratory distress syndrome, Hb – hemoglobin concentration

Table 5 cont.

TREATMENT INTERVENTIONS

Study No.	Year	Province	Cohort	Cohort Size	Sample size (Intervention 1)	Sample size (Intervention 2)	Sample size (Intervention 3)	Sample size (Control)	Outcome	Indicators of outcome			
										1	2	3	4
• Corticosteroids for preterm labour													
1	2000	Anhui	Hospital	–	–	18	19	–	5	Hyaline membrane disease (<34 weeks gestation): I<C, P<0.001	–	–	–
• Oral rehydration therapy													
1	2001–2005	Heilongjiang	Hospital	–	60	–	–	60	–	Temperature recovery speed (days): I=1.51±0.89, C=3.87±2.03, P<0.01	Diarrhoea recovery speed (days): I=2.97±1.45 C=5.72±2.43 P<0.01	General recovery speed (days): I=4.70±1.98 C=7.28±2.86 P<0.01	–
• Antibiotics for dysentery													
1	1994–1996	Jiangsu	Hospital	–	24	30	23	–	–	2 preferred based on temperature recovery speed and anti-diarrhoea duration: both Ps<0.01	–	–	–
• Vitamin A													
1	2003–2006	Jiangxi	Hospital	–	42	–	–	35	Recurrent respiratory infections	Temperature recovery speed (days): I=3.5, C=6.0, P<0.01	Diarrhoea recovery duration (days): I=5, C=8, P<0.01	Diarrhoea recovery duration (days): I=5; C=8 P<0.01	Recurrence (%): I<C, P<0.05
2	1990–2000	Chongqing	Hospital	–	30	–	–	30	Measles	VA (μmol/L): I=1.17±0.12, C=0.84±0.24, P<0.01	Cough recovery duration (days): I=8.12±1.24 C=9.36±1.68 P<0.01	Diarrhoea recovery duration (days): I=7.88±1.87 C=9.13±1.20 P<0.01	Complications (%) I<C, Ps<0.05

I – intervention, C – control, RR – risk ratio, AR – attribute ratio, ARP – attribute ratio percentage, RDS – respiratory distress syndrome, Hb – hemoglobin concentration

tivities focusing on the most underdeveloped region of China, where implementing, evaluating and further developing appropriately customized interventions may achieve highest potential impact on child mortality reduction and other aspects of child health in China as a whole.

Comprehensive and accurate data and evidence on child health interventions are indispensable for prioritizing prevention and treatment strategies in order to achieve optimal policy decisions. It is clear that considerable research interests and initiatives from both inside and outside the country have been concentrating on child health interventions, especially preventive interventions in China. How to best harness and facilitate those potential strengths in this still new and fast growing field could be the next opportunity and challenge that the country has to take.

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PAPERS

Leadership for child health in the developing countries of the Western Pacific

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The content and landscape of global child health is increasingly complex. There is strong evidence for the effectiveness of local, national and institutional leadership in reducing child mortality, but this has not been a focus of global health initiatives. Interventions to strengthen health systems should include support for local leadership: building-up institutions of training, empowering national paediatric professional associations, creating opportunities for contribution and leadership at national, provincial and local level, and networks of support for staff working in child health in remote areas. In the poorer high mortality burden countries of the Pacific, to meet the clinical and public health gaps, there is a need for increases in the education of child health nurse practitioners, and development of systems of continuing professional development for paediatric doctors and nurses. Involvement in local research, especially that which contributes directly to critical issues in child health policy or strengthening national data systems builds capacity for leadership.

The 524 000 child deaths each year in countries in the Western Pacific are much higher than what would be expected given the body of available knowledge and interventions (1,2). This gap has been attributed to the failure to deliver essential health services in a timely, sustainable and equitable way to children who need them (3). Health systems in the poorer developing countries with high death rates for children are often described as weak. Accounts point to deficiencies in each building block of the system: in the quality of health services, the workforce, health information systems, access to essential medical devices, financing, leadership and governance (4). The need for health systems strengthening is frequently cited (5). Yet, it is only recently that there has been a common definition (3), and that the major players in global health have proposed a joint approach to collaboration on health systems strengthening (6). As yet, the evidence-base for the impact of these approaches on health outcomes is mixed and generally weak (7).

The challenges in achieving a concerted effort to strengthen weak health systems are inherent in the breadth of the WHO's definition of health system as "all organizations, people and actions whose primary intent is to promote, restore or maintain health" (3). With the multiplicity of partner

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agencies, their vertical approaches yet calls for integration and harmonization of health and non-health initiatives, the increasing complexity of health care, and many threats from outside and within, countries are challenged in coordinating, setting and sustaining national priorities, and developing quality health services.

In 1997, the Partnership for Maternal, Newborn and Child Health released a statement calling for leadership at global and national levels to achieve the Millennium Development Goals (MDGs) for child (MDG 4) and maternal health (MDG 5) (8). The statement asserted the important role of health professional associations, and called for actions to develop local leadership in high mortality burden countries. In 2005, the Western Pacific Regional Office of WHO launched the Child Survival Strategy. This also included a call for leadership from political figures and policy-makers (9): "Policy-makers in different government sectors must provide strong and consistent leadership. Accelerating child survival efforts will require leadership from influential political figures at the highest possible level. To ensure wide support and that children's rights to health and health care are addressed, highly visible and well-respected champions will be needed across different sectors of society."

So what does leadership actually entail for child health? We set out to explore its role in the high mortality burden countries of East Asia and the Pacific: who does or can provide leadership, how to strengthen it, and whether this would have an impact on child health. We argue that this is an unmet need. We explain the reasons why leadership is so important and that in addition to political and policy leadership, the scope of leadership must be extended to clinical and public health leadership at all levels of the health service if child health is to improve.

IDENTIFYING BACKGROUND EVIDENCE

To discuss these issues with a sound evidence-base we searched PubMed (1980–2011), CINAHL (1970–2011) and Embase (1980–2011) using combinations of the terms 'leadership', 'child', 'health', 'mortality', and 'professional associations/societies'. The search was limited to articles in English. A sensitive search was performed on PubMed, and complemented with more specific searches by omitting some of the keywords on subsequent searches (details available on request from authors). As it was possible that more information on this was available in the grey literature, key terms were also entered in Google Scholar, the New York Academy of Medicine library and the World Health Organization databases. The International Pediatric Association (IPA) database was used to identify professional associations in countries in the Pacific and East Asia. We anticipated a scarcity of literature dealing with these issues. Therefore, we broadened the search to include literature on the impact of leadership on health (not specifically child health) that was relevant to developing and least developed countries. The United Nations Statistical Division classifications were used when referring to 'least developed' and 'small island developing' countries (10).

There is limited evidence in this field. We identified 16 publications of varying relevance. The search results are summarised here primarily to highlight the paucity of published literature, and the varying interpretations of what leadership for child health means. Five articles dealt with national leadership: three articles from Papua New Guinea (PNG) (11), Mexico (12) and Thailand (13) were specific for child heath, and two articles from Thailand (14) and Sub-Saharan Africa (15) were more general. Three articles discussed the role of professional associations for maternal and child health (16–18), and one outlined the development of paediatric services in Singapore (19). Three articles addressed clinical leadership: two from developed countries evaluated the impact of nursing leadership on patient outcomes (20,21), and one described the postgraduate paediatric training program in PNG (22). Four articles outlined interventions to improve public health and clinical leadership: South Africa's experience with mortality audit and policy for maternal and child health (23); the development of leadership training for paediatric residents (24) and designing nurse leadership training (25) in the United States; and an evaluation of the Fiji nurse practitioner training program (26). Nine additional reports that were directly relevant were retrieved from the gray literature search (3,4,7–9,27–30). The examples and data retrieved were used as background in the broader discussion that follows.

Data on the health situation for children in the East Asia and Western Pacific Region were sourced from UNICEF, WHO, the published literature, and are cited where used.

COUNTRIES OF THE EAST ASIA AND WESTERN PACIFIC REGION

The countries of the East Asia and Western Pacific Region are heterogeneous. Based on their child health characteristics, many child health challenges are shared by countries classified by WHO and UNICEF as Group 1 countries (Cambodia, Kiribati, Marshall Islands, Lao PDR, Papua New Guinea, Solomon Islands and Vanuatu), the other Pacific Island nations and Timor-Leste (31,32). In these countries infectious diseases and under-nutrition remain prominent throughout most of the population. While some countries are on-track to achieving MDG 4 targets, no country in the Region is on track for achieving all its Millennium Development Goals. It is for these countries that this review is predominantly relevant. In these countries poverty rates are high; one in four households is below national poverty lines and protein energy and micronutrient malnutrition is com-

mon. Other shared features include geographical isolation, poor health infrastructure, limited human resources, and in many countries, frequent natural disasters, risks from climate change, limited access to safe water and sanitation, and limited domestic markets. PNG has the highest burden of child deaths in the Pacific region, with about 14,000 child deaths per year. Lao PDR, Timor Leste and Cambodia have among the highest child mortality rates in the East Asian Region. In Pacific Island states more than 70% of child deaths occur in infancy, and neonatal mortality rates have not appreciably fallen in the last 10 years.

THE NEED FOR LEADERSHIP

Child health is becoming more complex

There are many reasons why leadership is needed now more than ever. The content and landscape of child health in developing countries has become increasingly complex in the last two decades. Twenty years ago there was no artemisinin-based treatment for malaria, rapid diagnostic tests, antiretroviral therapy, programs for prevention of mother to child transmission, fixed-dose combination therapy for tuberculosis, insecticide-treated bed nets, Integrated Management of Childhood Illness, zinc or vitamin A, conjugate vaccines against *Pneumococcus* or *Haemophilus influenzae type b*, rotavirus or *Human Papilloma Virus*, little use of third-generation cephalosporins or concerns over antibiotic resistance for common infections such as meningitis and dysentery. Twenty years ago there was little focus in developing countries on the care of the neonate, the needs of adolescents, child welfare, disability or human rights. Now all these areas are part of a comprehensive child health program, and to be properly implemented, especially in large or decentralised health systems there needs to be technical and leadership capacity at a national, provincial and a district level. Not only is the content of child health more complex, countries now interact with a global health landscape that has many more players with varied agendas and methods, and varied recognition of local capacity and its importance.

National leadership, and effective professional bodies can lead to improved health outcomes for children, and strengthen local capacity

While not proving the case for leadership, improvements in child survival in a number of countries in Asia, including Malaysia, Thailand and Singapore, occurred in conjunction with the development of national leadership and strong roles by professional associations for the introduction of national strategies (13,19,27).

In Thailand improved health service quality and equity has resulted from a range of financial and public health reforms. Some of these have been initiated by governments; others were a product of advocacy from professional bodies, including the Rural Doctors' Society (13). While not specific for child health, this Society, founded in 1978, initiated management training programmes, developed management handbooks and designed activities to support rural district hospital doctors. These included publication of a rural doctor journals/newsletters, public recognition for extraordinary performance, coordinating visits to rural hospitals by senior doctors to improve morale and organising provincial rural doctor coaches. The Rural Doctors' Society supported essential medicines policy, highlighted corruption, and advocated for better conditions for rural health professionals (14).

In Singapore, the first group of child health leaders initiated the national program of Maternal and Child Health Welfare services. The program included promotion of breastfeeding, and healthy birthing and rearing practices, and led the paediatric training in medical schools, training the country's first paediatrician in 1932. Associated with these was a reduction in infant mortality in rural areas in Singapore from 263 per 1000 live births in 1927 to 86 per 1000 in 1938 (19).

There are examples of national leadership in implementing vertical programs. Malawi's recent success in scaling-up anti-retroviral therapy – a product of strong national leadership and coordinated effort by partner agencies – has been associated with a reduction in adult mortality rates, and a significant increase in the number of HIV-infected adults on long-term anti-retroviral therapy (15).

Strong links have been drawn between the work of professional societies of obstetrics and midwifery and reductions in maternal deaths in many countries in a wide-ranging review (16). Historical and current links are described, as are the roles of such professional organizations. In 19th Century Sweden – one of the first countries to adopt national policies for maternal health and promote professional midwifery practice – the rate of maternal mortality was half of the rest of Europe at a time before antibiotics and anaesthetics. There are also published experiences of the positive impact that the collaboration between the Association of Obstetrics and Gynaecologists in Guatemala and the Society of Obstetricians and Gynaecologists of Canada has had on building institutional and individual leadership capacity for women's health in Guatemala (17).

NATIONAL LEADERSHIP, AND THE ROLE OF PROFESSIONAL BODIES IN THE WESTERN PACIFIC REGION

The Western Pacific Regional Child Survival Strategy called each country to have a single national child health plan, and mechanisms for coordinated implementation of pro-

grams, monitoring and evaluation (9). Some countries in the Western Pacific Region have adopted this Strategy, but few of these are Pacific Island States (33). Where progress has been achieved, such as in PNG, the processes is generally led by a central coordinating committee, which is composed of representatives from the ministry of health and a permanent national representative body (professional association or society) for child and maternal health, university academics in child health, UN agency representatives and community groups (11). Such local institutional organisations do not exist in many countries that have not taken up the strategy.

National paediatric societies, working closely with ministries of health, can be effective in upholding the child health agenda by accepting responsibilities for providing technical advice on national child health priorities, maintaining standards for clinical care, leading child health training, and advocating and lobbying for broad child health issues and turning policy into practice (**Table 1**).

PROFESSIONAL ASSOCIATIONS FOR CHILD HEALTH IN THE PACIFIC

Of 194 countries throughout the world, 132 have professional associations registered with the International Pediatric Association (IPA) (34). There is regional variation in the proportion of countries with paediatric associations (**Figure 1**). For 13 of the 14 Pacific Island countries, and for Timor-Leste, there is no registered association. PNG is the exception in the Region, where the Paediatric Society has led child health policy, the development of paediatric training, local treatment guidelines and programmes for equipping generalists in managing children in rural areas, public health initiatives such as the introduction of new vaccines, and the integration of global strategies (11).

Table 1 The roles of a national paediatric association or society

To develop and maintain standards of paediatric clinical care and public health, according to the latest evidence. The Paediatric Society is the custodian of these treatment policies, and ensures they are kept up to date.
To provide technical advice to the Ministry of Health on all aspects of child health, including social, environmental, developmental, curative and preventative health. The advice should be based on evidence and professional experience and wisdom.
To provide advice to the community on important aspects of child health, for example through public awareness campaigns about breast-feeding, immunization, nutrition and school attendance
To link with institutions of training to provide input on health training curricula, so that nursing, under-graduate medical and other health worker courses reflect the national child health policies and guidelines
To develop continuing professional development for paediatricians and child health nurses to ensure the maintenance of professional skills, knowledge and standards
To be a collegiate society providing professional and personal peer support

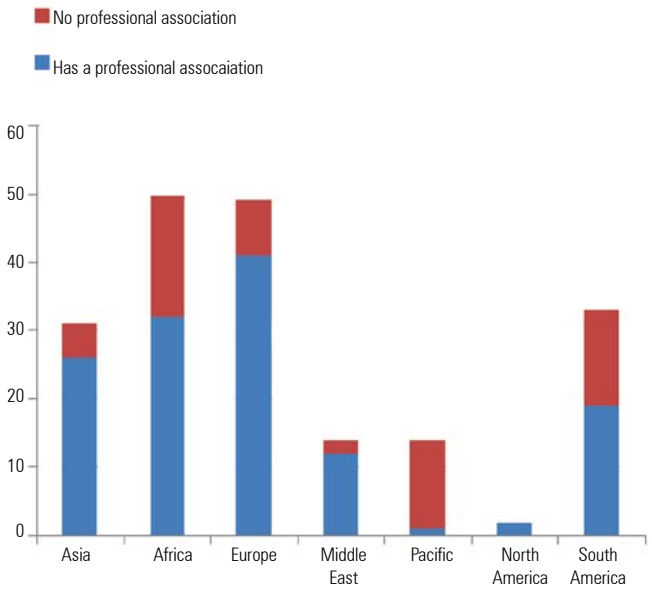

Figure 1 Number of countries in each region with professional associations for paediatrics (34).

Lack of registration with the IPA does not mean there are no informal national leadership groups for child health. For example, Fiji and the Solomon Islands have committees overseeing paediatrics and child health, with the potential to fulfil many of the same roles that a registered paediatric society can. However in general, without a formal paediatric association, the capacity for fulfilling national leadership roles is thinner.

LOCAL AND INDIVIDUAL LEADERSHIP

With the decentralisation of health systems in the Region, provincial or district governments are taking on greater responsibilities (35). The need for technical capacity and leadership in child health programs applies for managers coordinating programs at the district health office, and for health workers at the front-line. Surveys of districts in developing countries have shown deficiencies, amongst others, in program management and evaluation (36) and quality of care (37). Committed and well trained individuals are needed to: oversee child public health programs; manage, understand and use child health data effectively; coordinate the up-skilling of health workers in current treatment approaches for children; advocate and promote standards for good quality care, and communicate with the national leadership for child health. Paediatricians and child health nurses can carry out these roles. However many such individuals are under-supported, receiving little continuing professional development and no extra remuneration or time allowance.

Many countries will not have a trained paediatrician at every province or district in the foreseeable future. In these

countries there is often no cadre of adequately skilled health workers to fill this gap. Pacific Island countries with the highest child mortality rates have low physician densities (4), and therefore nurses are the first-line cadre of health workers caring for sick children. Nurses need advanced training in child health to function effectively, and often, independently. PNG is currently the only country in the Pacific with a program for training child health nurses, and that country now has one program, where there were formerly four. Smaller countries in the Pacific, with even more limited number of practicing paediatricians, have no such training programs. This is in contrast to midwifery training, which exists in all but 6 of the smallest Pacific countries (**Table 2**).

BARRIERS TO THE DEVELOPMENT OF LEADERS

Leadership positions within the public sector, whether in academia or public health, are often not well remunerated, and there is therefore much less financial incentive as compared to private or overseas practice (38,39). The hierarchy and bureaucracy within health departments and across other government departments may make it difficult for leaders to have influence over the broad and multi-sectoral activities outlined within maternal and child health plans. Countries in which there are opportunities for training and accreditation in overseas institutions are particularly vulnerable to attrition of the most highly trained individuals either to migration or the private sector (38–40). Individuals at the district level have much lower opportunities for further training (41). In addition to these are personal barriers (eg. time constraints and family commitments), political barriers (tolerance of organised professional associations), and cultural barriers (influence of age, gender and ethnicity on being able to take on national leadership positions).

In many countries, leading the translation of policy into practice is met by key challenges including complex national bureaucratic health systems, inadequate links between government departments (such as maternal and child health departments, finance and pharmaceuticals departments), and lack of human resources and technical capacity in peripheral areas.

APPROACHES TO IMPROVING LEADERSHIP THROUGH ADVANCED TRAINING

Increasing the capacity of nurses and doctors through local post-graduate training would encourage retention of these leaders within the public sector (42). There have been several models for this in the Region (**Table 2**), including paediatric training for doctors, child health nurses, and nurse practitioners.

In Fiji and Vanuatu, nurse practitioners – mid-level health workers (usually graduate nurses) – are trained to function independently in remote settings, across several disciplines

Table 2 Child health and midwifery training programs in the Pacific Island countries (29,44)

Country	Under-5 mortality rate	Paediatric nursing training	Midwifery training	Nurse practitioner training
Cook Islands	18–26	No	UNFPA certificate	9 month in-country course for graduate nurses, funded by NZAID
Federated State of Micronesia	40–47	No	Diploma: Fiji School of Nursing & University of South Pacific	No
Fiji	18–22	No	Diploma: Fiji School of Nursing; some nurses training in Tonga and Western Samoa	Fiji Nurse Practitioner Program
Kiribati	63–69	No	Diploma: Kiribati Midwifery Program.	No
Nauru	30–38	No	Diploma: Fiji School of Nursing	No
Niue	19	No	Diploma: Fiji School of Nursing	No
Palau	10–39	No	Diploma: Fiji School of Nursing	No
Papua New Guinea	74	Diploma of child health	Bachelor in University of PNG; diplomas in Pacific Adventist University, University of Goroka and Lutheran School of Nursing.	No
Republic of Marshall Islands	54–46	No	Diploma: College of the Marshall Islands Nursing School	No
Samoa	27–25	No	Bachelor of nursing, followed by post-graduate midwifery training: National University of Samoa or University of the South Pacific	No
Solomon Islands	71–37	No	Diploma, Solomon Islands School of Higher Education	No
Timor Leste	56	No	Yes	No
Tokelau		No	Diploma: Fiji School of Nursing	No
Tonga	23–22	No	Diploma: Queen Salote School of Nursing, Tonga	No
Tuvalu	37–36	No	Diploma: Fiji School of Nursing	No
Vanuatu	34–30	No	Vanuatu College of Nursing Education	Vanuatu College of Nursing Education

UNFPA – United Nations Population Fund, NZAID – New Zealand Aid

not specifically in child health (26,29). Evaluation of this program in Fiji showed high acceptance by candidates and the community, although further paediatric training was identified as a need if nurses are to practice independently in settings with no medical officer. Fiji and PNG currently train post-graduate nurses from surrounding countries, but this is limited by cost of international travel and accommodation, and coverage across the Pacific is very low.

In the Pacific Region post-graduate training for doctors in child health occurs in only PNG and Fiji. In PNG more than 40 paediatricians have been trained in the last 20 years, and there has been a doubling of capacity for provincial-level leadership in the last decade.

Another example from a Group 1 priority country in the Western Pacific is Lao PDR. In this country a Paediatric Residency Program – a 3-year course that trains doctors from each province in the central tertiary hospital in clinical paediatrics and public child health - has been running for over 12 years. A survey of graduates showed that Lao paediatricians have leadership roles in provincial hospitals where they teach and supervise other staff, and the Paediatricians Network is increasingly leading child health programs (30).

DISCUSSION

There is indirect evidence to guide approaches for strengthening leadership in the Pacific and poor Asian countries. A number of approaches seem appropriate.

Greater support for professional associations and training

Effective leadership at a higher political and policy level can be transformational for countries' health outcomes (12,13). However, there are other important facets of leadership for child health that also warrant more attention than has recently been given.

Effective paediatric, obstetric and midwifery associations have been important historically in the development of maternal and child health services. They require a critical mass of committed and well-trained professionals, working closely with the ministry of health. The challenge in many Pacific Island countries and in East Timor is the insufficient numbers of such people, and a lack of cohesive coordination. At a Pacific regional level the scale-up of post-graduate paediatrician training should be a medium term goal, and is a necessary pre-requisite to having this critical mass. In the immediate term, there are individuals in each country who fulfil leadership roles, and these need to be properly recognised and supported by ministries of health and development partners. The involvement of such people in policy decisions, particularly clinical leaders in provinces and districts, will be particularly important for bridging the policy-implementation gap.

There is a need for post-graduate training for nurses in child health, and these contribute to the critical mass. Nurse training needs to be clinically orientated and practical, but also equip nurses with basic public health and practical epidemiological skills necessary to support national child health programs and understand health information systems. Many countries in the Pacific would be able to deliver this training locally, therefore saving costs and avoiding the problems of overseas migration of regional and international training. The PNG diploma of child health or the Fiji Nurse Practitioner training with additional child health components may provide the comprehensive clinical and public health training model that is needed in the Pacific context.

Gradually, countries need a larger group of public child health professionals skilled in a variety of areas. This is being achieved in PNG through their now well-established post-graduate paediatric training program (22). In Lao PDR graduate paediatric doctors work in almost all provinces and maintain a collegiate professional network, increasingly engaged in policy work, standard setting and research. The approach in each country will differ, but there are common principles shared by the PNG and Lao programs that can be used in other countries (**Table 3**).

To keep up with the changing content and landscape of child health, there is a need for continuing professional development (CPD) for both nurses and doctors. This creates challenges for training institutions, professional bodies and ministries of health. The most common forms of CPD in the Pacific in recent decades have been multiple in-service training programs supported by donor partners to implement vertical programs. These continue to be driven by availability of funds and trends in global health, but have not been part of coordinated programs that reflect and are

Table 3 Features of post-graduate paediatric education that can promote leadership

Aim to train independent child health nurse practitioners, skilled in clinical diagnosis, basic treatment and procedures and when to refer
Align the course content with the national child health plan, clinical guidelines and public child health programs
Teach an understanding of global approaches that can be adapted nationally
Convey an understanding of locally important burdens of disease and mortality
Learn about national and local systems of surveillance and data
Introduce training in quality of care, and minimal standards
Ensure that intake policies promote geographical and ethnic representation that supports equity, i.e. from rural and remote provinces where human resources need most strengthening
Encourage input into the course content and structure from the national paediatric association
Follow-up and ongoing mentorship: provide mechanisms for graduates working at the provincial and district level to communicate and obtain advice from training institutions, senior clinicians, or academics
Establish a child health professional organization, including paediatricians and child health nurses

aligned to national priorities. It is time to put effort and resources into CPD that is led by local institutions and reflects national priorities. CPD does not have to be expensive in developing countries and can be introduced at scale, led by the national paediatric association (18).

Involvement in local research, especially that which contributes directly to critical issues in child health policy or strengthening national data systems builds capacity for leadership. There are challenges to achieving this in countries with limited manpower, but positive examples from PNG and Laos.

Common goals

Adaptation and implementation of the Western Pacific Regional Child Survival Strategy can be used as a starting point to work towards unified goals, and to provide existing professional organisations for maternal and child health with a framework for supporting the implementation of local plans. Uptake of this Strategy by smaller Pacific Island countries has been poor (33).

The national implementation of the Integrated Management of Childhood Illness (IMCI) at the community and primary health facility level and the WHO Pocketbook of Hospital Care for Children at the hospital level are also unifying goals that address issues of health service quality and the new technical content of child health (43). There is a need to provide sustained support to these initiatives in a coordinated way, by countries, donor partners and agencies, and to evaluate them.

Development and implementation of a National Child Health Plan, which brings together the strategies in the Child Survival Strategy, interventions to improve quality of care, other vertical programs as they relate to children (TB, HIV, malaria), immunization, newer areas of focus (such as child disability, child protection, neonatal care, adolescent health, sub-specialty paediatrics) and human resource plans, can provide the framework for a comprehensive child health service, and requires many skilled leaders (11).

Providing talented people in provincial areas with national portfolio responsibility for areas of child health can keep them in touch with national progress, assist in engagement and job satisfaction, and build enthusiasm for working towards shared national goals.

Providing networks of support, and opportunities for dialogue, contribution and research

Mentorship for individuals working in remote areas is important, and rarely done in the Pacific and rural Asia. Successful examples of this include the Thailand Rural Doctor Coaching Program (14), and less formal approaches being taken in Laos and PNG. There are increasing opportunities to build support networks with modern methods of communication and social networking.

Annual meetings where child health professionals convene to discuss policy and clinical issues have been running for many years in PNG and Laos, and are an essential element of supporting individuals in remote areas. Dialogue in such meetings between provincial paediatricians and provincial public health administrators has been important in improving the technical and policy understanding between professional groups. The sharing of local research and the interpretation of global research in the local context has also been important.

There are currently regional associations for child health, such as the Asian Pacific Paediatric Association and the Pasifika Medical Association, and these have the potential to provide a forum for sharing of ideas and experiences of senior leaders from each Pacific Island country.

CONCLUSIONS

Strong local leadership is needed to address the complexities and challenges of child health, at national, provincial and district level, among paediatricians, child health nurses and policy makers. Each country's efforts at this will be different, but it is a need not currently met in a serious way by governments or other agencies. It requires collaboration between governments, professional associations, training institutions, and decentralized health authorities. A substantial increase in skilled human resources in the Pacific Region is necessary if child health services are to be fully developed and health targets are to be reached. This will take a reconsideration of the complex roles that need to be played by clinical and public health staff and their professional development needs. The recent interest in strengthening health systems needs to include support for local institutions of training – large and small – and support for the roles of professional associations of paediatrics.

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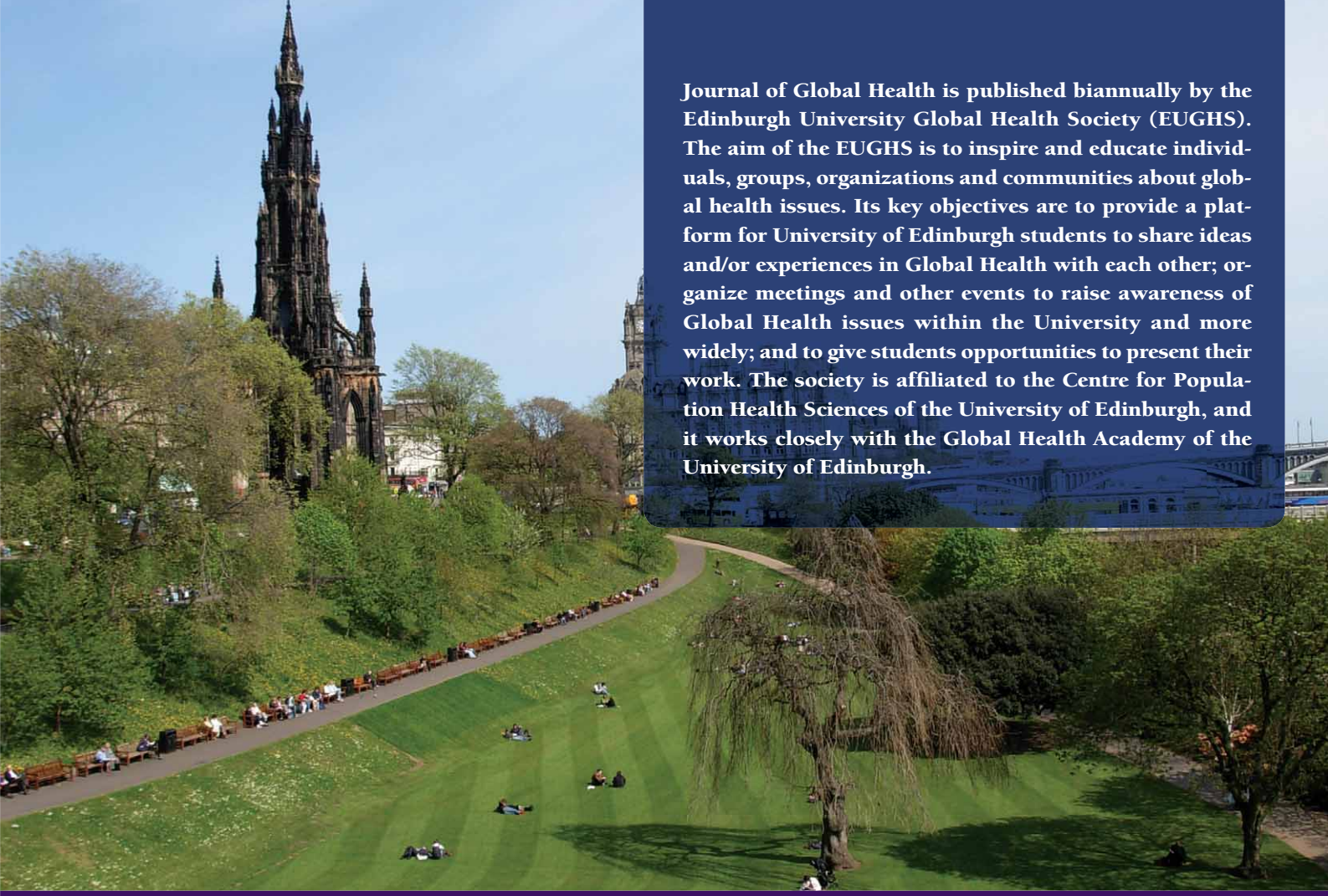

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