A Role for Science Investments in Advancing Newborn Health

Zulfiqar A. Bhutta and Gary L. Darmstadt

Progress in reducing the mortality of young children cannot be maintained without prioritization, funding, and implementation of neonatal interventions worldwide. Efforts to develop and deliver successful interventions must take a local perspective on problems and solutions, work through local policy processes and health care providers, and link to broader multisector efforts.

Few areas of global public health have garnered as much recent attention as newborn survival, in part because slow progress has hampered the achievement of Millennium Development Goal (MDG) 4 for child survival. This goal, which was to be achieved by 2015, was to reduce the deaths of children under age 5 by two-thirds relative to 1990 base figures. Here, we briefly review the progress and challenges in global newborn health over the past decade and highlight the critical contributions of research and development. Additionally, we underscore the importance of understanding household behaviors and community perspectives and investing in broader interventions to address health systems, policies, and social determinants of health.

DEATH AND DISABILITY
We estimated that 4 million neonatal deaths (defined as deaths in the first 28 days after birth) occurred globally in the year 2000 (1) and despite progress, 2.9 million newborn deaths continue to occur every year, constituting 44% of all deaths of children under 5 years of age (2). Although the neonatal mortality rate has decreased between 1990 and 2012, the improvement has been much slower than for older children or mothers, and the rate of decline in stillbirths has been even lower (2). Nearly all (99%) newborn deaths occurred in low- and middle-income countries (LMICs). Five high-burden countries alone accounted for more than half (1.5 million per year) of all newborn deaths and also had a disproportionate clustering of maternal deaths and stillbirths (3).

The major killers of newborns are well established. Prematurity (36%), intrapartum events (23%), and serious infections (23%) (4, 5) account for more than 80% of all neonatal deaths. Preterm birth, in particular, is now the number-one cause of death in children before their fifth birthday (2), and neonatal complications among survivors can cause serious and costly disabilities (6). Of the estimated 15 million children who are born prematurely every year, 1.1 million survive with long-term neurodevelopmental impairments (2, 7), mostly in middle-income countries with inadequate neonatal intensive care. Intrapartum complications, severe infections, and pathological jaundice also result in ~400,000, 30,000, and 60,000 impaired survivors, respectively (2). In sum, neonatal conditions account for an estimated 8.1% of worldwide disability adjusted life years (DALYs), similar to the burden for all DALYs due to cardiovascular disease and threefold that for AIDS (8).

ADDRESSING MORTALITY AND DISABILITY DETERMINANTS
Nearly 800,000 neonatal deaths per year are associated with small for gestational age (SGA) births, defined as a birth weight below the 10th percentile for a gestational age and sex-specific reference (9, 10). SGA infants who survive have increased lifetime risks for deficits in cognition and adult-onset metabolic and cardiovascular diseases, as well as reduced economic productivity.

Other determinants of newborn mortality include poverty and gender inequalities, such as access to primary and secondary education and young age at marriage and first birth (11). Access to family planning and healthy timing and spacing of births are critical to newborn survival through reducing high-risk pregnancies and extending inter-pregnancy intervals and may be closely related to issues of female empowerment (12).

To optimize the impact of evidence-based interventions on maternal and newborn survival, broader systems and societal processes and interventions must be considered (Fig. 1, conceptual framework) (13). The design of any successful intervention must begin from a community (or user) perspective regarding prioritized problems and solutions and engage them all along the research and development pathway. It must also work through local policy processes; take into account the characteristics of the health system, including networks of health care providers and intervention delivery channels; and link to broader multisector efforts to address the social determinants of health. This systemic approach requires working with partnerships across a wider set of domains than has been typical for many research endeavors.

Scale-up of evidence-based interventions and innovations. Over the past decade, considerable advances have been made in identifying evidence-based interventions that decrease the risk of stillbirth and newborn death and disability in LMICs. Key examples include insecticide-treated bednets and antimalarial drugs to prevent malaria in pregnancy, misoprostol for prevention and treatment of maternal hemorrhage, newborn resuscitation, and chlorhexidine application to the umbilical cord (14, 15). These interventions can be delivered in a range of settings, including communities, primary care clinics, and facilities for higher levels of care. For example, small and sick preterm babies can be stabilized in home settings with prevention of hypothermia, including skin-to-skin care. Then, as required, they can be referred for appropriate care in facility settings, including respiratory support, such as continuous positive airway pressure, and simplified antibiotic regimens.

Summarized in table S1 are key evidence-based interventions (14, 15) that can affect newborn health and survival by addressing a range of risk factors and causes of mortality and disability. These interventions—such as tetanus toxoid immunization, newborn resuscitation, prevention of hypothermia, cord care, and early initiation of breastfeeding—can be delivered by a variety of care providers, including community health workers, nurse-midwives, and physicians. They also require key commodities, such as medications, devices, and educational materials. Several of these commodities—such as resuscitation equipment, chlorhexidine, antenatal corticoste-
The concept of reducing financial barriers and deploying operations (such as supply-chain logistics, removal of maternal and newborn mortality are highest. In addition, coverage rates vary between and within high-burden countries, with major inequities between populations of different ethnicity, geography, gender, and social marginalization. It is critical to address these disparities as we move forward in order to achieve equitable coverage at scale in countries with a high burden of neonatal deaths. This will require investments in health systems, including innovations that accelerate the scale-up of interventions (such as supply-chain logistics, removal of financial barriers, and deployment of well-trained community health workers). Measurement and accountability are critical, as are feedback loops that will enable continual improvements in implementation, targeting the hardest-to-reach and most marginalized segments of the population.

Delivery platforms for scaling-up coverage. Research in some South Asian and African countries suggests that a combination of supply-and-demand factors can affect the coverage of key interventions, including community-based strategies such as women’s groups (17) and frontline health workers—especially to promote birth and newborn care preparedness, recognition of danger signs, and seeking referral for health facility care (18). A big challenge is the linkage of community and primary care for mothers and newborns with referral-level facilities, with a focus on provision of quality care, including a hygienic environment, facilities for fetal monitoring, and clean childbirth practices.

A promising approach to facilitate uptake of these interventions is the removal of financial barriers to seeking and receiving care (15). Although cash transfer schemes have rarely been implemented with objective impact assessment in mind, a recent evaluation of the large Bolsa Família program in Brazil, which transfers cash to poor households (maximum income US$70 per person per month) if they comply with conditions related to health and education, showed 17% reduction in mortality in children under 5 years of age between 2004 and 2009 (19). Similarly, the Janani Suraksha Yojana, the Safe Motherhood program in India, which provides a conditional cash transfer to poor women who deliver in health facilities, has led to increased facility deliveries and also opens the door for improving quality of care for mothers and newborns (20).

Innovations that address large-scale delivery and improve quality of care have the potential to extend the impact of programs among at-risk populations. A recent modeling exercise with some of these innovations and delivery platforms—such as the use of community-based approaches (women’s groups, community health workers for health promotion, and provision of key commodities) across the continuum of care for reproductive, maternal, newborn, and child health and nutrition—suggests that we have the potential to reduce newborn deaths by 71%, as well as to reduce maternal deaths by half and stillbirths by a third (15). The suggested global investments needed to make this happen are US$5.85 billion per year in running costs, or US$1928 for each maternal or newborn life saved or stillbirth averted (15). This investment of $5 per person per year (based on the population of 74 high-burden countries that account for over 99% of the burden of newborn mortality) could prevent a total of 147 million child deaths (including 60 million newborn babies), 32 million stillbirths, and 5 million maternal deaths by 2035 and could yield a return of close to nine times the amount of money invested in the form of social and economic benefits during the 23-year period from 2012 to 2035 (21).

**Fig. 1. Conceptual framework.** The scientific research and development process to define and test intervention efficacy and effectiveness, and to package interventions for delivery, must link with broader processes (policy process), systems (communities and health systems), and factors (social determinants) that influence the intervention’s potential to save lives, promote health, and enhance societies.

- **Communities:** Social norms and aspirations, local solutions, demand generation, knowledge sharing and transfer, accountability
- **Health System:** Workforce management, commodities, channels for healthcare delivery at scale (governments, private sector/markets, communities), data for decision-making (civil registrations and vital statistics, Health Monitoring Information Systems)
- **Policy Process:** Agenda setting (issue attention, political prioritization), policy formulation, and adoption (policies, laws)
- **Interventions for Social Determinants of Health:** User-centered design, Typical focus of scientific inquiry

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<th>Outcomes</th>
<th>Lives Saved</th>
<th>Maternal, newborn, under-5, stillbirths</th>
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<tr>
<td>Healthy Lives</td>
<td>Reduced illness, disability, stunting</td>
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<tr>
<td>Equitable &amp; Productive Societies</td>
<td>Increased human capital, employment, productivity, income, gender equality; stronger communities and societies; reduced population pressure on resources</td>
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characterized as inevitable, inconsequential, unpreventable, too expensive, or too complicated to address or are seen as a threat to other global health agendas. Some fear that intervening will increase the burden of disabilities. Some have assumed that “trickle-down” from programs that focus on maternal health or the care of older children will adequately address newborn health, whereas others assert that low-income country health systems and economies must develop further before investments in newborn health will be effective.

Data are available to debunk each of these myths (detailed data and recommendations for action are provided in table S2), but advocacy to counter the myths remains too weak to influence policy. To move forward, we need concerted efforts to address misperceptions among lay people, health professionals, government policy-makers, and program managers, as well as the global development community. These are critical to increase political and donor support in order to enhance investments in implementation as well as appropriate research to support innovations.

Global research investments to address newborn health and survival. To gain insight into research spending for newborn health and survival, we analyzed all open, competitive requests for proposals (RFPs) from 2005 to 2014, which addressed key risk factors and causes of newborn mortality and morbidity in LMICs. We identified RFPs that met these criteria from several leading global research funders, including Wellcome Trust, United States Agency for International Development (USAID), Grand Challenges Canada, and the Bill & Melinda Gates Foundation (BMGF), as well as one RFP with cofunding from the government of Norway and the UK’s Department for International Development, and one with cofunding from the Brazilian Ministry of Health. We excluded newborn health research not focused on LMIC settings, and research funded through mechanisms other than open, competitive RFPs. Thus, we did not assess overall global spending on newborn health research or total newborn health research spending in LMICs.

We plotted funding allocations across these RFPs according to the newborn condition being addressed (Fig. 2A) [prevention or management of preterm birth, infections, intrapartum-related conditions, jaundice, nutrition, integrated (>1 condition), and other categories (primarily pregnancy monitoring)], and the country where the research took place, dividing the funding equally by the number of countries involved. These data were grouped by the regional classification used by the World Health Organization (WHO). We also plotted the funding according to the country of residence of the principal investigator, and according to whether the research was primarily descriptive or focused on discovery.
development, or delivery (Fig. 2B). These data were projected onto a map of the world that displays countries according to their neonatal mortality rates, as reported by Lawn et al. (Fig. 2) (2).

We identified 330 projects totaling $180 million. Pitt et al. previously attempted to capture research funding for newborn health in LMICs by conducting a key-word search of donor disbursement records in the Organization for Economic Co-operation and Development’s Creditor Reporting System database from 2002–2010 (26). Very little research funding was identified among donors who reported in all years: $75,000 for 2002–2004, rising to just $2M in 2010. In comparison, BMGF reported $109 million in 2009 and $58 million in 2010.

We estimate that about two-thirds (67%) of the funding for innovations in global newborn health goes to North America and Europe for work done there. More than three-fourths (76.5%) of funding goes to principal investigators located in these geographical areas. The extent to which these efforts incorporate user-centered design principles and include community input alongside other considerations (Fig. 1) is unknown but likely is weak given the lack of investigators and research in LMICs. Only ~18.5% of funding goes to Africa and 9% to South Asia, although the vast majority of the burden lies in these two regions. The largest portion of the funding (35%) goes to integrated efforts that address more than one condition at a time. An additional 11 to 15% each is spent on the prevention and treatment of infections, prevention of preterm birth, and prevention and management of malnutrition, and another 6% is allocated to managing intrapartum-related events. Only 1.5% of the funding is dedicated to the treatment of premature infants, despite the fact that preterm birth is the top killer of children globally, and available interventions could prevent an estimated 58% of the deaths due to complications of preterm birth (15). Similarly, very little funding (<1%) goes to address jaundice, although recent estimates suggest that Rhesus disease and extreme hyperbilirubinemia cause 114,000 newborn deaths annually (3.9% of the total) (27).

Investments were distributed across descriptive/epidemiological studies (16.1%), intervention/product development (26.4%), intervention/product development (19.5%), and solution delivery (38%). Although investment was greatest for solution delivery, the share of funds allotted for this purpose did not match the priorities identified in a recent WHO-led exercise, in which 9 of the top 10 research challenges in newborn health were found to be in the delivery domain (28). Our analysis suggests the need for closer consultation among various research sponsors and between researchers and funders to rationalize the prioritization of funding for research. As an example of this approach, a group of funders and researchers worked together recently to develop a solution pathway and prioritize research across discovery, development, and delivery to accelerate progress on prevention and management of preterm birth, including development and validation of methods for determining gestational age (29). There is also greater need for coordination among science-funding bodies across the world in order to reduce duplication and address orphan areas of research. In addition, there is a clear need for greater public-private partnerships in this area, with inclusion of technology and engineering sectors from middle-income countries.

**ACTION PLAN**

Reducing newborn mortality is central to achieving global child survival goals and is supported by a new global Every Newborn Action Plan (ENAP; www.everynew-born.org) (30). The ENAP provides an unprecedented opportunity to form new partnerships among researchers, funders, policy-makers, program implementers, and communities to facilitate prioritization of newborn health in a variety of countries and integration of newborn interventions into reproductive, maternal, and child health and nutrition programs. Common myths and wrongly held beliefs must also be addressed. In addition, recognizing that intra-partum stillbirths are an extension of neonatal deaths will be critical for influencing policy to reduce this burden.

Although the deadline for achieving the MDGs will be upon us in 2015, reducing newborn mortality and morbidity must become a global priority over the next decade. This will require large-scale delivery strategies based on robust local situational and bottleneck analysis with appropriate community participation. Investing in research to define these actions is critical and is best supported by ongoing monitoring of implementation and evaluation of results, including intervention coverage. Current investments are disproportionate to the actual burden, causes, and distribution of stillbirths and newborn morbidity and associated morbidity but offer an extremely useful platform for future enhancements in research to advance maternal and newborn health.

**SUPPLEMENTARY MATERIALS**

www.sciencetranslationalmedicine.org/cgi/content/full/6/253/253cm8/DC1

Table S1. Common myths related to newborn survival and actions to counter them

Table S2. Evidence-based interventions to address major causes of stillbirths and neonatal deaths, and innovations for scaling up.

**REFERENCES AND NOTES**


20. B. Randive, V. Diwan, A. De Costa, India’s Conditional Cash Transfer Programme (the JSY) to promote institu- tory learning and action to improve maternal and new- born health, and Z. Charat (BMGF) for creating the maps. The views of the authors are their own and do not necessarily represent those of their organizations. Competing interests: The authors have no competing interests.

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