Born Too Soon

The Global Action Report on Preterm Birth

march of dimes
The Partnership for Maternal, Newborn & Child Health
Save the Children
World Health Organization

Born Too Soon: The Global Action Report on Preterm Birth features the first-ever estimates of preterm birth rates by country and is authored by a broad group of 45 international multi-disciplinary experts from 11 countries, with almost 50 organizations in support. This report is written in support of all families who have been touched by preterm birth. This report is written in support of the Global Strategy for Women's and Children's Health and the efforts of Every Woman Every Child, led by UN Secretary-General Ban Ki-moon.

Cover photo: *Colin Crowley/Save the Children*

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Photo: *March of Dimes*

Main Abbreviations

ANC	Antenatal Care
BMI	Body Mass Index
CHERG	Child Health Epidemiology Research Group
CPAP	Continuous positive airway pressure
DHS	Demographic and Health Surveys
EFCNI	European Foundation for the Care of Newborn Infants
GAPPS	Global Alliance to Prevent Prematurity and Stillbirth
GNI	Gross National Income
HIV	Human Immunodeficiency Virus
IMCI	Integrated Management of Childhood Illnesses
IPTp	Intermittent presumptive treatment during pregnancy for malaria
IUGR	Intrauterine growth restriction
IVH	Intraventricular hemorrhage
KMC	Kangaroo Mother Care
LAMP	Late and moderate preterm
LBW	Low birthweight
LiST	Lives Saved Tool
LMP	Last menstrual period
MDG	Millennium Development Goal
MMR	Maternal mortality ratio
MOD	March of Dimes Foundation
NCD	Non-communicable disease
NGO	Non-governmental organization
NICU	Neonatal intensive care unit
NIH	National Institutes of Health, USA
NMR	Neonatal mortality rate
PMNCH	Partnership for Maternal, Newborn & Child Health
PREBIC	International PREterm BIrth Collaborative
pPROM	Prelabor premature rupture of membranes
RCT	Randomized controlled trials
RDS	Respiratory distress syndrome
RMNCH	Reproductive, maternal, newborn and child health
SNL	Saving Newborn Lives, Save the Children
STI	Sexually transmitted infection
UN	United Nations
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
WHO	World Health Organization

Country groups used in the report

Millennium Development Goal regions:	Central & Eastern Asia, Developed, Latin America & the Caribbean, Northern Africa & Western Asia, Southeastern Asia & Oceania, Southern Asia, sub-Saharan Africa. For countries see http://mdgs.un.org
World Bank country income classification:	High-, middle- and low-income countries (details in Chapter 1)
Countdown to 2015 priority countries:	75 countries where more than 95% of all maternal and child deaths occur (full list in Chapter 6)

Foreword

Ban Ki-moon

The United Nations Secretary-General

The response to the 2010 launch of the *Every Woman Every Child* effort has been very encouraging. Government leaders, philanthropic organizations, businesses and civil society groups around the world have made far-reaching commitments and contributions that are catalyzing action behind the Global Strategy for Women's and Children's Health and the health-related Millennium Development Goals (MDGs). Born Too Soon is yet another timely answer by partners that showcases how a multi-stakeholder approach can use evidence-based solutions to ensure the survival, health and well-being of some of the human family's most defenseless members.

Every year, about 15 million babies are born prematurely — more than one in 10 of all babies born around the world. All newborns are vulnerable, but preterm babies are acutely so. Many require special care simply to remain alive. Newborn deaths — those in the first month of life — account for 40 per cent of all deaths among children under five years of age. Prematurity is the world's single biggest cause of newborn death, and the second leading cause of all child deaths, after pneumonia. Many of the preterm babies who survive face a lifetime of disability.

These facts should be a call to action. Fortunately, solutions exist. Born Too Soon, produced by a global team of leading international organizations, academic institutions and United Nations agencies, highlights scientifically proven solutions to save preterm lives, provide care for preterm babies and reduce the high rates of death and disability.

Ensuring the survival of preterm babies and their mothers requires sustained and significant financial and practical support. The Commission on Information and Accountability for Women's and Children's Health, established as part of the *Every Woman Every Child* effort, has given us new tools with which to ensure that resources and results can be tracked. I hope this mechanism will instill confidence and lead even more donors and other partners to join in advancing this cause and accelerating this crucial aspect of our work to achieve the MDGs by the agreed deadline of 2015.

I launched the Global Strategy for Women's and Children's Health to draw attention to the urgency of saving the lives of the world's most vulnerable people. I was driven not only by my concern, but by the fundamental reality that what has been lacking in this effort is the will, not the techniques, technologies or science. We know what to do. And we all have a role to play. Let us act on the findings and recommendations of this report. Let us change the future for millions of babies born too soon, for their mothers and families, and indeed for entire countries. Enabling infants to survive and thrive is an imperative for building the future we want.

Commitments to preterm birth

In support of the *Every Woman Every Child* effort to advance the Global Strategy on Women's and Children's Health, more than 30 organizations have provided commitments to advance the prevention and care of preterm birth. These statements will now become part of the overall set of commitments to the Global Strategy, and will be monitored annually through 2015 by the independent Expert Review Group established by the Commission on Information and Accountability for Women's and Children's Health. For the complete text of each commitment, please visit: http://everywomaneverychild.org/borntoosoon

The Association of Women's Health, Obstetric and Neonatal Nurses' Late Preterm Infant (LPI) Research-Based Practice Project, supported by Johnson & Johnson, will raise awareness of risks associated with late preterm birth, help reduce complications and improve care. Outcomes include expanding the body of knowledge about LPI morbidity and increasing nurses' ability to provide appropriate care. An Implementation Tool Kit will include strategies for effective nursing care as pivotal to eliminating preventable late preterm infant complications.

The Bill & Melinda Gates Foundation commits to reducing preterm birth through its Family Health agenda with grants of $1.5 billion from 2010 to 2014 to support three core areas: coverage of interventions that work (e.g. Kangaroo Mother Care, antenatal corticosteroids); research and development of new interventions; and tools to better understand the burden and reduce the incidence of preterm birth, such as the Lives Saved Tool and MANDATE Project.

CORE Group will increase awareness about practical steps to prevent and treat preterm complications to the CORE Group's Community Health Network, a community of practice of over 70 member and associate organizations, by disseminating this report and other state-of-the-art information through its working groups, listservs, and social media channels that reach 3,000 health practitioners around the world.

The Council of International Neonatal Nurses, Inc. is strongly committed to increasing awareness of the dangers of premature birth and in supporting the actions in this report, Born Too Soon, and to the prevention and care of babies not only because of the key role that neonatal nurses play in their early lives but also because of the urgent action needed in reducing the rates of preterm birth and related mortality and disability.

DFID has set out clear plans to help improve the health of women and young children in many of the poorest countries and help save the lives of at least 250,000 newborn babies and 50,000 women during pregnancy and childbirth by 2015. The UK's commitments to improve the lives of women and children can be found in "UK AID: Changing lives, delivering results", on DFID's website.

The European Foundation for the Care of Newborn Infants in partnership with the Global Alliances, March of Dimes and other organizations, looks forward to reducing the severe toll of prematurity in all countries. As prematurity poses a serious and growing threat to the health and well-being of the future European population, EFCNI commits to making maternal and newborn health a policy priority in Europe by the year 2020.

The Flour Fortification Initiative joins efforts to see babies delivered at full term through communication, advocacy and technical support for increased fortification of foods in developing countries. Studies indicate a link between maternal iron deficiency anemia in early pregnancy and a greater risk of preterm delivery, and insufficient maternal folic acid can lead to neural tube defects, one cause of preterm deliveries. Projects include campaigns in Nigeria and Ethiopia and support to Uganda, Mozambique and elsewhere.

The GAVI Alliance will help developing countries advance the control and elimination of rubella and congenital rubella syndrome through immunisation. Each year, 110,000 babies are born with severe birth defects from congenital rubella syndrome because their mothers were infected with rubella virus early in pregnancy. About 80% of those babies are born in GAVI-eligible countries. By 2015, over 700 million children will be immunised through campaigns and routine immunisation with combined measles-rubella vaccine.

The Global Alliance for Clean Cookstoves at the UN Foundation will fund up to US$ 800,000 over the next two years for research on the link between the use of traditional cookstoves and child survival. It will focus on adverse pregnancy outcomes, including low birth weight, pre-term birth, and birth defects; and/or severe respiratory illness including pneumonia in children under-five years of age. This research will hopefully identify new interventions to reduce premature births worldwide.

Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) commits to leading global efforts to discover the causes and mechanisms of preterm birth through the Preventing Preterm Birth initiative and operating the GAPPS Repository. GAPPS commits to expanding collaborative efforts for a global advocacy campaign to promote the critical need for strategic investment in research and catalyze funding for it. GAPPS will work to make every birth a healthy birth.

The Home for Premature Babies (HPB) is China's largest association of those affected by preterm birth. We unite 400,000 families and work to raise awareness and provide rehabilitation service for preterm infants. Within 3 to 5 years we plan to double our membership; publish a monthly magazine on premature infants; establish a medical tele-consultation system; develop and implement a continuing education program for paediatricians; and establish a branch of HPB in every province in China.

The International Confederation of Midwives will maintain its commitment to working towards enhancing the reproductive health of women, and the health of their newborn, including preventing preterm birth and care for premature babies, by promoting autonomous midwives as the most appropriate caregivers for childbearing women and their newborn and midwifery services as the most effective means of achieving MDGs 4&5 for child survival and maternal health.

The International Pediatric Association's (IPA) 177 pediatric societies support neonatal, child, adolescent and maternal health through policy advocacy, planning, expanded health services, pregnancies that are supported by the entire community and safe delivery for mother and baby. IPA will feature Born Too Soon on its website and in the organizational newsletter, encouraging national pediatric societies to feature this fundamental topic in educational meetings and policy discussions.

The Japan International Cooperation Agency supports partner countries in building and strengthening systems for a "Continuum of Care for Maternal and Child Health" through technical cooperation US$ 25 million and grant aid projects of around US$ 13 million annually, and initiating concessional loans to support partner countries to achieve MNCH-related MDGs. Japan's Global Health Policy 2011-2015 commits to saving approximately 11.3 million children's lives and 430,000 maternal lives in cooperation with other donors.

The Johns Hopkins Bloomberg School of Public Health is committed to strengthening evidence on the extent and causes of preterm births globally and to developing culturally and economically appropriate interventions to reduce the burden of premature birth around the world. We also commit to working with governments and their partners on the translation of evidence into effective policies and programs. We aim to achieve measurable results of our efforts by 2015.

The Kinshasa School of Public Health in the Democratic Republic of the Congo, with its partner the University of North Carolina, has joined the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) and submitted a proposal aimed at preventing preterm birth. The goal of this initiative is to encourage scientific studies that will lead to or refine preventive interventions for preterm birth and still birth related to preterm birth, primarily in developing world settings.

The London School of Hygiene & Tropical Medicine (LSHTM) has a strategic long-term commitment to research through the MARCH Centre for Maternal, Reproductive and Child Health and will continue to improve the data and evidence base and to advance and evaluate innovative solutions for the poorest women and babies. LSHTM will work with partners to increase the numbers and capacity of scientists and institutions in the most affected countries.

The March of Dimes commits to its Prematurity Campaign through 2020, devoting approximately $20 million annually to research into the causes of premature birth; collaboration with key stakeholders to enhance quality and accessibility of prenatal and newborn care; education and awareness campaigns to identify and reduce risk of prematurity. March of Dimes has worked with parent groups to create and promote World Prematurity Day, November 17, to advocate for further action, including the recommendations in this publication.

Paediatrics and Child Health, College of Medicine, University of Malawi is committed to improving the care of newborns in Malawi. Specific efforts are being made to help premature babies with respiratory distress by introducing appropriate technologies and enhancing the Kangaroo Mother Care through teaching and outreach.

The Partnership for Maternal, Newborn & Child Health commits to developing a companion knowledge summary to this report; supporting preterm private sector commitments linked to the Commission on Life-saving Commodities for Women and Children; promoting World Prematurity Day, November 17; and tracking yearly progress of these commitments for the annual report of the independent Expert Review Group related to the Global Strategy and the recommendations of the Commission on Information and Accountability for Women's and Children's Health.

Preterm Birth International Collaborative (PREBIC) supports prematurity prevention programs by organizing workshops for scientists and clinicians around the globe aimed to build consortiums of investigators. These consortiums identify knowledge gaps in various areas of preterm birth research and develop protocols to fill these gaps. PREBIC organizes scientific symposiums in association with major Obstetrics Congresses to educate health care professionals regarding ongoing preterm birth research. PREBIC's research core supports investigators in high throughput research.

The Preterm Clinical Research Consortium of Peking University Center of Medical Genetics (PUCMG) will work closely with global, regional and national communities and organizations to raise public awareness of the toll of preterm birth in China, and continue existing programs directed at reducing the rate of preterm birth and associated mortality and disability. Within three years, PUCMG will have completed a prospective cohort study identifying major risk factors for preterm birth in the Chinese population.

Save the Children commits to working with partners to make preventable newborn deaths unacceptable and to advance implementation of maternal and newborn services, enabling frontline health workers and empowering families to provide the care every newborn needs. By 2015, Save the Children will promote increases in equitable access for high-impact interventions for preterm babies including: antenatal corticosteroids to strengthen premature babies' lungs; Kangaroo Mother Care; neonatal resuscitation; improved cord care; breastfeeding support; and effective treatment of neonatal infections.

COMMITMENTS
TO PRETERM BIRTH

Sida is committed to reducing the incidence of prematurity by capacity building of the midwifery workforce for this purpose. As partners in the global movement to reduce maternal, new-born and child mortality, Sida will advocate to increase awareness of the need for professional midwives. Moreover to improve education and working conditions to allow midwives to play a significant role in the prevention of premature birth and competent care for the pre-term baby.

UNFPA commits to working with countries to address the following priorities by the end of 2013: strengthening midwifery in 40 countries; strengthening emergency obstetric and newborn care in 30 countries; ensuring no stock-outs of contraceptives at service-delivery points for at least six months in at least 10 countries; and supporting key demand generation interventions, especially for modern contraceptives, in at least 35 countries.

UNICEF commits to supporting global advocacy efforts; helping governments implement and scale up preterm and newborn care interventions, including community programs to improve equitable access for the most disadvantaged mothers and babies; working with WHO and countries to strengthen the availability and quality of data on preterm births and provide updated analyses and trends every three to five years; and advancing the procurement and supply of essential medicines and commodities for preterm births, neonatal illnesses and deaths.

University of the Philippines Manila commits to continue research and advocacy work on models for preconception care. The current project will produce counseling modules for the workplace, community level, and youth peer counseling, and is being piloted city-wide in Lipa City in cooperation with the Local Government.

The University of Texas Medical Branch and the Department of Obstetrics & Gynecology, Maternal-Fetal Medicine Division, studies preterm-birth risk factors, pathophysiology, pathways, and designs prevention strategies. In addition, the division is dedicated to understanding causes and consequences of fetal programming due to preterm birth.

USAID is committed to saving newborn lives in an effort to reduce under-five mortality by 35 percent. We will support high-impact affordable interventions that can prevent and manage complications associated with preterm birth. This includes service delivery approaches, innovations to reduce maternal and neonatal mortality, global guidelines and policies for governments, and engaging the private sector and global public-private alliances to harness the resources and creativity of diverse organizations.

Women Deliver commits to making family planning one of the key themes of its international conference Women Deliver 2013 in Kuala Lumpur, Malaysia, and developing conference sessions on newborn health. Spacing births through voluntary family planning is key to reducing the risk of preterm births. The global conference will explore solutions on how to reduce the unmet need for family planning by 100 million women by 2015, and 215 million women by 2020.

The World Health Organization is committed to working with countries on the availability and quality of data; regularly providing analyses of global preterm birth levels and trends every three to five years; working with partners on research into the causes, prevention and treatment of preterm birth; updating clinical guidelines including "Kangaroo Mother Care", feeding low birth-weight babies, treating infections and respiratory problems, and home-based follow-up care; as well as tools to improve health workers' skills and assess quality of care.

Photo: © March of Dimes

TO ADVANCE PREVENTION AND CARE

Photo: *Save the Children*

Grace from Malawi gave birth to her daughter, Tuntufye, 8 weeks early (pictured above). She survived against the odds and is now a healthy young girl (pictured below).

Photo: *Save the Children*

Photo: *William Hirtle/Save the Children*

Behind every statistic is a story

"We held our daughter in our arms... we shed our tears, said goodbye and went home to tell our little boy that he wouldn't have a sister." — Doug, USA

"I felt devastated watching my newborn fight for his life, yet our beautiful baby, Karim, with the help of his dedicated medical support team, continued to fight and survive." — Mirvat, Lebanon

"Weighing less than a packet of sugar, at only 2.2 lbs (about 1kg), Tuntufye survived with the help of Kangaroo Mother Care." — Grace, Malawi

The power of parent groups

Parents affected by a preterm birth are a powerful advocacy force around the world. Increasingly, parents are organizing among themselves to raise awareness of the problem, facilitate health professional training and public education, and improve the quality of care for premature babies. Parent groups are uniquely positioned to bring visibility to the problem of preterm birth in their countries and regions and to motivate government action at all levels. The European Foundation for the Care of Newborn Infants is an example of an effective parent group that is successfully increasing visibility, political attention and policy change for preterm birth across Europe (more information in Chapter 5).

The Home for Premature Babies is a parent group taking action forward in China, providing nationwide services in support of prevention and care (more information in Chapter 6).

"As we have experienced in China, groups of parents affected by preterm birth can be an independent and uniquely powerful grassroots voice calling on government, professional organizations, civil society, the business community and other partners in their countries to work together to prevent prematurity, improve care of the preterm baby and help support affected families." *Dr. Nanbert Zhong, Chair, Advisory Committee for Science and International Affairs, Home for Premature Babies*

Executive Summary

Headline Messages

15 million babies are born too soon every year

- More than 1 in 10 babies are born preterm, affecting families all around the world.
- Over 1 million children die each year due to complications of preterm birth. Many survivors face a lifetime of disability, including learning disabilities and visual and hearing problems.

Rates of preterm birth are rising

- Preterm birth rates are increasing in almost all countries with reliable data.
- Prematurity is the leading cause of newborn deaths (babies in the first 4 weeks of life) and now the second-leading cause of death after pneumonia in children under the age of 5.
- Global progress in child survival and health to 2015 and beyond cannot be achieved without addressing preterm birth.
- Investment in women's and maternal health and care at birth will reduce stillbirth rates and improve outcomes for women and newborn babies, especially those who are premature.

Prevention of preterm birth must be accelerated

- Family planning and increased empowerment of women, especially adolescents, plus improved quality of care before, between and during pregnancy can help to reduce preterm birth rates.
- Strategic investments in innovation and research are required to accelerate progress.

Photo: *Jenn Warren/Save the Children*

Premature babies can be saved now with feasible, cost-effective care

- Historical data and new analyses show that deaths from preterm birth complications can be reduced by over three-quarters even without the availability of neonatal intensive care.
- Inequalities in survival rates around the world are stark: half of the babies born at 24 weeks (4 months early) survive in high-income countries, but in low-income settings, half the babies born at 32 weeks (two months early) continue to die due to a lack of feasible, cost-effective care, such as warmth, breastfeeding support, and basic care for infections and breathing difficulties.
- Over the last decade, some countries have halved deaths due to preterm birth by ensuring frontline workers are skilled in the care of premature babies and improving supplies of life-saving commodities and equipment.

Everyone has a role to play

- Everyone can help to prevent preterm births and improve the care of premature babies, accelerating progress towards the goal of halving deaths due to preterm birth by 2025.
- The *Every Woman Every Child* effort, led by UN Secretary-General Ban Ki-moon, provides the framework to coordinate action and ensure accountability.

Definition of preterm birth: Babies born alive before 37 weeks of pregnancy are completed.

Sub-categories of preterm birth, based on weeks of gestational age:

Extremely preterm (<28 weeks)
Very preterm (28 to <32 weeks)
Moderate to late preterm (32 to <37 weeks)

Note: Births at 37 to 39 weeks still have suboptimal outcomes, and induction or cesarean birth should not be planned before 39 completed weeks unless medically indicated

Inform

Why do preterm births matter?

Urgent action is needed to address the estimated 15 million babies born too soon, especially as preterm birth rates are increasing each year (Figure 1). This is essential in order to progress on the Millennium Development Goal (MDG) for child survival by 2015 and beyond, since 40% of under-five deaths are in newborns, and it will also give added value to maternal health (MDG 5) investments (Chapter 1). For babies who survive, there is an increased risk of disability, which exacts a heavy load on families and health systems.

Photo: *March of Dimes*

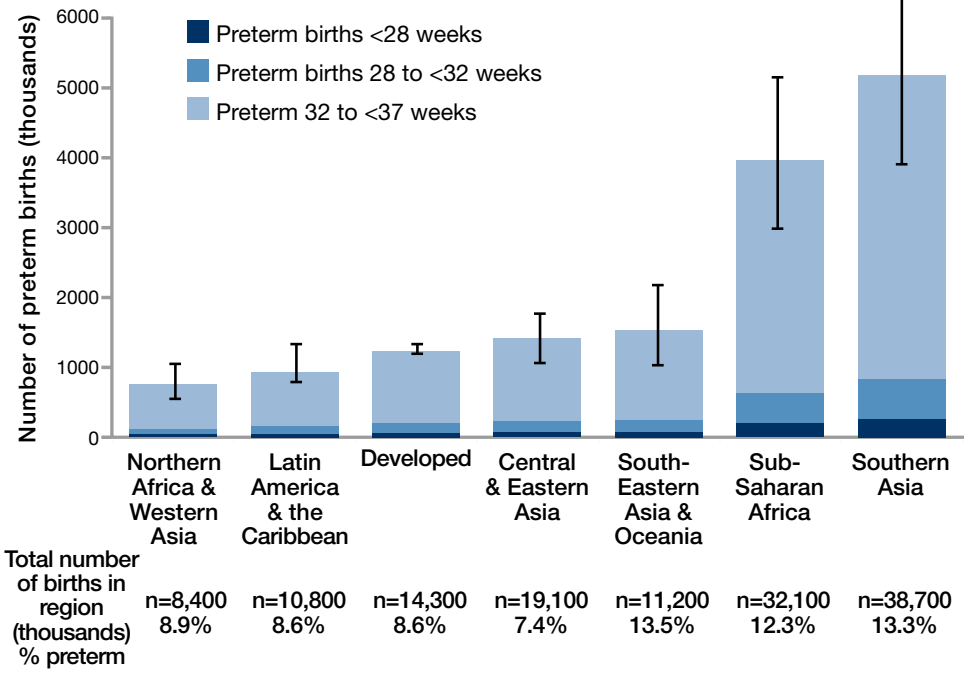
Why does preterm birth happen?

Preterm birth occurs for a variety of reasons (Chapter 2). Some preterm births result from early induction of labor or cesarean birth whether for medical or non-medical reasons. Most preterm births happen spontaneously. Common causes include multiple pregnancies, infections and chronic conditions, such as diabetes and high blood pressure; however, often no cause is identified. There is also a genetic influence. Better understanding of the causes and mechanisms will advance the development of prevention solutions.

Where and when?

Over 60% of preterm births occur in Africa and South Asia (Figure 1). The 10 countries with the highest numbers include Brazil, the United States, India and Nigeria, demonstrating that preterm birth is truly a global problem. Of the 11 countries with preterm birth rates of over 15%, all but two are in sub-Saharan Africa (Figure 2). In the poorest countries, on average, 12% of babies are born too soon compared with 9% in higher-income countries. Within countries, poorer families are at higher risk.

Figure 1: Preterm births by gestational age and region for 2010



Preterm birth by the numbers:

- 15 million preterm births every year and rising
- 1.1 million babies die from preterm birth complications
- 5-18% is the range of preterm birth rates across 184 countries of the world
- >80% of preterm births occur between 32-37 weeks of gestation and most of these babies can survive with essential newborn care
- >75% of deaths of preterm births can be prevented without intensive care
- 7 countries have halved their numbers of deaths due to preterm birth in the last 10 years

Based on Millennium Development Goal regions.
Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications

Of 65 countries with reliable trend data, all but 3 show an increase in preterm birth rates over the past 20 years. Possible reasons for this include better measurement and improved health such as increases in maternal age and underlying maternal health problems such as diabetes and high blood pressure; greater use of infertility treatments leading to increased rates of multiple pregnancies; and changes in obstetric practices such as more caesarean births before term.

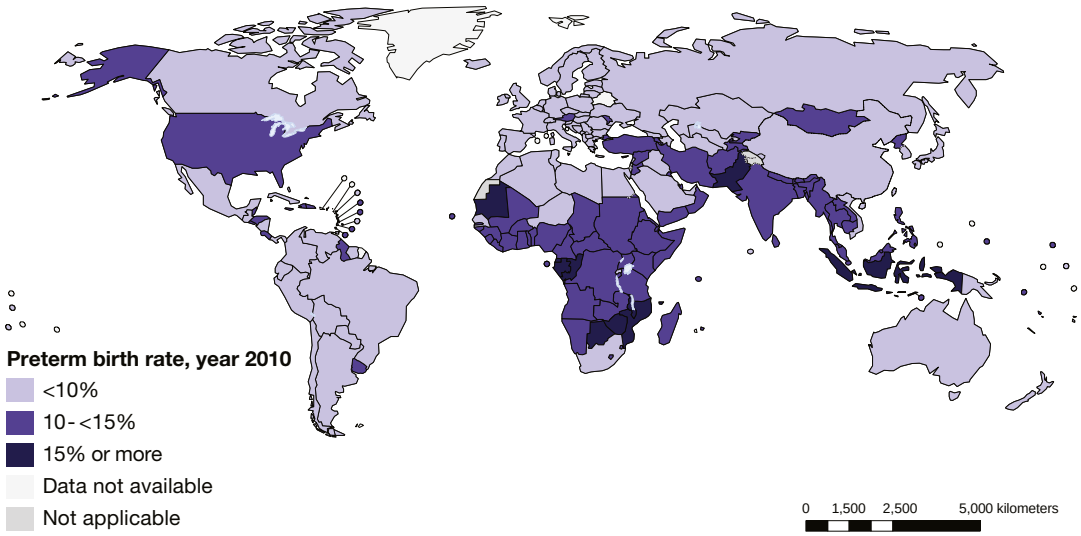
There is a dramatic survival gap for premature babies depending on where they are born. For example, over 90% of extremely preterm babies (<28 weeks) born in low-income countries die within the first few days of life; yet less than 10% of babies of this gestation die in high-income settings, a 10:90 survival gap.

Counting preterm births

The preterm birth rates presented in this report are estimated based on data from national registeries, surveys and special studies (Blencowe et al., 2012). Standard definitions of preterm birth and consistency in reporting pregancy outcomes are essential to improving the quality of data and ensuring that all mothers and babies are counted.

Photo: *Pep Bonet/Noor/Save the Children*

Figure 2: Global burden of preterm birth in 2010



11 countries with preterm birth rates over 15% by rank:

1. Malawi
2. Congo
3. Comoros
4. Zimbabwe
5. Equatorial Guinea
6. Mozambique
7. Gabon
8. Pakistan
9. Indonesia
10. Mauritania
11. Botswana

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

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Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications.
Note: rates by country are available on the accompanying wall chart.
Not applicable= non WHO Members State

Photo: Susan Warner/ Save the Children

Preconception

Empowering and educating girls as well as providing care to women and couples before and between pregnancies improve the opportunity for women and couples to have planned pregnancies increasing chances that women and their babies will be healthy, and survive. In addition, through reducing or addressing certain risk factors, preterm birth prevention may be improved (Chapter 3).

Invest and plan

Adolescent pregnancy, short time gaps between births, unhealthy pre-pregnancy weight (underweight or obesity), chronic disease (e.g., diabetes), infectious diseases (e.g., HIV), substance abuse (e.g., tobacco use and heavy alcohol use) and poor psychological health are risk factors for preterm birth. One highly cost-effective intervention is family planning, especially for girls in regions with high rates of adolescent pregnancy. Promoting better nutrition, environmental and occupational health and education for women are also essential. Boys and men, families and communities should be encouraged to become active partners in preconception care to optimize pregnancy outcomes.

Implement priority, evidence-based interventions

- Family planning strategies, including birth spacing and provision of adolescent-friendly services;
- Prevention, and screening/ management of sexually transmitted infections (STIs), e.g., HIV and syphilis;
- Education and health promotion for girls and women;
- Promoting healthy nutrition including micronutrient fortification and addressing life-style risks, such as smoking, and environmental risks, like indoor air pollution.

Inform and improve program coverage and quality

Consensus around a preconception care package and the testing of this in varying contexts is an important research need. When researching pregnancy outcomes or assessing reproductive, maternal, newborn and child health strategies, preterm birth and birthweight measures should be included as this will dramatically increase the information available to understand risks and advance solutions.

Premature baby care

The survival chances of the 15 million babies born preterm each year vary dramatically depending on where they are born (Chapter 5). South Asia and sub-Saharan Africa account for half the world's births, more than 60% of the world's preterm babies and over 80% of the world's 1.1 million deaths due to preterm birth complications. Around half of these babies are born at home. Even for those born in a health clinic or hospital, essential newborn care is often lacking. The risk of a neonatal death due to complications of preterm birth is at least 12 times higher for an African baby than for a European baby. Yet, more than three-quarters of premature babies could be saved with feasible, cost-effective care, and further reductions are possible through intensive neonatal care.

Photo: Sanjana Shrestha/Save the Children

Invest and plan

Governments, together with civil society, must review and update existing policies and programs to integrate high-impact care for premature babies within existing programs for maternal, newborn and child health. Urgent increases are needed in health system capacity to take care of newborns particularly in the field of human resources, such as training nurses and midwives for newborn and premature baby care, and ensuring reliable supplies of commodities and equipment. Seven middle-income countries have halved their neonatal deaths from preterm birth through strategic scale up of referral-level care.

Pregnancy and birth

Pregnancy and childbirth are critical windows of opportunity for providing effective interventions to improve maternal health and reduce mortality and disability due to preterm birth. While many countries report high coverage of antenatal care and increasing coverage of facility births, significant gaps in coverage, equity and quality of care remain between and within countries, including high-income countries (Chapter 4).

Photo: Aubrey Wade/ Save the Children

Invest and plan

Countries need to ensure universal access to comprehensive antenatal care, quality childbirth services and emergency obstetric care. Workplace policies are important to promote healthy pregnancies and reduce the risk of preterm birth, including regulations to protect pregnant women from physically-demanding work. Environmental policies to reduce exposure to potentially harmful pollutants, such as from traditional cookstoves and secondhand smoke, are also necessary.

Implement priority, evidence-based interventions

- Ensure antenatal care for all pregnant women, including screening for, and diagnosis and treatment of infections such as HIV and STIs, nutritional support and counseling;
- Provide screening and management of pregnant women at higher risk of preterm birth, e.g., multiple pregnancies, diabetes, high blood pressure, or with a history of previous preterm birth;
- Effectively manage preterm labor, especially provision of antenatal corticosteroids to reduce the risk of breathing difficulties in premature babies. This intervention alone could save around 370,000 lives each year;
- Promote behavioral and community interventions to reduce smoking, secondhand smoke exposure, and other pollutants; and prevention of violence against women by intimate partners;
- Reduce non-medically indicated inductions of labor and cesarean births especially before 39 completed weeks of gestation.

Photo: Pep/Noor/Save the Children

Inform and improve program coverage and quality

Better measurement of antenatal care services will improve monitoring coverage and equity gaps of high-impact interventions. Implementation research is critical for informing efforts to scale up effective interventions and improve the quality of care. Discovery research on normal and abnormal pregnancies will facilitate the development of preventive interventions for universal application.

Implement priority, evidence-based interventions

- Essential newborn care for all babies, including thermal care, breastfeeding support, and infection prevention and management and, if needed, neonatal resuscitation;
- Extra care for small babies, including Kangaroo Mother Care (carrying the baby skin-to-skin, additional support for breastfeeding), could save an estimated 450,000 babies each year;
- Care for preterm babies with complications:
- Treating infections, including with antibiotics;
- Safe oxygen management and supportive care for respiratory distress syndrome, and, if appropriate and available, continuous positive airway pressure and/or surfactant;
- Neonatal intensive care for those countries with lower mortality and higher health system capacity.

Inform and improve program coverage and quality

Innovation and implementation research is critical to accelerate the provision of care for premature babies, especially skilled human resources and robust, reliable technologies. Monitoring coverage of preterm care interventions, including Kangaroo Mother Care, as well as addressing quality and equity requires urgent attention. Better tracking of long-term outcomes, including visual impairment for surviving babies, is critical.

Photo: March of Dimes

Implement

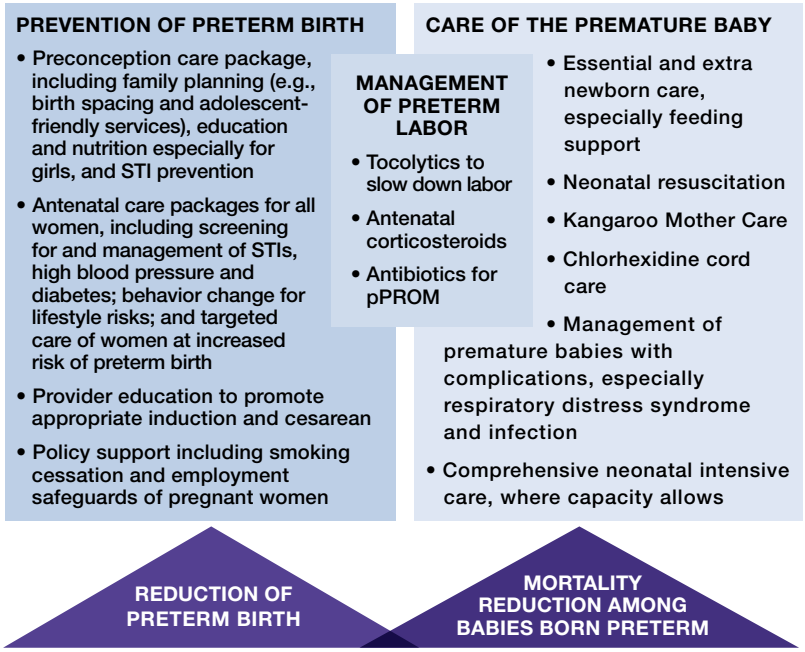
Priority interventions, packages and strategies for preterm birth

Reducing the burden of preterm birth has a dual track: prevention and care.

Interventions with proven effect for prevention are clustered in the preconception, between pregnancy and pregnancy periods as well as during preterm labor (Figure 3).

Interventions to reduce death and disability among premature babies can be applied both during labor and after birth. If interventions with proven benefit were universally available to women and their babies (i.e., 95% coverage), then almost 1 million premature babies could be saved each year.

Figure 3: Approaches to prevent preterm births and reduce deaths among premature babies



A global action agenda for research

Preterm birth has multiple causes; therefore, solutions will not come through a single discovery but rather from an array of discoveries addressing multiple biological, clinical, and social-behavioral risk factors. The dual agenda of preventing preterm birth and addressing the care and survival gap for premature babies requires a comprehensive research strategy, but involves different approaches along a pipeline of innovation. The pipeline starts from describing the problem and risks more thoroughly, through discovery science to understanding causes, to developing new tools, and finally to research the delivery of these new tools in various health system contexts. Research capacity and leadership from low- and middle-income countries is critical to success and requires strategic investment.

For preterm prevention research, the greatest emphasis should be on descriptive and discovery learning, understanding what can be done to prevent preterm birth in various contexts. While requiring a long-term investment, risks for preterm birth and the solutions needed to reduce these risks during each stage of the reproductive, maternal, newborn and child health continuum, are becoming increasingly evident (Chapters 3-5). However, for many of these risks such as genital tract infections, we do not yet have effective program solutions for prevention.

For premature baby care, the greatest emphasis should be on development and delivery research, learning how to implement what is known to be effective in caring for premature babies, and this has a shorter timeline to impact at scale (Chapter 6). Some examples include adapting technologies such as robust and simplified devices for support for babies with breathing difficulties, or examining the roles of different health care workers (e.g., task shifting).

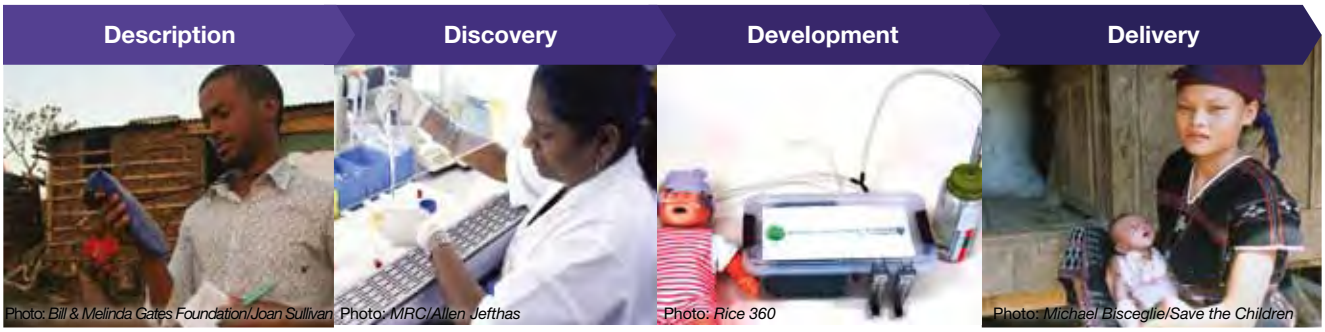


Photo: *Bill & Melinda Gates Foundation/Joan Sullivan* Photo: *MRC/Allen Jefthas* Photo: *Rice 360* Photo: *Michael Bisceglie/Save the Children*

Goal by 2025

Since prematurity contributes significantly to child mortality, Born Too Soon presents a new goal for the reduction of deaths due to complications of preterm birth.

- For countries with a current neonatal mortality rate level of more than or equal to 5 per 1,000 live births, the goal is to reduce the mortality due to preterm birth by 50% between 2010 and 2025.
- For countries with a current neonatal mortality rate level of less than 5 per 1,000 live births, the goal is to eliminate remaining preventable preterm deaths, focusing on equitable care for all and quality of care to minimize long-term impairment.

After the publication of this report, a technical expert group will be convened to establish a goal for reduction of preterm birth rate by 2025, for announcement on World Prematurity Day 2012.

Details of these goals are given in Chapter 6 of the report.

Everyone has a role to play...

to reach every woman, every newborn, every child

Reducing preterm births and improving child survival are ambitious goals. The world has made much progress reducing maternal, newborn and child deaths since the MDGs were set, but accelerated progress will require even greater collaboration and coordination among national and local governments, donors, UN and other multilaterals, civil society, the business community, health care professionals and researchers, working together to advance investment, implementation, innovation and information-sharing (Figure 4, Chapter 6).

Photo: *Ritam Banerjee for Getty Images/Save the Children*

Figure 4: Shared actions to address preterm births

✓ Primary role ✓ Secondary role: supporting effort

		Governments and policymakers	Donor countries and philanthropy	UN and other multilaterals	Civil society	Business community	Health care workers & associations	Academics and researchers
Invest	Ensure preterm interventions and research given proportional focus, so funding is aligned with health burden	✓	✓	✓	✓	✓		
Implement	Plan and implement preterm birth strategies at global and country level and align on preterm mortality reduction goal	✓		✓				✓
	Introduce programs to ensure coverage of evidence-based interventions, particularly to reduce preterm mortality	✓		✓	✓	✓	✓	
Innovate	Perform research to support both prevention and treatment agendas	✓		✓		✓	✓	✓
	Pursue implementation research agenda to understand how best to scale up interventions	✓		✓		✓	✓	✓
Inform	Significantly improve preterm birth reporting by aligning on consistent definition and more consistently capturing data	✓		✓	✓		✓	✓
	Raise awareness of preterm birth at all levels as a central maternal, newborn and child health issue	✓	✓	✓	✓	✓	✓	✓
Continue support for *Every Woman Every Child* and other reproductive, maternal, newborn and child health efforts, which are inextricably linked with preterm birth								
Ensure accountability of stakeholders across all actions								

PRETERM BIRTH MATTERS

Photo: © *March of Dimes*

Chapter 1. Preterm birth matters

— Christopher Howson, Mary Kinney, Joy Lawn

The numbers

More than 1 in 10 of the world's babies born in 2010 were born prematurely, making an estimated 15 million preterm births (defined as before 37 weeks of gestation), of which more than 1 million died as a result of their prematurity (Chapter 2) (Blencowe et al., 2012). Prematurity is now the second-leading cause of death in children under 5 years and the single most important cause of death in the critical first month of life (Liu et al., 2012). For the babies who survive, many face a lifetime of significant disability. Given its frequent occurrence, it is likely that most people will experience the challenge, and possible tragedy, of preterm birth at some point in their lives, either directly in their families or indirectly through friends.

Prematurity is an important public health priority in high-income countries.[1] However, lack of data on preterm birth at the country level has hampered action in low- and middle-income countries. *Born Too Soon* presents the first published country-level estimates on preterm birth. These estimates show that prematurity is rising in most countries where data are available (Blencowe et al., 2012). The reasons for the rise in prematurity, especially in the later weeks of pregnancy, are varied and are discussed in later chapters of the report.

The implications of being born too soon extend beyond the neonatal period and throughout the life cycle. Babies who are born before they are physically ready to face the world often require special care and face greater risks of serious health problems, including cerebral palsy, intellectual impairment, chronic lung disease, and vision and hearing loss. This added dimension of lifelong disability exacts a high toll on individuals born preterm, their families and the communities in which they live (Institute of Medicine, 2007).

The global rise in non-communicable diseases (NCDs) such as diabetes and hypertension and their association with an elevated risk of preterm birth also demand increased attention to maternal health, including the antenatal diagnosis and management of NCDs and other conditions known to increase the risk of preterm birth (Chapter 4). Premature babies, in turn, are at greater risk of developing NCDs, like hypertension and diabetes, and other significant health conditions later in life, creating an intergenerational cycle of risk (Hovi et al., 2007). The link between prematurity and an increased risk of NCDs takes on an added public health importance when considering the reported increases in the rates of both worldwide. Currently, 9 million people under the age of 60 years die from NCDs per year, accounting for more than 63% of all deaths, with the greatest burden in Africa and other low-income regions (United Nations General Assembly, 2011).

The Millennium Development Goals and beyond

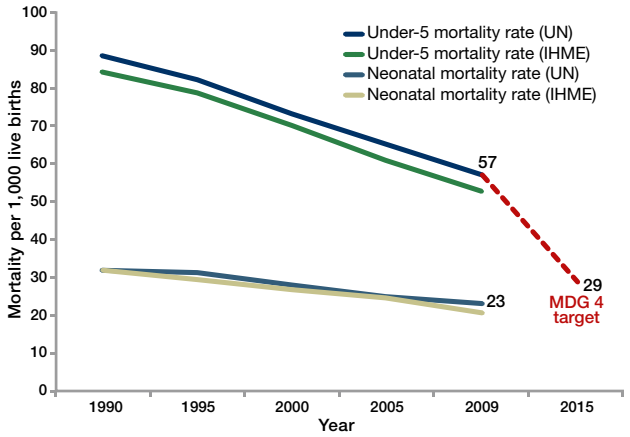
The substantial decline in high-income countries in maternal, newborn and child deaths in the early and middle 20th century was a public health triumph. Much of this decline was due to improvements in socioeconomic, sanitation and educational conditions and in population health, most notably a reduction in malnutrition and infectious diseases (Howson, 2000; World Bank, 1993). These advances in public health also resulted from strengthened political will prompted by public pressure, often by health professionals, who demanded attention to and investment in the necessary sanitary measures, drugs and technologies that were responsible for the decline in maternal and child mortality in industrialized countries in the 20th century (de Brouwere et al., 1998). Many low- and middle-income countries are now experiencing a similar "health transition," defined as an "encompassing relationship among demographic, epidemiologic and health changes that collectively and independently have an impact on the health of a population, the financing of health care and the development of health systems" (Mosley et al., 1993).

1. This report uses the World Bank classification of national economies on the basis of gross national income (GNI) per head. Using 2010 GNI figures, the World Bank describes countries as low-income (<$1,005), lower middle-income ($1,006 to $3,975), upper middle-income ($3,976 to 12,275), or high-income (>$12,276) (World Bank, 2012). Low- and middle-income countries are sometimes referred to as developing and high-income economies as industrialized. Although convenient, these terms should not imply that all developing countries are experiencing similar development or that all industrialized countries have reached a preferred or final stage of development (World Bank, 2012).

Recent acceleration in mortality reduction for mothers and for children aged between 1 and 59 months has been driven, in part, by the establishment of the Millennium Development Goal (MDG) framework (UNICEF, 2011; WHO, 2010). Established by 189 member states in 2000 with a target date of 2015 (United Nations General Assembly, 2000), the eight interlinking global goals provide benchmarks by which to measure success (UN, 2011). As such, they have mobilized common action to accelerate progress for the world's poorest families. These goals put reproductive, maternal, newborn and child health (RMNCH) on the global stage by raising their visibility politically and socially and helped unite the development community in a common framework for action. The need to monitor progress has also led to improved and more frequent use of health metrics and to collaboration and consensus on how to strengthen primary health care systems from community-based interventions to the first referral-level facility at which emergency obstetric care is available (Walley et al., 2008).

MDG 4 calls for a reduction in the under-5 mortality rate by two-thirds between 1990 and 2015 and MDG 5 for a reduction in the maternal mortality ratio by three-quarters during the same period. Even with the visibility and increased progress that MDGs 4 and 5 have brought to maternal and child survival, the rate of decline for mortality reductions remains insufficient to reach the set targets, particularly in sub-Saharan Africa and South Asia (Figure 1.1). For example, only 35 developing countries are currently on track to achieve the MDG 4 target in 2015 (UNICEF, 2011). One important barrier to progress on MDG 4 has been the failure to reduce neonatal deaths and deaths from its single most important cause, prematurity (Lawn et al., 2009). Child survival programs have primarily focused on important causes of death after the first 4 weeks of life such as pneumonia, diarrhea, malaria and vaccine-preventable conditions (Martines et al., 2005), resulting in a decline in under-5 mortality rates. While important, the concomitant lack of attention to important

Figure 1.1: MDG 4 Progress



Source: Adapted from Lawn et al., 2012. Data from UN Interagency Group for Child Mortality Estimates (UNICEF, 2011) and the Institute for Health Metrics and Evaluation (Lozano et al., 2011).
Note: MDG 4 target reflects a 2/3 reduction from the under-5 mortality rate in 1990.

Figure 1.2: How the Millenium Development Goals Link to Prevention and Care of Preterm Births

Millenium Development Goal	Links to Preterm Birth	Millenium Development Goal	Links to Preterm Birth
1 ERADICATE EXTREME POVERTY AND HUNGER	• Poverty is a risk factor for preterm birth • Women who were underfed or stunted as girls are at higher risk of preterm birth	5 IMPROVE MATERNAL HEALTH	• Family planning to avoid adolescent pregnancy and promote spacing births reduces the risk of preterm birth • Effective antenatal, obstetric and postnatal care for all pregnant women saves lives of mothers and babies
2 ACHIEVE UNIVERSAL PRIMARY EDUCATION	• Education especially of girls reduces adolescent pregnancy, which is a risk factor for preterm birth • Age appropriate health education may reduce preconception risk factors	6 COMBAT HIV / AIDS, MALARIA AND OTHER DISEASES	• Prevention and treatment before and during pregnancy of infectious and non-communicable diseases known to increase risk of preterm birth
3 PROMOTE GENDER EQUALITY AND EMPOWER WOMEN	• Gender equality, education and empowerment of women improve their outcomes and their babies' survival	7 ENSURE ENVIRONMENTAL SUSTAINABILITY	• Ensured access to improved water and sanitation facilities to reduce transmission of infectious diseases
4 REDUCE CHILD MORTALITY	• Newborn deaths account for 40% of under-5 mortality, which is the indicator for MDG4. Deaths from preterm birth have risen and now are one of the leading causes of under-5 deaths.	8 A GLOBAL PARTNERSHIP FOR DEVELOPMENT	• Identification of actions that key constituencies can take individually and together to mobilize resources, address commodity gaps and ensure accountability in support of RMNCH and preterm birth prevention and care

Note: With thanks to Boston Consulting Group for assistance on this figure.

causes of neonatal mortality like preterm birth (the single largest cause of neonatal mortality, contributing to 29% of neonatal deaths) has resulted in neonatal deaths becoming an increasing proportion of under-5 deaths (from 37% in 1990 to 40% in 2010), and demonstrating a slower rate of decline than that for under-5 deaths (Figure 1.1) (Lawn et al., 2012; Oestergaard et al., 2011). The actions in this report, if implemented quickly, will accelerate the reduction of neonatal deaths. In addition, they will benefit women directly by helping their babies survive, but also indirectly since the solutions for newborns, and especially preterm newborns, are intimately linked to maternal health and care.

The actions outlined in this report are importantly linked to all eight MDGs (Figure 1.2). This underlines a key theme of the report, namely, that to be effective, the proposed actions cannot exist in isolation by creating a new program of "prematurity care and prevention." Rather, they will require the engagement of organizations and expertise, not only from across the RMNCH spectrum, but also from

Box 1.1: Myths and Misconceptions

Myth 1: *Preterm birth is not a significant public health problem in low- and middle-income countries.*
Fact. Until recently, higher-level health policy-makers in many low- and middle-income countries have not prioritized preterm birth as a health problem partly despite mortality data being available since 2005. One challenge has been the lack of data showing the national toll of prematurity and associated disabilities. It was not until 2009 that the first global and regional rates of preterm birth were published by the World Health Organization (WHO) and the March of Dimes (March of Dimes, 2009; Beck et al., 2010). New estimates presented in this report show that the global total of preterm birth is even higher than reported in 2009.

Myth 2: *Effective care of the high-risk mother and premature newborn requires the same costly, high-technology interventions that are common in high-income countries, but is beyond the national health budgets of low- and middle-income countries.*
Fact. As Chapter 5 demonstrates, there exists a range of low-cost interventions such as Kangaroo Mother Care and antenatal corticosteroids that, if fully implemented, could immediately and substantially reduce prematurity-related death and disability in high-burden countries. High-income countries such as the United States and the United Kingdom experienced significant reductions in neonatal mortality before the introduction of neonatal intensive care units, through a combination of public health campaigns, dissemination of antimicrobials, and basic thermal care and respiratory support. In low-resource settings, therefore, immediate and significant progress can be made in preventing deaths related to complications from preterm birth with similar cost-effective interventions and improved public health services.

Myth 3: *The solutions to prevent preterm birth are known; all that is needed is the scale up of these solutions to reach all mothers.*
Fact. Very little is known about the causes and mechanisms of preterm birth, and without this knowledge, preterm birth will continue. Before pregnancy, some solutions are known to prevent preterm birth such as family planning, especially for girls in regions with high rates of adolescent pregnancy; yet there are few other effective prevention strategies available for clinicians, policy-makers and program managers (Chapter 3). Once a woman is pregnant, most of the interventions to prevent preterm birth only delay onset, turning an early preterm birth into a late preterm birth. Much more knowledge is needed to address the solution and reach a point where preterm birth is prevented.

Myth 4: *Programs' attention to care and, where possible, prevention of prematurity will draw funding away from other high-priority RMNCH interventions.*
Fact. The actions outlined in Chapter 6 are both feasible and affordable in financially constrained environments and have a cascade of beneficial effects on the health of women, mothers and newborns, in addition to reducing the rate of preterm birth and the mortality and disability associated with prematurity.

non-health sectors such as education. In addition, they must be firmly embedded in existing frameworks for action and accountability, most notably the United Nations' *Every Woman, Every Child* (see below). Such engagement, in turn, will serve to accelerate progress towards all eight MDGs and have an effect beyond improving maternal, newborn and child survival.

Recognition of preterm birth as a public health problem

Preterm births have been accorded a high public health priority in high-income countries due, in part, to champions among medical professionals and the power of affected parents. In high-income countries, improved care of the premature baby led to the development of neonatology as a discrete medical sub-specialty and the establishment of neonatal intensive care units (Chapter 5). The high prevalence and costs of prematurity have captured the attention of policy-makers and have demanded attention in many high-income countries. In the United States, for example, nearly 12 out of every 100 babies born in 2010 were premature, and this rate has increased by 30% since 1981 (NCHS, 2011). In addition, the annual societal economic cost in 2005 (medical, educational and lost productivity combined) associated with preterm birth in the United States was at least $26.2 billion. During that same year, the average first-year medical costs, including both inpatient and outpatient care, were about 10 times greater for preterm ($32,325) than for term infants ($3,325). The average length of stay was nine times as long for a preterm newborn (13 days), compared with a baby born at term (1.5 days) (Institute of Medicine, 2007). While health plans paid the majority of total allowed costs, out-of-pocket expenses were substantial and significantly higher for premature and low-birthweight newborns, compared with newborns with uncomplicated births (March of Dimes, 2012).

In low- and middle-income countries, there are common myths and misconceptions that have restricted attention and the implementation of interventions to prevent preterm birth and improve the survival and outcome of premature babies (Box 1.1).

Context for this report

With the establishment of the MDGs and recent global efforts such as *Every Woman, Every Child* launched by UN Secretary General Ban Ki-moon in support of the Global Strategy for Women's and Children's Health, there is growing urgency worldwide to improve health across the RMNCH continuum of care (Box 1.2). There also is a growing consensus on what needs to be done, as evidenced by the report on essential packages of interventions for preconception and antenatal and post-natal care (PMNCH, 2011). Over the past decade, the problem of newborn survival has also begun to receive greater attention globally in an increased volume of publications and meetings, with a major step forward being the 2005 *The Lancet* Neonatal Survival Series, which presented the first national estimates of the cause of 4 million neonatal deaths and also highlighted the importance of preterm birth (Lawn et al., 2005). However, despite the large burden, the availability of cost-effective

Box 1.2: *Every Woman, Every Child*

Launched by UN Secretary-General Ban Ki-moon during the United Nations Millennium Development Goals Summit in September 2010, *Every Woman Every Child* aims to save the lives of 16 million women and children by 2015. It is an unprecedented global movement that mobilizes and intensifies international and national action by governments, multilaterals, the private sector and civil society to address the major health challenges facing women and children around the world. The effort puts into action the UN Secretary-General's Global Strategy for Women's and Children's Health, which presents a roadmap on how to enhance financing, strengthen policy and improve service on the ground for the most vulnerable women and children.

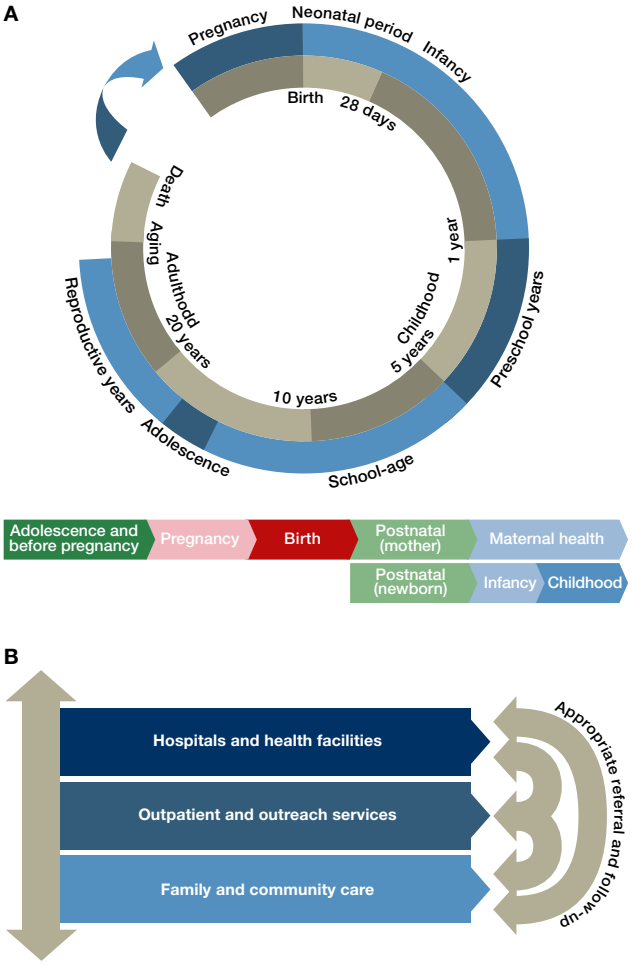
The *Every Woman, Every Child* strategy has mobilized over 200 commitments from national governments, non-governmental organizations (NGOs) and the private sector. The establishment of the Commission on Information and Accountability for Women's and Children's Health has led to a proposed transparent method for tracking these commitments, and will also track the commitments made for preterm birth. In addition, the Commission on Life-saving Commodities includes several high-impact medicines and technology to reduce the burden of preterm birth (see Chapter 6).

solutions and some increase in program funding, a recent global analysis suggests that newborn survival will remain vulnerable on the global agenda without the high-level engagement of policy-makers and adequate funding and without specific attention to the problem of preterm birth (Shiffman, 2010).

Global attention to preterm birth has recently increased. Global and regional estimates of preterm birth were released by the WHO Department of Reproductive Health Research (RHR) in 2008 (Beck et al., 2010) and presented in the 2009 *March of Dimes White Paper on Preterm Birth* (March of Dimes, 2009). These estimates suggested approximately 13 million preterm births in 2005. Media coverage reached more than 600 million people and triggered a commentary in *The Lancet* calling for increased international attention to the problem of preterm birth ("The global burden of preterm birth," 2009). Other key events were the establishment in 2004 of the International Preterm Birth Collaborative (PREBIC, 2010), *The Lancet* Series on preterm birth in 2008 (Goldenberg et al., 2008), and the launch of the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS) in 2009 (Lawn et al., 2010).

With leadership from global experts and big organizations, *Born Too Soon: The Global Action Report on Preterm Birth* was needed to document the severe toll of preterm birth for each country as well as identify the next steps that stakeholders — including policy-makers, professional organizations, the donor community, NGOs, parent groups, researchers and the media — could take to accelerate international efforts to reduce this toll. The report benefited from a broad coalition of organizations and individuals that contributed importantly to the review and the strengthening of the report's findings and actions.

Figure 1.3: Continuum of Care



Source: Adapted from Kerber et al., 2007

The continuum of care for mothers, newborns and children

The report has been structured to reflect the continuum of care, a core organizing principle for health systems, which emphasizes the delivery of health care packages across time and through service delivery levels. An effective continuum of care addresses the health needs of the adolescent or woman before, during and after her pregnancy, as well as the care of the newborn and child throughout the life cycle, wherever care is provided (Kerber et al., 2007). Figure 1.3 shows the continuum of care by time of caregiving, throughout the life cycle, from adolescence into pregnancy and birth and then through the neonatal and post-neonatal periods and childhood; and place of caregiving, that is, households, communities and health facilities (Kerber et al., 2007). Providing RMNCH services through the continuum of care approach has proven cost-effective, and there is evidence that this finding holds for the prevention and treatment of prematurity as well (Adam et al., 2005; Atrash et al., 2006; de Graft-Johnson et al., 2006; Kerber et al., 2007; Sepulveda et al., 2006).

The report chapters are presented in order of time of caregiving (preconception, Chapter 3, during pregnancy and birth, Chapter 4, and in the postnatal period for the preterm baby, Chapter 5). In each chapter the place of caregiving — at home, at the primary care level and in district and regional hospitals — is discussed.

The promise of change

While the causes and multiple events during pregnancy that result in a preterm birth remain a subject of increasingly vigorous research, there are available interventions which, if scaled up and delivered through integrated packages across the RMNCH continuum of care, would contribute to a modest reduction in preterm birth rates but would have a major impact on reducing mortality and disability in premature babies, helping women and their vulnerable babies to survive and thrive.

The report offers hope in its review of the evidence for these interventions and robust actions deriving from these that key actors can take, individually and together, to ensure delivery of the best possible care to all women before and during pregnancy, at birth and to all preterm babies and their mothers and families, wherever they live. In addition, it points to areas of research that require increased attention, funding and collaboration among partners in the governmental and nongovernmental, including the private, sectors.

Finally and importantly, the report offers promise by presenting actions that require mobilization across all constituencies (see Chapter 6). Indeed, it is the many partners identified on the cover of this report with their diversity of expertise, experience and affiliation who represent the core strength of this report. Their contributions and the commitments captured here for each of the constituencies identified in the *Every Woman, Every Child* framework for accountability will help ensure that the report's actions are acted upon quickly and sustained over the long term.

Photo: *Save the Children*

My wife, Chris, was 24 weeks pregnant with our second child. She was getting ready to go to her office in Mount Kisco, NY, one morning, when she noticed a blood spot. We called the doctor, thinking she would reassure us that it was "no big deal." To our surprise, she urged us to come straight to the hospital where a quick exam confirmed that premature labor had begun. My wife was told that she might have the baby that day. If not, she'd be in the hospital for the rest of the pregnancy. We were stunned: it was November 16, and the baby wasn't due until Valentine's Day.

An ambulance took Chris to Westchester Medical Center for delivery. This center had a Level 3 Neonatal Intensive Care Unit with highly-trained staff and the best facilities medical science has to offer, and it was considered the best place to deliver a high-risk baby. A few hours later, our daughter, Mallory was born, very tiny in her incubator, but very much alive. Doctors said she had about a 25% chance of survival. Over the next 16 days, she overcame many obstacles. My wife began pumping breast milk for the baby, and our hopes grew of having a daughter, as well as a sister for our five-year-old son, Sam.

... the baby wasn't due until Valentine's Day.

One day later, our dreams dissolved. Mallory developed necrotizing enterocolitis, an intestinal infection, and we were called urgently to the hospital. When we got there, the doctors told us that there was nothing further they could do. This incredible medical team that had done so much to help our daughter survive her first 16 days was at a standstill. We held our daughter in our arms for a few more hours until her little heart stopped beating. Then we shed our tears, said goodbye and went home to tell our little boy he wouldn't have a sister.

UNITED STATES

MALLORY

14 WEEKS PREMATURE

25% CHANCE OF SURVIVAL

On the way home in the car, we felt that we wanted to fight back somehow, so that other parents wouldn't have to go through the incredibly painful experience of losing a baby. We asked friends and family to donate in Mallory's name to organizations fighting for the prevention of preterm birth and were astounded by their generosity and outpouring of support. As we learned more about prematurity and how common it is, we realized that preterm birth is an event that touches most families at some point in time, either directly, as we experienced, or indirectly through the experiences of extended family or friends. And we realized that living in the richest country in the world with the best medical care offers no protection against losing a child.

Chris and I feel this this report is a milestone for all families and families-to-be worldwide, whether we live in the North or South, in an industrialized or developing country. We hope that the report will elevate prematurity on the world health agenda as this is desperately needed. Most importantly, we hope that it will offer a critical next step in the building of a dialogue that improves understanding of prematurity and its causes, leads to change and saves lives.

Photo: *Bill and Melinda Gates Foundation/ /John Ahern*

Chapter 2. 15 million preterm births: priorities for action based on national, regional and global estimates

— Hannah Blencowe, Simon Cousens, Doris Chou, Mikkel Z Oestergaard, Lale Say, Ann-Beth Moller, Mary Kinney, Joy Lawn

Why focus on preterm birth?

Preterm birth is a major cause of death and a significant cause of long-term loss of human potential amongst survivors all around the world. Complications of preterm birth are the single largest direct cause of neonatal deaths, responsible for 35% of the world's 3.1 million deaths a year, and the second most common cause of under-5 deaths after pneumonia (Figure 2.1). In almost all high- and middle-income countries of the world, preterm birth is the leading cause of child death (Liu et al., 2012). Being born preterm also increases a baby's risk of dying due to other causes, especially from neonatal infections (Lawn et al., 2005) with preterm birth estimated to be a risk factor in at least 50% of all neonatal deaths (Lawn et al., 2010).

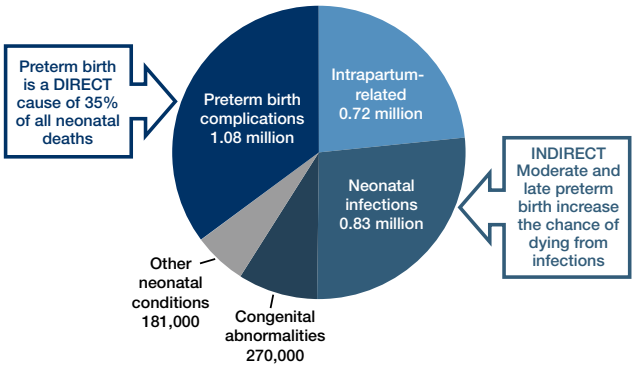
Addressing preterm birth is essential for accelerating progress towards Millennium Development Goal 4 (see Chapter 1) (UN, 2011; Valea et al., 1990). In addition to its significant contribution to mortality, the effect of preterm birth amongst some survivors may continue throughout life, impairing neurodevelopmental functioning through increasing the risk of cerebral palsy, learning impairment and visual disorders and affecting long-term physical health with a higher risk of non-communicable disease (Rogers and Velten, 2011). These effects exert a heavy burden on families, society and the health system (Table 2.1) (Institute of Medicine, 2007). Hence, preterm birth is one the largest single conditions in the Global Burden of Disease analysis given the high mortality and the considerable risk of lifelong impairment (WHO, 2008).

Table 2.1: Long-term impact of preterm birth on survivors

Long-term outcomes		Examples:	Frequency in survivors:
Specific physical effects	Visual impairment	• Blindness or high myopia after retinopathy of prematurity • Increased hypermetropia and myopia	Around 25% of all extremely preterm affected [a] Also risk in moderately preterm babies especially if poorly monitored oxygen therapy
	Hearing impairment		Up to 5 to 10% of extremely preterm [b]
	Chronic lung disease of prematurity	• From reduced exercise tolerance to requirement for home oxygen	Up to 40% of extremely preterm [c]
	Long-term cardiovascular ill-health and non-communicable disease	• Increased blood pressure • Reduced lung function • Increased rates of asthma • Growth failure in infancy, accelerated weight gain in adolescence	Full extent of burden still to be quantified
Neuro-developmental/ behavioral effectse	Mild Disorders of executive functioning	• Specific learning impairments, dyslexia, reduced academic achievement	
	Moderate to severe Global developmental delay	• Moderate/severe cognitive impairment • Motor impairment • Cerebral palsy	Affected by gestational age and quality of care dependent [f]
	Psychiatric/ behavioral sequelae	• Attention deficit hyperactivity disorder • Increased anxiety and depression	
Family, economic and societal effects	Impact on family Impact on health service Intergenerational	• Psychosocial, emotional and economic • Cost of care [h] – acute, and ongoing • Risk of preterm birth in offspring	Common varying with medical risk factors, disability, socioeconomic status [g]

References:
a O'Connor et al. (2007). "Ophthalmological problems associated with preterm birth." Eye (Lond) 21(10): 1254-1260.
b Marlow et al. (2005). "Neurologic and developmental disability at six years of age after extremely preterm birth." N Engl J Med 352(1): 9-19., Doyle et al (2001). "Outcome at 5 years of age of children 23 to 27 weeks' gestation: refining the prognosis." Pediatrics 108(1): 134-141.
c Greenough, A. (2012). "Long term respiratory outcomes of very premature birth (<32 weeks)." Semin Fetal Neonatal Med 17(2): 73-76.
d Doyle et al. (2003). "Health and hospitalistions after discharge in extremely low birth weight infants." Semin Neonatol 8(2): 137-145., Escobar, G. J., R. H. Clark et al. (2006). "Short-term outcomes of infants born at 35 and 36 weeks gestation: we need to ask more questions." Semin Perinatol 30(1): 28-33.
e Mwaniki et al., Long-term neurodevelopmental outcomes after intrauterine and neonatal insults: a systematic review. Lancet, 2012.
f Hagberg et al. (2001). "Changing panorama of cerebral palsy in Sweden. VIII. Prevalence and origin in the birth year period 1991-94." Acta Paediatr 90(3): 271-277.
Doyle et al (2001). "Outcome at 5 years of age of children 23 to 27 weeks' gestation: refining the prognosis." Pediatrics 108(1): 134-141.
g Singer et al. (1999). "Maternal psychological distress and parenting stress after the birth of a very low-birth-weight infant." JAMA 281(9): 799-805.
Moore M., H. Gerry Taylor et al. (2006). "Longitudinal changes in family outcomes of very low birth weight." J Pediatr Psychol 31(10): 1024-1035.
h Institute of Medicine of the National Academies (2006). "Preterm Birth: Causes, Consequences, and Prevention." from http://www.iom.edu/Reports/2006/Preterm-Birth-Causes-Consequences-and-Prevention.aspx

Figure 2.1: Estimated distribution of causes of 3.1 million neonatal deaths in 193 countries in 2010



Preterm birth is a risk factor for neonatal and postneonatal deaths
At least 50% of all neonatal deaths are preterm

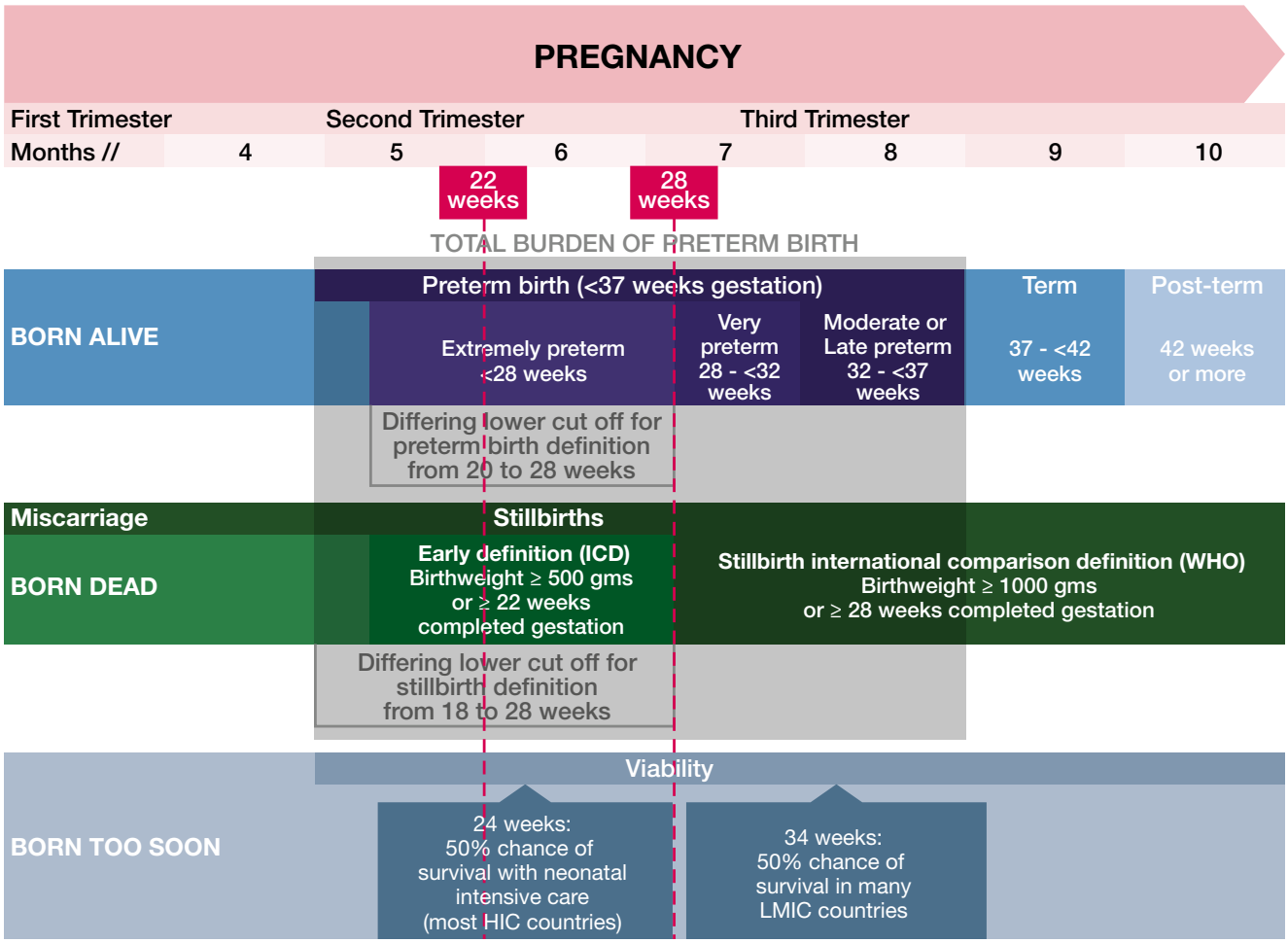
Source: Updated from Lawn et al., 2005, using data from 2010 published in Liu Let al., 2012.

Routine data on preterm birth rates are not collected in many countries and, where available, are frequently not reported using a standard international definition. Time series using consistent definitions are lacking for all but a few countries, making comparison within and between countries challenging. In high-income countries with reliable data, despite several decades of efforts, preterm birth rates appear to have increased from 1990 to 2010 (Joseph, 2007; Langhoff-Roos et al., 2006; Martin et al., 2010; Thompson et al., 2006), although the United States reports a slight decrease in the rates of late preterm birth (34 to <37 completed weeks) since 2007 (Martin et al., 2011).

There has been limited assessment of the size of the burden of preterm birth globally. Previous global level estimates of preterm birth published by WHO suggested that in 2005, 13 million babies were born too soon, 10% of babies worldwide (Beck et al., 2010).

This chapter presents new data from the first set of estimates of preterm birth rates (all live births before 37 completed weeks) for 184 countries in 2010 and a time series

Figure 2.2: Overview of definitions for preterm birth and related pregnancy outcomes



Source: Adapted from Blencowe et al. National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications
World Bank income groupings: HIC=High-Income Countries LMIC=Low and Middle Income available from http://data.worldbank.org/about/country-classifications/country-and-lending-groups

for 65 countries with sufficient data (Blencowe et al., 2012). Additionally, we estimate three preterm subgroups useful for public health planning (Blencowe et al., 2012). The chapter also presents the key risk factors for preterm births, and makes recommendations for efforts to improve the data and use the data for action to address preterm birth.

Understanding the data

Preterm birth — what is it?

Defining preterm birth

Preterm birth is defined by WHO as all births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period (WHO, 1977). Preterm birth can be further sub-divided based on gestational age: extremely preterm (<28 weeks), very preterm (28 - <32 weeks) and moderate preterm (32 - <37 completed weeks of gestation) (Figure 2.2). Moderate preterm birth may be further split to focus on late preterm birth (34 - <37 completed weeks).

The international definition for stillbirth rate clearly states to use stillbirths > 1,000 g or 28 weeks gestation, improving the ability to compare rates across countries and times (Cousens et al., 2011; Lawn et al., 2011). For preterm birth, International Classification of Disease (ICD) encourages the inclusion of all live births. This definition has no lower boundary, which complicates the comparison of reported rates both between countries and within countries over time since perceptions of viability of extremely preterm babies change with increasingly sophisticated neonatal intensive care. In addition, some reports use non-standard cut-offs for upper gestational age (e.g., including babies born at up to 38 completed weeks of gestation).

In some high- and middle-income countries, the official definitions of live birth or stillbirth have changed over time. Even without an explicit lower gestational age cut-off in national definitions, the medical care given and whether or not birth and death registration occurs may depend on these perceptions of viability (Goldenberg et al., 1982; Sanders et al., 1998). Hence, even if no "official" lower gestational age cut-off is specified for

Photo: *March of Dimes*

recording a live birth, misclassification of a livebirth to stillbirth is more common if the medical team perceives the baby to be extremely preterm and thus less likely to survive (Sanders et al., 1998). Eighty percent of all stillbirths in high-income countries are born preterm, accounting for 5% of all preterm births. Counting only live births underestimates the true burden of preterm birth (Flenady et al., 2011; Kramer et al., 2012).

In addition to the definition and perceived viability issue, some reports include only singleton live births, complicating comparison even further. From a public health perspective and for the purposes of policy and planning, the total number of preterm births is the measure of interest. Some countries only include live births after a specific cut-off, for example, 22 weeks. Given the limited accuracy of gestational age assessment, the upper limit of 37 completed weeks should be the standard for all studies (Zhang and Kramer, 2009).

For the purpose of this report and its estimates, the following definition of preterm birth rate is used:

DEFINITION OF PRETERM BIRTH RATE

All live births before 37 completed weeks (whether singleton or multiple)

Per 100 live births

Preterm birth – why does it occur?

Preterm birth is a syndrome with a variety of causes which can be classified into two broad subtypes: (1) *spontaneous* preterm birth (spontaneous onset of labor or following prelabor premature rupture of membranes (pPROM)) and (2) *provider-initiated* preterm birth (defined as induction of labor or elective caesarian birth before 37 completed weeks of gestation for maternal or fetal indications (both "urgent" or "discretionary"), or other non-medical reasons) (Table 2.2) (Goldenberg et al., 2012).

Spontaneous preterm birth is a multi-factorial process, resulting from the interplay of factors causing the uterus to change from quiescence to active contractions and to birth before 37 completed weeks of gestation. The precursors to spontaneous preterm birth vary by gestational age (Steer, 2005), and social and environmental factors, but the cause of spontaneous preterm labor remains unidentified in up to half of all cases (Menon, 2008). Maternal history of preterm birth is a strong risk factor and most likely driven by the interaction of genetic, epigenetic and environmental risk factors (Plunkett and Muglia, 2008). Many maternal factors have been associated with an increased risk of spontaneous preterm birth, including young or advanced maternal age, short inter-pregnancy intervals and low maternal body mass index (Goldenberg et al., 2008; Muglia and Katz, 2010).

Another important risk factor is uterine over distension with multiple pregnancy. Multiple pregnancies (twins, triplets, etc.) carry nearly 10 times the risk of preterm birth compared to singleton births (Blondel et al., 2006). Naturally occurring multiple pregnancies vary among ethnic groups with reported rates from 1 in 40 in West Africa to 1 in 200 in Japan, but a large contributor to the incidence of multiple pregnancies has been rising maternal age and the increasing availability of assisted conception in high-income countries (Felberbaum, 2007). This has led to a large increase in the number of births of twins and triplets in many of these countries. For example, England and Wales, France and the United States reported 50 to 60% increases in the twin rate from the mid-1970s to 1998, with some countries (e.g. Republic of Korea) reporting even larger increases (Blondel and Kaminski, 2002). More recent policies, limiting the number of embryos transferred during in vitro fertilization may have begun to reverse this trend in some countries, (Kaprio, 2005) while others continue to report increasing multiple birth rates (Lim, 2011; Martin et al., 2010).

Infection plays an important role in preterm birth. Urinary tract infections, malaria, bacterial vaginosis, HIV and syphilis are all associated with increased risk of preterm birth (Gravett et al., 2010). In

Table 2.2: Types of preterm birth and risk factors

Type:	Risk Factors:	Examples:	Interventions:
Spontaneous preterm birth:	Age at pregnancy and pregnancy spacing	Adolescent pregnancy, advanced maternal age, or short inter-pregnancy interval	Preconception care, including encouraging family planning beginning in adolescence and continuing between pregnancies (see Chapter 3)
	Multiple pregnancy	Increased rates of twin and higher order pregnancies with assisted reproduction	Introduction and monitoring of policies for best practice in assisted reproduction
	Infection	Urinary tract infections, malaria, HIV, syphilis, bacterial vaginosis,	Sexual health programs aimed at prevention and treatment of infections prior to pregnancy. Specific interventions to prevent infections and mechanisms for early detection and treatment of infections occurring during pregnancy. (see Chapters 3 and 4)
	Underlying maternal chronic medical conditions	Diabetes, hypertension, anaemia, asthma, thyroid disease	Improve control prior to conception and throughout pregnancy (see Chapters 3 and 4)
	Nutritional	Undernutrition, obesity, micronutrient deficiencies	(see Chapters 3 and 4)
	Lifestyle/ work related	Smoking, excess alcohol consumption, recreational drug use, excess physical work/activity	Behavior and community interventions targeting all women of childbearing age in general and for pregnant women in particular through antenatal care with early detection and treatment of pregnancy complications (see Chapters 3 and 4)
	Maternal psychological health	Depression, violence against women	(see Chapters 3 and 4)
	Genetic and other	Genetic risk, e.g., family history Cervical incompetence	
Provider-initiated preterm birth:	Medical induction or cesarean birth for: obstetric indication Fetal indication Other - Not medically indicated	There is an overlap for indicated provider-initiated preterm birth with the risk factors for spontaneous preterm birth	In addition to the above: Programs and policies to reduce the practice of non-medically indicated cesarean birth (Chapter 4)

addition, other conditions have more recently been shown to be associated with infection, e.g., "cervical insufficiency" resulting from ascending intrauterine infection and inflammation with secondary premature cervical shortening (Lee et al., 2008).

Some lifestyle factors that contribute to spontaneous preterm birth include stress and excessive physical work or long times spent standing (Muglia and Katz, 2010). Smoking and excessive alcohol consumption as well as periodontal disease also have been associated with increased risk of preterm birth (Gravett et al., 2010).

Preterm birth is both more common in boys, with around 55% of all preterm births occurring in males (Zeitlin, 2002), and is associated with a higher risk of dying when compared to girls born at a similar gestation (Kent 2012).
The role of ethnicity in preterm birth (other than through twinning rates) has been widely debated, but evidence supporting a variation in normal gestational length with ethnic group has been reported in many population-based studies since the 1970s (Ananth and Vintzileos, 2006). While this variation has been linked to socioeconomic and lifestyle factors in some studies, recent studies suggest a role for genetics. For example, babies of black African ancestry tend to be born earlier than Caucasian babies (Steer, 2005; Patel et al., 2004). However, for a given gestational age, babies of black African ancestry have less respiratory distress (Farrell and Wood, 1976), lower neonatal mortality (Alexander et al., 2003) and are less likely to require special care than Caucasian babies (Steer, 2005). Babies with congenital abnormalities are more likely to be born preterm, but are frequently excluded from studies reporting preterm birth rates. Few national-level data on the prevalence of the risk factors for preterm birth are available for modeling preterm birth rates.

Photo: *Joshua Roberts/Save the Children*

The number and causes of provider-initiated preterm birth are more variable. Globally, the highest burden countries have very low levels due to lower coverage of pregnancy monitoring and low cesarean birth rates (less than 5% in most African countries). However, in a recent study in the United States, more than half of all provider-initiated preterm births at 34 to 36 weeks gestation were carried out in absence of a strong medical indication (Gyamfi-Bannerman et al., 2011). Unintended preterm birth also can occur with the elective delivery of a baby thought to be term due to errors in gestational age assessment (Mukhopadhaya and Arulkumaran, 2007). Clinical conditions underlying medically-indicated preterm birth can be divided into maternal and fetal of which severe pre-eclampsia, placental abruption, uterine rupture, cholestasis, fetal distress and fetal growth restriction with abnormal tests are some of the more important direct causes recognized (Ananth and Vintzileos, 2006). Underlying maternal conditions (e.g., renal disease, hypertension, obesity and diabetes) increase the risk of maternal complications (e.g., pre-eclampsia) and medically-indicated preterm birth. The worldwide epidemic of obesity and diabetes is, thus, likely to become an increasingly important contributor to global preterm birth. In one region in the United Kingdom, 17% of all babies born to diabetic mothers were preterm, more than double the rate in the general population (Steer, 2005). Both maternal and fetal factors are more frequently seen in pregnancies occurring after assisted fertility treatments, thus increasing the risk of both spontaneous and provider-initiated preterm births (Kalra and Molinaro, 2008; Mukhopadhaya and Arulkumaran, 2007).

Differentiating the causes of preterm birth is particularly important in countries where cesarean birth is common. Nearly 40% of preterm births in France and the United States were reported to be provider-initiated in 2000,

compared to just over 20% in Scotland and the Netherlands. The levels of provider-initiated preterm births are increasing in all these countries in part due to more aggressive policies for caesarean section for poor fetal growth (Joseph et al., 1998, 2002). In the United States, this increase is reported to be at least in part responsible for the overall increase in the preterm birth rate from 1990 to 2007 and the decline in perinatal mortality (Ananth and Vintzileos, 2006). No population-based studies are available from low- or middle-income countries. However, of the babies born preterm in tertiary facilities in low- and middle-income countries, the reported proportion of preterm births that were provider-initiated ranged from around 20% in Sudan and Thailand to nearly 40% in 51 facilities in Latin America and a teaching hospital in Ghana (Barros and Velez Mdel, 2006; Alhaj et al., 2010; Ip et al., 2010; Nkyekyer et al., 2006). However, provider-initiated preterm births will represent a relatively smaller proportion of all preterm births in these countries where access to diagnostic tools is limited. These pregnancies, if not delivered electively, will follow their natural history, and may frequently end in spontaneous preterm birth (live or stillbirth) (Klebanoff and Shiono, 1995).

Preterm birth — how is it measured?

There are many challenges to measuring preterm birth rates that have inhibited national data interpretation and multi-country assessment. In addition to the variable application of the definition, the varying methods used to measure gestational age and the differences in case ascertainment and registration complicate the interpretation of preterm birth rates across and within nations.

Assessing gestational age

Measurement of gestational age has changed over time. As the dominant effect of gestational age on survival and long-term impairment has become apparent over the last 30 years, perinatal epidemiology has shifted from measuring birthweight alone to focusing on gestational age. However, many studies, even of related pregnancy outcomes, continue to omit key measures of gestational age. The most accurate "gold standard" for assessment is routine early ultrasound assessment together with fetal measurements, ideally in the first trimester. Gestational assessment based on the date of last menstrual period (LMP) was previously the most widespread method used and remains the only available method in many settings. It assumes that conception occurs on the same day as ovulation (14 days after the onset of the LMP). It has low accuracy due to considerable variation in length of menstrual cycle among women, conception occurring up to several days after ovulation and the recall of the date of LMP being subject to errors (Kramer et al., 1988). Many countries now use "best obstetric estimate," combining ultrasound and LMP as an approach to estimate gestational age. The algorithm used can have a large impact on the number of preterm births reported. For example, a large study from a Canadian teaching hospital found a preterm rate of 9.1% when assessed using ultrasound alone, compared to 7.8% when using LMP and ultrasound (Blondel et al., 2002).

Any method using ultrasound requires skilled technicians, equipment and for maximum accuracy, first-trimester antenatal clinic attendance. These are not common in low-income settings where the majority of preterm births occur. Alternative approaches to LMP in these settings include clinical assessment of the newborn after birth, fundal height or birthweight as a surrogate.

Photo: *Michael Bisceglie/Save the Children*

While birthweight is closely linked with gestational age, it cannot be used interchangeably since there is a range of "normal" birthweight for a given gestational age and gender. Birthweight is likely to overestimate preterm birth rates in some settings, especially in South Asia where a high proportion of babies are small for gestational age.

Accounting for all births

The recording of births and deaths and the likelihood of active medical intervention after preterm birth are affected by perceptions of viability and social and economic factors, especially in those born close to the lower gestational age cut-off used for registration. Any baby showing signs of being live at birth should be registered as a livebirth regardless of the gestation (WHO, 2004). The registration thresholds for stillbirths vary between countries from 16 to 28 weeks, and under-registration of both live and stillbirths close to the registration boundary is well documented (Froen et al., 2009). The cut-off for viability has changed over time and varies across settings, with babies born at 22 to 24 weeks receiving full intensive care and surviving in some high-income countries, whilst babies born at up to 32 weeks gestation are perceived as non-viable in many low-resource settings. An example of this reporting bias is seen in high-income settings where the increase in numbers of extremely preterm (<28 weeks) births registered is likely to be due to improved case ascertainment rather than a genuine increase in preterm births in this group (Consultative Council on Obstetric and Paediatric Mortality and Morbidity, 2001) and three community cohorts from South Asia with high overall preterm birth rates of 14 to 20%, but low proportions (2%) of extremely preterm births (<28 weeks) compared to the proportion from pooled datasets from developed countries (5.3%). In addition, even where care is offered to these very preterm babies, intensive care may be rationed (MRC PPIP Users and the Saving Babies Technical Task Team, 2010; Miljeteig et al., 2010).

Other cultural and social factors that have been reported to affect completeness of registration include provision of maternity benefits for any birth after the registration threshold, the need to pay burial costs for a registered birth but not for a miscarriage and increased hospital fees following a birth compared to a miscarriage (Lumley, 2003). In low-income settings, a live preterm birth may be counted as a stillbirth due to perceived non-viability or to "protect the mother" (Froen et al., 2009).

The definition of preterm birth focuses on live-born babies only. Counting all preterm births, both live and stillbirths, would be preferable to improve

Table 2.3: Gestational age methods, accuracy and limitations

Method	Accuracy	Details	Availability/feasibility	Limitations
Early ultrasound scan	+/- 5 days if first trimester +/- 7 days after first trimester	Estimation of fetal crown-rump length +/- biparietal diameter / femur length between gestational age 6 – 18 weeks	Ultrasound not always available in low-income settings and rarely done in first trimester	May be less accurate if fetal malformation, severe growth restriction or maternal obesity
Fundal Height	~ +/- 3 weeks	Distance from symphysis pubis to fundus measured with a tape measure	Feasible and low cost	In some studies similar accuracy to LMP Potential use with other variables to estimate GA when no other information available
Last menstrual period	~ +/- 14 days	Women's recall of the date of the first day of her last menstrual period	Most widely used	Lower accuracy in settings with low literacy. Affected by variation in ovulation and also by breastfeeding. Digit preference
Birthweight as a surrogate of gestational age	More sensitive/specific at lower gestational age e.g. <1500 g most babies are preterm		Birthweight measured for around half of the world's births	Requires scales and skill. Digit preference
Newborn examination	~ +/- 13 days for Dubowitz, higher range for all others	Validated scores using external +/or neurological examination of the newborn e.g. Parkin, Finnstrom, Ballard and Dubowitz scores	Mainly specialist use so far. More accurate with neurological criteria which require considerable skill. Potential wider use for simpler scoring systems	Accuracy dependant on complexity of score and skill of examiner. Training and ongoing quality control required to maintain accuracy
Best obstetric estimate	Around +/- 10 days (between ultrasound and newborn examination)	Uses an algorithm to estimate gestational age based on best information available	Commonly used in high-income settings	Various algorithms in use, not standardized

Adapted from Parker, Lawn and Stanton (unpublished Master's thesis)

Box 2.1: Overview of estimation methods for national, regional and global preterm birth rates

World Health Organization estimates of preterm birth rates

To compare preterm birth estimates across countries, the methods used to produce estimates need to be comparable across countries, otherwise one is not comparing like-with-like. The process is complicated by having only limited data for the majority of countries (the exception being primarily developed countries), from definitions of preterm births that may vary across countries and data sources, and from the need to develop a statistical model to account for all these issues.

Inputs

Preterm birth rate data were identified through a systematic search of online databases, National Statistical Offices and Ministry of Health data and assessed according to pre-specified inclusion criteria. National Registries (563 data points from 51 countries), surveys (13 Reproductive Health Surveys from 8 countries), and other studies identified through systematic searches (162 datapoints from 40 countries) were included. Preliminary data with methods and identified inputs were sent to countries as per WHO's country consultation process. Additional data points identified at this stage were included for the final analysis.

Statistical modelling

For 13 countries with data available using a consistent definition for most years 1990 – 2010, a model using the country's own data only was used to estimate the preterm birth rates. Two statistical models were developed to estimate for all other countries, one to estimate for MDG regions "Developed regions" and "Latin America and the Caribbean" (Model I), and the other to estimate for all other regions of the world (Model II). Each model included a set of predictors or factors associated with preterm birth rate and was used to estimate for the countries in the model. Uncertainty ranges were estimated for all countries:

Model I was developed for 65 countries based on a total of 547 data inputs. Most of these countries had reported national data and data for time trends. The model included the following predictors: log LBW rate, mean maternal BMI, year, and also data variables data source, method of gestational age assessment and denominator (singleton or all births).

Model II was developed for 106 countries based on a total of 191 data inputs, in most cases population data. The model included the following predictors; log LBW rate, malaria endemicity, female literacy rate, and also data variables data source, denominator (singleton or all births) and method of gestational age assessment.

Gestational age subgroups

We reviewed all data that separate preterm births to gestational age subgroups: extremely preterm (<28 weeks), very preterm (28 to <32 weeks), moderate preterm (32 to <37 weeks). The distribution was remarkably similar across the 345 data points from 41 countries in the period 1990 to 2010 (Table 2.4), which suggests a biological basis. There was no evidence of differences between regions or a change in the distribution over time. Given this remarkable consistency, we applied the proportions to the estimates for 2010 for all countries without their own data for these subgroups.

Limitations

Table 2.4: Distribution of preterm birth according to gestational age subgroup based on meta-analysis of 345 datapoints from 41 countries (n= 131,296,785 live births)

Preterm birth grouping	Gestational age	Proportion of all <37 weeks (%)	Lower 95% uncertainty interval	Higher 95% uncertainty interval (%)
Extremely preterm	<28 weeks	5.2%	5.1%	5.3%
Very preterm	28-<32 weeks	10.4%	10.3%	10.5%
Moderate or Late	32-36 weeks	84.3%	84.1%	84.5%

For 85 countries the systematic searches found no data on the rate of preterm birth. Few population-based data reporting preterm birth rates were identified for developing countries. Estimates for developing countries have relied on modeling using data from sub-national or facility based studies when available. These may not be representative of the population. For the Model II countries, time trend information was generally not available so trends in preterm birth rate were only estimated for countries with more consistent data over time, including 65 countries from Latin America and Caribbean, and from "Developed region", but excluding countries with fewer than 10,000 live births in 2010.

Source: Blencowe et al. National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications

comparability especially given stillbirth/livebirth misclassification. An increasing proportion of all preterm infants born will be stillborn with decreasing gestational age. The pathophysiology is similar for live and stillbirths; thus, for the true public health burden, it is essential to count both preterm babies born alive and all stillbirths (Golenberg et al., 2012).

Photo: Nicole Amoroso/Save the Children

Until these classification differences based on method (Table 2.3), lower gestational age cut-offs for registration of preterm birth, the use of singleton versus all births (including multiples), the inclusion of live births versus total births (including live and stillbirths) and case ascertainment have been resolved, caution needs to be applied when interpreting regional and temporal variations in preterm birth rates.

Using the data for action

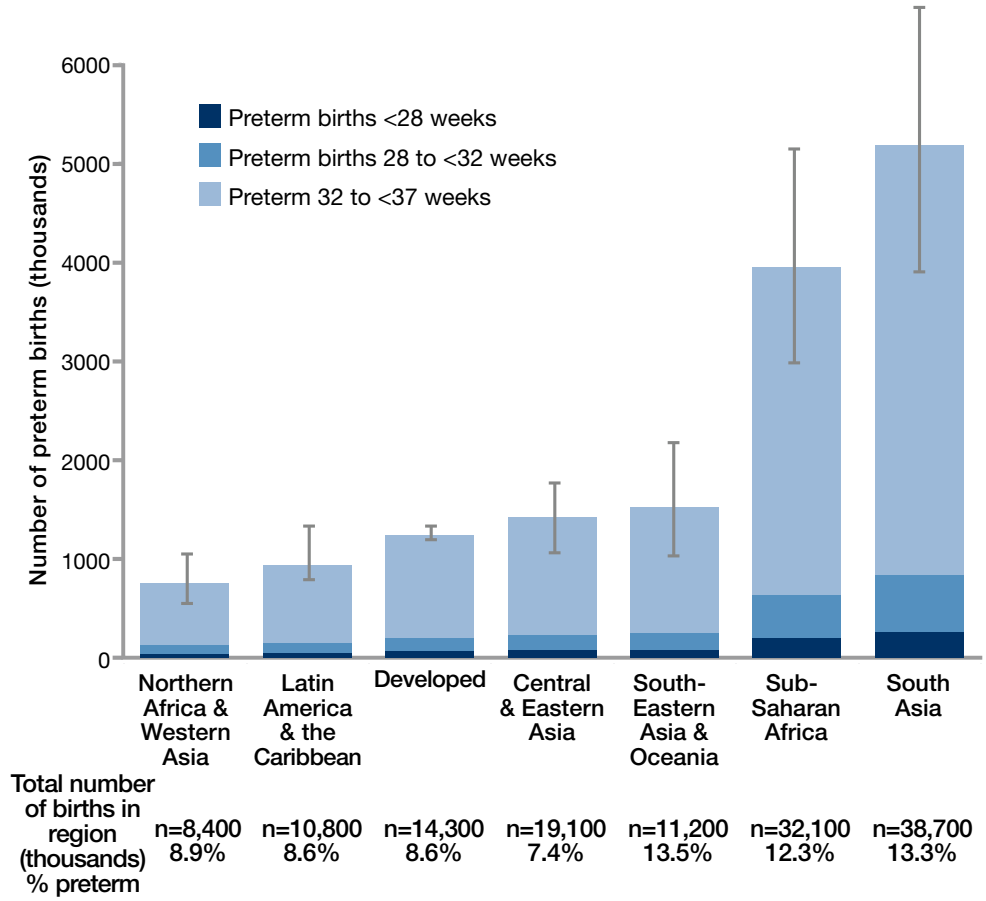
Preterm birth rates — where, and when?

Global, regional and national variation of preterm birth for the year 2010

New WHO estimates of global rates of preterm births (see Box 2.1 for methodology) indicate that of the 135 million live births worldwide in 2010, about 15 million babies were born too early, representing a preterm birth rate of 11.1% (Blencowe et al., 2012). Over 60% of preterm births occurred in sub-Saharan Africa and South Asia where 9.1 million births (12.8%) annually are estimated to be preterm (Figure 2.3). The high absolute number of preterm births in Africa and Asia are related, in part, to high fertility and the large number of births in those two regions in comparison to other parts of the world.

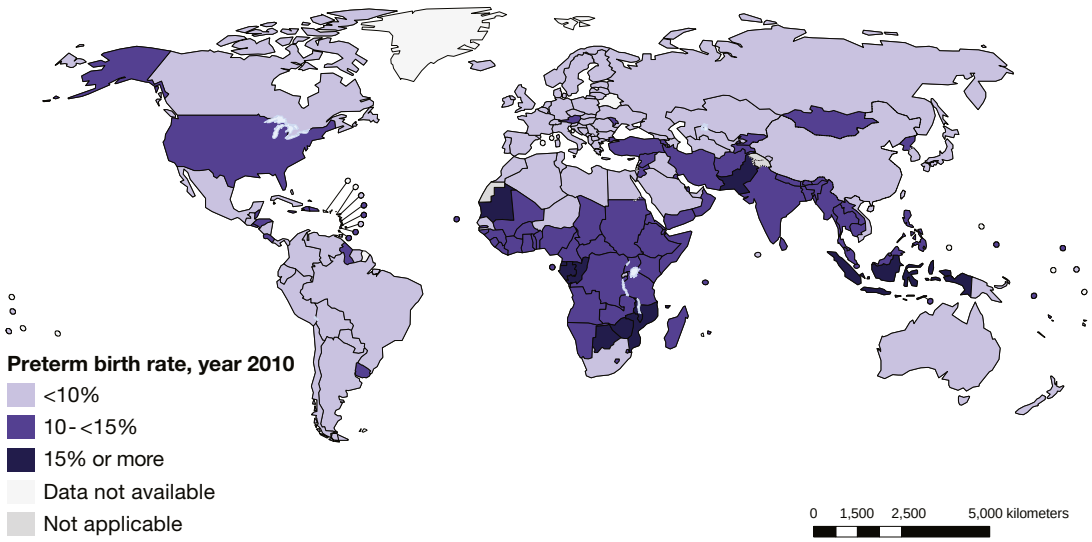
The variation in the rate of preterm birth among regions and countries is substantial and yield a different picture to other conditions in that some high-income countries have very high rates. Rates are highest

Figure 2.3: Preterm births by gestational age and region for year 2010



Based on Millennium Development Goal regions. Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications

Figure 2.4: Estimates rates of preterm birth in 2010



11 countries with preterm birth rates over 15% by rank:

1. Malawi
2. Congo
3. Comoros
4. Zimbabwe
5. Equatorial Guinea
6. Mozambique
7. Gabon
8. Pakistan
9. Indonesia
10. Mauritania
11. Botswana

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

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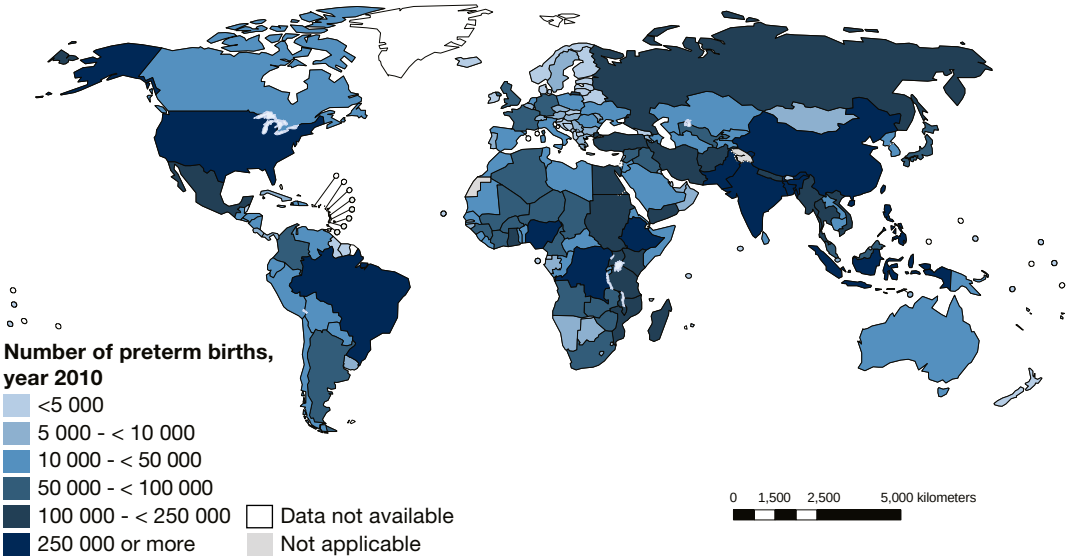
Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications .
Note: rates by country are available on the accompanying wall chart.
Not applicable= non WHO Members State

on average for low-income countries (11.8%), followed by lower middle-income countries (11.3%) and lowest for upper middle- and high-income countries (9.4% and 9.3%). However, relatively high preterm birth rates are seen in many individual high-income countries where they contribute substantially to neonatal mortality and morbidity. Of the 1.2 million preterm births estimated to occur in high-income regions, more than 0.5 million (42%) occur in the United States. The highest rates by Millennium Development Goal Regions ("Millennium Development Indicators: World and regional groupings,"Barker, 1983) are found in Southeastern and South Asia where 13.4% of all live births are estimated to be preterm (Figure 2.3).

Figure 2.5: Estimated numbers of preterm births in 2010



10 countries account for 60% of the world's preterm births by rank:

1. India
2. China
3. Nigeria
4. Pakistan
5. Indonesia
6. United States of America
7. Bangladesh
8. Philippines
9. Dem. Rep. of Congo
10. Brazil

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

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World Health Organization

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Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications.
Note: preterm birth numbers by country are available on the accompanying wall chart.
Not applicable= non WHO Members State

The uncertainty ranges in Figure 2.3 are indicative of another problem — the huge data gaps for many regions of the world. Although these data gaps are particularly great for Africa and Asia, there also are gaps in data from high-income countries. While data on preterm birth-associated mortality are lacking in these settings, worldwide there are almost no data currently on acute morbidities or long-term impairment associated with prematurity, thus preventing even the most basic assessments of service needs.

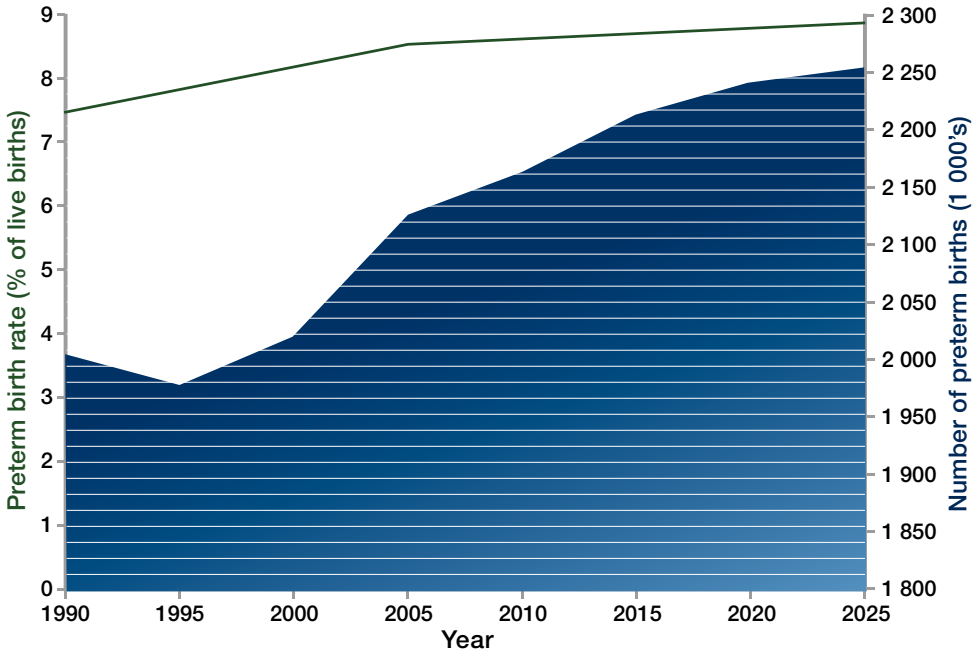
The maps in Figures 2.4 and 2.5 depict preterm birth rates and the absolute numbers of preterm birth in 2010 by country. Estimated rates vary from around 5 in several Northern European countries to 18.1% in Malawi. The estimated preterm birth rate is less than 10% in 88 countries, whilst 11 countries have estimated rates of 15% or more (Figure 2.4). The 10 countries with the highest numbers of estimated preterm births are India, China, Nigeria, Pakistan, Indonesia, United States, Bangladesh, the Philippines, Democratic Republic of the Congo and Brazil (Figure 2.5). These 10 countries account for 60% of all preterm births worldwide.

Mortality rates increase with decreasing gestational age, and babies who are both preterm and small for gestational

Photo: *Bill & Melinda Gates Foundation/Frederic Courbet*

age are at even higher risk (Qiu et al., 2011). Babies born at less than 32 weeks represent about 16% of all preterm births (Box 6.1). Across all regions, mortality and morbidity are highest among those babies although improvements in medical care have led to improved survival and long-term outcomes among very and extremely preterm babies in high-income countries (Saigal and Doyle, 2008). In 1990, around 60% of babies born at less than 28 weeks gestation survived in high-income settings, with approximately two-thirds surviving without impairment (Mohangoo et al., 2011). In these high-income countries, almost 95% of those born at 28 to 32 weeks survive, with more than 90% surviving without impairment. In contrast, in many low-income countries, only 30% of those born at 28 to 32 weeks survive, with almost all those born at <28 weeks dying in the first few days of life. In all settings, these very or extremely preterm babies account for the majority of deaths, especially in low-income countries where even simple care is lacking (see Chapter 5).

Figure 2.6: Time trends in preterm birth rate for regions with adequate data (Developed, Latin America and Caribbean) projecting to 2025 assuming the average annual rate of change from 2005 to 2010 is maintained



Based on Millennium Development Goal regions
Source: Blencowe et al National, regional and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications

Preterm births time trends 1990 to 2010

Annual national preterm birth rates were estimated for 65 countries in Europe, the Americas and Australasia with more than 10,000 live births in 2010. These regions include

almost all the countries with national reported time series. The absolute numbers and rates from 1990 to 2010 for these countries suggest an increasing burden of preterm birth (Figure 2.6). Despite a reduction in the number of live births, the estimated number of preterm births in these countries increased from 2.0 million in 1990 to nearly 2.2 million in 2010.

Only three countries, Croatia, Ecuador and Estonia, had estimated reductions in preterm birth rates from 1990 to 2010. Fourteen countries had stable preterm birth rates (<0.5% annual change in preterm birth rates). In all other countries, the preterm birth rate was estimated to be the same or greater in 2010 than in 1990.

in the first month of life, more from indirect effects, and millions have a lifetime of impairment. The burden of preterm birth is highest in low-income countries, particularly those in South Asia. Yet unlike many other global health issues, preterm birth is truly a global problem with a high burden being found in high-income countries as well (e.g. the United States where almost 1 in 8 babies is born too soon). However, while the risk of preterm birth is high for both the poorest and the richest countries, there exists a major survival gap in some regions for babies who are preterm. In high-income settings, half of babies born at 24 weeks may survive, but in low-income settings half of babies born at 32 weeks still die due to a lack of basic care (see Chapter 5).

The two big priorities from the data are firstly to close the survival gap for preterm babies in lower-income countries by implementing improved obstetric and newborn care, and secondly to develop innovative solutions to prevent preterm birth all around the world.

An increase in the proportion of preterm births occurring at 32 to <37 weeks (late and moderate preterm [LAMP]) has been reported over the past decades in some countries (Davidoff et al., 2006). For countries with available data in this exercise, there was no strong evidence of a change in the proportion of all preterm births that were LAMP from 1990 to 2010.

Caution is required in interpreting preterm estimates from many low- and middle-income countries where significant data gaps exist and modeling relies on reported figures from sub-national or facility-based studies which may not be representative of the population. Preterm birth rate trends for low- and middle-income countries suggest an increase in some countries (e.g., China) and some regions (e.g., South Asia) but given changes in the data type and the measurement of gestational age, these remain uncertain.

Priority policy and program actions based on the data

In 2010, approximately 15 million babies were born preterm, and more than 1 million died due to complications

Preterm birth rates appear to be increasing in most of the countries where data are available. Some of this increase may be accounted for by improved registration of the most preterm babies associated with increased viability and by improved gestational assessment, with change to near universal ultrasound for dating pregnancies in these settings. It may, however, represent a true increase. Possible reasons for this include increases in maternal age, access to infertility treatment, multiple pregnancies and underlying health problems in the mother, especially with increasing age of pregnancy and changes in obstetric practices with an increase in provider-initiated preterm births in moderate and late preterm infants who would not have otherwise been born preterm (Joseph et al., 2002). In the 1980s and 1990s, the increases seen in many high-income countries were attributed to higher multiple gestation and preterm birth rates amongst assisted conceptions after treatment for sub-fertility. Recent changes in policies limiting the number of embryos that can be implanted have led to a reduction in preterm births due to assisted fertility treatments in many countries (Mohangoo et al., 2011). However, in many

middle-income regions with newer, relatively unregulated assisted fertility services, a similar increase may be seen if policies to counteract this are not introduced and adhered to. A reduction in preterm birth was reported from the 1960s to 1980s in a few countries (e.g. Finland, France, Scotland), and this was attributed, in part, to improved socioeconomic factors and antenatal care. For the majority of countries in low- and middle-income regions, it is not possible to estimate trends in preterm birth over time as there are not sufficient data to provide reliable evidence of a time trend for preterm birth overall. Some countries in some regions (e.g. South and Eastern Asia) have data suggesting possible increases in preterm birth rates over time, but this may represent measurement artifact due to increases in data and data reliability.

Distinguishing spontaneous and provider-initiated preterm birth is of importance to programs aiming to reduce preterm birth. For spontaneous preterm births, the underlying causes need to be understood and addressed (see Chapters 3 and 4), while in the case of provider-initiated preterm births both the underlying conditions (e.g. pre-eclampsia) and obstetric policies and practices require assessment and to be addressed.

The proportion of neonatal deaths attributed to preterm births is inversely related to neonatal mortality rates, because in countries with very high neonatal mortality, more deaths occur due to infections such as sepsis, pneumonia, diarrhea and tetanus as well as to intrapartum-related "birth asphyxia" (Lawn et al., 2005). However, although the proportion of deaths due to preterm birth is lower in low-income countries than in high-income countries, the cause-specific rates are much higher in low- and middle-income than in high-income countries. For example, in Afghanistan and Somalia, the estimated cause-specific rate for neonatal deaths directly due to preterm birth is 16 per 1,000 compared to Japan, Norway and Sweden where it is under 0.5 per 1,000. This is due to the lack of even simple care for premature babies resulting in a major survival gap for babies depending on where they are born (see Chapter 5).

Photo: *Ritam Banerjee/ Getty Images for Save the Children*

Preterm birth can result in a range of long-term complications in survivors, with the frequency and severity of adverse outcomes rising with decreasing gestational age and decreasing quality of care (Table 2.1). Most babies born at less than 28 weeks need neonatal intensive care services to survive, and most babies 28 to 32 weeks will need special newborn care at a minimum. The availability and quality of these services are not yet well established in many low- and middle-income countries. Many middle-income countries, currently scaling up neonatal intensive care, are just beginning to experience these long-term consequences in survivors. These effects are most marked amongst survivors born extremely preterm; however, there is increasing evidence that all premature babies regardless of gestational age are at increased risk. The vast majority (84%) of all preterm births occur at 32 to 36 weeks. Most of these infants will survive with adequate supportive care and without needing neonatal intensive care. However, even babies born at 34 to 36 weeks have been shown to have an increased risk of neonatal and infant death when compared with those born at term and contribute importantly to overall infant deaths (Kramer et al., 2000). Babies born at 34 to <37 weeks also experience increased rates of short-term morbidity associated with prematurity (e.g., respiratory

"The true costs of prematurity, especially on a long-term global level, are poorly understood and likely to be grossly underestimated." (Simmons et al., 2010).

distress and intraventricular hemorrhage) than their peers born at term (Femitha and Bhat, 2011; Escobar et al., 2006; Teune et al., 2011). In the longer term, they have worse neurodevelopmental and school performance outcomes and increased risk of cerebral palsy (Quigley et al., 2012; Woythaler et al., 2011). On a global level, given their relatively larger numbers, babies born at 34 to 36 weeks are likely to have the greatest public health impact and to be of the most importance in the planning of services (e.g., training community health workers in Kangaroo Mother Care (KMC), essential newborn care and special care of the moderately preterm baby) (see Chapter 5).

We have highlighted the differences in preterm birth rates among countries, but marked disparities are also present within countries. For example, in the United States in 2009, reported preterm birth rates were as high as 17.5% in black Americans, compared to just 10.9% in white Americans, with rates varying from around 11 to 12% in those 20 to 35 years of age to more than 15% in those under age 17 or over 40 (Martin et al., 2011). Disparities within countries need to be better understood in order to identify high-risk groups and improve care.

The economic costs of preterm birth are large in terms of the immediate neonatal intensive care and ongoing long-term complex health needs frequently experienced. These costs, in addition, are likely to rise as premature babies increasingly survive at earlier gestational ages in all regions. This survival also will result in the increased need for special education services and associated costs that will place an additional burden on affected families and the communities in which they live (Petrou et al., 2011). An increased awareness of the long-term consequences of preterm birth (at all gestational ages) is required to fashion policies to support these survivors and their families as part of a more generalized improvement in quality of care for those with disabilities in any given country. In many middle-income countries, preterm birth is an important cause of disability. For example, a third of all children under 10 in schools for the visually impaired in Vietnam and more than 40% of under-5's in similar schools in Mexico have blindness secondary to

Table 2.5: Actions to improve national preterm birth rate data

Definition consistency Consensus on definition of preterm birth for international comparison, specifying gestational age	**Numerator (number of preterm births)** Simplified, lower cost, consistent measures of gestational age (GA) Widespread use and recording of GA Consistent inclusion of all live births of all gestations or weight, and noting if singleton or multiple births and noting the proportion that are under 500 g/22 weeks and under 1,000 g/28 weeks for international comparison Also record all stillbirths from 500 g/22 weeks and 1,000 g/28 weeks (whilst collecting by other national definition for stillbirth if different e.g., 20 weeks in United States)
	Denominator (number of births) Consistent measurement of all live births of all gestations noting if less than 22 weeks and if singleton or multiple births Also record all stillbirths
Actions to improve the data	**Focus on capture and consistency:** Gestational age and birthweight recording for all births Improve reporting of neonatal cause of death with preterm as direct cause and as risk factor (counting deaths of preterm babies who die from other causes) Collection of impairment data e.g., cerebral palsy and retinopathy of prematurity (ROP) rates according to a basic minimum dataset to increase consistency For settings where additional capacity available: Improve measurement e.g. gestational age assessment using early, high-quality ultrasound scan, development and refinement of improved gestational age assessment tools for use in low- resource settings **Increase the granularity of the data:** Record if provider-initiated, e.g., cesarean birth, or spontaneous and the basic phenotype, e.g. infection/relative contribution of each cause especially multiple births Improve the linkage of data to action: e.g., collating data by gender, socioeconomic status, ethnicity, subnational e.g. state Impairment data according to a more comprehensive standard dataset
Data for action	Set goals for national and global level for 1. Reduction of deaths amongst preterm babies by 2025 2. Reduction of preterm birth rates by 2025 Regular reporting of preterm birth rates and preterm-specific mortality rates at national level and to global level to track against goals

Note that weight is the preferred measure in ICD 10, but GA is commonly used now. The weight and GA "equivalents" are approximate.

retinopathy of prematurity (Limburg et al., 2012; Zepeda-Romero et al., 2011).

Actions to improve the data

The estimates in this report represent a major step forward in terms of presenting the first-ever national preterm birth estimates. However, action is required to improve the availability and quality of data from many countries and regions and, where data are being collected and analyzed, to improve consistency among countries. These are vital next steps to monitor the progress of policies and programs aimed at reducing the large toll of preterm birth (Table 2.5). Efforts in every country should be directed to increasing the coverage and systematic recording of all preterm births in a standard reporting format. Standardization of the definition in terms of both the numerator (the number of preterm births) and the denominator (the number of all births) is essential if trends and rankings are to be truly comparable. Collecting data on both live and stillbirths separately will allow further quantification of the true burden, while data focusing on live births only are required for monitoring of neonatal and longer-term outcomes. These estimates indicate the large burden amongst live-born babies. However, in developed countries with available data, between 5 and 10% of all preterm births are stillbirths, and the figure may be higher in countries with lower levels of medically-induced preterm birth. Distinguishing between live births and stillbirths may vary depending on local policies, the availability of intensive care and perceived viability of babies who are extremely preterm. If estimates for live-born preterm babies were linked to estimates for stillbirths, this would improve tracking among countries and over time. Achieving consensus around the different types of preterm birth and comparable case definitions, whilst challenging, are required where resources allow to further understand the complex syndrome of preterm birth (Goldenberg et al., 2012).

In many low- and middle-income countries without wide-scale vital registration, no nationally representative data are available on rates of preterm birth. Substantial investment and attention are required to improve vital registration systems and to account for all birth outcomes (Commission on Information and Accountability, 2011). In the meantime, the amount of population-based data available in high-burden countries could be dramatically increased to better inform future estimates and monitor time trends if data on preterm birth rates were included in nationally representative surveys such as the Demographic and Health Surveys (DHS) and demographic surveillance sites, but this will require developing and testing preterm-specific survey-based tools. Innovation for simpler, low-cost, sensitive and specific tools for assessing gestational age could improve both the coverage and quality of gestational age assessment. Data from hospital-based information systems would also be helpful, but potential selection and other biases must be taken into account. Simpler standardized tools to assess acute and long-term morbidities-associated preterm birth also are critically important to inform program quality improvement to reduce the proportion of survivors with preventable impairment.

Conclusion

There are sufficient data to justify action now to reduce this large burden of 15 million preterm births and more than one million neonatal deaths. Innovative solutions to prevent preterm birth and hence reduce preterm birth rates all around the world are urgently needed. This also requires strengthened data systems to adequately track trends in preterm birth rates and program effectiveness. These efforts must be coupled with action now to implement improved antenatal, obstetric and newborn care to increase survival and reduce disability amongst those born too soon.

Photo: Joshua Roberts/Save the Children

CARE BEFORE PREGNANCY

Photo: *Lucia Zoro/Save the Children*

Chapter 3. Care before and between pregnancy

— Sohni Dean, Zulfiqar Bhutta, Elizabeth Mary Mason, Christopher Howson, Venkatraman Chandra-Mouli, Zohra Lassi, Ayesha Imam

The importance of preconception health and care before pregnancy

Preconception care has, until recently, been a weak link in the continuum of care. Providing care to women and couples before and between pregnancies (interconception care) improves the chances of mothers and babies being healthy, and awareness is growing. Preconception care may be defined as "any intervention provided to women and couples of childbearing age, regardless of pregnancy status or desire, before pregnancy, to improve health outcomes for women, newborns and children" (Bhutta et al., 2011a), or "a set of interventions that aim to identify and modify biomedical, behavioral and social risks to a woman's health or pregnancy outcome through prevention and management" (Johnson et al., 2006). An expanded scope and definitions for preconception care are provided in Box 3.1.

Box 3.1: Scope and definitions of preconception care

Preconception care "Any intervention provided to women of childbearing age, regardless of pregnancy status or desire, before pregnancy, to improve health outcomes for women, newborns and children."

Periconception care "Any intervention provided to women of childbearing age preceding, including and immediately following conception to improve health outcomes for women, newborns and children."

Interconception care "Any intervention provided to women of childbearing age between pregnancies, to improve health outcomes for women, newborns and children."

Reproductive age encompasses adolescent girls age 15 and older, and women up to age 49.

Preconception Care envisages a continuum of healthy women, healthy mothers and healthy children; and promotes reproductive health for couples. Preconception care recognizes that boys and men are affected by, and contribute to, many health issues and risk factors that influence maternal and child health, such as sexually-transmitted infections, smoking and partner violence. Preconception care must reach girls and women, boys and men so that they are healthy in their own right, and so that they promote the health of mothers and newborns.

Source: Bhutta et al., 2011a

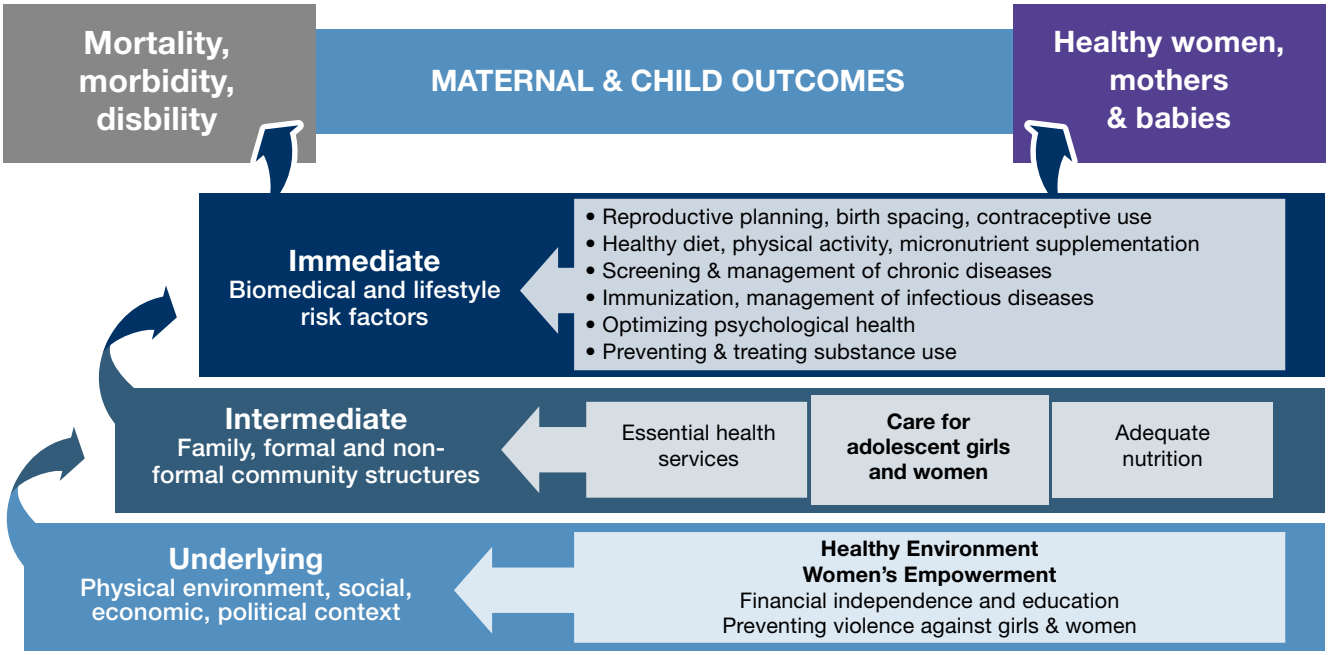
Preconception care emphasizes maternal and child health; however, it is vital to recognize that all girls and boys have the right to grow and develop in good health, just as all women and men have the right to be healthy—physically, psychologically and socially. Extending the RMNCH continuum to the preconception period improves the health and wellbeing of mothers, newborns and children as well as the health and wellbeing of girls and women, and boys and men, in their own right.

As shown in Figure 3.1, the conceptual framework for preconception care encompasses broader initiatives such as women's education and empowerment, and more targeted health interventions such as vaccination and micronutrient supplementation. Preconception care allows the time necessary for behavioral interventions to take effect. In various countries, it has been provided in schools, primary health care facilities or community centers, and has involved husbands, health care providers, youth leaders and community volunteers in achieving healthier outcomes for mothers and babies.

Many women, however, are unaware of how their health before conception may influence their risk of having an adverse outcome of pregnancy. As shown by the RMNCH continuum of care described in Chapter 1, health education and other programs delivered to all women during adolescence, before conception and between pregnancies can improve women's own health

1. Unless otherwise specified, the term preconception care in this chapter refers to both preconception and interconception care.

Figure 3.1: Conceptual framework for preconception care



Source: Bhutta et al., 2011a

during pregnancy as well as that of their babies (Institute of Medicine, 2007; Wise, 2008; Kerber et al., 2007). The imperative for preconception health is even greater given that 41% of all women report that their pregnancies were unplanned (Singh et al., 2010). Thus, waiting to provide needed health interventions until a woman and her partner decide to have a child will be too late in 4 out of 10 pregnancies.

Preconception care simultaneously promotes reproductive planning and interventions to reduce risk, allowing women to enter pregnancy in the best possible health and to have the best possible chance of giving birth to a healthy newborn. Outreach and awareness must begin in adolescence if it is to truly improve the health of women and newborns and reduce the rates of prematurity and low birthweight (Box 3.2). The contextual and individual risks that increase the likelihood of preterm births and other adverse pregnancy outcomes are present from the time a girl reaches adolescence, and they continue during and between pregnancies.

Priority packages and evidenced-based interventions

There is growing evidence that reducing risks in the preconception period improves the health of the pregnant woman and also contributes to the prevention of preterm birth. Table 3.1 presents risk factors associated with an increased risk of preterm birth. These estimates were derived from a detailed review of the evidence base on preconception risk factors for all adverse outcomes of pregnancy and landmark reviews on the causes of preterm birth (Barros et al., 2010; Bhutta et al., 2011a; Goldenberg et al., 2008; Iams et al., 2008).

Factors that have been shown to be strongly predictive of preterm risk, but cannot be modified, include history of previous spontaneous preterm birth, cervical procedures (including biopsies), primiparity, grand multiparity and multiple gestations. Factors associated with socioeconomic and racial disadvantage (see Chapter 2) will, hopefully, be amenable to positive transformation over the longer term, but this will require fundamental structural changes to society and a deep-seated shift in social values and norms.

Table 3.2 presents the priority packages and evidence-based interventions during the preconception period and

2. Although RMNCH is the accepted term for the continuum of health, as noted in Chapter 1, preconception health extends beyond reproductive health (the "R") encompassing a broad range of interventions.
3. Until now, preconception care has focused primarily on women since their health more directly impacts pregnancy outcomes, and in many contexts their needs are not adequately addressed. There is now a growing realization that involving men in preconception care is critical since the health of both the potential father and mother determines pregnancy outcome. Further, preconception care that engages men can help to make them supportive partners who promote healthy behaviors and increase women's access to care.

Box 3.2: Importance of preconception care for adolescent girls

It has been estimated that 16 million adolescent girls between the ages of 15 and 19 give birth each year, representing approximately 11% of all births worldwide (WHO, 2007). These girls are not physically prepared for pregnancy and childbirth and without the nutritional reserves necessary are at disproportionately greater risk of having premature and low-birthweight babies (Haldre et al., 2007; Mehra, and Agrawal 2004; Paranjothy et al., 2009; WHO, 2007). Both hospital- and population-based studies in developed and developing countries show that adolescent girls are at increased risk for preterm birth compared with women ages 20 to 35 (Ekwo and Moawad, 2000; Hediger et al., 1997; Khashan et al., 2010). The risk is especially high for younger adolescent girls (Khashan et al., 2010; Sharma et al., 2008).

Married and unmarried adolescent girls often lack education, support and access to health care that would allow them to make decisions about their reproductive health (WHO, 2001). One in 5 pregnant adolescent girls report shaving been abused in pregnancy (Parker et al., 1994). Violence against girls and women, not only has been shown to result in adverse physical, psychological and reproductive consequences for them, but also is reported to increase the risk for prematurity and low birthweight (Krug et al., 2002). Adolescent girls, in particular, are more likely to experience violence than adult women, and are less likely to seek care or support during pregnancy as a result (Jejeebhoy, 1998). Additionally, adolescent girls are more likely to have multiple risk factors for adverse pregnancy outcomes, including being socially disadvantaged, undernourished and having higher rates of sexually transmitted and other infections.

Despite the increased risks for adolescent mothers and their newborns, social and cultural norms in developing countries perpetuate early marriages with 60 million women reporting that they were married below the age of 18 (UNICEF, 2007). Married or unmarried adolescents are less likely to use any contraceptive method during sexual activity than adults in sexual partnerships (Blanc et al., 2009). Although adolescence is a period of increased risk, it also provides a unique opportunity to influence the development of healthy behaviors early on. Preconception interventions to promote reproductive planning, improve nutrition, encourage healthy sexual behaviors and prevent substance use and partner violence are likely to have greater benefit if targeted towards adolescent girls and boys.

before pregnancy that have potential to reduce preterm birth rates. These include interventions currently recommended by the WHO in the preconception period (e.g., family planning and prevention and treatment of STIs) (PMNCH, 2011). Only interventions with evidence of strong or moderate effectiveness are described in the section below. Efforts are now underway to develop guidelines for preconception care and expand the package of interventions to include those listed in Table 3.2—for example, optimizing pre-pregnancy weight, screening for and treating mental health disorders and other chronic diseases like diabetes and hypertension, preventing intimate partner violence and promoting cessation of tobacco use and exposure to secondhand smoke in the home and workplace. It should be noted that because preconception care is a relatively new concept, the evidence base for risks and interventions before conception is still being strengthened. Thus, broad consensus regarding a package of evidence-based interventions for care in the preconception period has yet to be decided.

Preconception care services for prevention of preterm birth for all women

Prevent pregnancy in adolescence

Preconception care that begins early on and continues between pregnancies will help to ensure that women have a reproductive life plan and are able to decide when to have children, how many children they desire and methods used to prevent unintended pregnancy. In some regions, cultural norms promote early marriage, which is a factor in high rates of adolescent pregnancy. Regulations to increase the legal age at marriage and educating communities to change cultural norms that support early marriage may be ways to prevent adolescent pregnancy in those countries. In an effort to discover what interventions are most effective to prevent adolescent pregnancy, a wide variety of programs carried out in low-, middle-, and high-income countries has revealed that the most successful programs are responsive to the unique educational, social, economic, nutritional,

Table 3.1: Risk factors associated with an increased risk of preterm birth and the effectiveness of intervention arrayed according to the strength of evidence

How Great Is The Risk?		
Pregnancy in adolescence	+	Increased prevalence of anemia, pregnancy-induced hypertension, low birthweight, prematurity, intra-uterine growth retardation and neonatal mortality
Birth spacing	+	
Short intervals		PTb: OR 1.45, LBW: OR 1.65
Long intervals		PTb: OR 1.21, LBW: OR 1.37
Pre-pregnancy weight status	+	
Underweight		PTb: OR 1.32, LBW: OR 1.64
Overweight & obesity		PTb: OR 1.07 Maternal overweight is a risk factor for many pregnancy complications including hypertensive disorders, gestational diabetes, postpartum hemorrhage, stillbirth, congenital disorders Both underweight and overweight women have a higher chance for requiring obstetric intervention at delivery
Micronutrient deficiencies	+/-	
Folic acid		Folic acid deficiency is definitively linked to neural tube defects (NTDs) in newborns
Iron		Anemia increases the risk for maternal mortality, low birthweight, preterm birth and child mortality
Chronic diseases	+	
Diabetes mellitus		Babies born to women with diabetes before conception have a much higher risk of stillbirths, perinatal mortality, congenital disorders, as well as spontaneous pregnancy loss, preterm labor, hypertensive disorders, and delivery by cesarean birth
Hypertension		
Anemia		A study shows that anemia before conception increases the risk of low birthweight (OR 6.5)
Poor mental health (especially depression) **and Intimate partner violence**	++	Increased risk for preterm birth, low birthweight and depression during pregnancy and the postpartum period IPV-PTb OR: 1.37, LBW OR: 1.17 Also increased risk for spontaneous pregnancy loss, stillbirth, gynecological problems including sexually-transmitted infections, depression
Infectious diseases	++	
STIs - syphilis HIV/AIDS Rubella		Infectious diseases increase the risk for spontaneous pregnancy loss, stillbirths and congenital infection
Tobacco use	++	A single study shows risk for PTb OR: 2.2 Smoking increases the risk for spontaneous pregnancy loss, placental disorders, congenital malformations, sudden infant death syndrome, stillbirths and low birth weight

For magnitude of risk:

++ means strong evidence of risk and implicated in biological pathways leading to preterm birth and low birthweight

+ means moderate evidence of risk on preterm birth and low birthweight

+/- means weak evidence of risk on preterm birth and low birthweight

Acroynms used: PTb = preterm birth; OR = odds ratio; IPV = intimate partner violence

Source: Barros et al., 2010; Bhutta et al., 2011a; Goldenberg et al., 2008; Iams et al., 2008

psychological and medical needs of adolescents (Gavin et al., 2010). Particular emphasis must also be placed on ensuring universal access to primary and secondary education for girls through increasing formal and informal opportunities, because girls who complete their education are less likely to become pregnant in adolescence (Guttmacher Institute, 1998). While expanded sexual education programs increase adolescents' knowledge of risk, they have not been shown to change behaviors. In a combined analysis, personal development programs that incorporated skills-building and include contraceptive provision were shown to prevent 15% of first adolescent pregnancies (DiCenso et al., 2002; Origanje et al., 2009), and programs that taught parenting skills and enabled teen mothers to complete their education decreased repeat adolescent pregnancies by 37% (Corcoran and Pillai, 2007; Bhutta et al., 2011a; Harden et al., 2006). Across all contexts, programs demonstrated greater success if they were holistic in scope rather than solely focused on sexual education and STI/teen pregnancy prevention. It is important to note that programs with a longer duration were more effective since adolescents require time to integrate new information, practice the skills that will

Table 3.2: Priority interventions and packages during the preconception period and before pregnancy to reduce preterm birth rates

Preconception care services for the prevention of preterm birth for all women
• Prevent pregnancy in adolescence • Prevent unintended pregnancies and promote birth spacing and planned pregnancies • Optimize pre-pregnancy weight • Promote healthy nutrition including supplementation/fortification of essential foods with micronutrients • Promote vaccination of children and adolescents
Preconception care services for women with special risk factors that increase the risk for preterm birth
• Screen for, diagnose and manage mental health disorders and prevent intimate partner violence • Prevent and treat STIs, including HIV/AIDS • Promote cessation of tobacco use and restrict exposure to secondhand smoke • Screen for, diagnose and manage chronic diseases, including diabetes and hypertension

allow them to negotiate safe behaviors and develop confidence in themselves to broaden their life options (Bhutta et al., 2011a; Corcoran and Pillai, 2007; DiCenso et al., 2002; Harden et al., 2006; Origanje et al., 2009).

Prevent unintended pregnancies and promote optimal birth spacing

One way to ensure that mothers and babies have good outcomes is to encourage pregnancy planning. Women who have very closely spaced pregnancies (within 6 months of a previous live birth or pregnancy) are more likely to have preterm or low-birthweight babies (Conde-Agudelo et al., 2006). This may be because they have not had enough time to replenish their nutritional reserves or treat an infection or other systemic illness. The correct, consistent use of family planning methods leads to more women spacing their pregnancies 18 to 24 months apart, which is ideal (Tsui et al., 2010). Encouraging family planning and the use of contraceptive methods (hormonal and barrier methods) has other advantages including reductions in maternal and infant mortality, lower rates of unintended pregnancies, and prevention of STIs, including HIV (Conde-Agudelo et al., 2006; Tsui et al., 2010).

Breastfeeding promotion for 24 months can prevent closely spaced pregnancies, a method that continues to be underused despite strong evidence of its positive effect on maternal and newborn health. On its own, 12 months of contraception-only coverage in the preceding birth interval can reduce the mortality risk for the next newborn by 31.2%, whereas 12 months of contraceptive use overlapping with breastfeeding reduces the risk by 68.4% (Tsui, 2010). Programs to make effective contraception available to women and couples of reproductive age must also include counseling and follow-up to determine if the chosen method of contraception is being used correctly, and so that the method may be changed if necessary. It has been demonstrated that contraceptive counseling by trained care providers in the immediate postpartum period, or as part of comprehensive care after pregnancy loss, increases women's uptake and their partner's support for contraceptives (Bhutta et al., 2011a). Appropriate birth spacing after a previous live birth or pregnancy loss decreases the risk for prematurity in subsequent pregnancies (Shah and Zao, 2009; Conde-Agudelo et al., 2005).

Although contraceptive use, particularly amongst adolescents, currently falls far short of the optimal with only 56% of the demand for family planning satisfied among the Countdown to 2015 priority countries (Requejo et al., 2012), the renewed interest in family planning and contraceptive commodity security (UK Govt Family Planning Summit forthcoming July 2012, UN Commission on Life-saving Commodities for Women and Children) gives an unprecedented opportunity to scale up use of contraception and allows for women and partners to plan their pregnancy. Strategies for improving coverage, especially

Photo: Susan Warner/Save the Children

in low-resource settings, are urgently needed and require vigorous research.

Optimize pre-pregnancy weight

Optimizing weight before pregnancy is recommended, since weight gain or loss during pregnancy increases the risk of adverse pregnancy outcomes. Monitoring nutritional status through measurement of women's body mass index prior to pregnancy is feasible, even in low-income contexts, and should be used as a baseline to develop a regimen for healthy eating and physical activity to optimize their weight.

Women who are underweight before pregnancy (body mass index less than 18.5 kg/m2) are at significantly greater risk of having premature, low birthweight newborns (Han et al., 2011). Given that maternal undernourishment is a risk factor for being underweight, improving food security could reduce the rates of preterm birth, especially in impoverished nations. It is important, therefore, to evaluate whether local and national food programs largely targeted towards children could be replicated for adolescent girls and women.

Obesity is a problem of increasing magnitude globally with estimated 300 million women of reproductive age who are obese (WHO, 2011). Overweight and obese women (body mass index greater than 25 kg/m2) have a higher risk for preterm births (McDonald et al., 2010; Torloni et al., 2009). While existing evidence indicates that weight loss at any age is difficult to achieve and sustain, successful programs for women in their reproductive years reaffirm that women can overcome environmental pressures like easy access to low-cost, high-calorie foods and develop healthy eating habits. These programs promote dietary modification and increased physical activity through sustained daily changes, with the help of a support system and regular monitoring (Eiben and Lissner, 2005; Faucher and Mobley, 2010; Amorim et al., 2007; Chang et al., 2010; Galtier et al., 2008; Kinnunen et al., 2007; Mediano et al., 2010; Ostbye et al., 2009; Rock et al., 2010). Women should be encouraged to include moderate physical activity in their daily routine to improve weight and cardiovascular status before pregnancy and reduce the likelihood of developing weight-related complications during gestation (Gavard and Artail, 2008). Programs should be tailored to women's weight at baseline and their lifestyle, to build motivation and increase the chances of sustaining weight loss.

Promote healthy nutrition including supplementation/fortification of essential foods with micronutrients

Studies of the biological mechanisms leading to preterm birth indicate that more severe congenital disorders, including neural tube defects, might result in preterm delivery (Honein et al., 2009). Consuming a multivitamin containing 400 µg of folic acid in the preconceptional period is the best way to ensure adequate micronutrient intake to help prevent neural tube and other birth defects (Christianson et al., 2006). Multivitamin supplementation reduces the risk of congenital malformations (e.g., neural tube, congenital heart, urinary tract and limb defects) by 42-62% and the risk

Photo: *Jane Hahn/Save the Children*

of preeclampsia by 27%. Folic acid supplementation or fortification reduces the risk of neural tube defects by 53% (Bhutta et al., 2011a). Although folic acid is known to protect against neural tube defects, there is little evidence to show that folic acid supplementation alone reduces the risk for preterm birth (Bukowski et al., 2009). In addition, providing folic acid supplementation to all women of childbearing age poses a major logistical challenge. In middle- and low-income countries, iron and folic acid supplementation reaches fewer than 30% of women (PAHO, 2004). Even in the United States where there are aggressive promotional campaigns, only 1 in 3 women of childbearing age takes a vitamin with folic acid daily (March of Dimes, 2003). For this reason, iron and folic acid fortification of foods for mass consumption is considered an important strategy to increase micronutrient levels in the population. A number of countries have already opted to increase population folic acid intake through inexpensive, large-scale fortification, which has proven to be moderately effective and safe (CDC, 2004; Calvo and Biglieri, 2008; Blencowe et al., 2010; De Wals et al., 2003; Gucciardi et al., 2002; Honein et al., 2001; Liu et al., 2004; Lopez-Camelo et al., 2005; Persad et al., 2002; Ray et al., 2002; Sadighi et al., 2008; Sayed et al., 2008; Simmons et al., 2004; Williams et al., 2002, 2005). However, legislation for mandatory fortification of food staples has still not been enacted in many countries.

Promote vaccination of children and adolescents

Infections transmitted around the time of conception or during pregnancy may result in preterm birth (Goldenberg et al., 2000). Not only does infection, especially with rubella virus, increase the risk for prematurity, but it may also lead to other devastating consequences such as congenital rubella syndrome or miscarriage (Christianson et al., 2006; Cutts et al., 1997; Robertson et al., 1997). Many of these infections could be prevented through routine childhood vaccinations. However, the rubella vaccine can also be given at least 3 months prior to pregnancy to women who are not already immune (Coonrod et al., 2008). Vaccination campaigns against rubella have been able to increase coverage for adolescent girls and women (Gudnadottir, 1985; Su and Guo, 2002; Menser et al., 1985; Miller et al., 1985; Wang et al, 2007).

Preconception care services for women with special risk factors that increase the risk for preterm birth

Screen for, diagnose and manage mental health disorders and prevent intimate partner violence

Maternal stressors such as depression, socioeconomic hardship and intimate partner violence have been linked to preterm birth (Austin and Leader, 2000; Coker et al., 2004; Copper et al., 1996; Hegarty et al., 2004; Sharps et al., 2007). It has been hypothesized that physical and psychological stress acts through inflammatory pathways involving maternal cortisol to cause premature birth (Challis and Smith, 2001; Wadhwa et al., 2001). Importantly, when such risks are present before pregnancy, they are likely to continue throughout pregnancy as well. Moreover, women with psychosocial stressors have a greater likelihood of engaging in risky behaviors such as smoking and alcohol use and are less likely to seek health care (Schoenborn and Horn, 1993; Zuckerman et al., 1989). Risky sexual behaviors also put these women at greater risk for unintended pregnancies and STIs (Bauer et al., 2002; Bonomi et al., 2006; Seth et al., 2010). Interventions to improve the psychological health of women before conception have included group counseling and development of coping and economic skills. These have shown some promise in reducing risk, but so far have not demonstrated reductions in adverse birth outcomes including prematurity. Further research in this area is needed since the burden of mental health disorders—particularly depression, anxiety and somatic disorders—is high in women, and the safety of some medications used to manage these conditions during pregnancy is unclear. A Joint Statement by the American Psychiatric Association and American College of Obstetrics and Gynecology indicates that the higher risk of preterm birth may be related to depression itself, or the antidepressants used for treatment (Yonkers et al., 2009). Behavioral therapy for couples before marriage, for men who have been violent with their partners, and for married couples in a violent relationship has shown a reduction in aggression, largely in more severe forms of violence (Feder and Forde, 2000; Markman et al., 1993; O'Leary et al.,

1999; Simpson et al., 2008). Two programs that integrated interventions for domestic violence and substance use also showed some success, however, the effect generally faded with time (Rychtarik and McGillicuddy, 2005; Scott and Easton, 2010).

Prevent and treat STIs, including HIV/AIDS

Reducing the incidence of infectious diseases, particularly syphilis, is a high priority to lowering the rates of stillbirths and preterm birth (Donders et al., 1993). A number of interventions have been piloted in various countries to prevent and treat STIs, especially since such interventions also impact teen pregnancy, HIV/AIDS and contraceptive use. Focusing interventions on high-risk groups, including women, adolescents and intravenous drug users, can effectively reduce the transmission of STIs to the population in general and subsequently reduce preterm births and stillbirths (Over and Piot, 1993; Wasserheit and Aral, 1996). Behavioral and counseling interventions may lead to a 25% rise in the practice of safe sexual behaviors and a 35% drop in the incidence of STIs (Bhutta et al., 2011a). Mass treatment interventions with antibiotics also have been shown to decrease the prevalence of STIs by one-fifth (Kamali et al., 2003; Maynaud et al., 1997; Wawer et al., 1999). Counseling and behavioral interventions that focus on educating women are especially crucial, given that women are physically more vulnerable to contracting a STI during intercourse than men, and are less likely to have the ability to negotiate safe behaviors with their partners such as condom use (Mize et al., 2002). Focused interventions for preventing the broad range of STIs may be helpful in preventing preterm births, though more research is needed.

Promote cessation of tobacco use and restrict exposure to secondhand smoke

Cigarette smoking approximately doubles the threat of preterm birth (Andres and Day, 2000). Despite the risk of fetal growth restriction and preterm birth (Cnattingius, 2004; Honein et al., 2007; Siero et al., 2004), a survey of women in low- and middle-income countries found that many pregnant women currently used tobacco or were exposed to secondhand-smoke (Bloch et al, 2008). A few studies have shown, however, that preconception counseling and the involvement of husbands or partners in smoking cessation programs can increase the number of women who quit smoking before pregnancy (Elsinga et al., 2008; Park et al., 2004). In many instances even when women themselves do not use tobacco, they are exposed to environmental tobacco smoke and indoor air pollution; interventions and regulatory measures must therefore target male partners and behavioral change on a wider level to minimize women's exposure.

Screen for, diagnose and manage chronic diseases

In the United States alone, 12% of women of reproductive age suffer from diabetes and hypertension (Dunlop et al., 2008). Although testing and treatment for women diagnosed with such medical problems prior to pregnancy are cost-effective and prevent further complications for the mother and baby, they do not necessarily lower the incidence of preterm births (Iams et al., 2008). For example, achieving good control of diabetes through counseling, weight management, diet and insulin administration could reduce the risk of perinatal mortality and congenital disorders by approximately 70%, but does not significantly lower the rate of preterm birth among diabetic mothers (Bhutta et al., 2011a). At any contact with health care services, women of reproductive age should, therefore, be asked about other medical conditions and the use of medications. Until adequate control of the medical condition is achieved, women should be educated about the possible risks to themselves and their newborn, and be encouraged to use effective contraception (Tripathi et al., 2010). Multivitamin supplementation for women with chronic medical conditions is especially important because it has been shown to lower their risk for adverse pregnancy outcomes (Mahmud and Mazza, 2010). For women with other chronic conditions, such as cardiorespiratory disease, systemic lupus erythematosus, hypertension and renal disease, a cesarean birth may be indicated, leading to a baby being born prematurely; however, even in such cases, achieving optimal control of the condition before pregnancy may lead to better long-term outcomes for the mother and newborn.

Limitations of the evidence

The growing interest in preconception care is fairly recent; thus, there are limited data specific to the period prior to and between pregnancies, particularly relating to preterm birth risks and outcomes. Risk factors and interventions that have been studied only in adolescents or only during pregnancy also may be relevant in the preconception period. For instance, exposure to indoor air pollution during pregnancy leads to 20% more stillbirths and low birthweight babies (Pope et al., 2010). Yet many women are exposed to biomass smoke and second-hand tobacco smoke long before pregnancy is established. Similarly, interventions such as smokeless stoves or smoking cessation programs that reduce overall levels of exposure also would benefit women who later become pregnant. For many women, a positive pregnancy test is a stimulus to cease smoking, yet most women require multiple attempts to quit. Smoking cessation programs for adult men and women have been evaluated and demonstrate higher rates of women who quit before or during the first trimester (Floyd et al., 2008). Given the strong evidence of risk for preterm birth and low birthweight with tobacco use in pregnancy, it may be inferred that fewer women smoking translates to lower rates of preterm birth.

Many interventional studies in the preconception period report different health outcomes, which is also the case for studies on pregnancy and childbirth (Chapter 4). This precludes a complete assessment of the impact that an intervention could have on multiple pregnancy outcomes. For instance, research to reduce the prevalence of STIs among women may assess safe sexual behaviors or rates of transmission as outcomes; however, many studies do not indicate how many women later became pregnant or change in rates of preterm birth.

Until now, preconception care has been provided through three avenues: pre-pregnancy health visits for couples contemplating pregnancy; programs to increase awareness, screening and management for a particular risk; or participatory women's groups in the community. The diversity of contexts and risks among adolescent girls and women will require that preconception care be tailored to different settings and groups. The approaches used are a step in the right direction; but could be broadened to include earlier health care and health promotion for women and couples and address risks more holistically.

Program opportunities to scale up

There is widespread agreement that in order to reduce maternal and childhood mortality, a continuum of care needs to be provided and that actions are needed at the community, primary care and referral care levels to deliver this continuum (Chapter 1). Packages of interventions to improve maternal and newborn health have been developed; however, these focus largely on care during pregnancy and after birth (WHO, 2010). Tracking progress and scaling up delivery of preconception interventions has been a challenge, with preconception initiatives in individual countries delivering different services to different segments of the population (women, couples or adolescents).

In some high-income countries, such as the United States, Hungary, Australia and the Netherlands, an attempt has been made to provide preconception care to couples of reproductive age through family physicians or a special preconception clinic (Czeizel, 1999; Lumley and Donohue, 2006; Elsinga et al., 2008; Hillemeier et al., 2008; Jack et al., 1998; Moos et al., 1996). Evidence-based recommendations for the content of preconception care also have been published (Jack et al., 2008, Berghella et al., 2010; Johnson et al., 2006; Korenbrot et al., 2002), and components have been incorporated into major national and international health guidelines (Victora et al., 2010; PMNCH, 2011). In the United States, a website has been developed to support clinical education and practice in this area (www.beforeandbeyond.org).

In some countries (India, Pakistan, Bangladesh and Nepal), women's support groups have been teaching birth preparedness to women and their partners (Midhet and Becker, 2010; Azad et al., 2010; Bhutta et al., 2011b; Manandhar et al., 2004;; Tripathy et al., 2010). Many large-scale trials for individual preconception interventions also have been carried out in low- and middle-income countries. While

Table 3.3: Research priorities for preterm outcomes related to preconception

Description
• Maintain and expand global databases on the prevalence of preconception risk factors, incidence of preterm birth • Develop indicators to evaluate progress in scaling up coverage of preconception care • Evaluate impact of preconception care programs on rates of preterm birth and other adverse pregnancy outcomes
Discovery
• Basic science research on preconception risk factors for preterm birth
Development
• Develop and test screening tool to assess risk of preterm birth based on risk factors in the preconception period • Develop ways to increase demand for and access to preconception interventions
Delivery
• Define and test preconception care guidelines and intervention package • Explore means to integrate effective preconception interventions into broader programs and initiatives • Adapt effective interventions to maximize uptake by adolescents • Improve health systems (infrastructure, management, distribution of goods, training of providers) to deliver preconception care

individual settings will require context-specific approaches to providing preconception care, a number of effective and culturally acceptable interventions already exist. An example of an opportunity to build on existing programs is the integration of interconception health into home visits during the postnatal period.

The evidence base for risks and interventions before conception is still being strengthened because preconception care, as noted, is a relatively new concept. Therefore, an agreed-upon package of evidence-based interventions and opportunities for scale up in the preconception period has yet to be decided.

Priorities for research for preconception care

The limited evidence on the effectiveness of preconception care in reducing preterm births presents a major barrier for reducing the global burden of preterm birth; thus, across the research pipeline — from description to delivery, development and discovery — there is much to be done (Table 3.3). Some important risk factors have been identified, and certain interventions have proven effective in the preconception period; however, these have limited impact on preterm birth. Replicating these interventions in larger studies of adolescent girls and women before first pregnancy, or between pregnancies, is needed to assess the relative benefit that may be obtained through preconception care across different populations. There also is a need to identify innovative ways to assess and reduce exposure to risk factors that are not amenable to medical intervention, such as environmental pollution.

The development of national and international guidelines specific to preconception care would increase the visibility of the issue for health care providers and the population in general. While there is need for a defined and tested preconception care package, that can be adapted to various settings and models of service delivery at scale, much is still undiscovered, both in terms of what works and how to integrate effective preconception interventions into broader programs and initiatives across the continuum of RMNCH. Even if there was consensus and evidence for interventions during this period for preventing preterm births, national and global data are lacking. A current initiative to maintain a database of the number of adolescent girls and women exposed to a particular risk (e.g., anemia) or receiving a particular preconception intervention (e.g., folic acid fortification) is necessary. Such a global database will allow the risk reduction for an intervention to be calculated in various populations. It will also permit assessment of tailored or packaged strategies to improve health in high-risk populations.

The interventions with proven benefit and national data, such as family planning, require further operational research including how to maximize uptake by adolescents and assessing feasibility and impact of scaling up. To monitor quality of care, mid-level health care workers providing preconception care must be evaluated and provided with additional support or training if gaps exist. Improvements to infrastructure, supply chain and health management systems also may increase coverage of preconception services.

Piloted interventions to improve the health of adolescent girls and women, which can lead to prevention of preterm birth, are often not categorized as preconception care; thus, they present a missed opportunity for linking to preterm birth research. Continued research into the etiology of preterm birth will be necessary in order to identify variations in the

Table 3.4: Actions before and between pregnancy to reduce the risk of preterm birth

Invest and plan
• Assess situational need for preconception care services and opportunities in local health system to deliver. • Use every opportunity to reach girls and women and couples with preconception messages, beginning in school and extending to health care settings and community events. Preconception health must also involve boys and men, to improve their health; and to engage them in ensuring better outcomes for women and girls.
Implement
Seize opportunities through existing programs (including non-health programs) to: • Educate women and couples of reproductive age to have a reproductive plan that includes age at first pregnancy, method to prevent unintended pregnancy, and number of children they wish to have • Scale up personal development programs and skills-building to negotiate safe sexual behavior in adolescence. Adapt preconception interventions to maximize uptake by adolescents • Implement universal coverage of childhood and booster vaccinations for infectious diseases known to cause adverse pregnancy outcomes • Screen for and treat infectious diseases, particularly sexually transmitted infections. • Promote healthy nutrition and exercise to prevent both underweight and obesity in girls and women • Promote food security for communities and households. Expand nutrition programs to include adolescent girls and women. Particularly for underweight women, provide protein calorie supplementation and micronutrients. A cost-effective way to ensure adequate levels of micronutrient consumption would be to enact large-scale fortification of staple foods. • Implement public health policy to reduce the number of men and women of reproductive age who use tobacco • Implement strategies for community development and poverty reduction, since living environments and socioeconomic constructs have a significant impact on health • Ensure universal access to education to empower girls and women with the basic knowledge and skills they need to make decisions for themselves, such as when to access care **Scale up** • Promote effective contraception for women/couples to space pregnancies 18 to24 months apart • Screen for chronic conditions, especially diabetes, and institute counseling and management as early as possible to improve neonatal outcomes
Inform and improve program coverage and quality
• Develop indicators for baseline surveillance and to monitor progress in preconception care • Include preterm birth among tracking indicators
Innovate and undertake implementation research
• Invest in research and link to action We all share in the responsibility of making sure that all women before and between pregnancies receive the care they need for healthy pregnancies and birth outcomes

risk profiles and therefore, specific interventions, for women in different contexts and from different strata within the same communities. There also is need for innovation such as the development of a screening tool to assess individual risk of having a preterm birth or technology and software to provide individualized preconception care in user-friendly ways.

Addressing contextually relevant ways to increase demand for and access to preconception care services is especially necessary in developing countries. While many countries have implemented behavior change strategies to increase awareness on birth preparedness and women's empowerment, more strategies for assessing benefit particularly for preterm birth are needed, especially culturally appropriate ways to involve adolescent boys, men and communities.

For preconception care, there is still much that needs to be discovered, such as exploring new medical interventions for women at high risk of having a preterm birth, based on knowledge of biological pathways. Even with current tools used to diagnose disease such as hypertension, the development of simpler, cost-effective diagnostic tests will enable efficient point-of-care testing with timely results and minimize the need for multiple visits. Likewise, affordable, easy-to-administer preventive and treatment options that are woman-friendly are in demand, such as oral insulin or better female-controlled contraceptive methods. With the knowledge gaps for preconception care, there is room for testing innovative technology and for implementation research.

Prescription for action

To prevent preterm births, proven interventions need to be scaled up and integrated so that they reach more women more often. In the health care setting, an essential package of interventions (contraception, micronutrient supplements, vaccination, STI screening, etc.) and a checklist of risk factors to be screened for might be a feasible starting point. In some countries, mandatory screening for hereditary diseases before marriage drastically reduced rates of thalassemia, and whether preconception care could be delivered through a similar means has not been explored (Samavat and Modell, 2004). This must be supported by ways to educate providers of the benefits of preconception care to increase their willingness to provide it. Provision of preconception care must also be extended beyond those who are traditionally involved in women's health, by incorporating the concept into training for current and future health care providers. For some risks, such as chronic diseases, until diagnosis and treatment can become more affordable, policy-makers and donor organizations must work

in conjunction to make screening and care widely available. Increasing coverage of postpartum care would also help to improve women's health in future pregnancies, for example, through the integration of preconception care in postnatal home visits.

Also of importance will be the development of partnerships with other sectors such as education, food and agriculture, telecommunications and media, to promote greater demand for preconception care, and to reach girls, women and couples beyond the health care system. In some cases, integrated programs have already been shown to be feasible and effective, such as youth development programs, contraceptive provision in school for adolescents and incorporating maternal health into child vaccination days. It is also essential to develop a way to involve men, community leaders and volunteers in support for and provision of preconception care. Specific action points are listed in Table 3.4.

Conclusion

Until recently, the provision of care to women and couples before and between pregnancies to improve maternal and newborn health has not had sufficient priority on the RMNCH continuum of care. As with research, care must focus increasingly "upstream" from birth if the true potential for prevention of preterm birth is to be realized. Effective preconception care involves a broad variety of partners, including men, health care providers, youth leaders and community volunteers; and delivery sites such as schools, primary health care facilities and community centers. Outreach and awareness must begin in adolescence if it is to truly improve the health of women and newborns and reduce the rates of prematurity. If tackled, however, with vigorous and evidence-based interventions, preconception care offers the earliest opportunity to reduce risk, allowing women to enter pregnancy in the best possible health and to have the greatest chance of giving birth to a healthy baby.

Photo: *Ahman El-Nemr/Save the Children*

Baby Karim Kobeissy was born and admitted to the Neonatal Intensive Care Unit at the American University of Beirut Medical Center on the 2nd of June 2009 at 24 weeks of gestation and weighing 575 grams (1.3 lbs.). Mirvat and Mohamed Kobeissy did not expect the birth of their newborn so early after the normal birth of their two older children who are now 15 and 13 years old, respectively. When Mrs. Kobeissy presented to the hospital to deliver her precious baby, she was informed that her son's chances of living were minimal at best. Doctors explained how hard the situation was for such a tiny baby to be able to fight for survival, yet Mrs. Kobeissy was buoyed by her strong faith and belief that this tiny soul, her son, would be a survivor and make it through the difficult times ahead.

Due to his extreme prematurity, baby Karim had under-developed lungs and pulmonary problems requiring immediate intubation. He could not eat for nearly three months except by tube feeding. At one point, due to his critical illness, Mrs. Kobeissy was told that her son was at risk of losing his tiny fingers and toes, yet with the support of the highly experienced medical team in the NICU Mrs. Kobeissy says, baby Karim surmounted this challenge. He also developed retinopathy of prematurity, a complication common in extremely premature babies. He underwent laser surgery to correct it but, unfortunately, still lost sight in one eye. Yet by the beginning of month three of his stay in the NICU, baby Karim had reached the weight of one kilogram, a sign of real progress!

I felt devastated watching my newborn fight for his life...

LEBANON

BABY KARIM

12 WEEKS PREMATURE

CHANCE OF SURVIVAL: MINIMAL

With all of the medical problems, financial concerns and ups and downs of hope and despair during baby Karim's first four months in the NICU, Mrs Kobeissy said it was a nightmare for her, her husband and family—one that they thought would never end. She said "I felt devastated watching my newborn fight for his life, yet our beautiful baby Karim, with the help of his dedicated medical support team, continued to fight and survive."

When he left the NICU after four months weighing 2.5 kilograms, Mrs. Kobeissy said that baby Karim's ordeal was not over. Due to his low immune level and the increased risk of infection it posed, baby Karim had to stay another three months in his room at home to avoid exposure to others. But he fought on and continued to grow. Now at 2½ years of age, Karim the little hero—born at 24 weeks of gestation and a mere 575 grams—is full of life, healthy and goes to day care, where he is loved for his energy and sense of humor. And to his family, Karim continues to be a source of joy and faith in life day after day. Baby Karim survived overwhelming odds because of his courage, the love of his family and the skill and dedication of the NICU staff. May his story be one of hope for all babies born too soon, wherever they are.

In Lebanon, the rate of preterm birth is on the rise and this is the greatest risk factor for neonatal death. Over 5,000 Lebanese babies are born premature each year.

CARE DURING PREGNANCY AND CHILDBIRTH

Photo: *Aubrey Wade/Save the Children*

Chapter 4. Care during pregnancy and childbirth

— Jennifer Requejo, Mario Merialdi, Fernando Althabe, Matthais Keller, Joanne Katz, Ramkumar Menon

Pregnancy period and childbirth - the importance of antenatal care

Pregnancy and childbirth represents a critical window of opportunity for providing effective interventions to prevent preterm birth and to reduce stillbirths as well as maternal and neonatal deaths plus other adverse health outcomes associated with an early birth. These interventions encompass services delivered during antenatal care for all pregnant women and women at high risk of preterm birth, services provided to manage preterm labor and interventions targeted at improving health behaviors and knowledge about early warning signs of pregnancy complications, including preterm labor. They also include the provision of needed social and financial support to disadvantaged mothers as well as workplace, professional and other supportive policies promoting safe motherhood and women's universal access to antenatal care.

Increasing access to care during pregnancy is an essential step towards addressing the growing problem of preterm birth. Research has shown that women who receive antenatal care services are at lower risk for having a preterm birth than women who are not reached by the health system prior to delivery (Iams et al., 2008). Further studies are needed to determine if this association is related to the content of services provided during antenatal care visits or to differences between women who do and do not receive antenatal care.

Many countries around the world report high coverage levels of antenatal care, making antenatal care visits an opportune time to deliver proven interventions to all pregnant women (UNICEF, 2012). Yet, there are large and unacceptable inequities in coverage between and within counties. In order to help reduce preterm birth rates, it is critical that all pregnant women receive at least the basic package of recommended antenatal care services.

This chapter presents information about available interventions that can be delivered during pregnancy to reduce preterm birth rates and improve the health outcomes of the premature baby. The chapter also focuses on promising avenues of research on the pregnancy period that will contribute to a better understanding of the causes of preterm birth and ability to design interventions at the policy, health care system and community levels for scale up.

Priority packages and evidence-based interventions

Chapter 2 describes in detail the complex risk factors and multiple mechanisms believed responsible for both spontaneous and indicated types of preterm delivery, including possible epigenetic/genetic predispositions. As noted, the majority of preterm births occur spontaneously often with prelabor Premature Rupture of the Membranes (pPROM). Medically and non-medically indicated preterm births are related to early induction of labor or cesarean birth. Medical indications include pregnancy complications such as placental abnormalities (e.g., placenta previa), multiple gestations, maternal diabetes, high blood pressure, pre-eclampsia, asthma, and thyroid and heart disease. Strategies for preventing or managing these two types of preterm births during the pregnancy period may differ due to variances in their underlying pathophysiological processes. There are a large number of preventive interventions for spontaneous and indicated types of preterm birth that are currently part of the standard of care in high-income countries. Many of these interventions are not readily available or feasible to introduce in low- and middle-income countries, and supportive evidence of their effectiveness is lacking.

Available and proposed preterm birth interventions are tailored for delivery to three population groups: (1) all pregnant women; (2) pregnant women with a history of previous preterm delivery or other risk factors, including multiple gestation, bleeding during pregnancy, hypertensive

Table 4.1: Priority packages and evidence-based interventions during pregnancy to reduce preterm birth rates and to benefit the premature baby

Services delivered during antenatal care:
• Basic package for all pregnant women • Situational interventions (e.g., identification and treatment of malaria, tuberculosis and HIV) • Additional interventions as needed (e.g., behavioral, social support and financial interventions, nutritional interventions including calcium supplementation)
Management of pregnant women at higher risk of preterm birth including:
• Identification and treatment of hypertensive disease in pregnancy • Monitoring multiple pregnancies • Administration of progesterone to prolong pregnancy • Identification and treatment of structural abnormalities (e.g., cervical cerclage, cervical pessary)
Management of women in preterm labor including:
• Tocolytics to slow down labor • Antenatal corticosteroids to reduce mortality in the newborn • Antibiotics for pPROM to prevent infection • Provision of magnesium sulphate for neuro-protection of the newborn
Community interventions:
• Promote antenatal and skilled delivery care for all women • Smoking cessation and reducing exposure to secondhand smoke and other pollutants
Policy interventions:
• Policies to support safe motherhood and universal access to antenatal care • Workplace policies regulating working hours and strenuous working conditions • Professional and hospital policies to regulate infertility treatments and to reduce cesarean birth rates and early induction of labor

disorders and diabetes; and (3) pregnant women experiencing or recovering from preterm labor. Interventions for the first two population groups are aimed primarily at prevention and range from basic and specialized packages of antenatal care services as well as supportive workplace and professional policies. Interventions designed for the third group are focused on improving the health outcomes of the premature baby. At the individual level, quality clinical care involves practitioners identifying each woman's own set of risk factors throughout the pregnancy period and responding with appropriate care.

Only those interventions or intervention areas with proven or potential effectiveness in either reducing preterm birth rates or improving birth outcomes for the premature baby are identified in Table 4.1. Exhaustive systematic reviews on preterm birth interventions for the pregnancy period serve as the source of information for these descriptions (Haas, 2011; Barros et al., 2010; Blencowe et al., 2011; Cousens et al., 2010; Goldenberg et al., 2008; Imdad et al., 2011; Mwansa-Kambafwile et al., 2010; PMNCH, 2011; Rubens et al., 2010) and the Cochrane database (The Cochrane Collaboration, 2012), which includes regularly updated systematic reviews on available evidence from clinical trials, considered the most robust evidence for guiding policy and program development. A list of Cochrane reviews on preterm birth-related interventions for delivery during the pregnancy period is provided in the web annex.

Antenatal care services for prevention of preterm birth for all women

Culturally appropriate and effective care during pregnancy is essential for increasing the likelihood of positive birth outcomes (WHO, 2005b). Antenatal care is a service delivery platform through which all women can be reached at multiple times during pregnancy with a package of interventions that can prolong a healthy pregnancy and improve maternal and perinatal health. Basic services that can be delivered during antenatal care with a potential impact on reducing preterm birth rates include identification of women at high risk of preterm birth; screening for and treatment of sexually transmitted diseases including HIV and other infections (tuberculosis, malaria, bacterial vaginosis, bacteriuria); identification and correction of malnutrition and nutrition counseling; counseling on birth preparedness and complication readiness for identification of early labor and other risk factors; and behavioral and social support interventions such as smoking cessation programs and programs aimed at the prevention of violence against women (NICE, 2008; WHO, 2003a, 2003b, 2003c, 2005a, 2005b; Holbrook and Kaltenbach, 2011).

Infections during pregnancy can cross into the intra-amniotic

cavity, establish intra-amniotic infection and result in preterm labor. In some women, such infections are associated with prelabor rupture of the membranes (Goldenberg et al., 2008). Screening for and treatment of infections such as asymptomatic bacteriuria and bacterial vaginosis during antenatal care may reduce preterm births, although study findings show inconsistent results. Systematic reviews and meta-analyses show that antibiotic treatment for infection and periodontal care does not reliably reduce the risk of preterm birth, and effectiveness may depend upon when during pregnancy the infection or periodontal disease is detected and treated. This finding emphasizes the need for more research on the inter-relationships between infection, pregnant women's immune response, and the cascade of events resulting in preterm birth (Menon, 2008). Such research can inform the development of optimal screening and treatment protocols based on underlying risk factors that will take into consideration when in pregnancy screening and treatment for infections should occur to reduce the preterm birth rate (Iams et al., 2008).

The advantages of prophylactic treatment for malaria (intermittent presumptive treatment during pregnancy for malaria [IPTp]) and the use of bednets to prevent malaria transmission in malaria-endemic areas on reducing preterm birth similarly needs further investigation. More rigorous studies examining the impact of HIV infection and the use of antiretrovirals and TB medication during pregnancy on the risk of preterm birth that control for disease stage and other potential confounding factors are also needed (Barros et al., 2010).

Women's nutritional status during pregnancy has been linked to preterm birth, with underweight and obese pregnant women at elevated risk of preterm birth and other poor obstetrical outcomes as noted in Chapter 3 (Institute of Medicine, 2007; Goldenberg et al., 2008). Malnutrition increases vulnerability to infection and predisposes pregnant women to adverse obstetrical outcomes including preterm delivery, although findings on obesity and the risk of preterm birth are mixed. Recent research suggests that the association between body mass index (BMI) and risk of preterm birth may differ by race or ethnic group, underscoring the complexity of the role nutrition plays in triggering preterm birth (Torloni et al., 2012). Providers can administer nutritional supplements and counseling services during routine antenatal visits. Evidence from clinical trials to date does not, in general, show a clear beneficial effect of dietary supplements (e.g. zinc, calcium, magnesium, fish oil), nutritional counseling, or protein and calorie supplements during pregnancy on the preterm birth rate. Further research is needed to determine the optimal timing during a woman's life course of introducing nutritional interventions for reducing the risk of preterm birth and how best to implement these interventions within the broader context of efforts to improve the overall nutritional status of pregnant women and women of reproductive age. Pregnant women should be encouraged to take multivitamin supplements and to gain an adequate amount of weight based on their nutritional status at the beginning of their pregnancy for other health-promoting reasons such as reducing the risk of low birthweight and neural tube defects.

Photo: Thomas L. Kelly/Save the Children

Antenatal care services for prevention of preterm births, women at higher risk

Women at increased risk of preterm delivery can be identified during antenatal care based on obstetric history (e.g., known uterine or cervical anomaly or previous preterm birth) or presenting pregnancy characteristics (e.g., hypertensive disorder of pregnancy, diabetes, multiple gestation, bleeding). Young adolescents also are at greater risk (Moore, 2002; Tsikouras et

Box 4.1: Antenatal corticosteroids

Evidence from more than 20 clinical trials and additional studies in middle-income countries such as Brazil, Jordan, South Africa and Tunisia indicate that antenatal corticosteroids administered to pregnant women at high risk of preterm birth is a highly effective and safe intervention for reducing neonatal mortality ("The effect of antenatal steroids for fetal maturation on perinatal outcomes-statement," 1994; Roberts and Dalziel, 2006; Amorim et al., 1999; Fekih et al., 2002; Pattinson et al., 1999; Qublan et al., 2001). A summary of the trial data shows a 34% relative reduction in the incidence of respiratory distress syndrome (risk ratio [RR] 0.66, 95% confidence interval [CI] 0.59–0.73), a 46% relative reduction in intraventricular hemorrhage (RR 0.54, 95% CI 0.43–0.69) and a 31% relative reduction in neonatal mortality (RR 0.69, 95% CI 0.58–0.81). Similar findings were recorded in the studies carried out in low- and middle-income countries. The results suggest that for every 100 women treated appropriately with antenatal corticosteroids, 4 neonatal deaths, 9 cases of RDS, 4 intraventricular hemorrhages and 12 cases of surfactant use would be avoided.

An analysis using the Lives Saved Tool (described in Chapter 6) shows that achievement of universal (95%) coverage of antenatal corticosteroids across the 75 Countdown to 2015 priorities countries would result in an approximate 40% decrease in preterm-associated mortality in 2015 — translating to around 373,000 deaths averted per year in comparison to 2010 levels.

The WHO lists antenatal corticosteroids as a priority intervention for the prevention of respiratory distress syndrome in premature babies, and considers antenatal corticosteroids (both betamethasone and dexamethasone) as a priority medicine for reducing mortality among babies born too early (PMNCH, 2011). Dexamethasone is included on the WHO essential medicines list, but at the time of publication this is for treating allergies only (Lawn et al., 2012).

Use in low- and middle-income countries – A need for scale up

Although the evidence of the effectiveness of antenatal corticosteroids was established more than 15 years ago, usage rates remain unacceptably low. In 2000, it was estimated that in the 42 countries with 90% of the worldwide childhood deaths, only 5% of appropriate candidates received the intervention (Jones et al., 2003). Another study based on data from 75 countries estimated that only 10% of eligible mothers received antenatal corticosteroids (Darmstadt et al., 2005). In Latin America, six studies between 1999 and 2009 reported that the use of antenatal corticosteroids in premature babies ranged between 4% and 71% (Colomar et al., 2004; Forteza et al., 2002; Krauss Silva et al., 1999; Vallejo Valdivieso et al., 2002; Vargas-Origel et al., 2000). These figures are a clear indication of major missed opportunities around the world for improving the survival chances of preterm babies.

Research gaps

To date, all trials have been conducted in hospital settings, most of them referral facilities with availability of high-level care (oxygen, incubators, ventilators). The next step is to assess the effect of antenatal corticosteroids on maternal and neonatal health in lower-level facilities or home births where no specialized care is available at childbirth.

Lessons learned – an implementation agenda

In the United States, low provider use of antenatal corticosteroids 20 years ago was successfully addressed through the development of a multifaceted intervention including informing local opinion leaders, the introduction of the intervention into clinical grand rounds, chart reminders, group discussions, and audit and feedback practices (Leviton et al., 1999). WHO conducted a trial in 22 hospitals in Mexico and 18 hospitals in Thailand to evaluate the effect of a multifaceted educational strategy to promote the use of the WHO Reproductive Health Library (Development and Research Training in Human Reproduction, 2012) on several obstetric practices, including the use of antenatal corticosteroids in preterm births at less than 34 weeks gestation. The results showed no changes in the low use of antenatal corticosteroids in these hospitals (Gulmezoglu et al., 2007). The findings of the WHO study suggest that education alone is not enough to change clinical practice. Instead interventions need to be designed that combine training with appropriate supervision and clinic reminders. In low- and middle-income countries, implementation strategies that address supply-chain problems must also be prioritized to reduce occurrence of stock-outs.

In recognition of the many challenges related to the uptake of proven interventions such as antenatal corticosteroids, the United Nations established a Commission on Life-saving Commodities for Women and Children in 2012. The Commission is reviewing recommendations for addressing the supply-chain, training requirements, and other implementation barriers faced by low- and middle-income countries in their efforts to scale up antenatal corticosteroids (the aims of the Commission are described in Chapter 6) (Lawn et al., 2012).

al., 2012) (see Chapter 3 for more details). Although prospective studies that evaluate the use of risk-screening tools based on epidemiologic, demographic biomarkers and clinical indicators in routine antenatal care are still needed, there are several approaches for providing preventive care for these women. One such approach includes specialized antenatal clinics for women with evident risk of preterm birth that provide enhanced health education and more rigorous monitoring and treatment of risk factors and pregnancy complications. The evidence is scanty on such approaches in reducing the risk of preterm birth, but trials were conducted prior to the introduction of new screening tests.

Administration of progesterone to prolong pregnancy in high-risk women with a history of previous preterm birth has been shown effective in preventing a recurrence of preterm birth in these women and in decreasing the prevalence of low birthweight (Barros et al., 2010). Recent guidelines and professional opinion recommend administering vaginal progesterone to women with singleton pregnancies and short cervical length to reduce preterm birth and perinatal morbidity and mortality (Berghella V., & The Society for Maternal-Fetal Medicine: Publication Committee, 2012). Most studies to date on the use of progesterone have been conducted in high-income countries. There is a need for evidence generation on progesterone use in resource-constrained settings including how this intervention can be scaled up at national level and the feasibility of introducing universal cervical length measurement screening.

Cochrane reviews have shown small reductions in preterm birth rates with treatment interventions for pre-eclampsia such as calcium supplementation. A recent randomized controlled trial has shown promising results for the use of a cervical pessary to lower rates of spontaneous preterm birth among women with a short cervix (Goya et al., 2012). Another promising intervention in reducing the risk of preterm birth that requires further investigation is the placement of circumferential stitches on a structurally weak cervix (cerclage) (Haas, 2011; Barros et al., 2010).

These interventions are only applicable to a small number of high-risk women, however, and the overall effect on general population rates of preterm birth is likely to be limited.

Management of women in preterm labor to improve survival chances of the premature baby

Once preterm labor has commenced, there are interventions that can prolong pregnancy and improve health outcomes and survival for the premature baby. To date, these interventions have not been designed to address the underlying mechanisms that trigger preterm labor.

Interventions to prolong pregnancy include the provision of tocolytic agents that inhibit uterine contractions to suppress labor (e.g., oxytocin antagonists, betamimetics, calcium channel blockers, magnesium sulphate), and clinical practices to ensure the optimal timing of cesarean birth and labor induction for indicated preterm births. The provision of tocolytics has been shown effective in slowing down labor, enabling the administration of antenatal corticosteroids and transfer of mother and baby to a higher-level facility where appropriate care may be available. Any use of strategies to prolong labor, including delaying cesarean birth, must be evaluated against the potential risk of continued exposure of mother and fetus to sub-optimal conditions that may result in harmful effects. Further research is needed on the short- and long-term health consequences for mother and baby from efforts to prevent preterm labor.

There are three key interventions that can be delivered during the pregnancy period with evidence of effectiveness in improving health outcomes in the premature baby: antenatal corticosteroids, antibiotics for pPROM, and magnesium sulphate.

The administration of antenatal corticosteroids to pregnant women at high risk of preterm birth possibly as early as 23 weeks can significantly reduce the premature baby's risk of death, respiratory distress and developmental problems (Box 4.1).

Premature rupture of the membranes is strongly associated with infection of the amniotic membranes contributing to preterm birth and other poor fetal outcomes such as cerebral palsy and chronic lung disease. Antibiotic treatment for pPROM has been shown to delay onset of labor for up

to 48 hours and to reduce neonatal infections and abnormal cerebral ultrasound scans prior to hospital discharge.

The administration of magnesium sulphate to women at risk of preterm birth helps to protect the baby's brain, reduce rates of cerebral palsy and improve long-term neonatal health outcomes. Further studies are needed, however, to investigate side effects of the treatment for the mother (e.g., flushing, sweating, nausea, vomiting, headaches and a rapid heartbeat) and how these can be reduced.

Behavior and community interventions for the prevention of preterm birth

Lifestyle factors including depression, intimate partner violence, smoking, substance abuse and stress are risk factors for preterm birth. Antenatal care models that address these issues and provide social and financial support for pregnant women and particularly disadvantaged/at-risk population groups have been associated with reduced rates of preterm birth. There are numerous efforts underway to determine how best to integrate psychological and behavioral interventions, including programs to prevent violence, into antenatal care to improve preterm birth rates and other maternal and neonatal health outcomes. Controlled trials need to be designed to further test the efficacy of antenatal care approaches that incorporate social and financial support measures so that such approaches can be introduced at scale in settings where they are most needed.

Smoking during pregnancy is a well-known cause of preterm birth, especially preterm birth complicated by pPROM. Smoking cessation interventions in high-income countries that combine counseling with additional social support services have been found to significantly reduce preterm birth and should be adapted for application in low- and middle-income countries where the large majority of smokers live (Ballard and Radley, 2009; "Committee opinion no. 471: Smoking cessation during pregnancy," 2010).

Other programs such as the Healthy Babies are Worth the Wait™ campaign of the March of Dimes and the "humanization of childbirth" social movement in Brazil and other Latin American countries that educate women with healthy pregnancies about the advantages of vaginal delivery and waiting until 39 weeks to deliver should be promoted, particularly in contexts characterized by high and rising elective cesarean birth rates (Davis-Floyd, 2007; March of Dimes, 2011). Health care provider education on the adverse health outcomes of late preterm birth and of inducing delivery for non-medical reasons prior to 39 weeks has been shown to be effective in reducing preterm birth rates in some countries such as Brazil (Behague et al., 2001; Campbell, 2009; Rattner et al., 2009).

Photo: *Ahman El-Nemr/Save the Children*

Policy interventions to promote healthy pregnancies

Pregnant women can experience a reduced risk of preterm birth and other health benefits from professional and public policies based on sound scientific evidence. Chapter 2 shows that the risk of preterm birth increases in women with twins and higher-order births. Policies on infertility treatments and use of assisted reproductive technologies directed to limiting the number of embryos that can be transferred have shown success in reducing the number of higher-order births and the associated high risk of preterm birth in Europe, Australia and the United States (Iams et al., 2008; Jain et al., 2004; Min et al., 2006).

Hospital policies aimed at lowering the primary cesarean birth rate and early induction rates, particularly for non-medically indicated reasons, are part of a growing effort to prolong pregnancy, promote healthy newborn outcomes and reverse the increasing trend of preterm birth. Such policies are especially needed in regions where cesarean birth rates, and particularly elective cesarean birth rates, are high or rising like Latin America and in many high-income countries.

Legislation mandating universal access to maternal health care services and eliminating user fees in low- and middle-income countries also have been shown to be an important prerequisite to ensuring all women receive antenatal care.

Workplace policies designed to promote healthy pregnancies and protect pregnant women from occupational hazards can potentially reduce the risk of preterm birth. Examples include, but are not limited to, time off for antenatal care visits, paid pregnancy leave for a set number of weeks and exemption from night shifts and tasks requiring heavy lifting or standing for long periods of time (Saurel-Cubizolles et al., 2004). Studies have shown that carrying heavy workloads and working more than 5 days a week are associated with preterm birth (Agbla et al., 2006). Measures that can improve general working conditions are especially important for pregnant women in low- and middle-income countries where they are more likely to be engaged in agricultural labor and other physically demanding tasks.

Pregnant women can benefit from legislation reducing their exposure to potentially harmful environmental risk factors such as second-hand smoke and air pollution (combustion and household sources). There is growing interest in understanding and developing policy and programmatic solutions to the association between air pollution and adverse pregnancy outcomes including preterm birth (Ritz and Wilhelm, 2008; Leonardi-Bee et al., 2008; Pearce et al., 2012; Sram et al., 2006; Sapkota et al., 2010). For example, the UN Foundation houses the Global Alliance for Clean Cookstoves, a multi-partner effort launched in 2010 to promote clean and efficient cookstoves. Traditional cookstoves and open fires, the primary means of cooking and heating for nearly three billion people in the developing world, place pregnant women at increased risk of preterm birth and other poor obstetrical outcomes.

Limitations of the evidence

The clinical trial literature shows a lack of evidence for many of the preventive interventions currently in use. The multi-causal and complex nature of preterm birth is likely responsible for single interventions not showing a significant public health effect and it is thus doubtful that rates of preterm birth can be reduced by the delivery of one single intervention. There is, therefore, an imperative need for well-designed studies examining the effectiveness of interventions delivered alone or as an integrated package of antenatal care. Epidemiological research is needed to assess the effectiveness of introducing a comprehensive set of science-based interventions delivered at the policy, health system and community or home levels on reducing the rate of preterm birth. The scientific literature and technical reports similarly show evidence for only a handful of interventions delivered during pregnancy that can improve the health outcomes of babies born too early, again stressing the need for more research on available and promising interventions. This emphasis on research and generation of quality data, however, needs to be balanced with the further promotion and worldwide scale up of interventions with proven effectiveness.

The brevity of the list of interventions delivered during the pregnancy period with evidence of effectiveness for preterm birth prevention and for improving survival chances of the premature baby is related to long-standing neglect of the newborn period and to insufficient research on the biological complexities of pregnancy and childbirth. The growing concentration of child deaths in the newborn period and the emergence of organizations and efforts focused on the newborn (e.g., The Healthy Newborn Partnership in the mid-2000s, and Saving Newborn Lives) have served as a catalyst for focused attention on preterm birth, a leading cause of newborn mortality (Shiffman, 2010; Bustreo et al., 2012). There is an increasing emphasis on research that can inform the development of cohesive strategies for addressing the underlying determinants of preterm delivery with the goal of reducing the numbers of preterm births.

Program opportunities to scale up

Coverage of antenatal care (at least one visit) is approximately 80% worldwide, with coverage levels dropping to about 56% for four or more visits. Inequities in coverage are pervasive, with coverage levels of four or more antenatal care visits hovering around 40% for the least developed countries (UNICEF, 2012). These figures indicate that efforts aimed at improving availability of antenatal care, demand for care and women's ability to reach these services throughout the pregnancy period are needed, particularly in low-resource settings and amongst

the most disadvantaged population groups. Adolescents are another group at high risk of preterm birth due to their young age and typically limited access to preconception and prenatal care (see Chapter 3).

Figure 4.1 shows missed opportunities in the provision of antenatal care services to pregnant women living in the Countdown to 2015 priority countries where more than 95% of all maternal and child deaths occur (Requejo et al., 2012). Consistent with the global data, the figure shows high levels of at least one visit of antenatal care across the Countdown countries, but considerably lower levels of the recommended four or more antenatal care visits. This indicates that the majority of women in these countries are not benefiting from the recommended basic package of antenatal care services. The figure also highlights substantial gaps in the quality of care pregnant women are receiving during antenatal care visits, with coverage levels of specific evidence-based interventions considerably lower than the ideal of universal coverage. A similar review of gaps in the provision of key components of antenatal care in sub-Saharan Africa, where the rates and absolute numbers of preterm birth are among the highest in the world, similarly showed low levels of coverage of several recommended components (Beck et al., 2010; Kinney et al., 2010). These missed opportunities are a call to action for strengthening health systems in the Countdown priority and other low- and middle-income countries including ensuring practitioners are equipped with the skills and necessary drugs and equipment to deliver effective antenatal care that can potentially reduce the risk of preterm birth and improve health outcomes of the premature baby.

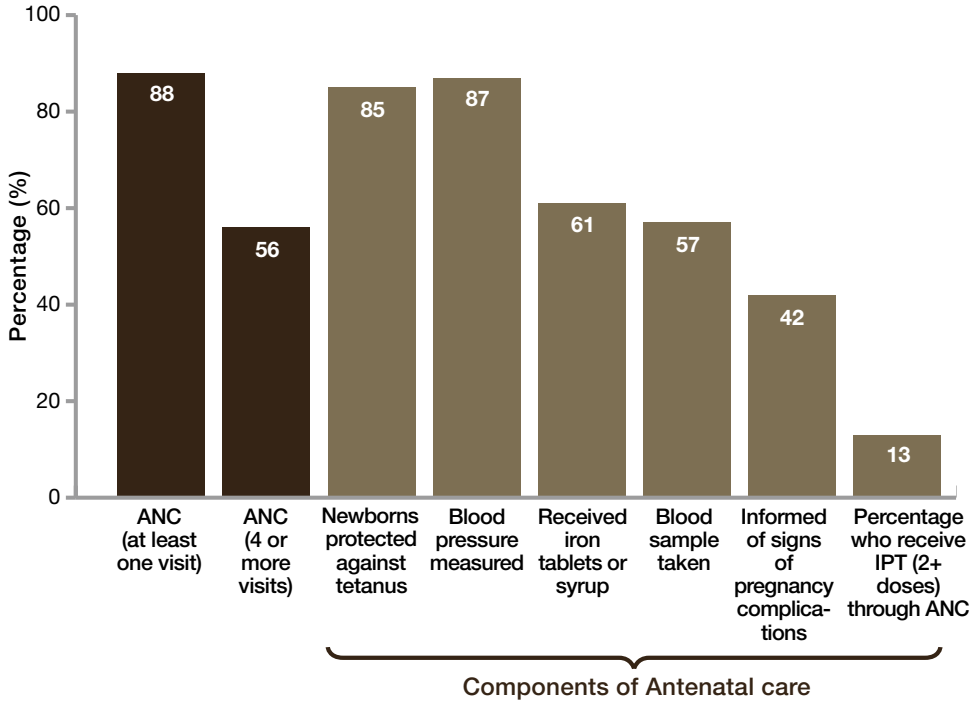
Table 4.2: Coverage levels of key interventions, pregnant women in labor, 24 to 34 weeks, after 3 hours in the hospital, World Health Organization 18 country study

Intervention	All countries*	Mexico
Antenatal corticosteroids	56.4%	53.8%
Tocolytic agents		
Beta mimetics	15.8%	8.2%
Calcium channel blockers	9.9%	7.7%
Magnesium sulphate	7.8%	4.9%
Oxytocin antagonists	1.2%	2.4%

*Countries include Afghanistan, Argentina, Cambodia, China, Ecuador, Japan, Kenya, Mexico, Mongolia, Nepal, Nicaragua, Pakistan, Paraguay, Peru, Philippines, Thailand, Sri Lanka and Vietnam
Data source: Souza et al., 2011. Preliminary results, World Health Organization, Multi-country survey on maternal and newborn health.

Table 4.2 shows coverage levels of preterm birth-related interventions available from a World Health Organization multi-country study on the prevalence of maternal near-miss cases with a key objective of mapping the use of evidence-based interventions during childbirth in health care facilities (Souza et al., 2011). At the time of publication, country-specific data were available only for the Latin American countries involved in the study, and Mexico is presented as an example. The low coverage levels shown in Table 4.2 should serve as a starting point for dialogue with governments, development partners and health care providers in the study countries on developing strategies for increasing the uptake of these science-based interventions.

Figure 4.1: Missed opportunities to reach pregnant women with antenatal care services, median for Countdown to 2015 priority countries



Source: UNICEF Global Databases, February 2012, based on Demographic Health Surveys, Multiple Indicator Cluster Surveys and other national surveys.
Note: Countdown to 2015 priority countries with available data, 2006-2010. Acronyms used: ANC = antenatal care; IPT = intermittent presumptive treatment

Table 4.3: Research priorities during pregnancy to reduce preterm birth rates and to benefit the premature baby

Description
Epidemiological research to: • Examine the relationships between maternal risk factors and preterm birth at a population level (e.g., nutritional, infection, age and other socio-demographic factors
Discovery
Basic science research on normal and abnormal pregnancies to: • Identify the causal pathways leading to preterm labor and delivery • Understand the gestational clock triggering the onset of labor • Explore the genetic determinants of preterm birth and genetic-environment interactions increasing risk of preterm birth
Development
Translational research to: • Develop simple screening tools based on the findings of biological and genetic research for identifying women at high risk of preterm birth and preterm labor • Develop robust diagnostic tools for universal application (e.g., anaemia, syphilis)
Delivery
Clinical trials and other studies to: • Build the evidence base on available and promising interventions • Determine effectiveness of interventions delivered individually and as packages of care Implementation research to: • Address coverage gaps by increasing the availability of antenatal care and women's ability to access services around the world • Address quality of care gaps by increasing the uptake of evidence-based interventions and intervention packages by health care providers (e.g., syphilis testing and screening, blood pressure monitoring during antenatal care visits, etc.)

Priority research themes for the pregnancy period and childbirth

There is an imperative need for research on preterm birth that can yield quality data on the efficacy of existing and promising interventions delivered individually or as a package during the pregnancy period. There is an equally critical need for implementation research to improve the scale up of proven policy and health care interventions in low- and middle-income countries. There has been growing interest in preterm birth in recent years and in developing a comprehensive research paradigm to address this growing cause of neonatal mortality. A major emphasis of the paradigm has been on discovery science to shed light on the basic biology of normal and abnormal pregnancies so that the pathological process of preterm birth can be understood and effective interventions developed. This research (described in more detail in chapter 6) will also potentially result in the development of better screening tools for the prediction and prevention of preterm labor. The link between genetics, gene-environment interactions and preterm birth is being investigated with the hope of gaining an understanding of differences in preterm birth rates across racial and ethnic groups that can be translated into more effective and equitable clinical care guidelines including counseling and screening services (Menon, 2008; Biggio et al., 2008). Research is underway to explore the connections between maternal infections, nutritional status and preterm birth within a broader framework of research on prematurity, low birthweight and intrauterine growth restriction (Box 4.2). In addition, research on the social determinants of preterm birth is being conducted to explore the pathways between social disadvantage, behavioral and lifestyle factors and preterm birth (Collins et al., 2004; Messer et al., 2010; Schempf et al., 2011). A major goal of this research is to help develop strategies for addressing social and economic disparities in preterm birth rates, inequities in access to needed care between and within countries as well as how to best integrate social and behavioral interventions into antenatal care.

Box 4.2 presents information on select ongoing research activities to generate the evidence needed to inform the development of effective preventive programs and policies. Table 4.3 summarizes the key interrelated areas of priority research on preterm birth in the pregnancy period, emphasizing that simultaneous progress in each of these areas is critical for achieving reductions in preterm birth rates and optimal birth outcomes for the premature baby.

Prescription for action during the pregnancy period and childbirth

A standard approach to preterm birth prevention during the pregnancy period hinges upon the findings of the ongoing research on the causal pathways to preterm delivery. Clinical management practices will need to remain flexible as practitioners decide upon a course of action based on the particular characteristics and set of risk factors of their individual women clients. There are, however, basic steps that countries around the world can introduce now and as resources permit to begin making strides towards addressing

this growing public health problem. These steps are summarized in Table 4.4 and described in more detail below.

As a first step, national policies and guidelines for comprehensive antenatal, labor and delivery, emergency obstetric and postnatal care should be established in all countries to promote universal access to quality maternal and perinatal services. Pro-poor legislation (e.g., to abolish user fees, introduce conditional cash transfer programs, etc.) for maternal and perinatal services should be considered in low- and middle-income countries where out-of-pocket expenses are high and/or coverage levels of antenatal and delivery care interventions are low. Protective legislation is needed to improve general working conditions for pregnant women, and to reduce pregnant women's exposure to potentially harmful environmental, behavioral and lifestyle risk factors such as second-hand smoke and violence against women.

The implementation of national and professional policies and guidelines that are in-line with science-based recommendations, such as those made by WHO, needs to be prioritized. All countries and their partners should allocate sufficient resources to strengthening health care systems to facilitate the implementation process and enable the equitable and early delivery of quality antenatal care. Resources also are needed to develop clearly defined care and referral pathways. Prevention needs to be prioritized through improving access to screening and diagnostic tests and appropriate treatment during antenatal care with adequate follow-up and referral of women identified at high risk of preterm birth.

Efforts to strengthen health systems must include increased and regular training opportunities for health care providers on the use of effective interventions, and on tailoring clinical care to the individual woman based on her risk profile throughout the duration of her pregnancy. The delivery of all recommended components of antenatal care should be regularly instituted and monitored through supportive supervision.

These health care system readiness efforts need to be complemented by communication and education campaigns to increase demand for maternal and perinatal care services and to ensure prospective parents and community members are fully informed about a healthy pregnancy and potential complications.

In settings with greater capacity, professional policies regulating assisted reproductive technologies and infertility treatments should be put into place to reduce the number of multiple gestations at higher risk of preterm birth. Genetic counseling and adequate counseling for women over the age of 35 on pregnancy risks also should be included as components of antenatal care.

All women should be provided with access to quality antenatal care services and a functional referral system throughout pregnancy. Women should be encouraged to give birth in health care facilities and have access to health care facilities where quality maternal services are guaranteed. Community members need to be informed about the importance of all women receiving antenatal care and delivering in functioning health care facilities as well as warning

Table 4.4: Actions during pregnancy to prevent or manage preterm birth

Invest and plan
• Ensure national policies and guidelines exist and provide adequate protection of pregnant women and universal access to comprehensive antenatal, labor and delivery, emergency obstetric and postnatal care. • Allocate adequate resources for the provision of equitable and high-quality antenatal care, and removal of barriers to care such as user fees.
Implement
• Seize opportunities to leverage resources, approaches, and training opportunities from existing programs (including non-health programs) • Ensure the existence of a functional referral system, procurement system, an adequately trained and supervised health work force, and quality services for all pregnant women. Inform communities about the importance of antenatal, delivery and postnatal care for all women, and warning signs including early recognition of preterm labor.
Inform and improve program coverage and quality
• Address data gaps and increase sound monitoring and evaluation of programs to improve service quality and outreach to the poorest populations. • Prioritize implementation research to promote the scale up of effective interventions in different contexts and across different population groups.
Innovate and undertake implementation research
• Invest in discovery research on the basic biology of normal and abnormal pregnancy, genetic determinants of preterm birth, and epidemiological research on maternal risk factors to provide the evidence base needed for the development of effective prevention and treatment strategies.
We all share in the responsibility of making sure pregnant women around the world receive the care they need for healthy birth outcomes.

Photo: Michael Bisceglie/Save the Children

signs in pregnancy including preterm labor. In low- and middle- income countries, communities need to be supported in developing appropriate mechanisms that enable women to seek care, particularly the most disadvantaged women who face multiple barriers to accessing timely care.

The integration of effective services should be promoted to best use antenatal care visits as a platform for the delivery of a package of interventions and to leverage scarce resources for women's and children's health. The integration of HIV, malaria, and social and financial support programs into routine antenatal care, for example, represents an efficient use of resources with potential to reach a large majority of pregnant women.

Health care facilities need to be equipped with trained staff and ample and consistent supplies of drugs and equipment so that women can be guaranteed provision of antibiotics for pPROM, antenatal corticosteroids, progesterone, magnesium sulphate and tocolytics as needed.

Countries need to engage in collaborative and multi-center research for the development of high-quality evidence on available and promising interventions delivered singly and as a package during antenatal care or labor and delivery. Adequate funding is needed for basic science research on the etiology of preterm birth, the physiological processes of healthy and abnormal pregnancies and the linkages between preterm birth and genetics, environment, stress and depression, infection and nutrition. Findings from such research will guide the development of preventive interventions, diagnostic markers and related screening tools and better clinical management guidelines for all women and for women at high risk of preterm birth. These cross-country, multi-disciplinary research efforts will ultimately facilitate the discovery and development of interventions with universal application.

Implementation research is essential for determining how research findings can be best translated into practical application in low- and middle-income countries where resource constraints and inequities in intervention coverage are more pronounced and where innovations in service delivery strategies are most needed. Efforts are needed, for example, on how to most effectively integrate evidence-based interventions into antenatal care in specific contexts so that pregnant women are reached with comprehensive and culturally appropriate packages of care.

National audit and other monitoring and evaluation systems at facility level need to be put into place as a quality control measure to track preterm birth rates and the use of effective services during antenatal care and labor and delivery.

In all settings, ongoing monitoring and evaluation of the implementation of guidelines and policies are essential for ensuring that pregnant women receive high-quality care based on the best evidence.

Conclusion

The pregnancy period is a time of great excitement for prospective parents. It represents a time period when a woman can be reached through a variety of mechanisms with interventions aimed at reducing her risk of a preterm birth and improving her health and the health of her unborn baby. One key mechanism is routine antenatal care during which a woman should receive a range of effective services at multiple times throughout her pregnancy that are tailored to her individual risk profile. She also can benefit from supportive policies and programs that increase her access to quality care and protect her from potentially harmful exposures. The message is clear: We all need to work together to make it possible for women everywhere to receive the care they need during pregnancy, labor and delivery as a starting point for successfully addressing the growing problem of preterm birth.

This involves simultaneous and coordinated action in the three main areas of service delivery, discovery and development. Although there are substantial gaps in our knowledge of the underlying causal pathways of preterm labor and delivery, we know there are proven interventions that need to be scaled up now. Governments and their partners must prioritize the equitable delivery of these interventions through innovative and cost-effective strategies. At the same time, basic research and discovery science must be promoted to build the evidence base so that effective preventive and treatment interventions can be designed. This will require collaborative partnerships across institutions and countries. As the evidence is generated, resources need to be allocated to its translation into new and better screening and diagnostic tools and other interventions aimed at saving maternal and newborn lives. The time is now to put this action plan into motion.

Box 4.2: Building the evidence base on preterm birth

The International PREterm BIrth Collaborative (PREBIC):

A nonprofit organization, supported by WHO and the March of Dimes (www.prebic.net), is a multidisciplinary global network of clinicians and scientists conducting research to develop clinical interventions to reduce the rate of preterm birth globally. PREBIC's annual workshops hosted by WHO have resulted in concrete action steps to fill several knowledge gaps, including estimation of the global preterm birth rate, systematic reviews (e.g., on genetic markers, biomarkers and risk factors such as BMI) and guidelines on conducting basic and clinical research on preterm birth. PREBIC educational activities include organizing satellite symposiums in association with major perinatal and obstetric congresses. PREBIC is establishing research core centers and collaborating with other organizations to set up data and biological sample repositories to further promote preterm birth research.

The Preterm Birth Genome Project (PGP) is a multinational collaborative study of gene-environment Interactions in spontaneous preterm birth that is part of PREBIC and aims to identify genes that increase susceptibility to preterm birth, using genome-wide association as an initial tool. The project involves a five year five-phase research plan including a whole genome analysis to determine genetic variants associated with spontaneous preterm birth. PGP has conducted a two-phase genome-wide association study for preterm births at less than 34 weeks gestation using maternal DNA samples from Caucasian populations. Genes increasing susceptibility to preterm birth were identified, and risk of preterm birth was shown to increase directly with the number of adverse genes a woman has (odds of preterm birth increased from 1.5 with one adverse gene to 1.9 and 3.2 with two and three adverse genes, respectively). The PGP findings of common genetic variants linked to preterm birth have been replicated in three additional cohorts. The next step is to validate these results through multiple cohort studies with the hope that these identified genetic variants can be used to develop an early screening tool, even for use prior to pregnancy.

The Preterm Birth Biomarker Project (PBP) is a joint PREBIC/WHO/March of Dimes initiative aimed at identifying preterm birth biomarkers that can be used for risk screening. Research in the past four decades on more than 115 potential biomarkers has not yielded identification of a single biomarker that can accurately predict preterm birth risk, and suggests that preterm birth risk may be related to the interaction of multiple biomarkers. The PBP is testing this hypothesis with the long-term objective of using the results to inform the development of accurate screening tools (Menon et al., 2011).

The Child Health Epidemiology Research Group (CHERG):

CHERG was appointed by WHO and UNICEF to advise the United Nations on epidemiological estimates for child health (http://cherg.org/). CHERG developed the first national and global estimates of neonatal causes of death published in The Lancet Neonatal series in 2005, showing preterm birth to be the leading cause of neonatal deaths. These estimates are updated every two years by CHERG with WHO-led country review, and published in peer review journals. The 2010 estimates show preterm birth to be the second leading cause of child deaths. The CHERG neonatal team, with WHO, also developed the first national estimates of preterm birth featured in chapter 2 of this report as well as disability estimates for the Global Burden of Disease analyses. In addition, CHERG is undertaking an epidemiological assessment of intrauterine growth restriction (IUGR) as measured by small for gestational age (SGA), examining whether preterm birth modifies the associations between maternal risk factors and IUGR. The data sources are population-based or multiple facility-based data sets where gestational age, birthweight and maternal risk factors were measured. One source of data is the WHO Global Survey on Maternal and Perinatal Health. The analysis will estimate odds ratios for risk of preterm birth or SGA associated with various maternal risk factors to inform the development of tailored interventions to prevent these two causes of low birthweight.

Some other groups with global preterm birth prevention research as a major focus include, Global Alliance for Prevention of Prematurity and Stillbirths (GAPPS, see Chapter 6, Panel 11), the Genomic and Proteomic Network for Preterm Birth, and a number that are limited to within one country such as the US Maternal Fetal Medicine Units Network, or the Neonatal Research Network.

Grace Ngoto had tried to get pregnant for nine years and was overjoyed when she discovered that she was pregnant. Unfortunately in her seventh month of pregnancy, she began to have complications and her doctors decided to deliver the baby because her blood pressure was too high.

Photo: *Save the Children*

Her little girl was born in February 2006, arriving eight weeks early and weighing only 2.2 lbs (about 1 kg), "less than a packet of sugar," remembers Grace. She and her husband named their daughter Tuntufye, which means "Praise" in Malawi's Nkhonde dialect.

In her first couple of days, Tuntufye's weight dropped to 1.8 lbs (about 800 grams), and the doctors told Grace that her baby had a a less than 50% chance of survival because neonatal intensive care was not available. One of the nurses recommended Grace to a hospital in Malawi's capital city that taught mothers to practice Kangaroo Mother Care. Grace learned how to carry her little girl in Kangaroo position, tied with a cloth against her chest all day long. The skin-to-skin contact regulates the baby's body temperature since the mother's body acts as a heater, and the position promotes easy breast feeding and bonding between the mother and baby. The baby also feels secure close to the mother's heart.

Grace fed her little girl every hour, and with the help of Kangaroo Mother Care, little Tuntufye started to gain weight, adding grams every day. "You provide heat with the skin contact,

In her first couple days, Tuntufye's weight dropped to 1.8 lbs.

and you provide food easily, and when the baby is here the love is also here," says Grace. After a month at the Kangaroo Mother Care ward, Tuntufye had gained enough weight and was allowed to go home, where Grace continued the practice. Grace later became a community health worker and shares her story with pregnant women in the community, educating them about the benefits of Kangaroo Mother Care.

MALAWI

BABY TUNTUFYE

8 WEEKS PREMATURE

50% CHANCE OF SURVIVAL

Photo: *Save the Children*

Today Tuntufye is a happy young girl, going to school and playing with her friends. She might not have survived if she had lived in another African country where Kangaroo Mother Care was also not available or well known.

Malawi is one of two countries in sub-Saharan Africa on track to meet the Millennium Development Goal for child survival. Though estimated to have the highest preterm birth rate globally (18.1%), nearly every district in the country has an active Kangaroo Mother Care unit. Facility-based health care providers are being trained in the practice and community health workers are being sensitized to their role in supporting the intervention.

For more information on Kangaroo Mother Care, please see chapter 5 in this report.

CARE FOR THE PRETERM BABY

Photo: *Ritam Banergee/ Getty Images for Save the Children*

Chapter 5. Care for the preterm baby

— Joy E Lawn, Ruth Davidge, Vinod Paul, Severin von Xylander, Joseph de Graft Johnson, Anthony Costello, Mary Kinney, Joel Segre, Liz Molyneux

Preterm baby survival and care round the world

Each year 15 million babies are born preterm and their survival chances vary dramatically around the world (Blencowe et al., 2012) (Figure 5.1). For the 1.2 million babies born in high income countries, increasing complexity of neonatal intensive care the last quarter of the 20th century has changed the chances of survival at lower gestational ages. Middle-income and emerging economies have around 3.8 million preterm babies each year, and whilst some countries such as Turkey have halved deaths for preterm babies within a decade, other countries have made minimal progress (Chapter 6). South Asia and sub-Saharan Africa account for almost two-thirds of the world's preterm babies and over three-quarters of the world's newborn deaths due to preterm birth complications (Chapter 2). Worldwide, almost half of preterm babies are born at home, and even for those born in facilities, essential newborn care is often lacking.

Most premature babies (>80%) are born between 32 and 37 weeks of gestation (moderate/late preterm), and die needlessly for lack of simple, essential care such as warmth and feeding support. About 10% of preterm babies are born 28 to <32 weeks gestation, and in low-income countries more than half of those will die but many could be saved with feasible care, not including intensive care such as ventilation (Figure 5.2). For babies born before 28 weeks gestation, intensive care would be needed to save most of these, but it is important to

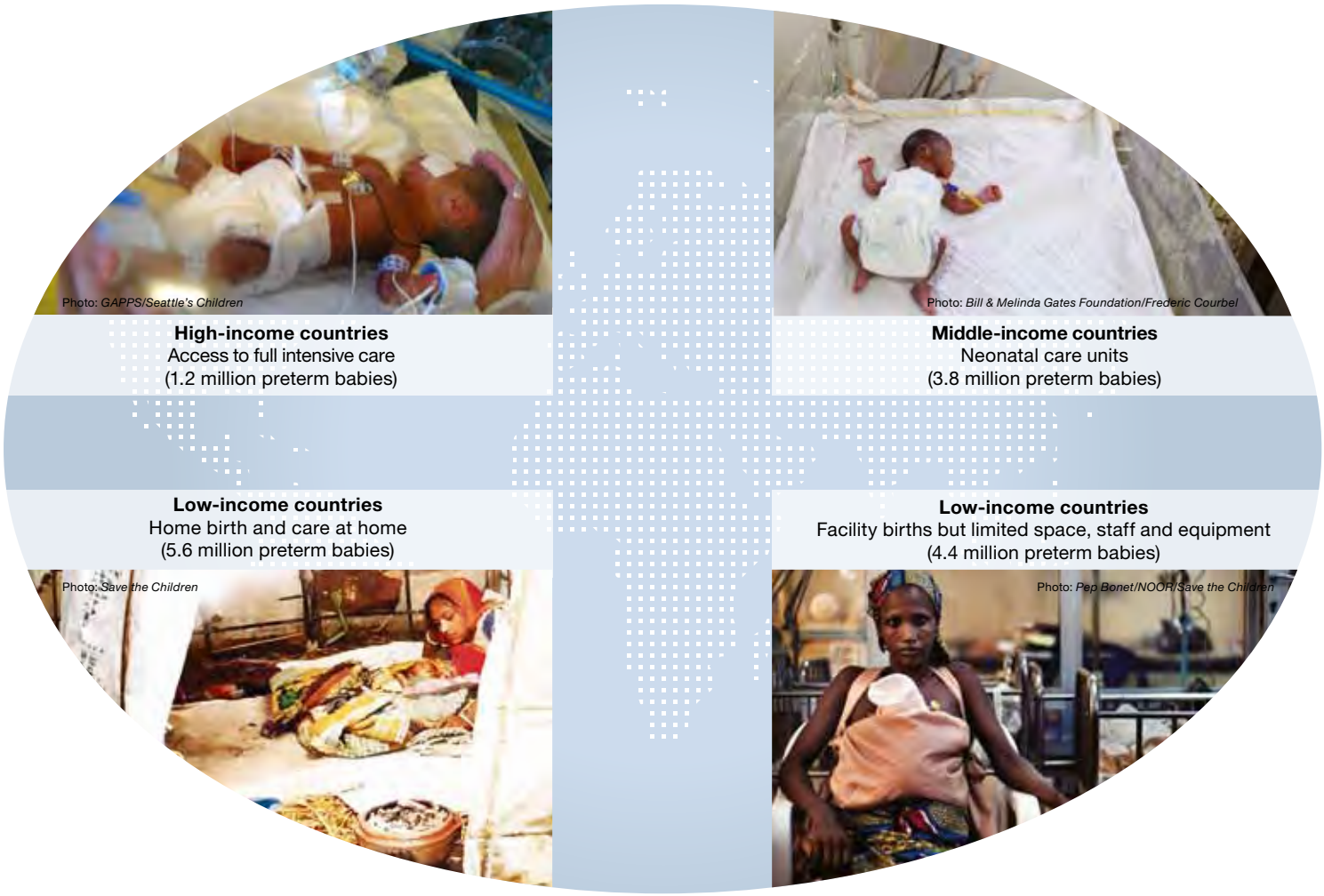


Figure 5.1: Worlds apart: the four settings where 15 million preterm babies receive care

> *"I never thought that this baby would survive; I thought it would die any time"*
>
> *— Mother of moderately preterm baby at home in Eastern Uganda (Waiswa et al., 2010)*

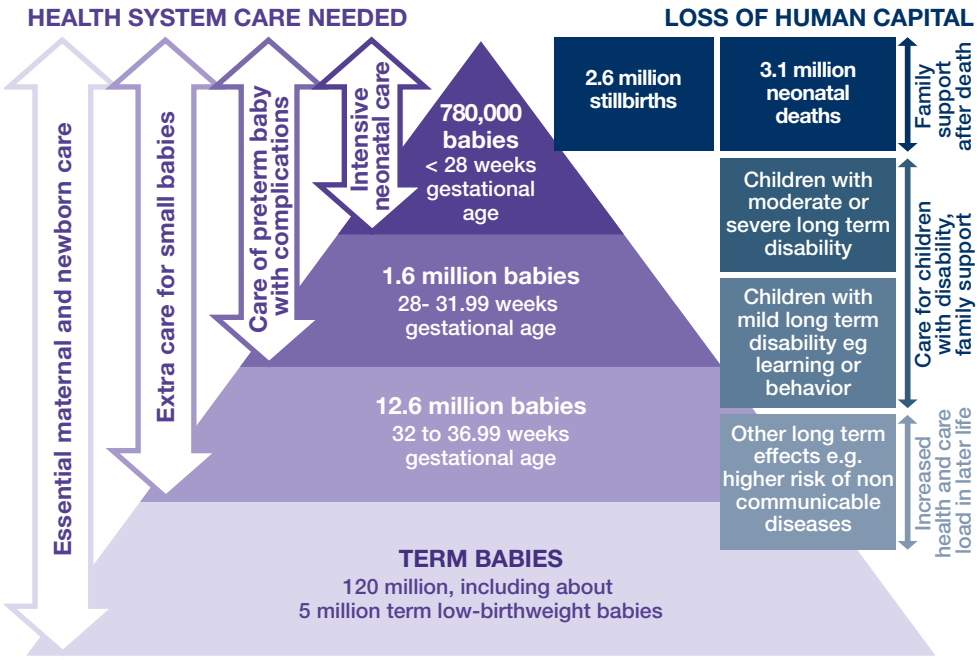
realize that these are the minority – about 5% of premature babies. Yet in many countries, families and health care providers still perceive the deaths of any premature baby as inevitable.

In contrast, neonatal survival is extending to lower and lower extremes of gestational age in high-income settings. In 1990, few babies under 25 weeks gestation were surviving; yet by 2010, 95% of preterm babies under 28 weeks survived, and more than half of the babies born before 25 weeks gestation survived, although the latter have a higher risk of impairment (Petrou et al., 2006).

Over the last few decades the survival gap for babies born in high-income countries and babies born in the poorest countries has widened dramatically, even though the pace of survival gains in high-income countries has slowed reaching the extremes of preterm gestation. For example, North America is still achieving an average annual reduction of more than 5% per year for preterm-specific mortality, yet Africa on average is improving mortality rates for preterm babies by only 1% a year (Figure 5.3). Those countries with the highest risk of death and the most feasible deaths to avert are still experiencing the least progress. The history of neonatal care in high income countries shows that the major reduction in deaths occurred before neonatal intensive care was established. Yet the risk of a neonatal death due to complications of preterm birth is about twelve times higher for an African baby than for a European baby (Liu et al., 2012) (Figure 5.2).

An important but under-recognized issue for all countries is that of disability for survivors of preterm birth (see Chapter 2). In the early days of neonatal intensive care, disabilities were common amongst survivors, ranging from some school learning disability through to severe cerebral palsy. Impairment outcomes have a heavy toll on families and on the health system. Indeed a recent report estimated that the average baby born 28 to 31 weeks gestation in the United States costs $95,000 in medical care in the first year alone (Behrman and Butler, 2006). Over time the pattern of impairment from preterm birth in high-income countries has shifted. The focus of intensive care has shifted to extremely premature babies (less than 28 weeks), or "micro preemies" as this smaller subset of babies has increased risk and severity of impairment (Marlow et al., 2005; Petrou et al., 2006).

Figure 5.2: 135 million newborns and 15 million premature babies - health system needs and human capital outcomes



Source: Analysis using data from Blencowe et al., 2012; Cousens et al., 2011; Liu et al., 2012

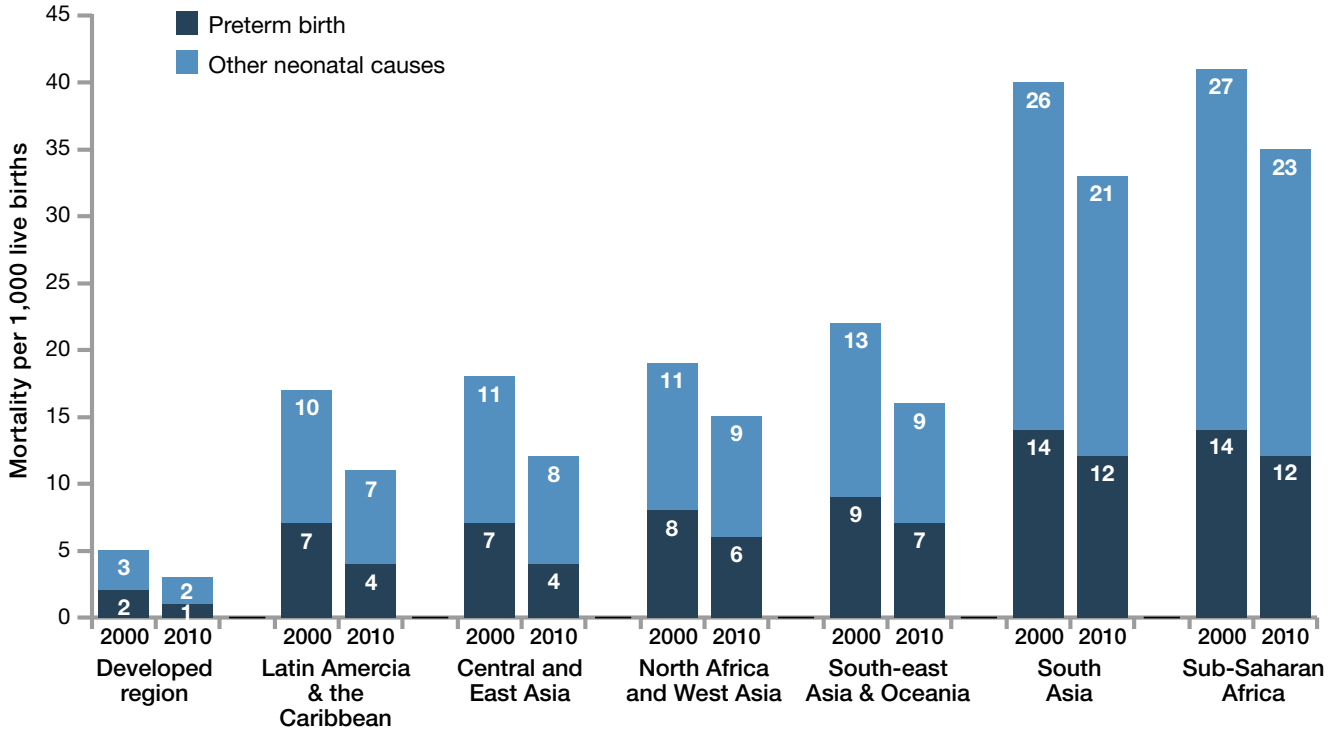
Recent data show that even late and moderate preterm (LAMP, or 32 to <37 weeks gestation) is also associated with significant adverse effects, including on school learning, prompting increasing debate regarding avoidable causes of moderate preterm birth such as high cesarean birth rates (Osrin, 2010; Shapiro-Mendoza and Lackritz, 2012). These long-term effects on society and on the health system as well as more evidence of the link with non-communicable diseases in later adult life (see Chapter 1) underline that importance of addressing preterm birth is beyond survival.

Over the last four decades with an increasing evidence-based care for premature babies in high-income countries, the risk of long-term impairments is reducing. Neonatal intensive care has also become less interventionist and hence some aspects are also potentially more feasible to adapt to lower-income settings. Notable advances in quality of intensive care for premature babies include:

- Widespread use of antenatal corticosteroids in high- and some middle-income countries following multiple RCTs and the National Institute of Health consensus statement ("The effect of antenatal steroids for fetal maturation on perinatal outcomes statement," 1994), ensuring that babies are less likely to develop respiratory distress syndrome (RDS), or have less severe RDS (Mwansa-Kambafwile et al., 2010; Roberts and Dalziel, 2006).
- A shift to less intensive ventilator pressures and increasing use of continuous positive airway pressure (CPAP), now often the respiratory support method of choice (De Paoli et al., 2003).
- Detailed quality of care protocols and "job aids" for almost every aspect of care have improved quality and also shifted more care to the responsibility of skilled neonatal nurses, particularly with respect to addressing infection prevention, feeding support, use of intravenous fluids, and safe oxygen use with careful tracking of oxygen saturation levels (Sola et al., 2008) and follow-up services.
- Deliberate attention to baby friendly care, reducing pain and over stimulation and more family friendly care, including family rooms linked to neonatal units and increased access for parents to their babies while in neonatal care units. (Symington and Pinelli, 2003).

In low- and middle-income countries, there are limited comparable data on long-term outcomes after preterm

Figure 5.3: Increasing survival gap for preterm babies around the world: Regional variation in preterm birth as direct cause of neonatal deaths showing change between 2000 to 2010



Source: Child Health Epidemiology Reference Group and World Health Organization estimates of neonatal causes of death (Liu et al. 2012)

Box 5.1: Preterm babies face specific risks

- Feeding difficulties since the coordinated suck and swallow process only starts at 34 weeks gestation. Preterm babies need help to feed and are more likely to aspirate.
- Severe infections are more common, and premature babies are at higher risk of dying once they get an infection. The majority of babies who die from neonatal sepsis are preterm.
- Respiratory Distress Syndrome due to lung immaturity and lack of surfactant in the alveoli, resulting in collapsing lungs that take extra pressure to inflate. Below 32 weeks gestation, the majority of babies develop RDS, although this risk can be reduced by antenatal corticosteroids injections to women at risk or preterm labor, or in preterm labor.
- Jaundice is more common in premature babies since the immature liver cannot easily metabolize bilirubin, and once jaundiced, the preterm baby's brain is at higher risk since their blood-brain barrier is less well developed to protect the brain.
- Brain injury in preterm babies is most commonly intraventricular hemorrhage, occurring in the first few days after birth in about 1 in 5 babies under 2,000 g and is often linked to severity of RDS and hypotension. Less commonly, preterm babies may have hypoxic brain injury with white matter loss which differs from that seen in the brain of term babies (Volpe, 2009).
- Necrotizing enterocolitis is a rarer condition affecting the intestinal wall of very premature babies, with a typical X-ray image of gas in the bowel wall. Formula feeding increases the risk tenfold compared to babies who are fed breast milk alone (Schanler, 2001).
- Retinopathy of prematurity due to abnormal proliferation of the blood vessels around the retina of the eye, which is more severe if the baby is given too high levels of oxygen.
- Anemia of prematurity, which often becomes apparent at a few weeks of age due to delay in producing red blood cells as the bone marrow is immature.

birth (Lawn et al., 2009b; Mwaniki et al., 2012). However, small studies suggest a high risk of moderate or severe neurodevelopmental impairment and an urgent need to improve awareness, data and care. Retinopathy of prematurity caused an epidemic of blindness for preterm babies in Europe and North America 50 years ago, especially after high or unmonitored use of oxygen. Data from Latin America show increasing rates of retinopathy of prematurity (Gilbert et al., 1997; Gilbert, 2008) and it is likely that areas without data such as Southeast Asia are also experiencing an increase, recreating an avoidable problem. As neonatal care is improved and complexity increases, monitoring quality of care and tracking impairment outcomes are critical and should not be considered an optional extra in low-resource settings. Urgent attention is needed to develop standard, simpler measures of such impairments and integrate these metrics into other measurement systems and also provide support for such babies and their families (Lawn et al., 2009b).

Priority packages and evidence-based interventions

All newborn babies are vulnerable given that birth and the following few days hold the highest concentrated risk of death of any time in the human lifespan. Every baby needs essential newborn care, ideally with their mothers providing warmth, breastfeeding and a clean environment.

Table 5.1: Life-saving essential and extra newborn care

Risk for all babies, especially those who are preterm	Essential care for all babies	Extra care for preterm babies
Hypothermia = low body temperature (increased risk of infections, mortality, and for preterm babies increased risk of RDS)	***Thermal care*** Drying, warming, skin-to-skin and delayed bathing	***Extra thermal care*** Kangaroo Mother Care, baby hats, blankets, overhead heaters, incubators
Cord and skin infections, neonatal sepsis	***Hygienic cord and skin care at birth and home care practices*** Hand washing and other hygiene Delayed cord clamping Consider chlorhexidine	***Extra attention to infection prevention and skin care*** Consider chlorhexidine and emollients
Hypoglycemia = low blood sugar (Increased risk of impairment or death)	***Early and exclusive breastfeeding***	***Extra support for breastfeeding*** e.g., expressing and cup or tube feeding, supplemented breast milk if indicated Lack of breast milk is a risk factor for necrotising enterocolitis in preterm babies
Hypoxia = low oxygen levels, (Increased risk of impairment or death and for preterm babies, higher risk of RDS and intracranial bleeding)	***Neonatal resuscitation if not breathing at birth*** Bag-and-mask resuscitation with room air is sufficient for >99% of babies not breathing at birth	***Safe oxygen use*** Monitored oxygen use e.g., in head box or with nasal cannula, routine use of pulse oximeters

Premature babies are especially vulnerable to temperature instability, feeding difficulties, low blood sugar, infections and breathing difficulties (Table 5.1). There are also complications that specifically affect premature babies (Box 5.1).

Saving lives and preventing disability from preterm birth can be achieved with a range of evidence-based care increasing in complexity and ranging from simple care such as warmth and breastfeeding up to full intensive care (Table 5.2). The packaged interventions in this chapter are adapted from a recent extensive evidence review and a consensus report, "Essential Interventions Commodities and Guidelines for Reproductive Maternal, Newborn and Child Health" (PMNCH, 2011).

Recognition of small babies and distinguishing which ones are preterm are essential first steps in prioritizing care for the highest risk babies. First trimester ultrasound assessment is the most accurate measure, but this is not available for most of the world's pregnant women (Chapter 2, Table 2.3). Other options include Last Menstrual Period, using birthweight as a surrogate or assessment of the baby to estimate gestational age (e.g., Dubowitz or other simpler scoring methods). The highest-risk babies are those that are both preterm and growth restricted.

Package 1: Essential and extra newborn care

Care at birth from a skilled provider is crucial for both women and babies and all providers should have the competencies to care for both mother and baby, ensuring that mother and baby are not separated unnecessarily, promoting warmth, early and exclusive breastfeeding, cleanliness and resuscitation if required (WHO, 2010). These practices are essential for full-term babies, but for premature babies, missing or delaying any of this care can rapidly lead to deterioration and death. For all babies at birth, minutes count.

Thermal care

Simple methods to maintain a baby's temperature after birth include drying and wrapping, increased environmental temperature, covering the baby's head (e.g., with a knitted cap), skin-to-skin contact with the mother and covering both with a blanket (McCall et al., 2005) (WHO, 1997a). Delaying the first bath is promoted, but there is a lack of evidence as to how long to delay, especially if the bath can be warm and in a warm room (Penny-MacGillivray, 1996). Kangaroo Mother Care (KMC) has proven mortality effect for babies <2,000 g and is discussed below. Equipment-dependent warming

Photo: *Sanjana Shrestha/Save the Children*

Table 5.2: Priority evidence-based packages and interventions for preterm babies

Essential Newborn Care For All Babies	Grade
Thermal care (drying, warming, skin-to-skin and delayed bathing) Hygienic cord and skin care Early initiation, exclusive breastfeeding	Evidence: Low to moderate Recommendation: Strong
Neonatal resuscitation for babies who do not breathe at birth	Evidence: Low to moderate Recommendation: Strong
Extra Care For Small Babies	
Kangaroo Mother Care for small babies (birthweight <2,000 g) Extra support for feeding	Evidence: Moderate to high Recommendation: Strong
Care For Preterm Babies With Complications	
Case management of babies with signs of infection Safe oxygen management and supportive care for RDS Case management of babies with significant jaundice	Evidence: Moderate to high* Recommendation: Strong
Hospital care of preterm babies with RDS including if appropriate, CPAP and/or surfactant	Evidence: Moderate to high* Recommendation: Strong
Intensive neonatal care	Evidence: High* Recommendation: Strong

Sources: Adapted from The Healthy newborn: A reference guide for program managers (Lawn et al., 2001), and PMNCH Essential Interventions (PMNCH, 2011) using WHO guidelines, LiST, Cochrane and other reviews, with detailed references in text. * Note that the evidence is mostly from high-income countries and more context specific research required in middle- and low-income settings

techniques include warming pads or warm cots, radiant heaters or incubators and these also require additional nursing skills and careful monitoring (WHO, 1997a). Sleeping bags lack evidence for comparison with skin-to-skin care or of large-scale implementation. There are several trials suggesting benefit for plastic wrappings but, to date, these have been tested only for extremely premature babies in neonatal intensive care units (Duman et al., 2006).

Photo: *Joshua Roberts/Save the Children*

Feeding support

At the start of the 20th century, Pierre Budin, a famous French obstetrician, led the world in focusing on the care of "weaklings," as premature babies were known then. He promoted simple care--warmth, breastfeeding and cleanliness. However, by the middle of the 20th century, formula milk was widely used and the standard text books said that premature babies should not be fed for the first few days. After 1960, the resurgence of attention and support for feeding of premature babies was an important factor in reducing deaths before the advent of intensive care (Greer, 2001).

Early initiation of breastfeeding within one hour after birth has been shown to reduce neonatal mortality (Bhutta et al., 2008; Edmond et al., 2006; Mullany et al., 2008). Premature babies benefit from breast milk nutritionally, immunologically and developmentally (Callen and Pinelli, 2005). The short-term and long-term benefits compared with formula feeding are well established with lower incidence of infection and necrotizing enterocolitis and improved neurodevelopmental outcome (Edmond et al., 2007; Hurst, 2007). Most premature babies require extra support for feeding with a cup, spoon or another device such as gastric tubes (either oral or nasal) (WHO, 2011a; Lawn et al., 2001). In addition, the mother requires support for expressing milk. Where this is not possible, donor milk is recommended (WHO, 2011a). In populations with high HIV prevalence, feasible solutions for pasteurisation are critical. Milk-banking services are common in many countries and must be monitored for quality and infection prevention. Extremely preterm babies under about 1,000 g and babies who are very unwell may require intravenous fluids or even total parenteral nutrition, but this requires meticulous attention to volume and flow rates. Routine supplementation of human milk given to premature babies is not currently recommended by WHO. WHO does recommend supplementation with vitamin D, calcium and phosphorus and iron for very low birthweight babies (WHO, 2011) and vitamin K at birth for low birthweight babies (WHO et al., 2003a; WHO, 2012).

Infection prevention

Clean birth practices reduce maternal and neonatal mortality and morbidity from infection-related causes, including tetanus (Blencowe et al., 2011). Premature babies have a higher risk of bacterial sepsis. Hand cleansing is especially critical in neonatal care units. However basic hygienic practices such as hand washing and maintaining a clean environment are well known but poorly done. Unnecessary separation from the mother or sharing of incubators should be avoided as these practices increase spread of infections. For the poorest families giving birth at home, the use of clean birth kits and improved practices have been shown to reduce mortality (Seward et al., 2012).

Recent cluster-randomized trials have shown some benefit from chlorhexidine topical application to the baby's cord and no identified adverse effects. To date, about half of trials have shown a significant neonatal mortality effect especially for premature babies and particularly with early application, which may be challenging for home births (Arifeen et al., 2012; Soofi et al., 2012; Tielsch et al., 2007). Another possible benefit of chlorhexidine is a behavior change agent — in many cultures around the world, something is applied to the

cord and a policy of chlorhexidine application may accelerate change by substituting a helpful substance for harmful ones.

The skin of premature babies is more vulnerable, and is not protected by vernix like a term baby's. Topical application of emollient ointment such as sunflower oil or Aquaphor™ reduces water loss, dermatitis and risk of sepsis (Soll and Edwards, 2000) and has been shown to reduce mortality for preterm babies in hospital-based trials in Egypt and Bangladesh (Darmstadt et al., 2004; Darmstadt et al., 2007). Three trials are now testing the effect of emollients in community settings in South Asia, but as yet there are none being conducted in African (Duffy et al., 2011). This is a potentially scaleable, simple approach to save lives even where most births are at home.

Another effective and low cost intervention is appropriate timing for clamping of the umbilical cord, waiting 2-3 minutes or until the cord stops pulsating, whilst keeping the baby below the level of the placenta. For preterm babies this reduces the risk of intracranial bleeding and need for blood transfusions as well as later anemia. Yet this intervention has received limited attention (McDonald and Middleton, 2008). Possible tension between delayed cord clamping and active management of the 3rd stage of labor with controlled cord traction has been debated, but the Cochrane review and also recent-evidence statements by obstetric societies support delayed cord clamping for several minutes in all uncomplicated births (Leduc et al., 2009).

Package 2: Neonatal resuscitation

Between 5 to 10% of all newborns and a greater percentage of premature babies require assistance to begin breathing at birth (Wall et al., 2009). Basic resuscitation through use of a bag-and-mask or mouth-to-mask (tube and mask) will save four out of every five babies who need resuscitation; more complex procedures, such as endotracheal intubation, are required only for a minority of babies who do not breathe at birth and who are also likely to need ongoing ventilation. Recent randomized control trials support the fact that in most cases assisted ventilation with room air is equivalent to using oxygen, and unnecessary oxygen has additional risks (Saugstad et al., 2006). Expert opinion suggests that basic resuscitation for preterm births reduces preterm mortality by about 10% in addition to immediate assessment and stimulation (Lee et al., 2011). An education program entitled Helping Babies Breathe has been developed by the American Academy of Pediatrics and partners for promotion of basic neonatal resuscitation at lower levels of the health system in low-resource settings and is currently being scaled up in over 30 low-income countries and promises potential improvements for premature babies (Chapter 6, Box 6.5) (WHO, 1997b; WHO, resuscitation guidelines, forthcoming, American Academy of Pediatrics et al., 2010; Singhal et al., 2012).

Package 3: Kangaroo Mother Care

KMC was developed in the 1970s by a Colombian pediatrician, Edgar Rey, who sought a solution to incubator shortages, high infection rates and abandonment among preterm births in his hospital (Charpak et al., 2005; Rey and Martinez, 1983). The premature baby is put in early, prolonged and continuous direct skin-to-skin contact with her mother or another family member to provide stable warmth and to encourage frequent and exclusive breastfeeding. A systematic review and meta-analysis of several randomized control trials found that KMC is associated with a 51% reduction in neonatal mortality for stable babies weighing <2,000g if started in the first week, compared to incubator care (Lawn et al., 2010). These trials

Photo: *Jenn Warren/Save the Children*

all considered facility-based KMC practice where feeding support was available. An updated Cochrane review also reported a 40% reduction in risk of post-discharge mortality, about a 60% reduction in neonatal infections and an almost 80% reduction in hypothermia. Other benefits included increased breastfeeding, weight gain, mother-baby bonding and developmental outcomes (Conde-Agudelo et al., 2011). In addition to being more parent and baby friendly, KMC is more health-system friendly by reducing hospital stay and nursing load and therefore giving cost savings (Lima et al., 2000). KMC was endorsed by the WHO in 2003 when it developed a program implementation guide (WHO, 2003b). Some studies and program protocols have a lower weight limit for KMC, e.g., not below 800g, but in contexts where no intensive care is available, some babies under 800g do survive with KMC and more research is required before setting a lower cut off. Despite the evidence of its cost effectiveness, KMC is underutilized although it is a rare example of a medical innovation moving from the Southern hemisphere, with recent rapid uptake in neonatal intensive care units in Europe (Lawn et al., 2010).

Package 4: Special care of premature babies and phased scale up of neonatal intensive care

Moderately-premature babies without complications can be cared for with their mothers on normal postnatal wards or at home, but babies under 32 weeks gestation are at greater risk of developing complications and will usually require hospital admission. Fewer babies are born under 28 weeks of gestation and most of these will require intensive care.

Photo: *March of Dimes*

Care of babies with signs of infection

Improved care involves early detection of such danger signs and rapid treatment of infection, while maintaining breastfeeding if possible (WHO, 2005; WHO, 2007). Identification is complicated by the fact that ill premature babies may have a low temperature, rather than fever. First level management of danger signs in newborns has relatively recently been added to Integrated Management of Childhood Illness guidelines (WHO et al., 2005; The Young Infants Clinical Signs Study Group, 2008). WHO recommends that all babies with danger signs be referred to a hospital. Where referral is not possible, then treatment at the primary care center can be lifesaving.

Care of babies with jaundice

Premature babies are at increased risk of jaundice as well as infection, and these may occur together compounding risks for death and disability (Mwaniki et al., 2012). Since severe jaundice often peaks around day 3, the baby may be at home by then. Implementation of a systematic predischarge check of women and their babies would be an opportunity to prevent complications or increase careseeking, advising mothers on common problems, basic home care and when to refer their baby to a professional.

Babies with Respiratory Distress Syndrome

For premature babies with RDS, methods for administering oxygen include nasal prongs, or nasal catheters. Safe oxygen management is crucial and any baby on continuous oxygen therapy should be monitored with a pulse oximeter (Duke et al., 2009).

The basis of neonatal care of very premature babies since the 1990s was assisted ventilation. However, reducing severity of RDS due to greater use of antenatal corticosteroids and increasing concerns about lung damage prompted a shift to less intensive respiratory support, notably CPAP commonly using nasal prongs to deliver pressurized, humidified, warmed gas (air and/or oxygen)

to reduce lung and alveoli collapse (Sankar et al., 2008). This model of lower intensity may be feasible for wider use in middle-income countries and for some low-income countries that have referral settings with stronger systems support such as high-staffing, 24-hour laboratories.

Recent trials have demonstrated that CPAP reduces the need for positive pressure ventilation of babies less than 28 weeks gestation, and the need for transfer babies under 32 weeks gestation to neonatal intensive care units (Finer et al., 2010; Gittermann et al., 1997; Morley et al., 2008). One very small trial in South Africa comparing CPAP with no ventilation among babies who were refused admission to neonatal intensive care units found CPAP reduced deaths (Pieper et al., 2003). In Malawi, a CPAP device developed for low-resource settings is being trialed in babies with respiratory distress who weigh over 1,000g. Early results are encouraging, and an important outcome will be to assess the nursing time required and costs (Williams, 2010).

Increasing use of CPAP without regulation is a concern. Many devices are in the "homemade" category; several low-cost bubble CPAP devices are being developed specifically for low-income countries but need to be tested for durability, reliability and safety (Segre, 2012a). CPAP-assisted ventilation requires adequate medical and nursing skill to apply and deliver safely and effectively, and also requires other supportive equipment such as an oxygen source, oxygen-monitoring device and suction machine.

Surfactant is administered to premature babies' lungs to replace the missing natural surfactant, which is one of the reasons babies develop RDS. The first trials in the 1980s demonstrated mortality reduction in comparison to ventiallation alone, but it was 2008 before the drug was added to the WHO Essential Medicine list (WHO, 2011b). Uptake is limited in middle- and especially low-income countries as the current products can only be feasibly administered in a well-equipped and staffed hospital that can intubate babies. The cost also remains a significant barrier. In India, surfactant costs up to $600 for a dose (Vidyasagar et al., 2011). Data from India and South Africa suggest that surfactant therapy is restricted to use in babies with potential for better survival, usually over 28 weeks' gestation due to its high price (Vidyasagar et al., 2011). Costs may be reduced by synthetic generics and simplified administration, for example with an aerosolized delivery system, but before wide uptake is recommended, studies should assess the additional lives saved by surfactant once antenatal corticosteroids and CPAP are used.

Photo: *Pep Bonet/Noor/Save the Children*

Evidence limitations

Most published trials come from high-income countries where care for premature babies assumes the presence of neonatal intensive care, and often large multi-site trials are required to examine the incremental effect of a change in care. Few rigorous trials are undertaken in lower-income settings where severe morbidity and even fatal outcomes are common and contextual challenges may be critical. Ironically, more of the large recently funded rigorous trials are community-based, such as those assessing chlorhexidine and emollients (Duffy et al., 2011), and there is an urgent need for more facility-based research addressing quality of care which includes cost analyses.

There were a number of interventions considered in the PMNCH essential interventions review process that are

used in high-income settings for premature babies but were not included in the global recommendations for scale up due to lack of context-specific evidence on cost effectiveness – for example, caffeine citrate to reduce the risk of apnea of prematurity (Bhutta et al., 2011). Thus, more evidence from low-income settings is required.

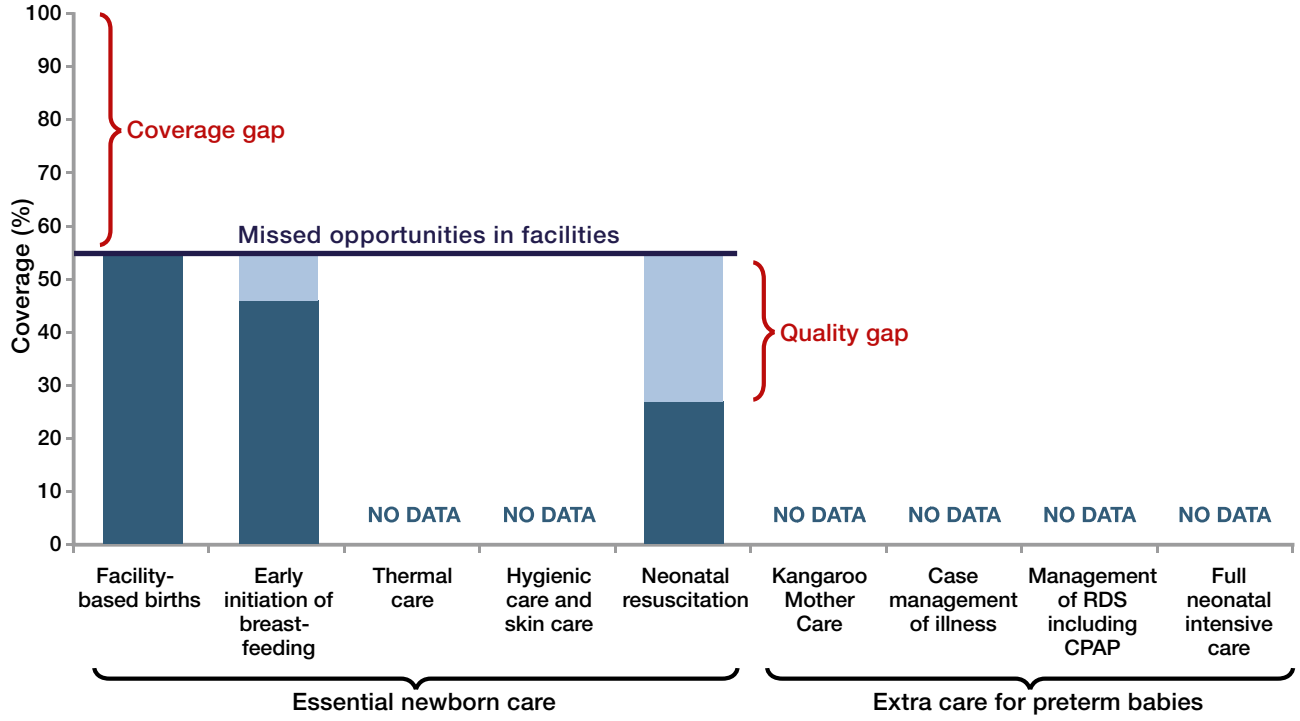
Program opportunities for scale up of care

National coverage data for many of the evidence-based interventions for premature babies are lacking even in high-income settings, hence it is difficult to assess the global situation for care of premature babies or indeed for several important newborn care interventions (Figure 5.4).

For the 50 million home births without skilled care, the poorest women in the poorest countries, a major care gap is obvious. In sub-Saharan Africa, more than half of home births are alone, with no attendant (UNICEF, 2012). In South Asia, around one-thirds of home births are without traditional birth attendants. In these instances, the primary caregivers of babies are their mothers and their families. Ensuring that women and communities are informed about healthy home care and enabled to care for their newborns and especially their preterm babies in the best possible way is critical. Women's groups offer peer counseling and community mobilsation have been shown to have a significant effect on neonatal mortality in at least half of the trials in Asia and Africa to date (Lassi et al., 2010; Manandhar et al., 2004).

The increasing pace of policy and program change for home-visit packages during pregnancy and after birth provides an opportunity to empower women to have a better outcome themselves and for their babies (WHO et al., 2009). An early postnatal visit (within two days of birth) is one of only seven coverage indicators along the continuum of care selected by the United Nations Commission on Information and Accountability and tracked by Countdown to 2015 (Commission on Information and Accountability, 2011; Requejo et al., 2012). In the 75 Countdown to 2015 priority countries, only 1 in 3 women and babies have an early postnatal visit —the lowest of the seven indicators. This early visit is critical for survival and health and an important opportunity to identify preterm babies. Novel methods for identification of premature babies include community health workers using foot size to identify those babies and then

Figure 5.4: Missed opportunities to reach preterm babies with essential interventions, median for Countdown to 2015 priority countries



Data sources: Adapted (Kinney et al., 2010) using data from UNICEF Global Databases (UNICEF, 2012) based on Demographic Health Surveys, Multiple Indicator Cluster Surveys and other national surveys, neonatal resuscitation from LiST ("LiST: The Lives Saved Tool. An evidence-based tool for estimating intervention impact," 2010).

Box 5.2: Kangaroo Mother Care – what works to accelerate progress towards scale?

Preparation and national buy-in by key stakeholders

- Identify national champions to understand and address the barriers to expansion of KMC.
- Interact with policymakers, service providers and donors regarding the evidence for KMC as a cost-effective intervention, sharing experiences from other countries.
- Enable catalytic learning visits - internal or external - for policymakers and service providers, to see KMC implementation, and tiny preterm babies surviving with KMC, recognize that KMC is used in neonatal intensive care units in high-income countries and is not just a second best option, and that initial cultural reluctance, or modesty concerns can be overcome.
- Establish a Ministry of Health led national level stakeholder process with support from implementing partners and ownership by nursing and medical associations.

Planning and introduction

- Develop national policy/strategy, service guidelines, training materials, job aids, supervisory systems and indicators to track implementation and monitor outcomes.
- Adapt KMC to the local setting, translation (e.g., "kumkumbatia mtoto kifuani" = cuddle your baby in Kiswahili), locally tested counseling materials and posters addressing specific barriers e.g., re modesty.
- Establish learning centers strategically to maximize expansion (e.g., regional hospitals) and implement master training, transfer training, ongoing mentoring.
- Promote systems focus and district ownership and sustainable resource commitment for training and supervision. Equipment or commodities are not the limiting factor for scale up. Staff skills, leadership, ongoing quality improvement are fundamental to success.

Photo: *Joshua Roberts/Save the Children*

Institutionalizing, increasing coverage and quality

- Integrate KMC with other training packages and supervision systems and institutionalize within pre-service medical and nursing education including adequate practical KMC experience.
- Integrate KMC and other newborn care indicators into national HMIS, national household surveys and quality improvement systems and use this data to review coverage and quality of services, linking to national, and district health annual workplans.
- Expand newborn care services using KMC as an entry point to improve the care of preterm babies including feeding support, safe oxygen use and training for preterm baby care especially for nurses.

providing extra visits, breastfeeding support and referral to a facility if needed (Marchant et al., 2010).

As well as gaps in coverage of crucial interventions for women and babies, there are equity gaps between rich and poor, public and private health sectors, provinces and districts and among rural, urban and peri-urban populations. Complex, facility-based interventions tend to have a higher level of inequity than simpler interventions that can be delivered closer to home (Barros et al., 2012). For example, there is low inequity for immunization and antenatal care, while higher disparities exist for skilled attendance coverage (Victora and Rubens, 2010). Among the 54 of 75 Countdown to 2015 priority countries with equity data, birth in a health facility is more than twice as likely for a richer family compared to a poorer family (Barros et al., 2012).

Many African and most South Asian countries are experiencing increases in health facility births, some very rapidly (Requejo et al., 2012). However, the quality of care has not kept pace with coverage, leaving a quality gap but also giving cost-effective opportunities for lifesaving care for

women and babies who are reachable in health facilities. For example, midwives are skilled and equipped to provide essential newborn care and resuscitation if needed. However, often key commodities or attention to infection prevention are lacking. Perinatal audit data are a powerful tool for improving quality of care and can also be collated and used for national or subnational improvement of care (Pattinson et al., 2009).

Figure 5.4 shows the coverage and quality gaps for premature baby care in the Countdown to 2015 priority countries, highlighting the data gaps. With just over 50% of all births taking place in health facilities, essential newborn care could be provided for all those babies. Yet data show even the apparently simple practices of hand cleansing and warmth in the labor room are poorly done around the world (Knobel et al., 2005). Early initiation of breastfeeding is tracked by national household surveys but the practices for premature babies and duration of breastfeeding preterm are not known at national level.

Neonatal resuscitation scale up is benefitting from recent innovation in technology and from public-private partnerships (American Academy of Pediatrics et al., 2010). However, data from Service Provision Assessment surveys suggested that under half of all skilled birth attendants had resuscitation skills and/or the correct equipment in terms of bag-and-mask (Figure 5.4) (Wall et al., 2009).

KMC, despite being established for more than 20 years, has had limited scale up (Box 5.2). It is currently implemented on a large scale in only a few countries such as Colombia, Brazil and South Africa. There has also been rapid uptake in neonatal intensive care units in high-income countries, including

Box 5.3: The right people for reducing deaths and disability in preterm babies

Community Level/Home

- Mothers and Fathers
- Community Health Workers, Extension workers and outreach nurses or midwives

First Level/Outreach

- Nurse and midwives also with skills for newbon care
- Medical assistants or clinical officers
- Extension workers
- Ward attendants

Referral Level/District Hospital

- Nurse and midwives with higher skills in newborn care (e.g., KMC, management of sepsis and RDS)
- Doctor and specialists
- Content-specific cadres e.g. medical assistants, clinical officers

Photos: *PMNCH essential interventions*

Table 5.3: Tools, technologies, and innovations required for the care of preterm babies

Priority packages and interventions	Current technology/Tools	Technological innovations required
ALL BABIES		
Essential newborn care and extra care for preterm babies • Thermal care (drying, warming, skin-to-skin and delayed bathing) • Early initiation, exclusive breastfeeding • Hygienic cord and skin care	• Protocols for care, training materials and job aids • Materials for counselling, health education and health promotion • Weighing scales • Cord clamp and scissors, clean birth kit if appropriate • Vitamin K for LBW babies	• Generic communications and counselling toolkit for local adaptation • Generic, modular training kit for adaptation, novel methods eg cell phone prompts • Birth kits for frontline workers • Chlorhexidine preparations for application to the umbilical cord • Simplified approaches to identifying preterm babies such as footsize
Neonatal resuscitation for babies who do not breathe at birth	• Materials for training and job aids • Training manikins • Newborn resuscitation devices (bag-and-mask) • Suction devices • Resuscitation stations with overhead heater • Clock with large face and second hand	• Wide scale novel logistics systems to increase availability of devices for basic resuscitation and training manikins • Additional innovation for resuscitation devices (eg upright bag-and-mask, adaptable, lower cost resuscitation stations)
PRETERM BABIES		
Kangaroo mother care for small babies (birthweight <2,000 g)	• Cloth or wrap for KMC • Baby Hats	Generic communications and counselling toolkit for local adaptation, Innovation to address cultural, professional barriers Generic, modular training kit and job aids for local adaptation
Care of preterm babies with complications including: • Extra support for feeding preterm and small babies • Case management of babies with signs of infection • Safe oxygen management and supportive care for RDS • Case management of babies with significant jaundice • Managing seizures	• Nasogastric tubes, feeding cups, breast milk pumps • Blood sugar testing sticks • IV fluids including glucose and more accurate giving sets • Syringe drivers • Injection antibiotics, 1 cc syringes/27G needles, preloaded syringes • Oxygen supply/concentrators • Nasal prongs, headboxes, other O2 delivery systems • Pulse oximeters to assess blood oxygen levels with reusable cleanable neonatal probes. • Bilirubinometers (table top and transcutaneous) • Phototherapy lamps and eye shades • Exchange transfusion kits • Hot cots, overhead heaters	Lower-cost and more robust versions of: • Blood sugar testing for babies on low volume samples, heel pricks • Oxygen condensers, including portable options • Pulse oximeters and robust probes, including with alternative power options • Syringe drivers able to take a range of syringes • Bilirubin testing devices including lower cost transcutaneous devices • Haemoglobin and blood Grouping, Rhesus Point of Care • Point of care for C-reactive protein/procalcitonin • Apnoea alarm • Phototherapy devices such as portable "bilibed" to provide both phototherapy treatment and heat
Neonatal intensive care	• Continuous Positive Air Pressure (CPAP) devices with standardized safety features	• Lower-cost robust CPAP equipment with standardized settings • Neonatal intensive care context specific "kits", e.g., district hospital with ongoing support for quality use and for equipment maintenance • Surfactant as more stable, lower cost preparations

Note this table refers to care after the baby is born so does not include other essential tools and technologies such as antenatal steroids, or critical commodities for the woman
Sources: (East Meets West; WHO et al., 2003; Lawn et al., 2006; 2009a; PMNCH, 2011)

for ventilated babies (Nyqvist et al., 2010). Systematic scale up of KMC is making progress in some countries in sub-Saharan Africa and South Asia including Malawi (Blencowe et al., 2009), Tanzania, Rwanda, Ghana (Nguah et al., 2011), Indonesia and Vietnam (Bergh et al., 2012). In other countries, a KMC unit established in one teaching hospital over a decade ago has yet to benefit babies in the rest of the country. Lessons are being learned in overcoming barriers such as lack of knowledge by policy makers and service providers. Countries that are making more rapid progress have a national policy for KMC, a learning site, national champions and a plan for national implementation and have integrated training along with essential newborn care and resuscitation into pre-service medical and nursing education (Box 5.2). KMC can be safely delivered by trained patient attendants under the supervision of nurses, allowing nurses to look after the sickest neonates – a successful example of taskshifting (Blencowe et al., 2009). A major impediment to program tracking and accountability is the lack of data for coverage of KMC, although this indicator could feasibly be tested for inclusion in household surveys.

Quality of service provision requires the availability of people with the right skills (Box 5.3) as well as essential equipment and drugs. Indeed, for newborn survival, skilled people are at least as critical as equipment and commodities (Table 5.3) (Honeyfield, 2009). Shortages of qualified health workers and inadequate training and skills for the care of premature babies are a major reason for poor progress in reducing neonatal deaths (Knippenberg et al., 2005; Victora and Rubens, 2010). Nurses or midwives with skills in critical areas such as resuscitation, KMC, safe oxygen management and breastfeeding support are the frontline worker for premature babies, yet in the whole of sub-Saharan Africa there are no known neonatal nurse training courses. Urgent systematic attention is required for preservice and inservice

training, non-rotation of nurses with skills in neonatal care, and where appropriate the development of a neonatal nurse cadre, as well as rewarding for those who work against the odds in hard-to-serve areas (Chapter 6).

While most premature babies are born just a few weeks early and can be saved with the right people and simple care, for more extreme premature babies, additional skills, equipment and commodities are critical, ranging from bag-and-mask and controlled IV fluid-giving sets, to CPAP and surfactant (Table 5.3). A premature baby suffering from RDS requires oxygen and safe monitoring of oxygen saturation levels with a pulse oximeter — however, this equipment is often unavailable. Likewise, prevention of hearing impairment for premature babies being treated for infection with gentamicin requires dose titration and, ideally, laboratory monitoring of gentamicin levels, which is often unavailable. The UN Commission on Life-saving Commodities for Women and Children has prioritized high-impact, neglected commodities, and these include several for the care of premature babies (Chapter 6, Box 6.6).

Addressing newborn care in district hospitals is a key priority for improving newborn survival and health. In most countries, district hospitals are understaffed and poorly resourced compared to teaching hospitals. There are a number of large-scale examples of improved newborn care in district hospitals including a network in rural Western Kenya (Opondo et al., 2009). In Limpopo, South Africa, a network of more than 30 district hospitals instituted an accreditation scheme and targeted quality improvement with mentor teams (Robertson et al., 2010), and in another province, a program called Neonatal Experiential Leaning reaches 16 hospitals with standard guidelines, a 2-week neonatal training course and monthly mentor visits. Across several Indian states, peripheral hospitals have developed a dedicated newborn care space, basic equipment and standard protocols and referral hospitals have had upgraded special-care baby units. Some also have experimented with the use of alternative cadres of ward aides specially trained in newborn care and restricted from rotations to other wards (Sen et al., 2007). Design and implementation of context-specific hospital newborn care packages is critical, especially as more births occur in facilities.

Priority reseach for care of the premature newborn

Although 92% of premature babies are born in low- and middle-income countries and 99% of premature babies in these countries die, to date the vast majority of published research has been conducted in high-income countries (Lawn et al., 2008). Important health gains are achievable in the short term with delivery or implementation research, prioritizing the highest-impact interventions and the most significant constraints to scale up (Table 5.4) (Martines et al., 2005). For preterm birth, there is a major gap in developing, delivering and testing community-based interventions. A recent systematic exercise ranked 55 potential research questions to address preterm birth and stillbirth at the community level and 29 experts applied a standardized scoring approach developed by the Child Health and Nutrition Research Initiative (George et al., 2011). The 10 top-ranked questions were all about delivery of interventions, notably demand approaches, such as

Table 5.4: Research priorities for reducing deaths and disability in preterm babies

Description
• Standardized, simplified metrics for assessing acute morbidities in premature babies and tools and protocols for comparable follow up of impairment and disability in premature babies
Discovery
• Biomarkers of neonatal sepsis • Sensitive, specific identification of sepsis in preterm and other newborns • Shorter course antibiotics, oral, fewer side effects • Stability of oral surfactant
Development
• Development of simpler, lower-cost, robust devices (See Table 5.3 for full list) • Simplified identification of preterm babies in communities, increased accuracy of GA in facilities • Community initiation of Kangaroo Mother Care
Delivery
Implementation research to understand and accelerate scaling up of facility based care: • KMC, including quality improvement, task shifting • Feeding support for preterm babies • Infection case management protocols and quality improvement • Improved care of RDS, including safe oxygen use protocols and practices • Infection prevention Implementation research at community level • Simplified improved identification for premature babies • Referral strategies • Feasibility and effect of home care for preterm babies in humanitarian emergencies or where referral is not possible

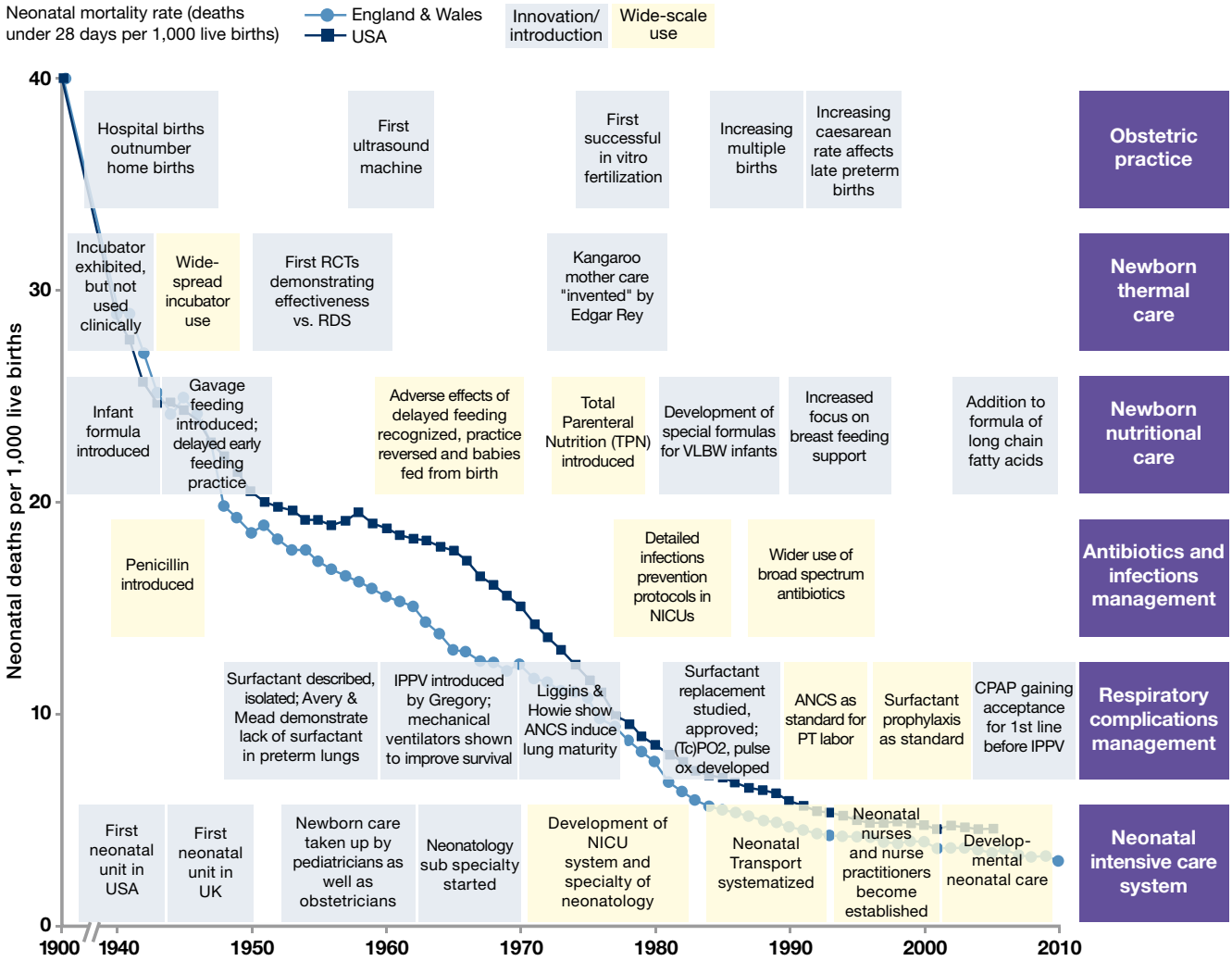
overcoming financial barriers and use of incentives, but also supply such as community health workers tasks and supervision. The need for simplified, validated methods to identify premature babies at community level was ranked second of 55. Since the exercise was focused at the community level, equipment and facility-based innovations were not listed but are widely recognized to be of critical importance (Table 5.4). Most equipment is developed for high-income countries and requires development and testing in varying contexts in low- and middle-income countries (Powerfree Education Technology, 2012). Discovery research often requires a longer time frame but potentially could have high return, especially with prevention of preterm birth. Description research is also important, especially to address major data gaps for impairment outcomes in low- and middle-income settings and promote more controlled assessment of some interventions, notably the impact of thermal care practices on mortality and morbidity.

Prescription for action

The neonatal mortality rate (NMR) in the United Kingdom and the United States was reduced to below 15 per 1,000 live births before neonatal intensive care was widely available, and the largest reduction in NMR from 40 to 15 was related to obstetric care and simpler improvements in individualized newborn care such as warmth, feeding and infection prevention and case management (Figure 5.5).

Seven low- and middle-income countries have halved their preterm deaths within a decade (Chapter 6). These

Figure 5.5: The history of neonatal care in the United Kingdom and the United States shows that dramatic declines in neonatal mortality are possible even before neonatal intensive care is scaled up



Acronyms used: ANCS = antenatal corticosteroids, CPAP = continuous positive airways pressure, NICU = neonatal intensive care, IPPV = intermittent positive pressure ventilation, VLBW = very low birth weigh
Sources: (Smith et al., 1983; NIH, 1985; Baker, 2000; Wegman, 2001; Philip, 2005; Jamison et al., 2006; Lissauer and Fanaroff, 2006; CDC, 2012; Office for National Statistics, 2012) with thanks to Boston Consulting Group

Table 5.5: Actions for reducing deaths and disability in preterm babies

Invest and plan
Assess and advocate for newborn and preterm baby care, mobilize parent power • Review existing policies and programs to integrate high-impact care for premature babies • Train nurses for newborn care and include skilled personnel for premature baby care in human resource planning for all levels of the health system where babies are cared for • Ensure essential equipment and commodities are consistently available
Implement
Seize opportunities through other programs including For all facility births ensure: • immediate essential newborn care and neonatal resuscitation if needed • infection prevention and management • At community level scale up: • Pregnancy and postnatal home visits, including behavior change messages for families, as well as identification, extra care and referral for premature babies, • Breastfeeding promotion through home visits, well baby clinics, baby friendly hospital initiative ***Reach high coverage with improved care for premature babies especially*** • Kangaroo mother care and improved feeding for small babies • Antenatal corticosteroid use • Respiratory distress syndrome support, safe oxygen use • Audit and quality improvement processes • Provide family support Where additional capacity consider: • Additional neonatal care such as CPAP, • Referral level neonatal intensive care, with safeguards to ensure the poor can also access this care Careful attention to follow up of premature babies (including extremely premature babies) and early identification of impairment
Inform and improve program, coverage and quality
• Improve the data including morbidity follow up and use this in programmatic improvement e.g. gestational specific survival, rates of retinopathy of prematurity etc • Address key gaps in the coverage data especially for kangaroo mother care
Innovate and undertake research
• Establish prioritized research agenda with emphasis on implementation • Invest in research and in research capacity • Conduct multi-country studies of effect, cost and "how to" and disseminate findings linked to action

countries are Sri Lanka, Turkey, Belarus, Croatia, Ecuador, El Salvador, Oman and China. Some of these countries also had fertility rate reductions, which may have contributed (Lawn et al., 2012), but the likely explanation is national focus on improved obstetric and neonatal care, and systematic establishment of referral systems with higher capacity of neonatal care units and staff and equipment helped in some cases by larger national budgets (Chapter 6). Over time, as neonatal care increases in scope, people skills, commodities and equipment become more critical and at a NMR below 15 per 1,000 live births, intensive care plays an increasing role. Hence low- and middle-income countries should be able to halve the risk of their newborns, their most vulnerable citizens, of dying with the right people and the right basic commodities. Yet human resource planning has not addressed this key need, and courses for nurse training in neonatal care are rare in sub-Saharan Africa and much of South Asia. Investing in frontline workers and skills is crucial to overcoming nervousness of many workers when looking after tiny babies, and building their lifesaving skills. A phased approach, for example using KMC as an entry point to show that babies under 1,000g at birth can and do survive and thrive can be a turning point for clinical staff as well as also hospital management.

Starting from existing program platforms at community level (e.g. home visit packages, women's groups) and at facility level to ensure effective care for all births at health facilities, is cost effective and more likely to show early results. However whilst families remain unreached, for example because of financial barriers to facility birth care, these gaps often mean those most at risk are unreached.

Action for preterm birth will start from increased visibility and recognition of the size of the problem— deaths, disability, later chronic disease, parent suffering and wider economic loss (Table 5.5). In many higher-income countries, visibility is driven by empowered parents or by professionals or synergy of the two (Box 5.4). Parents of premature babies are both those who experience the greatest pain and those who hold the greatest power for change. Societal mobilization has made it unacceptable for women to die while giving birth. The voice of women and families in low-income countries is yet to be mobilized for the issue of newborn deaths and stillbirths, and these deaths too often continue to be accepted as the norm despite the existence of highly cost-effective and feasible solutions.

Conclusion

Globally, progress is being made in reducing maternal deaths and child death after the first month of life. Progress for neonatal deaths is slower. Severe neonatal infection deaths may possibly be reduced through "trickle down" from child health programs. Neonatal

deaths due to intrapartum complications ("birth asphyxia") also are beginning to decline, although slowly, perhaps related to increased investments in care at birth and maternal health and care. However the 1.1 million deaths among premature babies are less likely to be reduced though "trickle down" from other programs and indeed it was the specific vulnerability and needs of the premature baby that catalyzed the specialty of neonatology. There are simple solutions that will reduce deaths among premature babies immediately for the poorest families at home in the lowest income settings — for example early and exclusive breastfeeding, chlorhexidine cord applications and skin-to-skin care. However, higher-impact facility-based care, such as KMC is needed and is dependent on nurses and others with skills in caring for small babies and can be phased over time to add increased complexity. Starting with intensive care will fail if simple hygiene, careful attention to feeding and other basic building blocks are not in place. Many countries cannot afford to rapidly scale up neonatal intensive care but no country can afford to delay doing the simple things well for every baby and investing extra attention in survival and health of newborns especially those who are preterm.

Box 5.4: Parents' pain and parents' power

Depending where in the European Union a woman becomes pregnant or a baby is born, the care received will vary. Wide differences still exist in morbidity and mortality for women and newborns between countries and within countries. Preterm deliveries in Europe make up 5-12% of all births, and disproportionately affect the poorer families. Preterm babies represent Europe's largest child patient group and the number of preterm survivors is increasing. Yet despite the growing prevalence and increasing costs, maternal and newborn health still ranks low on the policy agendas of EU countries.

Photo: March of Dimes

Parents and healthcare professionals felt the urgent need to act and to give our most vulnerable group - newborns – a voice. The European Foundation for the Care of Newborn Infants (EFCNI) was founded in 2008. EFCNI is a network between countries and between stakeholders across Europe and is motivated especially by parents whose lives have been changed by having or losing a preterm baby. The vision is that every child in Europe receives the best possible start in life, aiming to reduce the preterm birth rate, prevent complications and to provide the best possible treatment and care, also improving long-term health. So far this network has:

- Created a movement of over 30 parent organizations across 27 European countries, a platform for information exchange and targeted training, amplifying the power of parents.
- Published policy documents to promote accountability such as the EU Benchmarking Report "Too little, too late?", a comparison of policies impacting newborn healthcare and support to families across 14 European Member States and the European Call to Action for Newborn Health and "Caring for Tomorrow- EFCNI White Paper on Maternal and Newborn Health as well as Aftercare Services"
- Mobilized politicians through the European Parliament Interest Group on Maternal and Neonatal Health.
- Involved the general public through the first pan-European online awareness and information campaign on prematurity "ene, mene, mini. One baby in ten is born premature worldwide".

Placing maternal and newborn health more centrally in European and national health policies and research programs is an investment in the human capital of Europe's future generations.

More information is available at http://www.efcni.org/

ACTIONS

Photo: *Pep Bonet/Noor/Save the Children*

Chapter 6. Actions: everyone has a role to play

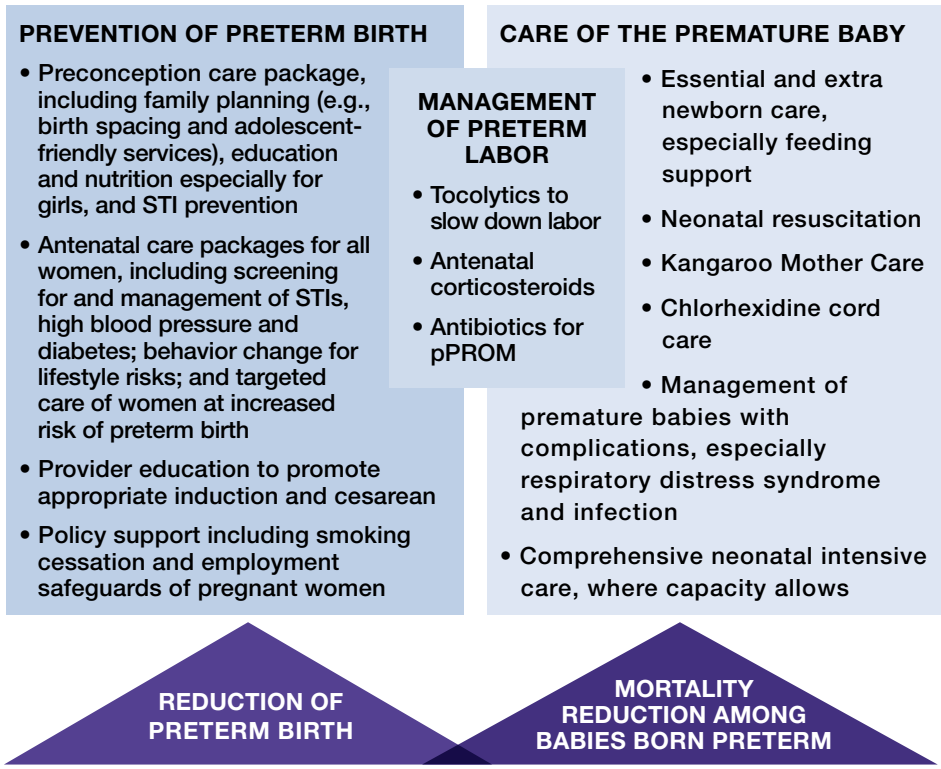
— Preterm Birth Action Group, including Preterm Birth Technical Review Panel and all the report authors

More than 1 in 10 of the world's babies are born too soon, and every page of this report shows the need for concerted action on the prevention of preterm birth and care of the premature baby, and the imperative to ensure mother and baby survive together. This final chapter summarizes the evidence-based interventions for preterm birth in the context of the wider health system, the implications for integrating and scaling up those available interventions and the potential lives saved as a result. Advancing the research agenda is a critical need to reduce the global burden of preterm birth, requiring innovations for both prevention and care. The previous chapters have identified gaps in coverage, quality, equity and metrics, highlighting actions that involve many constituencies. All partners are invited to join this global effort for preterm birth, which is linked closely to the health and care of women and girls, as well as to child survival and global development. Much is being accomplished by individual partners, and each has a unique role to play. By pooling our efforts collaboratively and transparently, with each organization playing to its strengths, our shared goal, as epitomized in *Every Woman Every Child,* can be realized — a day when pregnancies are wanted and safe, women survive, babies everywhere get a healthy start in life, and children thrive.

Action framework: Scale up what works while filling knowledge gaps

Addressing the burden of preterm birth has a dual track — prevention and care (Figure 6.1). Reducing risks during the preconception period and before birth in the pregnancy period advances preterm birth prevention, while actions taken during labor, delivery and after birth are necessary to reduce prematurity-associated mortality and disability. Interventions that can prevent preterm birth and reduce death and disability in premature babies have been identified through global reviews of the evidence and are summarized in Chapters 3, 4 and 5 and shown in Figure 6.1. Many of these interventions also benefit maternal health and prevent stillbirths (Bhutta et al., 2011). More research is urgently needed for preterm birth prevention, which is a longer-term investment but would have widespread impact on mortality, childhood disability and health-care expenditure. For care of premature babies, the emphasis is on scaling up implementations more rapidly as soon as possible, so that the maximum number of premature babies and their mothers benefit. In this way, hundreds of thousands of lives could be saved with the application of current knowledge.

Figure 6.1: Approaches to prevent preterm birth and reduce deaths among premature babies



Prevention of preterm birth is primarily a knowledge gap

Despite the burden of preterm birth, few effective prevention strategies are available for clinicians, policymakers and program managers. Multiple studies in high-income contexts have attempted to prevent preterm birth, yet have failed to identify high-impact interventions in the preconception and antenatal periods. Many interventions have been evaluated, and some have been identified as beneficial though limited in public health impact, such as progesterone therapy, which has only been studied in certain high-risk populations. Reducing the rate of elective cesarean births or inductions without medical indication before the recommended 39 completed weeks of gestation may have an important impact on prevention overall, but has yet to be broadly implemented (National Collaborating Centre for Women´s and Children´s Health, 2011).

Photo: *Chhandak Pradhan/Save the Children*

Hence, for preterm birth prevention, there is a large solution gap. In high-income settings, if all existing interventions, including smoking cessation, reached universal coverage, they would avert a small proportion of preterm births. However, low- and middle-income countries with the highest burden of preterm births also carry the greatest burden of higher-risk conditions that are preventable or treatable. Hence, interventions such as family planning; prevention and management of sexually transmitted infections (STIs); use of insecticide-treated bednets to prevent malaria in pregnancy; and antenatal care, especially to identify and treat pre-eclampsia and reduction of physical workload (e.g., working in fields or factories for long periods) would be expected to be more effective in preventing preterm birth in these locations. Unfortunately, to date, few studies have assessed preterm birth outcomes in these countries with accurate measures of gestational age (Lawn et al., 2010). The greatest potential for prevention of preterm birth, therefore, lies in strategic, sufficiently funded research of interventions that have strong potential to reduce the risk of preterm birth. This should be vigorously pursued.

There are some significant secondary prevention interventions that reduce the impact of preterm birth. Antenatal corticosteroid injections given to women in preterm labor are highly effective at preventing respiratory distress syndrome in premature babies, but remain underused in many low- and some middle-income countries. There is, thus, a need for delivery research that can help understand context-specific reasons for the continued low coverage in these countries and identify ways to adapt known effective strategies for use in low-resource settings. Tocolytic medicines rarely stop preterm labor, but may help delay labor for hours or days, allowing the baby additional precious time to develop before birth.

Care of premature babies is primarily an action gap

As evidenced by the large survival gap between babies born in high-income countries and those born in low- and middle-income countries, effective interventions exist to reduce death and disability in premature babies, yet this care does not reach the poorest and most disadvantaged populations where the burden is highest (Chapter 5). There is a “know-do gap” or a gap between what is known to work and what is done in practice. Bridging this gap will be critical for saving premature babies globally.

More than 60% of all premature babies are born in South Asia and sub-Saharan Africa (Chapter 2), with just over half now being born in facilities. Most preterm births

occur after 32 weeks of gestation (84%), and deaths in these babies can almost all be prevented by essential newborn care. For most such babies, intensive care is not needed (Chapter 5) (Figure 6.1). It is possible to implement some evidence-based interventions for the care of premature babies at the community level through behavior change initiatives and women's groups, as well as home-visit packages with extra care for premature babies, particularly breastfeeding support and awareness of the importance of seeking care when danger signs occur (Gooding et al., 2011). In a few countries, case management of neonatal sepsis is being scaled up using community-based health workers. However, the highest impact interventions, notably antenatal corticosteroids and Kangaroo Mother Care (KMC), require facility-based care, but it is highly feasible to scale them up in low-resource settings and have them act as entry points for strengthening health systems.

Photo: *Chris Taylor/Save the Children*

If scaled up and made universally available, especially in high-burden countries, community and facility interventions would have an immediate, significant effect on reducing the 1.1 million deaths of premature babies each year. This care would also address other causes of neonatal deaths, stillbirth and maternal death and reduce the risks of associated lifelong disability for survivors. Translating knowledge into action through existing health systems platforms will require a focus on systems issues, especially human resources and, notably, nursing skills for obstetric and newborn care. Also, increasing commodities for family planning, obstetric and newborn care are key opportunities for accelerating progress. An initiative on this is being led by the UN Commission on Life-saving Commodities for Women and Children.

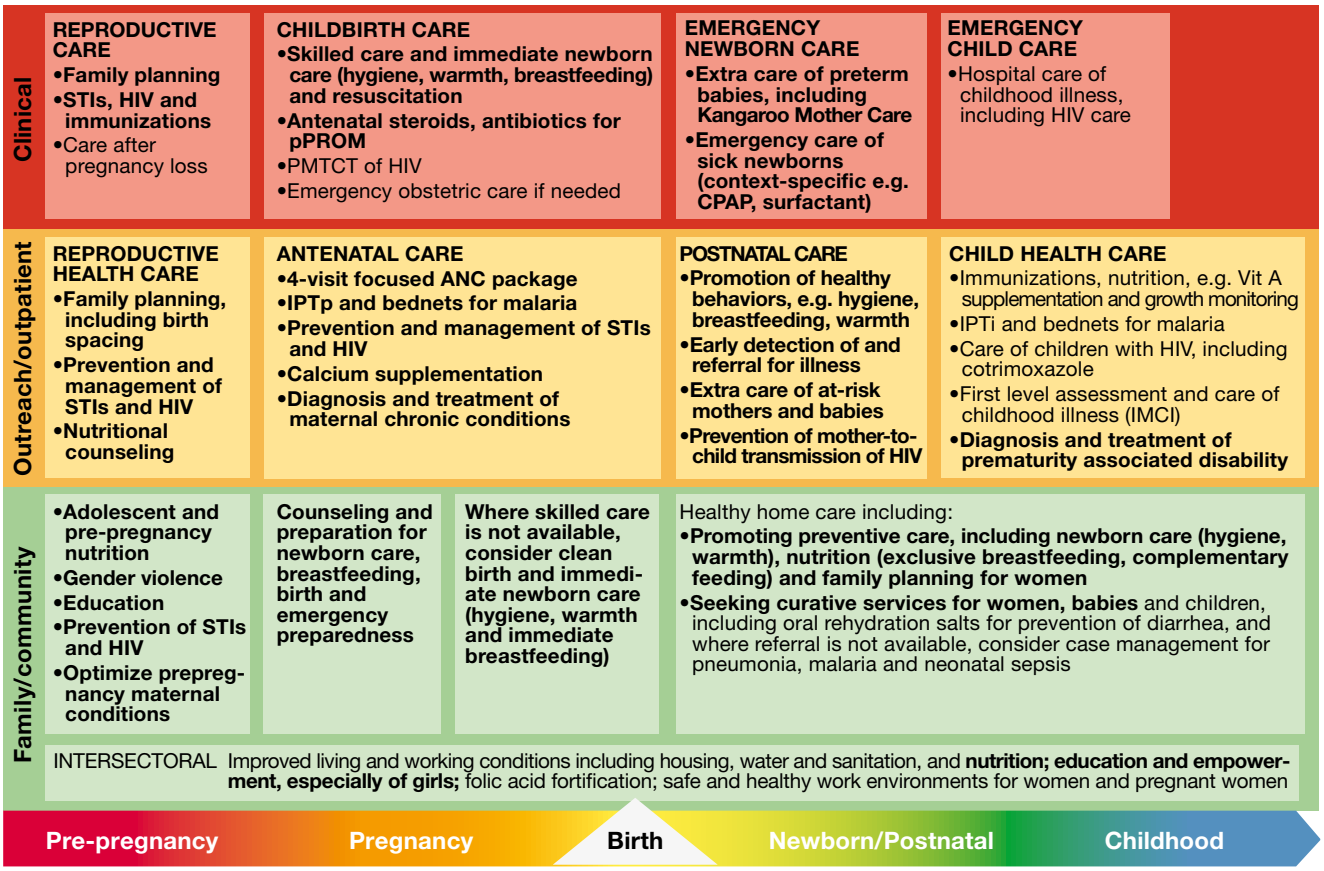
Packaging preterm birth interventions within the existing health system

There is increasing global consensus around essential reproductive, maternal, newborn and child health (RMNCH) interventions (PMNCH, 2011), including those to address preterm birth. The goal is to achieve universal, equitable coverage and high quality in all these RMNCH interventions. For sustainable effect, interventions to prevent preterm birth in the preconception and antenatal periods and to reduce death and disability in premature babies must be integrated within the existing health system.

The continuum of care is a core organizing principle for health systems emphasizing linkages between health-care packages across time and through various service delivery strategies (Chapter 1). An effective continuum of care addresses the health needs of the adolescent, woman, mother, newborn and child throughout the life cycle, wherever care is provided, whether it be at the home, primary care level or district and regional hospitals. Integrated service delivery packages within the continuum of care have many advantages: cost-effectiveness is enhanced; available human resources are maximized; and services are more family-friendly, reducing the need for multiple visits (Ekman et al., 2008). Most importantly, they can help prevent stillbirths, improve prevention and care of premature babies and save the lives of women, newborns and children (Friberg et al., 2010; Pattinson et al., 2011).

Interventions with the highest impact on the prevention of preterm birth and care of the premature baby can be

Figure 6.2: Integrated service delivery packages for maternal, newborn and child health



Source: Adapted from (Kerber et al., 2007; Lawn et al., 2012). Note: interventions for preterm birth are bold. Acryomns used: ANC = Antenatal care; CPAP = Continuous positive airway pressure; HIV = Human Immunodeficiency Virus; IMCI = Integrated Management of Childhood Illnesses; IPTp = Intermittent presumptive treatment during pregnancy for malaria; pPROM = Prelabor premature rupture of membranes; STI = Sexually Transmitted Illness

integrated into these health service delivery packages, which exist in most health systems and involve links with maternal and child health services, as well as immunization, malaria, HIV/AIDS, nutrition and other related programs (Kerber et al., 2007). A schematic matrix of the basic health packages (Figure 6.2) outlines these packages spanning the continuum of care and through various service delivery modes within the health system, highlighting the interventions included to address preterm birth.

While these packages may exist in nearly all settings, lower-income countries cannot scale up and implement all the individual RMNCH interventions within all the packages at once. Packages usually are initially comprised of the essential interventions and then increase in complexity over time according to local needs and capacity. The functionality of health systems, such as human resource capacity, health-facility infrastructure, supply and demand systems, financial resources, government stewardship, district-level management and use of data, will also determine the rate of scale-up within the continuum of care.

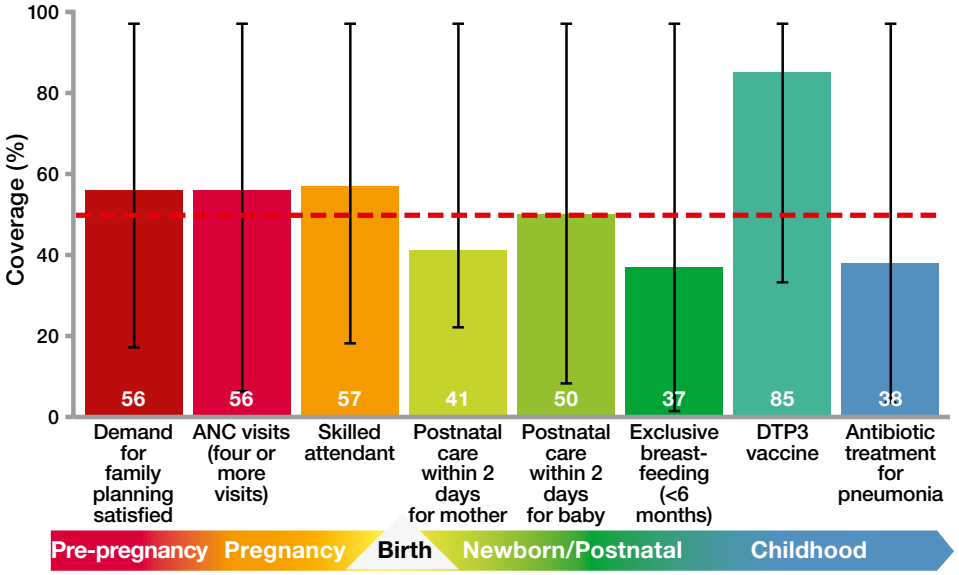
Closing gaps in coverage, equity and quality

In order for health services to save the maximum number of lives, coverage, quality and equity need to be high. Ensuring high coverage of care means reaching every woman, mother-to-be, mother, newborn, child and family with targeted interventions. Providing quality care means doing the right thing at the right time. Providing equitable care means ensuring care for all according to need, rather than income, gender or other social grouping. This holds true for the existing inequalities in care within and across high-income as well as low- and middle-income countries.

Current coverage levels across the continuum of care for the eight indicators, chosen by the United Nations Commission on Information and Accountability for Women's and Children's Health, are tracked for the

75 priority Countdown to 2015 countries that collectively account for 90% of maternal, newborn and child deaths. Essential care reaches only half of the people in need (Figure 6.3), and there is a wide variation in coverage levels among countries, with some countries achieving nearly universal coverage and others meeting less than a quarter of the need. In addition, quality gaps are a missed opportunity for reaching families, women and babies (Chapters 4 and 5). Substantial progress is still needed for the reduction of maternal and newborn deaths, especially for the vital contact times (e.g., skilled attendant at birth and postnatal care) and for the prevention of preterm births (e.g., demand for family planning satisfied and antenatal care) (Requejo et al., 2012). Currently, there are no routine data available for many of the interventions for preterm birth prevention and care.

Figure 6.3: Coverage along the continuum of care for 75 Countdown to 2015 priority countries



Source: Countdown to 2015 (Requejo et al., 2012). Note: Eight selected Commission on Information and Accountability for Women's and Children's Health indicators, showing median for Countdown priority countries. Acryomns used: ANC = Antenatal care; DTP3 = Three doses of diphtheria, tetanus and pertussis vaccine.

A research pipeline to address preterm birth

Preterm birth is not a single condition, but a single outcome due to multiple causes. Hence, there will not be a single solution, but rather from an array of solutions that address the various biological, social, clinical and behavioral risk factors that result in preterm birth. This report identifies risks for preterm birth and the solutions needed to reduce these risks across the RMNCH continuum; yet for many of these risks, we do not have effective solutions. Important research priorities have been highlighted in Chapters 3, 4 and 5. A strategic research approach is needed to understand why babies are born preterm or as stillbirths; how to identify women at risk, even in adolescence; how to close the global survival gap for premature babies; and how to reduce disability rates in the preterm population and improve their quality of life.

Important research themes can be summarized across the research pipeline of description, discovery, development and delivery science, showing the dual agenda of preventing preterm birth and addressing the care and survival gap for babies born preterm (Table 6.1). For the preterm prevention research agenda, the greatest emphasis is on discovery and descriptive research, which is a longer-term investment. For

Photo: *Bill & Melinda Gates Foundation/Joan Sullivan* Photo: *MRC/Allen Jefthas* Photo: *Rice 360* Photo: *Michael Bisceglie/Save the Children*

Table 6.1: A research pipeline advancing knowledge to address preterm birth

	Description Characterize the problem	**Discovery** Understand the problem	**Development** Create and develop new interventions	**Delivery** Advance equitable access to interventions
Research aim	Descriptive epidemiology to understand determinants, advance definitions	Development of new interventions or adapting or improving existing interventions	Development of new interventions or adapting or improving existing interventions	Delivery of interventions at scale through innovative approaches
Preterm prevention research themes	• Improve collection, analysis, interpretation, application of epidemiological data for: » Refining, disseminating standard definitions of exposures, outcomes and phenotypes » Further understanding of risk factors for preterm birth » Monitoring and evaluating impact of interventions » Improving the estimates and data collection systems	• Increase knowledge of the biology of normal and abnormal pregnancy • Better understand modifiable mechanisms contributing to preterm birth (e.g., preconceptual or antenatal nutrition, infection and immune response) • Advance understanding of underlying pathophysiology of preterm newborns and impact of co-morbidities on outcomes in different country settings	• Create, develop new interventions (e.g., novel approaches to preventing preterm birth) • Adapt existing interventions to increase effect, reduce cost, or expand utilization and access	• Evaluate impact, cost and process of known interventions to reduce preterm birth (e.g., family planning, STI management, malaria prevention) • Social behavior change research to address lifestyle factors and other risks for preterm birth • Effective approaches to increase use of antenatal steroids in low- and middle-income settings
Premature baby care research themes			• Create new devices and drugs for preterm babies that are feasible to use in low-income settings • Adapt existing interventions to increase effect, reduce cost, and/or improve deliverability in challenging settings or at community level (e.g., robust, simpler technologies)	• Implementation research to adapt and scale up context-specific packages of care for preterm babies (e.g., examining task shifting, innovative commodities, etc.) • Create and implement effective community-based approaches (e.g., community health workers home visit packages, women's' groups)
Typical timeline to impact	Near-term to Long-term (2 to 15 years)	Long-term (5 to 15 years)	Medium-term (5 to 10 years)	Near-term (2 to 5 years)

Source: Adapted from Lawn et al., 2008; Rubens et al., 2010; with thanks to Boston Consulting Group for help on the table

the premature baby care agenda, the greatest emphasis is on development and delivery research, with a shorter timeline to impact at scale.

Descriptive research

Improved and consistently applied epidemiologic definitions and methods are the foundation for tracking the burden of preterm birth and better addressing the multiple and often interrelated causes of preterm birth to help identify methods for prevention. Simpler and lower-cost methods for measuring gestational age are particularly needed in low- and middle-income countries where the burden of preterm birth is highest. Social and racial disparities in preterm birth rates are a major issue, yet remain poorly understood. Another important need is standardized methods for diagnosing and treating prematurity-related impairment in childhood and more consistent measures and timing for assessing multi-domain impairments.

Discovery research

Discovery research focuses on better understanding the causes and mechanisms of preterm birth and the physiological processes of pregnancy, labor and birth. A multidisciplinary approach is needed to identify women at risk and discover new strategies for prevention, related to the multiple biological, clinical, behavioral, social, infectious and nutritional causes of preterm birth. Although infectious and inflammatory processes contribute to many early spontaneous preterm births, antibiotic treatment of reproductive tract infections has generally failed to reduce preterm risk. Novel

strategies for prevention are urgently needed, especially those that are feasible solutions for low-resource settings.

Development research

Equipment and commodities are considered essential for neonatal care units in high-income countries, yet for many such units in low-income settings, basic equipment and essential medicines are not available or no longer functioning. Development of robust, fit-for-purpose equipment, as outlined in Chapter 5, is a critical next frontier for referral care for preterm babies in the settings where most die, especially for care in hospitals. Some examples include oxygen condensers and pulse oximeters to ensure safe oxygen use in babies, low-cost and effective methods for intervening in complications of labor and delivery, syringe drivers for safer intravenous fluid and drug administration, devices for testing bilirubin (jaundice levels) and innovative phototherapy equipment. Commodities, such as antenatal corticosteroids, could reach more women and babies if they could be prepackaged in single-dose syringes or, ideally, needle-free devices.

Delivery research

Delivery or implementation research addresses how interventions can be best implemented, especially in resource-constrained settings where coverage inequalities are more pronounced so that all families are reached with effective care.

Addressing preterm birth brings the focus back to the woman before, during and after pregnancy. This includes highlighting the critical need for basic and applied research in the complications of pregnancy and delivery and pre-existing chronic diseases in pregnant women, including pre-eclampsia, hypertension, diabetes, aberrations in placentation and placental growth and infectious diseases. Multiple socioeconomic, behavioral and biomedical factors are major contributors to poor fetal outcomes, both preterm births and stillbirths.

These require implementation research and program evaluation on how best to achieve broad delivery and uptake of interventions, including programs for emergency obstetric care and infectious diseases such as malaria, HIV and STIs; improved nutrition; smoking cessation; and reducing indoor air pollution. In many high-income countries and those with emerging economies, there is evidence of an increase in elective inductions and cesareans without clear medical indication. More information is urgently needed from both providers and patients on the reasons for these shifts in clinical practice and how to promote more conservative obstetric management.

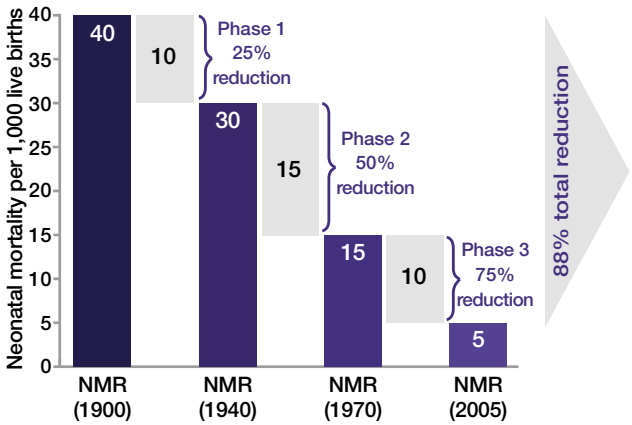
The vast majority of published studies on neonatal care relate to high-technology care in high-income settings. Implementation research from low- and middle-income settings is critical to inform and accelerate the scale up of high-impact care, such as KMC and neonatal resuscitation. Evaluation of context-specific neonatal care packages regarding outcome, cost and economic results is important, including adaptations such as task shifting to various cadres and use of innovative technologies. There is also a need to understand how to screen more effectively for and treat possible prematurity-related cognitive, motor and behavioral disabilities, even in older children. In addition, the economics of preterm birth prevention and care, including the cost/benefit and cost/effectiveness of interventions delivered singly or as a package across the continuum of care and in different settings and populations as well as the costs of doing nothing, need to be better studied.

Building the platform to accelerate research

Underlying this entire research agenda is the development and implementation of the capacity to advance the science of prevention of preterm birth, manage preterm labor and improve care of premature babies. Standard case definitions of the types and causes of preterm birth are being developed (Goldenberg et al., 2012; Kramer et al., 2012) and will be critical to accelerating discovery and making comparisons across studies from basic science to clinical trials and program evaluation. Multi-country studies tracking pregnant women with improved and accurate gestational dating will contribute to a better understanding of all pregnancy outcomes for women, stillbirths and newborns. Improved communication and collaboration among researchers investigating these linked outcomes will accelerate the discovery, development and delivery of innovation, especially across disciplines and between laboratory benches and remote and under-resourced

Box 6.1: Historical phasing of reductions in neonatal mortality rates in the United Kingdom and United States during the 20th century

Figure 6.4: Phased reductions of NMR in US and UK



PHASE 1: NMR reductions associated with public health approaches

- Early 20th century saw significant improvements in sanitary practices including at birth, mass education programs for hygiene, and rise of public health experts devoted to children's issues

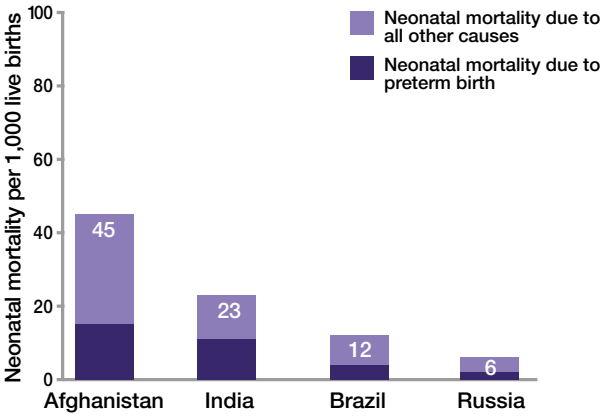
PHASE 2: Improved individual patient management associated with a further halving of NMR reduction prior to NICUs:

- Enhanced maternal health care, obstetric care, shift to facility births
- Wide uptake of antimicrobials
- Basic thermal care, further increased focus on neonatal and infant nutrition, introduction of incubators.

PHASE 3: Neonatal intensive care introduction and scale up:

- Incubators, ventilation, increasing complexity of care

Figure 6.5: Example countries in each NMR level



Start from where you are:

Some examples for countries in each NMR group show the preterm-specific mortality rates (Figure 6.5).

Afghanistan (NMR: 45) could reduce newborn deaths by about 10% through public health approaches, or more with increased focus on improved care of premature babies.

India (NMR: 23) could reduce deaths by 50% by increasing case management of neonatal infections and improved thermal care and feeding support for premature babies, and scaling up KMC.

Brazil (NMR: 12) could halve neonatal mortality with universal coverage of high-quality neonatal intensive care.

Data sources for UK and US historical data: (CDC, 2012, Office for National Statistics, 2012, NIH, 1985, Smith et al., 1983, Jamison et al., 2006, Lissauer and Fanaroff, 2006, Baker, 2000, Philip, 2005, Wegman, 2001).
With thanks to Boston Consulting Group
Note: more information on history of neonatal mortality reduction in UK and USA available in Chapter 5.
Data sources for Afghanistan, India, Brazil, and Russia from Child Health Epidemiology Reference Group/World Health Organization cause of death estimates for 2010 (Liu et al., 2012).

hospitals. Expanding training, research opportunities and mentorship for researchers in low-income settings will promote a pipeline of expertise to advance the science with the skills to use this science effectively to promote change.

Potential for lives saved

To understand the impact of evidence-based interventions on deaths due to complications of preterm birth, we considered both historical data and a new analysis using lives saved modeling.

History lessons

The historical data from the United States and United Kingdom (Box 6.1) demonstrate convincingly that a moderate increase in coverage of selected interventions results in a mortality reduction (Figure 6.4), even in the absence of neonatal intensive care. A number of lessons can be drawn from this historical data:

- Basic care and infection case management interventions have an important effect on neonatal deaths and on deaths amongst moderate and late preterm births, which account for over 80% of preterm births.
- More targeted care is necessary for reducing deaths among babies 28 to <32 weeks, and this reduction could be accelerated as higher-impact interventions are now known, such as KMC and antenatal corticosteroids which were not available in the mid-20th century in the the United States and United Kingdom.

- Intensive care may be necessary to reduce deaths among extremely premature babies (<28 weeks), who account for 5% of all premature babies though a larger proportion of deaths.

Table 6.2: Estimated lives saved of premature babies in settings with universal coverage of interventions

Intervention reaching 95% coverage	Also saves mothers or other babies	By 2015		By 2025	
		% deaths averted	Lives saved	% deaths averted	Lives saved
Family planning*	M, SB, N	24	228,000	32	345,000
Antenatal corticosteroids	N	40	373,000	41	444,000
Antibiotics for pPRoM	N	9	85,000	9	101,000
Immediate assessment and simple care of all babies	N	5	44,000	5	53,000
Neonatal resuscitation	N (SB)	7	65,000	7	77,000
Thermal care	N	15	142,000	16	171,000
Kangaroo mother care	N	48	452,000	48	531,000
Interventions implemented together	M, SB, N	81	757,000	84	921,000

Note: interventions marked with M will also save maternal lives, SB would avert stillbirth, and N will save newborns dying from causes other than preterm birth.
* Family planning scaled to 60% coverage or to a level whereby the total fertility rate is 2.5.
Note that obstetric care would also have an impact, but is not estimated separately

Lives saved modeling

A Lives Saved Tool (LiST) analysis was undertaken ("LiST: The Lives Saved Tool. An evidence-based tool for estimating intervention impact", 2010). LiST is a free and widely used module in a demographic software package called Spectrum, which allows the user to compare the effects of different interventions on the numbers of maternal, neonatal and child deaths and stillbirths, as well as stunting and wasting. National time series data for mortality, health status and intervention coverage is preloaded for 75 Countdown to 2015 priority countries[1]. The detailed review process to estimate the effect sizes of cause-specific mortality and the modeling assumptions in LiST are based on *The Lancet's* Series on Child Survival, Neonatal Survival, Maternal Health, Stillbirths and Child Undernutrition as well as about 40 published reviews. The modeling methods have been published elsewhere (Boschi-Pinto and Black, 2011; Stover et al., 2010).

The LiST analysis (Table 6.2) was conducted for 75 Countdown to 2015 priority countries. Table 6.2 lists the interventions included in the analysis that benefit preterm birth prevention and survival of premature babies. We considered the period from 2010 to 2015 and then up to 2025 to allow for a more feasible time frame to scale up care and progress on the prevention agenda. The results of the LiST analysis found that 84% of premature babies (more than 921,000 lives) could be saved in 2025 if these interventions were made universally available (95%). Full coverage of antenatal corticosteroids alone resulted in extremely high mortality reductions, a 41% decrease from 2010 (Mwansa-Kambafwile et al., 2010). Implementing KMC suggests even more dramatic results are possible (Lawn et al., 2010), averting approximately 531,000 deaths in 2025. If these were added to existing health system packages, especially noting the recent shifts to more facility births in Africa and Asia, then a high impact is possible even in a relatively short time frame.

Goals for action by 2025

This report initiates a process towards goals for preterm birth prevention and presents a new goal for the reduction of deaths due to complications of preterm birth (Box 6.2). This goal was set through consultation by a group of technical experts. Several analyses were undertaken, notably

(1) projections by country of the deaths due to preterm birth from now until 2025, assuming no change in trends and assuming expected changes in Gross National Income (GNI);
(2) reduction in preterm-specific neonatal mortality if the historical trends from the United Kingdom or the United States (Box 6.1) were applied or if more rapid recent reductions in middle-income countries were applied (Box 6.3);

1. These countries are: Afghanistan, Angola, Azerbaijan, Bangladesh, Benin, Bolivia, Botswana, Brazil, Burkina Faso, Burundi, Cambodia, Cameroon, Central African Republic, Chad, China, Comoros, Congo, Democratic Republic of the Congo, Côte d'Ivoire, Djibouti, Egypt, Equatorial Guinea, Eritrea, Ethiopia, Gabon, The Gambia, Ghana, Guatemala, Guinea, Guinea-Bissau, Haiti, India, Indonesia, Iraq, Kenya, Democratic Republic of Korea, Kyrgyz Republic, Lao People's Democratic Republic, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mexico, Morocco, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, Papua New Guinea, Peru, Philippines, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, South Africa, South Sudan, Sudan, Swaziland, Tajikistan, United Republic of Tanzania, Togo, Turkmenistan, Uganda, Uzbekistan, Vietnam, Yemen, Zambia, and Zimbabwe.

Box 6.2: Goals for action by 2025

As a specific action from this report, a technical expert group will be created to consider a ***goal for reduction of preterm birth rate*** by 2025 for announcement on World Prematurity Day 2012.

This report includes a new goal for the ***reduction of deaths due to preterm birth***. The global goal is broken down into two different country groups: those that have already achieved a low level of neonatal mortality (less than 5 per 1,000 live births) and those countries that have not yet achieved this level.

For the countries that have already reached a neonatal mortality rate (NMR) of 5 per 1,000 live births or below by 2010:

The goal is to eliminate remaining preventable preterm deaths, focusing on equitable care for all and quality of care to minimize long-term impairment.

For countries with a neonatal mortality rate above 5 per 1,000 live births in 2010:

The goal is to reduce their preterm birth-attributable mortality by 50% between 2010 and 2025. This reduction will mean that 550,000 premature babies will be saved each year by the target year of 2025. In addition, more babies will be saved who are moderately preterm but die of other causes (e.g. infections).

(3) preterm-specific neonatal mortality reductions predicted based on coverage changes according to Lives Saved Tool Modeling (Table 6.2).

All these analyses used data from UN demographic projections of births (UN, 2010) and the Child Health Epidemiology Reference Group/World Health Organization neonatal cause of death time series, 2000 to 2010 (Liu et al., 2012).

Using the results from analyses of the three future scenarios (Box 6.4), a target for mortality reduction of preterm births was set and agreed by the technical experts (Box 6.2).

Scenario 1: "Business as usual"

Should country governments and the global community take no further direct action to address deaths due to preterm birth, analysis of regional trends over the past decade and forward projection shows that mortality, will decline by 24% by 2025 (or 16%, if the projection is based on forecasted GNI change) (Box 6.4). Given this scenario and taking into account changing numbers of births, the global total of preterm deaths will not reduce significantly by 2025, with around 900,000 premature babies continuing to die every year.

Photo: *William Hirtle/Save the Children*

Scenario 2: Countries take action to catch up with top performers within their region

Should country governments take action now to match the improvements of the top performers within their regions or to match the historical reductions in the United States and the United Kingdom from basic interventions before widespread use of intensive care, preterm mortality could decline by 44 to 50% by 2025 (Box 6.1). The examples of Sri Lanka and Turkey (see Box 6.3) present models that could result in a significant reduction in mortality, halving deaths in 10 years, before the 2025 target. Even those countries with higher mortality rates that are not yet ready to scale up intensive care could see a 50% reduction as shown in the mid-20th century in the United States and the United Kingdom. This reduction is achievable with improved essential care of premature babies and better case management of infections and respiratory distress syndrome, especially since the deaths of moderately preterm babies are the most common and preventable ones.

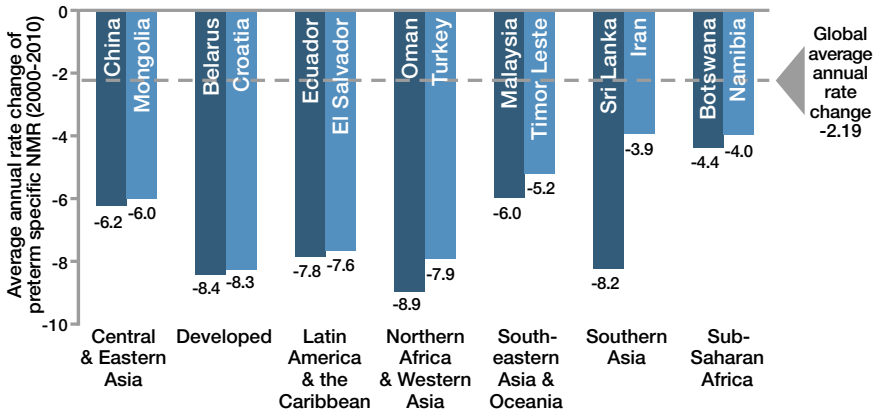
As this report shows, there are new high-impact, low-cost interventions currently at low coverage, such as

antenatal corticosteroids and KMC, that could significantly accelerate progress, which were not available in the United States and the United Kingdom in the middle of the 20th century when NMR was significantly reduced. Hence, it would be expected, with the inclusion of these and other innovations, that mortality reduction would be more rapid than for the historical examples.

Box 6.3: Some countries have halved their deaths due to preterm birth in just one decade

Several low- and middle-income countries have demonstrated a major reduction in preterm-specific neonatal deaths in low- or middle-resource settings (Figure 6.6). The experiences of two of these countries — Sri Lanka and Turkey — are briefly described here. Differences between approaches are immediately apparent, as countries customize their approach to availability of resources and "readiness" of the systems.

Figure 6.6: Well-performing countries for preterm-specific mortality reduction by region



TURKEY

Turkey, an upper middle-income country, has made significant progress in health care over the past decade. Health system transformation was comprehensive, but maternal and neonatal health policies, in particular, played a central role. As a result, the neonatal mortality rate dropped from 21 per 1,000 live births in 2000 to 10 per 1,000 live births in 2010 (UNICEF et al., 2011). Births with a skilled attendant rose from 83% in 2003 to more than 90% in 2009, and institutional facility births rose to more than 90% by 2009 (Demirel and Dilmen, 2011). In fact, Turkey achieved in a decade what took 30 years in the OECD countries.

Part of Turkey's success was through the implementation of demand and supply strategies. There was significant promotion of antenatal care and facility births, including cash incentives and free accommodation in maternity waiting homes in cities for expectant women from remote areas (Kultursay, 2011). In addition, wider public health approaches were an important foundation, such as focused elimination of maternal and neonatal tetanus, breastfeeding promotion and UNICEF "baby-friendly" hospitals campaigns. Turkey invested in health systems improvements, such as systematizing referral to neonatal care with transport systems, and upgrading neonatal intensive care units, focusing on nursing staff skills and standardization of care especially for neonatal resuscitation (Baris et al., 2011).

SRI LANKA

Sri Lanka, a lower middle-income country, has benefited from a reduction in its NMR as a result of policies and gradual improvements in health care that have been continually implemented over the past five decades. Despite relatively low per-capita income, Sri Lanka has achieved impressive results and has often been cited as an example of success for reduction of maternal mortality through a primary health care approach (WHO, 2006).

Many of these advances have come due to Sri Lanka's investment in primary care initiatives as well as provision of free health care at government facilities. Antenatal care coverage is at 99% for the country, with approximately 51% of pregnant woman having more than 9 antenatal visits. Skilled birth attendance at delivery is universal (99%). Postnatal care is also robust, with 90% of women receiving public health midwife visits within 10 days of discharge (United Nations Millennium Project, 2005; Senanayake et al., 2011).

From an NMR of 80 per 1,000 live births in 1945, Sri Lanka progressed steadily to 22 per 1,000 live births by 1980, and now to around 10 per 1,000 live births (Senanayake et al., 2011; UNICEF et al. 2010). More recent advances included reinvigoration of community-based health care, including maternity clinics, and strengthening of referral and transportation networks such that women in preterm labor are rapidly transported to appropriate secondary and tertiary care centers. A recent focus has been additional investment in tertiary care centers equipped for neonatal intensive care, training of specialists and investment in expensive technologies (WHO Country Cooperation, expert interviews).

Source: Analysis conducted using data from Liu et al., 2012. Credit: Boston Consulting Group with the Global Preterm Birth Mortality Reduction Analysis Group

Scenario 3: Countries achieve universal coverage of basic interventions

Should countries adopt universal coverage of interventions (95%) ensuring that every woman and child who needs an intervention receives it, then, according to both the LiST analysis (Table 6.2) and the historical data (Box 6.1), countries could achieve an 84% reduction of 1.1 million deaths due to preterm birth complications. While ensuring a 95% coverage rate is ideal and would result in a major mortality reduction, this process will take time. Working towards this goal will achieve significant progress from now until 2015 and beyond. Many other causes of newborn death, as well as maternal deaths and stillbirths, would be saved by such shared interventions as skilled care at birth.

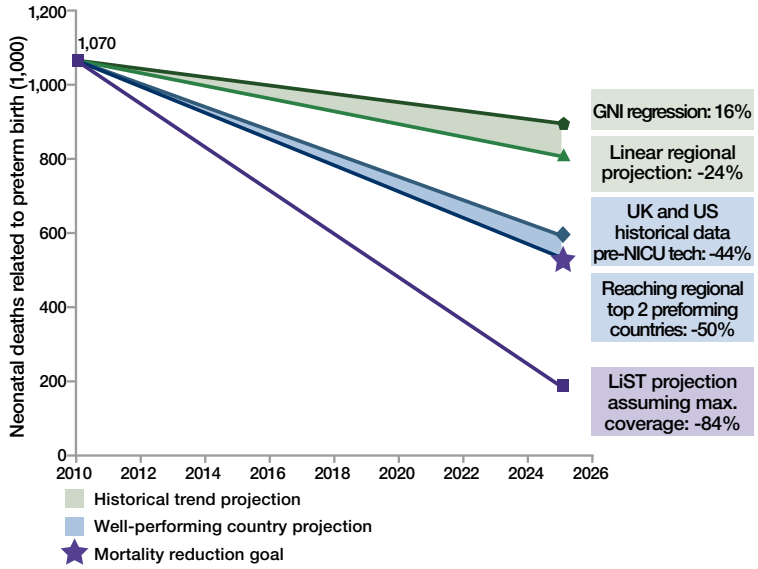
Call to action

This report is sobering in the news it delivers and in the personal stories of loss that it tells. Yet it is also a story of hope in the significant opportunities for change, especially as we approach the final sprint for the MDG 4 target and aim to maintain momentum beyond 2015. These first-ever country estimates for preterm birth tell a grim story (Chapter 2). In 2010, 15 million babies — more than 1 in 10 births — were born too soon, exacting an emotional and economic toll on families, the communities in which they live and their countries. The problem is not diminishing; for the countries with 20-year trend data, the majority show an increase in preterm birth rates. Even worse, the burden is not shared equally, with the impact of preterm birth falling most severely on the poorest families and in low- and middle-income countries where health systems are less prepared to respond. There are also high preterm birth rates in many high-income countries, including the United States. These facts demonstrate that the problem of preterm birth is one that we all share; therefore, the solutions must be ones that we not only share, but also tackle through cooperation, collaboration and coordination of the many constituencies and stakeholders that need to be involved if the toll of preterm birth is to be optimally reduced and the lives of mothers and newborns saved.

A number of specific actions, if pursued by all partners and applied across the RMNCH continuum of care, will not only help prevent preterm birth, but will have an immediate, profound and sustained impact on family health and human capital in the highest-burden countries. The seven constituencies, as identified by *Every Woman Every Child*

Box 6.4: Three scenarios inform a target for mortality reduction for premature babies

Figure 6.7: Results of three scenarios of preterm-specific mortality reduction to 2025



Scenario 1: Business as usual, assuming continuing trends (lowest option for goal)
Forward projection based on average annual rate of change of neonatal mortality due to preterm birth (-24%) or if adjusted for GNI forecast (-16%)

Scenario 2: Well-performing country analysis (midpoint)
Matching top global or regional performers indicates potential reduction of 40-50%

Scenario 3: LiST analysis of interventions without intensive neonatal care but very high coverage (potential upper target)
95% coverage of suite of interventions predicts 84% reductions, similar to historical data from the United Kingdom and the United States

Preterm mortality reduction target by 2025
- 50% for countries with NMR above 5 per 1,000 live births
- Eliminate all preventable preterm deaths for countries with NMR below 5 per 1,000 live births

Source: Analysis conducted by Mortality Reduction Goal Group and Boston Consulting Group using multiple data sources (Liu et al., 2012; EIU GDP projections 2010 to 2030; World Population Prospects, 2010; UN Department of Economic and Social Affairs; LiST analysis). Note: Analysis is for countries with NMR of more than 5 per 1,000 live births; other countries are excluded. Interventions in the LiST analysis included KMC, antenatal corticosteroids, antibiotics for pPRoM, skilled birth attendance, and others.

(Ban, 2010), have four action themes, which link closely to the principles of Act, Monitor and Review recommended by the Commission on Information and Accountability for Women's and Children's Health.

Invest:

Bring both financial and other resources to address maternal and newborn health and the burden of preterm birth.

Implement:

- Adapt integrated packages of care, taking into account national and local contexts, and tailored to national health service delivery models.
- Increase reach of existing preventive interventions in the preconception period, especially family planning, to all women, including adolescent-friendly services.
- Ensure that every woman receives the high-quality care she needs during pregnancy, at birth and post-natal, especially if she is at risk of preterm birth. There should be greater emphasis on the universal provision of antenatal corticosteroids, building on the work of the UN Commission on Life-saving Commodities for Women and Children as an opportunity to accelerate progress.
- Undertake immediate action to scale up KMC as a standard of care for all preterm babies under 2,000 grams, regardless of resource setting.
- Improve methods for diagnosing and treating prematurity-related impairment in childhood.
- Ensure that every family has the support they need, immediately after birth of a premature baby, following its loss, or living with a child with prematurity-associated disability.

Inform:

Improve the data for preterm birth rates, mortality, impairment and their causes, with regular tracking of coverage, quality and equity gaps, as is done through Countdown to 2015 and linked to the work of the Commission for Information and Accountability using the data for action and accountability, including the establishment of national birth registrations.

Innovate:

Conduct multi-country collaborative research on the:

- Etiology of preterm birth in order to develop innovative solutions to help reverse the almost universal rise in preterm birth rates, in particular, advancing the understanding of important maternal health conditions associated with preterm birth (e.g., preeclampsia and gestational diabetes) and improving identification of diagnostic markers and related screening tools.
- Implementation research to develop and deliver innovations to reach the poorest.

This agenda is ambitious, yet it can and must be accomplished if the actions detailed in this report are to be given the visibility, funding and attention they deserve. To be successful in our goals, the constituencies identified must work together collaboratively and in partnership in ways that are transparent to all, vigorous and accountable.

All of the partners, donors and contributors involved in the preparation and dissemination of this report see its publication not as a final step (see page viii for partner commitments), but as an important next step towards a world where every woman and every newborn is given the best chance to survive and thrive.

Everyone has a role to play...

to reach every woman, every newborn, every child

To be accountable to reaching the poorest,
reviewing information and accelerating change.

Partner commitments for addressing preterm birth detailed onpage viii and available at www.everywomaneverychild.org

Governments and policy-makers at local, national, regional and global levels:

Invest

- Commit to reducing neonatal deaths due to preterm birth by 2025, in the context of continued progress for child survival (MDG 4) and maternal health (MDG 5) to 2015 and beyond
- Set targets for improved survival of premature babies (50% for countries with NMR more than 5 per 1,000 live births) and for preterm prevention (target to be announced in November 2012)
- Commit more funds for preterm birth prevention and care, including increased funding for research and innovation to improve both in the context of national health plans
- Ensure equitable access to and provision of quality care before, between and during pregnancy, at birth and care of the premature baby

Implement

- Strengthen health systems for quality maternal and neonatal care, with a focus on the health systems, including key commodities and a priority workforce, specifically midwives and neonatal nurses
- Strengthen community care and increase awareness and demand for RMNCH services and link to referral systems
- Introduce or amend legislation and policies to promote universal access to quality preconception and maternal and perinatal services, including family planning services, and ensure labor rights for all women, especially pregnant women
- Harmonize stakeholder efforts to reduce the toll of preterm birth; include academic institutions, health care organizations, the private sector, civil society, health care workers and donors

Innovate:

- Promote the discovery, development and delivery of affordable, essential medicines, new technologies and novel models for training and service delivery, to prevent preterm birth and improve care of premature babies, in partnership with the private sector where needed

Inform:

- Track progress towards MDGs 4 and 5, RMNCH coverage as outlined by Commission on Information and Accountability for Women's and Child's Health: and specifically improve the data for preterm birth rates, mortality, disability, quality of life and equitable coverage of evidence-based interventions

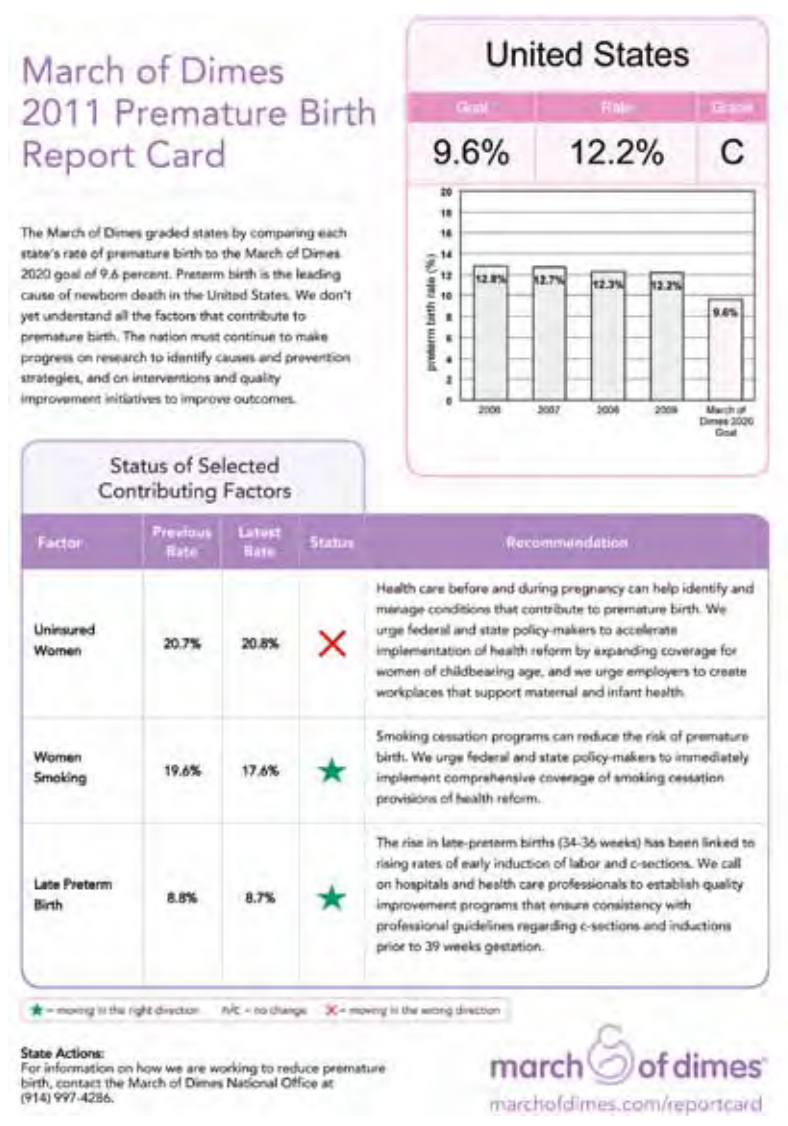
Box 6.5: National integrated campaign for preterm births

Parents, advocates and civil society have captured the attention of governments and monitored progress in the United States through support of an annual Premature Birth Report Card. The Report Card, a familiar means of assessing progress for school-age children, has been a powerful tool used in the United States to prevent preterm birth and its serious health consequences. These grades, used as a rallying point, have helped bring visibility and promote change. Issued by the March of Dimes every year since 2008, the Report Cards assign a letter grade to the United States and to each of 50 state governments. In addition, they summarize the actions that must be taken to fund prevention programs, address health care access and bring about needed change in health care systems.

One southern U.S. state, with the second highest preterm birth rate in the country, has received an "F" on its Report Card every year since 2008. The failing grade mobilized state health officials in early 2012 to launch a statewide initiative with the goal of reducing rates. An important factor in the success of the Report Cards is the accuracy and objectivity of the data and analysis used to derive the grades. For transparency, this information is made publicly available each year. In the first year, great care was taken to explain to the states the methodology and the basis of comparison. Media coverage and use of the Report Card grades by state governments have grown in each of the subsequent years.

The U.S. Surgeon General has participated in media outreach to publicize the Report Cards and their recommended actions. Sustained effort by health care leaders and advocates at all levels, inside and outside of government, has elevated the issue of preterm birth on the nation's health agenda, contributing to an announcement of new federal resources to test promising practices. As new resources are brought to bear on the problem, the Report Cards will continue to mobilize stakeholders and mark progress.

More information is available at http://www.marchofdimes.com/prematurity_reportcard.html



March of Dimes 2011 Premature Birth Report Card

The March of Dimes graded states by comparing each state's rate of premature birth to the March of Dimes 2020 goal of 9.6 percent. Preterm birth is the leading cause of newborn death in the United States. We don't yet understand all the factors that contribute to premature birth. The nation must continue to make progress on research to identify causes and prevention strategies, and on interventions and quality improvement initiatives to improve outcomes.

United States

Goal	Rate	Grade
9.6%	12.2%	C

Status of Selected Contributing Factors

Factor	Previous Rate	Latest Rate	Status	Recommendation
Uninsured Women	20.7%	20.8%	✕	Health care before and during pregnancy can help identify and manage conditions that contribute to premature birth. We urge federal and state policy-makers to accelerate implementation of health reform by expanding coverage for women of childbearing age, and we urge employers to create workplaces that support maternal and infant health.
Women Smoking	19.6%	17.6%	★	Smoking cessation programs can reduce the risk of premature birth. We urge federal and state policy-makers to immediately implement comprehensive coverage of smoking cessation provisions of health reform.
Late Preterm Birth	8.8%	8.7%	★	The rise in late-preterm births (34-36 weeks) has been linked to rising rates of early induction of labor and c-sections. We call on hospitals and health care professionals to establish quality improvement programs that ensure consistency with professional guidelines regarding c-sections and inductions prior to 39 weeks gestation.

★ = moving in the right direction N/C = no change ✕ = moving in the wrong direction

State Actions:
For information on how we are working to reduce premature birth, contact the March of Dimes National Office at (914) 997-4286.

march of dimes
marchofdimes.com/reportcard

The United Nations and other multilateral organizations:

Invest

- Help countries develop and align their national health plans, including implementation costing to achieve the health MDGs and preterm birth mortality-reduction targets
- Support systems that track progress of global and national preterm birth rates and associated mortality and morbidity, and advocate to address funding gaps

Implement

- Define norms and guidelines to support efforts to improve women's and children's health, and encourage their adoption
- Work together and with other partners outside the UN system to strengthen technical assistance and programmatic support for the prevention and treatment of preterm births, helping countries scale up high-impact interventions and strengthen their health systems, including health care workers and community-level care
- Ensure linkages along the continuum of care and among health sectors (e.g., education, environment and indoor air pollution) and integrate with other international efforts promoting the MDGs

Innovate

- Generate and disseminate evidence on preterm birth, and provide a platform for sharing best practices; generate and disseminate evidence on cost-effective interventions and research findings
- Utilize the UN Commission on Life-saving Commodities for Women and Children to innovate, in collaboration with the private sector and other partners, to address gaps for essential equipment and medicines (e.g., antenatal corticosteroids)

Inform:

- Promote standard definitions and advance sufficiently detailed metrics for measuring preterm birth outcomes, linking with other partners and collaborating on regular estimates for preterm birth, alongside other RMNCH tracking
- Support the production, dissemination and use of coverage data for evidence-based interventions through the Countdown to 2015 and Commission on Information and Accountability for Women's and Children's Health through the independent Expert Review Group

Box 6.6: Life-saving Commodities for Women and Children — potential for action to reduce preterm deaths

The United Nations (UN) Secretary General's The Global Strategy for Women's and Children's Health highlighted inequities for women and children around the world and advocated for universal access to basic health care for all essential medicines and other commodities necessary to achieve MDGs 4, 5 and 6. Too often, cost-effective, high-impact health commodities do not reach the women and children who need them. Some of the barriers to access include the lack of affordable products, lack of age-appropriate formulations, weak supply chains, lack of awareness of how, why and when to use these commodities and inadequate regulatory capacity at the country level to protect the public from sub-standard or counterfeit medicines that cause harm.

The UN has established a Commission to address this issue, bringing together industry, civil society and technical experts to champion the effort to reduce the barriers that obstruct access to essential health commodities. Selected commodities will be:

1. High-impact and effective, addressing major causes of death and disease among children under 5 years of age and women during pregnancy and childbirth
2. Inadequately funded by existing mechanisms
3. Ready for innovation and rapid scale up in product development and market shaping

An initial list of 13 commodities has been selected for consideration, and includes four with potential to reduce the 3.1 million deaths amongst newborns, especially those who are preterm. All of these commodities are high-impact, low-coverage, and none has had previous global funding:

- Antenatal corticosteroids reduce the risk of severe respiratory complications by half if given by injection to women in preterm labor, but this commodity is low-coverage even in middle-income countries, due to a number of supply and regulation issues and low awareness among health care providers. It has been estimated that up to 400,000 babies could be saved with this intervention, and the unit costs, if dexamethasone is used, is around one dollar per dose.
- Chlorhexidine cord care has recently been shown to be effective in reducing neonatal deaths due to sepsis: 320,000 babies die each year of sepsis and many of them are moderately preterm. Rapid policy and program uptake of chlorhexidine could save many of these babies.
- Resuscitation devices and training mannequins have undergone recent innovations, but are still not widely available in many high-burden countries with scope to reduce neonatal deaths from intrapartum insults, as well as from preterm birth complications.
- Injection antibiotics, including gentamicin, are crucial for treating neonatal infections and yet, due to low dosing, are often mis-administered; innovations such as pre-packaged doses and needle-free technology could have a major effect on reaching the poorest.

Photo: *CAPRISA*

Promotion of a robust supply of quality products with fair pricing is a unique opportunity to accelerate progress and save lives of women and children, and could contribute to halving the 1.1 million deaths due to preterm birth.

More information available at http://www.everywomaneverychild.org/resources/un-commission-on-life-saving-commodities

Donors and philanthropic institutions:

Invest

- Provide sustained long-term support (financial and programmatic) in line with national health and RMNCH plans that incorporate preterm births and are harmonized with other related global health initiatives
- Advocate for emphasizing preterm birth within the broader development, global health and RMNCH context, and align preterm birth mortality-reduction goals with country-specific needs
- Invest in national systems to improve measurement of risk factors for preterm birth, pregnancy and birth outcomes, and the strengthening of research institutions

Innovate

- Support high-priority research efforts to address solution gaps and implementation research to inform the scale up of evidence-based interventions to reduce preterm deaths

Inform:

- Promote transparent tracking of commitments and accountability, and long-term improvements in national health management and information systems

Box 6.7: Helping Babies Breathe as an example of a public-private alliance to save newborns

In 2010, the United States Agency for International Development (USAID) instituted a formal public-private partnership, called Global Development Alliance, to accelerate the scale up of a simplified neonatal resuscitation package, called Helping Babies Breathe (HBB). HBB brought together differing skills with a professional association, American Academy of Pediatrics (AAP), civil society and industry. Key constraints that had impeded scale up of neonatal resuscitation were in the lack of robust, fit-for-purpose equipment and the complexity of guidelines and training. AAP and others developed an evidence-based simplified pictorial algorithm for basic neonatal resuscitation. Laerdal designed and manufactured low-cost equipment, including bag and mask, a penguin suction device and Neonatalie (a robust training mannequin). A non-exclusive partnership with Laerdal facilitated the availability of these devices, as well as those of other manufacturers. Save the Children's role facilitated uptake, integration and sustainable scale up with ministries of health in lower-income countries. The U.S. National Institutes of Health (NIH) helped with evaluation. Other partners, including Johnson & Johnson and the Latter-day Saints Charities, have joined and generated momentum at global and country level.

Photo: Laerdal

In less than 2 years, HBB was rapidly introduced in 34 countries, 10 of which have developed national roll-out plans. A similar partnership model could be applied to other preterm birth interventions to accelerate progress.

More information available at http://www.helpingbabiesbreathe.org/GDAinformation.html

The business community:

Invest

- Invest additional resources to develop and adapt devices and commodities to prevent and treat preterm birth in low-income settings; look for innovative partnerships and business models for scalable, equitable and sustainable change

Implement

- Scale up best practices and partner with the public sector to improve service delivery and infrastructure for prevention and management of preterm birth

Innovate

- Develop affordable new diagnostics, medicines, technologies and other interventions, including social and behavioral change, for preterm birth and make them available to the most vulnerable and marginalized

Inform:

- Use and strengthen existing tracking systems for commodities and devices to improve supply-chain logistics

Box 6.8: Industry partnership for innovative technology for preterm baby care in Asia

Many countries lack the technical capacity and human and financial resources to successfully implement facility-based neonatal intensive care. Equipment failures, management and personnel training, and stock outs of consumables hamper health delivery efforts. GE Healthcare and the East Meets West Foundation (EMW) have forged an alliance to solve these challenges. Building on the success of a program called Breath of Life, EMW and GE Healthcare are creating a suite of neonatal technologies that are durable, require few consumables, are easy to use and are specifically designed for sustainability in low-resource settings. The equipment is delivered in the context of a multi-year program of training, monitoring, clinical supervision and technical support. Since its launch by EMW in 2005, the Breath of Life program has been implemented in more than 280 hospitals across eight countries of South Asia, currently treating more than 55,000 babies a year.

Designed locally in Vietnam, EMW's neonatal equipment has maintained a failure rate below 5% compared to more than 80% for donated equipment from Western countries. Beyond core technologies of bubble CPAP, LED phototherapy and radiant warmers, the program also provides infection-control systems, ambu-bags, baby bonnets and a long list of ancillary equipment. Monitoring and training — a pervasive shortcoming of many technology-based programs — are core strengths of the Breath of Life program. EMW staff typically monitor every hospital in the network 3 to 5 times per week, and visit as often as twice a month for extended technical and clinical training and supervision.

Photo: *Design that Matters*

In partnership with GE Healthcare, the Breath of Life program will be significantly expanded in scope and scale. Future devices will be engineered according to local design principles and follow stringent quality and regulatory review processes. As a global leader in the design and manufacture of advanced neonatal intensive care equipment, GE Healthcare can deliver and service these neonatal devices virtually anywhere in the world. Volume manufacturing should result in both lower costs and higher quality. This alliance of EMW and GE Healthcare is a powerful example of what partnerships can accomplish to help reduce the rate of preterm birth.

http://www.eastmeetswest.org and http://www.gehealthcare.com

Academic and research institutions:

Invest

- Agree upon and disseminate a prioritized and coordinated research agenda for preterm birth and pregnancy outcomes, including longer-term discovery science to address preterm prevention, and immediate implementation research to reduce deaths from preterm birth
- Encourage increased budget allocation for research into the causes of preterm birth, and innovative interventions for prevention and treatment

Implement

- Ensure accurate information on preterm birth outcomes are included in research studies assessing other pregnancy outcomes, and that preterm birth studies measure other relevant pregnancy outcomes
- Build capacity at research institutions, especially in low- and middle-income countries, and train professionals

Innovate

- Advance policy development by improving the metrics for impairment outcomes as well as preterm birth rates, and link to other pregnancy outcomes, reporting on trends and emerging issues relating to preterm births
- Advance innovative research into the multiple causes of preterm birth and innovative strategies for prevention

Inform:

- Disseminate new research findings and best practice related to preterm birth
- Strengthen global networks of academic providers, researchers and trainers through leveraging the momentum from this report and commitments of these institutions

Box 6.9: A global alliance to address knowledge gaps for preventing preterm birth

The Global Alliance to Prevent Prematurity and Stillbirth (GAPPS), an initiative of Seattle Children's, leads a collaborative effort to increase awareness and accelerate innovative research to improve maternal, newborn and child health. A global effort to prevent preterm birth and stillbirth requires an interdisciplinary research approach and a diverse network. GAPPS collaborates with a wide range of stakeholders, including families, foundations, corporations, hospitals, universities, governments, non-governmental organizations and research organizations.

At the International Conference on Prematurity and Stillbirth, key stakeholders developed the Global Action Agenda (GAA) on preterm birth and stillbirth. This defined strategic research priorities, including social and biological mechanisms of preterm birth and stillbirth, and testing new diagnostic, treatment and prevention interventions. The GAA also set goals to increase advocacy and scale up known prevention strategies, and strategies for funding organizations, while underscoring the need for better data on maternal mortality, stillbirths, preterm birth and the impact of preterm birth on newborn and child health.

Since the conference, GAPPS worked with scientists on preterm birth and stillbirth definitions and terminology for normal and abnormal pregnancy in order to improve comparability of research studies (Goldenberg et al., 2012; Kramer et al., 2012). The GAPPS Repository for data and specimen collection offers a standardized source of high-quality specimens linked to phenotypic data from diverse populations of pregnant women.

Photo: March of Dimes

Recently, the Preventing Preterm Birth initiative was launched, funded by a $20 million (USD) grant from the Bill & Melinda Gates Foundation, as part of the Grand Challenges in Global Health. The initiative provides grants to scientists around the world to investigate infectious, nutritional and immunologic factors contributing to preterm birth and preterm-related mortality, especially in the developing world.

More information is available at www.gapps.org

Health care workers and their professional associations:

Invest

- Advocate for and participate in evidence-based training, deployment and retention of workers with the necessary skills to address the burden of preterm birth

Implement

- Adapt and adopt evidence-based standards to prevent or treat preterm births; implement training plus continuing competency-based education, particularly for specialized health professionals such as neonatal nurses; and update curricula with evidence-based interventions
- Provide the highest-quality evidence-based care to prevent preterm birth in the preconception and antenatal periods and to improve care for premature babies; share best practices; test new approaches; use the best tools possible; and audit clinical practice
- Ensure that women, newborns and children are treated with respect and sensitivity when receiving health care, including provision of adolescent-friendly services

Innovate

- Identify areas for improved services and innovations to prevent or treat preterm birth
- Prioritize working in partnership to provide universal access to the essential package of interventions, including both prevention and care, and involving task shifting where appropriate

Inform:

- Improve data collection to track preterm births, such as consistent assessment of gestational age, birthweight, cause of death, data on impairment and retinopathy of prematurity

Box 6.10: Health care providers as champions of change for mothers and newborns

A premature baby's survival is dependent on both his mother's survival and on care received from several health care professional groups:
• Obstetricians, who provide effective care to the woman, prevent or manage preterm labor
• Midwives, who ensure safe delivery and resuscitate, if necessary
• Pediatricians, who undertake advanced resuscitation and ongoing care, if needed. Where most premature babies are born and die, there are few pediatricians and almost no neonatologists.

This cross-unit team can save lives; however, if none of these groups takes responsibility for premature babies, where minutes count between life and death, then more babies will die. Indeed, nurses and midwives are the front line workers for millions of premature babies in facilities in low- and middle-income countries. However, there is an acute shortage internationally of neonatal nurses, or nurses who receive specific training in newborn care, particularly in low-income countries. Those nurses, who commit to newborn care, often receive little or no recognition for providing excellent care against all the odds.

Regina Obeng has worked in the neonatal unit at the Komfo Anokye Teaching Hospital in Kumasi, Ghana for over 20 years. Not accepting newborn deaths as inevitable, she has dedicated her life to saving babies in her crowded ward, where 350 to 400 newborns are cared for each month. She has been a consistent voice for these babies and their mothers, speaking up for more space, better supplies and, especially, more staff and ways to retain skilled staff, and places for mothers to stay. Regina was awarded the International Neonatal Nursing Excellence Award in 2010, given by the International Conference of Neonatal Nurses (ICNN) together with Save the Children, the Council of International Neonatal Nurses (COINN) and the Neonatal Nurses Association of South Africa (NNASA). Now her voice is even stronger in Ghana, raising public awareness about the issues facing mothers and newborn babies, particularly prematurity, and has influenced even the highest levels of the Ministry of Health to ensure neonatal nurses' training will start in Ghana.

Photo: Jane Hahn/Getty Images for Save the Children

http://www.healthynewbornnetwork.org/success-story/international-neonatal-nursing-excellence-award-regina-obeng

Civil society:

Invest

- Advocate for increased attention to the health of women (including adolescents and mothers), newborns and children, with particular attention to strengthening prevention of and treatment for preterm birth, as well as strategic research
- Coordinate and support national campaigns, parent support groups and other agents of change

Implement

- Strengthen community and local capabilities to scale up implementation of effective, feasible and culturally appropriate interventions for prevention and care (e.g., KMC)
- Ensure family support for acute loss of stillbirth and preterm birth, or long-term support for disability

Innovate

- Develop and test innovative approaches to deliver essential services for prevention and care, particularly ones aimed at the most vulnerable and marginalized people, including women, newborns, and especially premature babies

Inform:

- Educate, engage and mobilize communities about preterm birth to encourage early care, beginning in adolescence, as well as to raise visibility of the problem of preterm birth and the availability of cost-effective solutions
- Track progress and hold all stakeholders at global, regional, national and local levels accountable for their commitments, to improve pregnancy outcomes and preterm birth.
- Promote accountability through annual Countdown to 2015 country data profiles, and global and national reports that document preterm birth rates and associated mortality and coverage of evidence-based interventions

Box 6.11: Chinese parents mobilizing for their preterm babies

Groups of parents affected by preterm birth are an influential civil society group, supporting affected families and being their voice in government and among health policy planners. The Home for Premature Babies (HPB) is an example of a parent group advocating for improvements in care and support. As the largest preterm birth association of parents and families among Chinese-speaking nations, the membership of HPB now exceeds 400,000 families.

Photo: *Home for Premature Babies*

Formed in 2005 by Mrs. Jianian Ma, a mother of a very preterm baby, HPB now encompasses several foundations that provide nationwide services in support of prevention and care. With the sponsorship of the China National Committee for the Well-being of the Youth, HPB was established as a semi-governmental organization. This close central government tie has helped ensure continuity of HPB's funding and the ability to partner more effectively with other organizations in China.

HPB has established three centers dedicated to the care of children with prematurity-related disabilities; launched an interactive website to allow parents and prospective parents to ask qualified medical experts about ways to help minimize the risk of having a preterm birth and how to care for their preterm baby; implemented a telephone hotline to provide immediate responses to parents' questions; and established a "Green Track" in more than 100 hospitals nationwide that allows families with a sick preterm child to see a pediatrician quickly.

"As we have experienced in China, groups of parents affected by preterm birth can be an independent and uniquely powerful grassroots voice, calling on government, professional organizations, civil society, the business community and other partners in their countries to work together to prevent prematurity, improve care of the preterm baby and help support affected families." *Dr. Nanbert Zhong, Chair, Advisory Committee for Science and International Affairs, HPB*

Together rapid change is possible

Over the last decade, the world has changed. Just as it is no longer acceptable for people with HIV/AIDS to remain untreated because they live in poor countries, it is no longer acceptable for women to die while giving birth. Likewise 3.1 million newborns, including those who are born too soon, do not need to die. We need more frontline health workers who are skilled and confident in newborn care. We need health clinics equipped with life-saving commodities. Girls, women and mothers must be educated, nourished and enabled, so that they can protect their own health, and that of their babies.

Over three-quarters of premature babies who die could be saved if basic care reached them and their mothers. Rapid progress is possible, contributing to greater advances in reaching the MDGs and beyond. At the same time research and innovation for preterm birth prevention is urgent. These actions would also improve reproductive and maternal health, reduce disability and chronic disease and build sustainable health systems.

Together, as professionals, as policy-makers and as parents, we commit to our common goal: all pregnancies wanted and healthy, all women survive, and all babies – including those born too soon – with a healthy start in life, and thriving as children, fulfilling their potential as adults.

More information:

www.who.int/pmnch/media/news/2012/preterm_birth_report/en/index.html
Related materials and interactive map of preterm births: www.marchofdimes.com/borntoosoon
Every Woman Every Child commitments to preterm birth: www.everywomaneverychild.org/
World Prematurity Day on November 17
www.facebook.com/WorldPrematurityDay

Photo: *Jeff Holt/Save the Children*

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Chapter 1: Preterm Birth Matters

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