

Preterm birth now leading global killer of young children

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For the first time in history, the complications of preterm birth outrank all other causes as the world's number one killer of young children.

Of the estimated 6.3 million deaths of children under the age of five in 2013, complications from preterm births accounted for nearly 1.1 million deaths, according to new findings published in *The Lancet* by a research team coordinated by Robert Black, M.D., of the Johns Hopkins Bloomberg School of Public Health, together with World Health Organization and London School of Hygiene & Tropical Medicine.

Specifically, direct complications from preterm births accounted for 965,000 deaths during the first 28 days of life, with an additional 125,000 deaths between the ages of one month and five years. Other main causes for young child deaths include pneumonia, which killed 935,000 children under-five, and childbirth complications, which caused 720,000 deaths (662,000 in the neonatal period, most on the first day of life, and 58,000 in the post-neonatal period).

"This marks a turning of the tide, a transition from infections to neonatal conditions, especially those related to premature births, and this will require entirely different medical and [public health](#) approaches," says Joy Lawn, M.D., Ph.D., of the London School of Hygiene & Tropical Medicine, a member of the research team and a long-term advisor to Save the Children. "The success we've seen in the ongoing fight against infectious diseases demonstrates that we can also be successful if we invest in prevention and care for preterm birth."

Groundbreaking research to discover why preterm births occur is now underway. These unprecedented efforts, backed by \$250 million in new funding, involve more than 200 researchers and are expected to identify ways to prevent or alleviate this global health problem within three to five years, saving countless infant lives.

The countries with the highest numbers of children under-five dying from preterm birth complications each year are: India (361,600), Nigeria (98,300), Pakistan (75,000), Democratic Republic of the Congo (40,600), China (37,200), Bangladesh (26,100), Indonesia (25,800), Ethiopia (24,400), Angola (15,900) and Kenya (13,300).

Some of the highest rates of preterm deaths are in West Africa, particularly in the countries currently being decimated by Ebola, where the risk will now be even higher given the challenges faced in those countries, notably Sierra Leone and Liberia.

The 10 countries with the highest percentage of under-five deaths directly resulting from preterm birth complications are: Macedonia, 51.0 percent; Slovenia, 47.5 percent; Denmark, 43.0 percent; Serbia, 39.8 percent; the United Kingdom, 38.7 percent; Hungary, 37.4 percent; Slovakia, 34.9 percent; Poland, 34.8 percent; Republic of Korea and Switzerland, 32.7 percent. All of these exceed the global average of 17.4 percent of under-five deaths, partly because of success in reducing infectious diseases.

In the U.S., 28.1 percent of under-five deaths are from direct complications due to preterm birth, which translates to 8,100 deaths of children under-five. The U.S. ranks 141th worst on the list of 162 countries, followed by Oman, Georgia, Egypt, Canada, Germany and Qatar.

The Epidemic of Prematurity

Since 2000, the worldwide mortality rate of children under-five has declined dramatically from 76 to 46 deaths per 1,000 live births in 2013. This is an annual reduction rate of 3.9 percent. Almost half of the overall reduction is a result of the massive progress made against deaths from pneumonia, diarrhea, measles, HIV and tetanus. In contrast, preterm mortality rates have declined at only 2.0 percent annually based on WHO global mortality rate for preterm birth in 2000 and 2013.

The reason: vaccines, bed nets for malaria, antibiotics, antimalarial and HIV treatment have received major investments. However, these have had a small impact on deaths resulting from preterm birth complications. Compounding the problem is the fact that the global prematurity rate of more than one in ten babies, or 15.1 million being born too soon, has continued to increase.

"Some 7,600 newborns die daily," explains Andres de Francisco, M.D., of the Partnership for Maternal, Newborn & Child Health (PMNCH), a coalition of more than 600 partners. "We have an epidemic of preterm and newborn deaths that represents one of the greatest health challenges of the 21st century. Two-thirds of these deaths could be prevented without intensive care."

Prematurity is moving higher up on the global agenda. In addition to new research to solve the problem, global health partners are intensifying joint efforts to advocate for investment and policy approaches to reduce preterm birth and improve newborn health. A key moment in this effort is World Prematurity Day (WPD).

World Prematurity Day

More than 200 countries, non-government organizations, UN agencies, medical and health organizations will participate this year in the Fourth

World Prematurity Day on Monday, November 17th. More than 60 countries have planned special events that focus on prematurity and premature babies.

Last year's WPD activities reached 1.4 billion people via radio, TV, print, Internet and social media. Of that, the global public service announcements featuring Celine Dion and Thalia reached more than a billion people on CNN International and CNN en Español. The partners of WPD also hosted a 24-hour Twitter relay that involved nearly 30 million people. WPD reached another 7.3 million people via Facebook through a collection of more than 3,000 personal family stories about prematurity.

National parent groups affiliated with the European Foundation for the Care of Newborn Infants and the US-based NGO March of Dimes lit some of the world's most famous buildings and landmarks purple, the representative color of WPD: Empire State Building (New York), Niagara Falls (New York/Canada), Brandenburg Gate (Germany), Peace Bridge (New York/Canada), Belfast City Hall (Ireland), First Direct Arena (England), CN Tower (Canada), Singapore Flyer, National Museum (Poland), Bratislava Castle (Slovakia), El Moro (Mexico City), the Bosphorus Bridge (Turkey), General Motors Headquarters (Detroit), and the Las Vegas Strip (Nevada).

WPD is part of the Every Women Every Child initiative. This umbrella initiative, spearheaded by the UN Secretary-General, was created to rapidly advance the UN Millennium Development Goals (MDGs) 4 and 5, to reduce under-five child and maternal mortality by two-thirds and three-fourths respectively.

"On World Prematurity Day, I urge all partners to recognize the vital importance of addressing prematurity as we strive to improve women's and children's health," says United Nations Secretary-General Ban Ki-

Moon.

"Intensifying our focus on prematurity will sustain gains in child survival, accelerate progress towards the Millennium Development Goals, and help lay the groundwork for ending all preventable deaths of women and children by 2030. The Every Woman Every Child movement is working with all stakeholders to end this tragic and preventable reality."

The Every Woman Every Child movement was launched four years ago and has grown to include 300 partners and 400 financial, policy and service delivery commitments, such as training midwives. In total, \$27.3 billion has already been disbursed, according to PMNCH.

"Adding to the successful Every Woman Every Child movement, WHO and partners have been working on two complementary approaches: the Every Newborn Action Plan (ENAP), led by WHO and UNICEF and adopted by 194 countries at the World Health Assembly this year, and Ending Preventable Maternal Mortality (EPMM)," says Flavia Bustreo, M.D., WHO's Assistant Director-General for Family, Women's and Children's Health. "ENAP and EPMM have articulated strategies and set targets to improve maternal and child health in the post-MDG era and both have attracted unprecedented commitments from countries and development partners."

ENAP has attracted some 40 commitments from a broad range of donors and partners, including the Islamic Development Bank, the Norwegian Government, Johnson & Johnson and Phillips. India and Nigeria have already launched their own ENAP programs.

New Research Initiatives to Address Premature Birth

Four major research initiatives, with some \$250 million in funding, are

now underway. Researchers seek to discover the unknown causes of prematurity and find effective ways to prevent or delay preterm births. Precisely what events trigger the start of labor at full-term, let alone preterm labor, remain a mystery. More than half of preterm births occur spontaneously.

1. The Global Coalition to Advance Preterm Birth Research (GCAPR) is a new partnership initiated by the National Institute of Child Health and Human Development (NICHD), the March of Dimes, the Bill & Melinda Gates Foundation, and the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS). Some 16 institutions are now members of the coalition. GCAPR will advance needed research into the field of preterm birth, a blueprint of which was detailed in *The Lancet Global Health* in December 2013.

2. The March of Dimes has launched a \$75 million Campaign to End Premature Birth, a "medical Manhattan Project" to create a specialized network of five research centers conducting team-based research to discover the unknown causes of prematurity. Two of these research programs are well underway. The remaining three will be named by the end of 2014.

"The March of Dimes initiative is looking at the whole spectrum of prematurity," says Joe Leigh Simpson, M.D., senior vice president for research and global programs at the March of Dimes. "Some 200 scientists from 20 disciplines already are involved in this research effort and those numbers are expected to double by next year."

3. The University of California at San Francisco's (UCSF) Preterm Birth Initiative (PTBi) has launched a 10-year global initiative to slow the epidemic of preterm births and improve the health of preterm babies. PTBi is currently in a planning phase to determine where UCSF and its partners can have the greatest impact. The Bill & Melinda Gates

Foundation and Marc and Lynne Benioff are co-funding this \$100 million initiative.

4. The last research effort led by the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS), a program started by Seattle Children's Hospital, is focusing its research on discovering the causes and mechanisms of prematurity, work that may lead to interventions to prevent it. Seven research projects are underway with more in planning stages. The work has \$20 million in funding from the Bill & Melinda Gates Foundation and a \$1.3 million USAID grant.

"To be successful, this has to be a team effort," says Larry Rand, M.D., director of Perinatal Services at UCSF and co-director of PTBi.

"Effective collaboration will accelerate discovery, increase access to interventions that work and optimize the project's impact on rates of early preterm birth and mortality."

Prematurity is complex. Thus, research groups are from 20 diverse fields. Besides obstetrics/gynecology, neonatology, genetics, immunology and infectious diseases, the trans-disciplinary initiatives include experts in engineering, statistics, physics, biochemistry and mathematics.

One group is working to identify a pacemaker in the uterus that initiates labor while another seeks to discover the source of the electric signals that initiate labor and discover whether the process is triggered by mother or fetus.

Another group is focused on identifying biomarkers, proteins and molecules in the circulations of both mother and fetus, gene-environment interaction and the maternal microbiome (the total collective of genomes of microorganisms in the mother).

One research team is investigating why Somali women living in the U.S. have very low rates of premature births, while most black women in the U.S. have very high rates of premature birth.

Researchers are studying how poverty, nutrition, pollution, stress and other compounding factors affect preterm birth.

"This unprecedented collaborative effort will yield results in three to five years," anticipates Dr. Simpson. "I expect the net effect to be greater than the sum of the parts, to be the product of collaboration among the centers."

Helping Premature Babies and Mothers

Measures to help premature babies and mothers include an emphasis on family planning, prevention of infections and use of antibiotics, and wider use of Kangaroo Mother Care, a technique that holds the infant skin-to-skin on the mother's chest to keep the baby warm and make breastfeeding easier.

An international conference on Kangaroo Mother Care is scheduled for the week of November 17th in Rwanda, coinciding with World Prematurity Day. It is estimated that greater use of this simple technique could save as many as 450,000 preterm newborns each year.

Known preventions to reduce risk of premature birth:

- Family planning to improve spacing and avoid pregnancy in women under 17 and over 40.
- Reducing the number of embryos transferred as part of fertility treatment.
- Eliminating C-sections before 39 weeks that are elective and not medically necessary.

Risk factors linked to premature births include obesity and high blood pressure. These also are risk factors for both stillbirths and birth defects.

Major donor countries are also recognizing the growing demand to improve survival rates of preterm babies. Last month, the U.S. Agency for International Development announced a new five-year, \$9 million program, called Every Premie—SCALE, to expand evidence-based and underutilized interventions to improve survival rates among preterm and low birth weight babies in 24 priority countries across Africa and Asia. The program is supported by a partnership among Project Concern International, GAPPS and the American College of Nurse-Midwives.

To assist professionals in scaling up proven interventions, the March of Dimes and the International Federation of Gynecology & Obstetrics have created a Global Collaborative Network to Prevent Preterm Birth that identifies best practices.

In addition, Survive and Thrive is a public-private partnership that engages U.S. pediatric, Ob/Gyn, and midwifery membership organizations with the private sector and the U.S. Government to collaborate with international and national professional associations and global health scholars to strengthen maternal, newborn, and child health programs. This initiative is working in the three highest burden countries - Ethiopia, India and Nigeria - to improve essential newborn care training including neonatal resuscitation and care for small and sick newborns.

Prematurity Major Problem in U.S.

The preterm birth rate in the U.S. declined between 2006 and 2013. The March of Dimes estimates that 231,000 fewer babies were born prematurely during this time, saving about \$11.9 billion in health care costs.

However, the U.S. still has one of the worst preterm birth rates of any high-resource country. In 2013, 11.4 percent of babies in the U.S. were born preterm, according to the National Center for Health Statistics. The statistics suggest some of the reasons. Nearly 10 percent of single births are premature, while 57 percent of twins and more than 90 percent of triplets are born prematurely and 46 percent of deliveries by C-section are premature.

The U.S., with 28.1 percent of its under-five deaths resulting from [preterm birth complications](#) appears awful, but there are other developed countries with higher rates: Denmark (43.0 percent), United Kingdom (38.7 percent), Switzerland (32.7 percent), Germany and Canada (29.1 percent).

In the U.S., race makes a difference with premature delivery rates of 16.3 percent among black women, 13 percent among American Indian, 11.3 percent among Hispanic, and about 10 percent for Caucasian and Asian/Pacific Islanders.

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