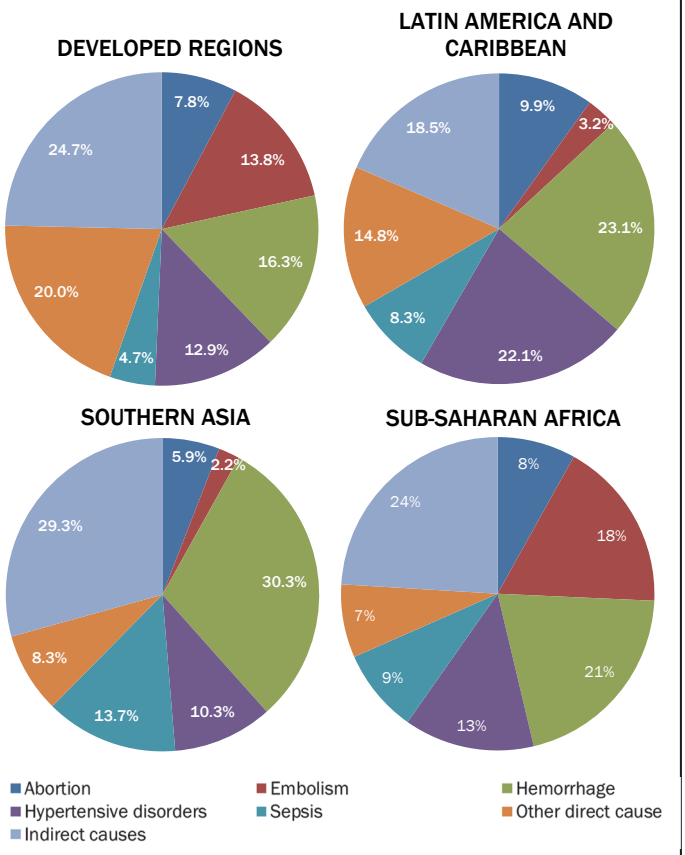
Intersecting Epidemics: An Overview of the Causes of Maternal Death and Infectious Diseases

Over the last 20 plus years, great achievements have been made in the reduction of deaths in women during pregnancy, childbirth, and the first six weeks postpartum. Globally, an estimated 289,000 women died during pregnancy in 2013, a decline of 45% from 1990.[1] Still, in too many parts of the world, maternal mortality remains unacceptably high, with wide regional and sub-regional variation in progress toward Millennium Development Goal 5.[2] The maternal mortality ratio in developing regions is still 14 times higher than in developed regions and, in 2013, sub-Saharan Africa and South Asia accounted for 62% of all maternal deaths worldwide.[1] This situation raises questions about how maternal health strategies can and should be increasingly customized and targeted to accelerate progress in saving mothers' lives.

WHY ARE MOTHERS DYING? CAUSES OF MATERNAL MORTALITY

While hemorrhage (27.1%), hypertensive disorders (14%), and sepsis (10.7%) remain the leading direct causes of maternal mortality globally,[3] a true appreciation for the causes of mortality, and how to address them, can come only from a closer look at local contexts. For example, Menendez et al.'s 2008 study of the causes of maternal mortality in a tertiary hospital in Mozambique found that infectious diseases such as HIV/AIDS, pneumonia, malaria, and meningitis accounted for at least half of all maternal deaths,[4] making these indirect causes of maternal mortality more substantial than the direct obstetric causes.

Figure 1: Estimated distribution of causes of maternal mortality by region, 2003-2009



Source: Say L et al. 2014. Global causes of maternal death: a WHO systematic analysis. *The Lancet Global Health* 2(6), e323-e333.

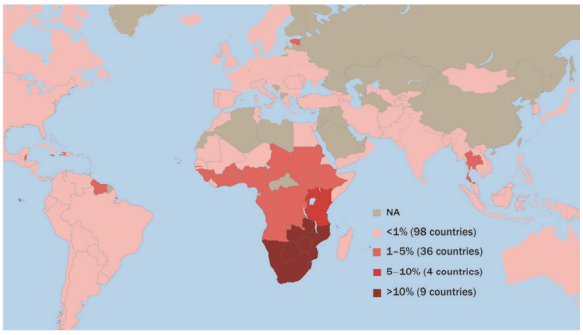
WHERE ARE MOTHERS DYING? REGIONAL BURDENS OF DISEASE

The global health community is growing more aware of the ways in which infectious diseases contribute to the challenges facing maternal health. Mothers affected by these conditions are more susceptible to serious intrapartum and postpartum bacterial infections. Moreover, infections with sexually transmitted organisms including syphilis and hepatitis B further complicate maternal and newborn health, leading to additional maternal morbidity as well as stillbirth, low birth weight, and congenital abnormalities for newborns.[5]

HIV/AIDS

For women aged 15-44, HIV/AIDS is the leading cause of death globally.[6] Recent data suggest that pregnant or postpartum women living with HIV have approximately eight times higher maternal mortality than those who are not infected.[7] Although data are limited, confidential enquiries made between 2008 and 2010 in South Africa suggest that most deaths in HIV-infected pregnant and postpartum women are due to non-obstetric infections including pneumonia, tuberculosis, and meningitis.[8] HIV also appears to increase the risk of infections in pregnancy, childbirth, and postpartum, with HIV-infected women experiencing three times the risk of puerperal sepsis.[9]

Figure 2: Adult HIV prevalence rates, 2012

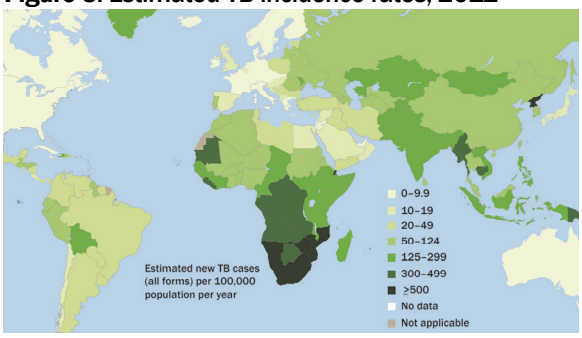


Data from UNAIDS Report on the Global AIDS Epidemic 2013.

TUBERCULOSIS

Tuberculosis (TB) is responsible for between 6% and 15% of maternal mortality, depending on the country and local burden.[10] The highest rates of TB are found in sub-Saharan Africa, India, China, and the islands of Southeast Asia and Micronesia. TB infection also has significant implications for newborns; pregnant women with pulmonary TB have approximately twice the risk of delivering a baby who is premature or low birth weight and six times the risk of a perinatal death.[10] Pregnant women living with HIV have 10 times the risk of developing active TB,[11] and pregnant women with HIV/TB co-infections face higher risks of maternal mortality. HIV-infected women with active TB are also more than two times as likely to transmit HIV to their infants.[12]

Figure 3: Estimated TB incidence rates, 2012

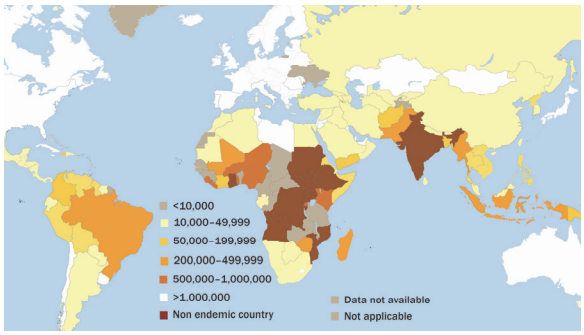


Data from WHO Global Tuberculosis Report 2013.

MALARIA

The serious consequences of *Plasmodium falciparum* malaria in pregnancy (MIP) are well-documented. Transmission is stable throughout the year in tropical areas of Africa, where 30 million women become pregnant each year and 11% of neonatal deaths are attributed to low birth weight from *P. falciparum* infections in pregnancy.[13] In areas of unstable *P. falciparum* malaria transmission, pregnant women are at increased risk of severe malaria, death, and fetal stillbirth. The impact of malaria on maternal health depends on age (young mothers are more vulnerable), gravidity (first pregnancies are riskier), nutritional status, immunity status, prophylactic treatment, and co-infection with other diseases.[14] For example, HIV infection lessens a pregnant woman's ability to control malaria infections, and placental infection with malaria parasites doubles the risk of transmission of HIV infection to newborns.[15]

Figure 4: Number of confirmed malaria cases reported, 2010

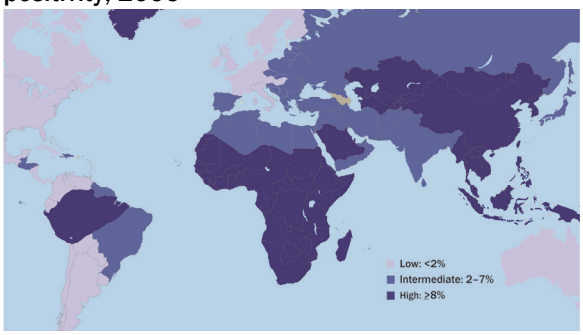


Data from WHO.

HEPATITIS B

Hepatitis B virus (HBV), an infection of the liver that can lead to chronic and acute liver disease, is easily-transmitted but preventable via vaccination. It is most commonly acquired sexually, through intravenous drug use, or from mother to child. Globally, over 2 billion people are infected with HBV at some point in their lives, and HBV accounts for 1.2% of mortality for women aged 15-49.[6] In areas where HBV is highly endemic, mainly in Southeast Asia and Africa, up to 70% to 90% of the population are infected and approximately 8% to 10% of those populations are thought to develop chronic HBV.[16] About half of new infections result from vertical transmission during pregnancy,[17] a statistic that is linked to the fact that HBV screening is rarely a part of routine antenatal care. Maternal HBV is associated with increased rates of antepartum hemorrhage, gestational diabetes, and preterm labor, as well as premature and low birth weight babies.[18] Rarely will infected infants or children develop acute HBV, but the majority of those who do will develop complications from chronic disease in later life, such as cirrhosis or primary liver cancer.[16]

Figure 5: Prevalence of HBV surface antigen positivity, 2006

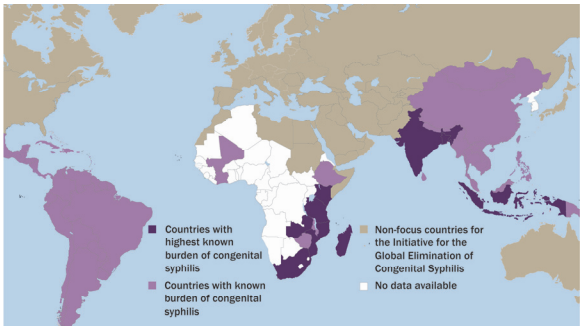


Data from U.S. Centers for Disease Control and Prevention.

SEXUALLY TRANSMITTED INFECTIONS

The World Health Organization (WHO) estimates that nearly 500 million incident cases of four curable, sexually transmitted infections (STIs)—gonorrhea, syphilis, chlamydia, and trichomonas—occur annually.[19] STIs are a public health problem in all countries, and infection rates range from a yearly incidence among people aged 15-49 of 2.2% in East Asia and the Pacific to 25.7% in sub-Saharan Africa. While STIs such as gonorrhea or chlamydia contribute to maternal mortality through puerperal sepsis, they are also associated with pelvic inflammatory disease, ectopic pregnancy, adverse psycho-social outcomes, and infertility. Neonatal outcomes can also be grave, and include prematurity, pneumonia, severe infant eye infection, and eventual blindness. The STI herpes simplex virus (HSV) is also widespread; an estimated 16% of people aged 15-49 worldwide live with the HSV-2 virus. Without clinical intervention, maternal HSV infection can lead to preterm birth, low birth weight babies, and neonatal sepsis. Additionally, genital herpes—like all STIs characterized by open sores or lesions—increases a woman's likelihood of acquiring HIV by two to three times.[20]

Figure 6: Eliminating mother-to-child transmission of syphilis



Data from WHO partner brief, 2010 (Advancing MDGs 4, 5 and 6: Impact of congenital syphilis elimination).

Syphilis warrants particular attention. WHO estimates that, worldwide, 2 million pregnant women are infected with syphilis each year and that more than half of them will transmit the infection to their newborns, causing approximately 650,000 fetal and neonatal deaths annually.[21] In sub-Saharan Africa alone, an estimated 1,640,000 pregnant women have undiagnosed syphilis every year.[22] Preventing needless morbidity and mortality due to syphilis is a global public health priority. Problems associated with syphilis in pregnancy can be almost entirely eliminated by universal antenatal screening and antibiotic treatment.

MATERNAL BACTERIAL INFECTIONS

Infection of the amniotic fluid or membranes, or chorioamnionitis, can develop during labor when cervical or vaginal microorganisms migrate through the cervical canal during prolonged labor or after a woman's membranes have ruptured. If untreated, chorioamnionitis leads to puerperal sepsis, a leading direct causes of global maternal mortality. Chorioamnionitis is also linked to serious adverse outcomes for newborns including asphyxia, early onset neonatal sepsis, pneumonia, meningitis, and perinatal death.[23]

Women who experience prolonged labor, prolonged rupture of membranes, multiple vaginal examinations, and other invasive procedures, or who have genital tract infections, are at increased risk for developing chorioamnionitis.[24] Simple, low-cost interventions—such as the use of the partograph to monitor the length and progress of labor and regular monitoring of women's temperatures—can prevent infection and promote early detection and management.

FROM CHALLENGES TO SOLUTIONS

The intersection of maternal health and infectious diseases is an area requiring increased focus and better clinical and programmatic evidence as well as improved measurement. However, a number of low-cost and effective tools already exist to address these challenges. We can accelerate progress toward improving maternal and neonatal health around the globe through antiretroviral therapy for maternal health and to prevent HIV transmission to newborns, routine screening and appropriate treatment for TB and STIs during pregnancy, intermittent prophylactic therapy for malaria, insecticide-treated bed nets, consistent infection prevention practices, evidence-based clinical decision-making, vaccination where available and indicated, availability of acceptable family planning options, and integration of infectious disease service provision with maternal and child health care platforms. While the global maternal health community has made substantial progress in the reduction of maternal mortality in the past two decades, additional progress will come only through collaborative partnerships and renewed attention to integrated clinical and public health approaches to infectious diseases and their impact on maternal health.

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