IMPROVING GLOBAL HEALTH THROUGH

Better Maternal Environments

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HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH





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Overview

The following provide the background on maternal and neonatal health and health trends over time in order to show the overall burden due to poor maternal and child health outcomes on mothers and their children, as well as families and the society at large.

They also provide an overview of the social determinants of maternal and child health, and ways in which the life course approach can help to prevent, detect, and manage causes and consequences of poor maternal and child health outcomes.

Finally, the section summarizes the role that our environments play in shaping our health, with a special focus on their significance during early fetal development that occurs during pregnancy.



24% decrease in maternal mortality over the past decade



from complications related to pregnancy and childbirth each year

Maternal and Child Health: an Unfinished Agenda

We start from the premise that human health globally can and needs to improve. We, as citizens of the world, need to work collectively to help each other live longer, healthier lives. It makes good sense to start at the very beginning of our lives – development in utero, as that stage is one of the most significant determinants of future health and well-being; therefore, we need to focus on the health and welfare of mothers and their children.

Ensuring safe pregnancy and childbirth for every woman and newborn is a critical goal of global health efforts. A pressing priority in today's world is guaranteeing that mothers and their children not just survive, but thrive. Achieving good health and quality of life for all women and children, especially those who are most vulnerable, remains an unfinished agenda. Overcoming existing challenges is essential, as ensuring positive birth outcomes for all is both a public health and an ethical imperative, and the foundation for sustainable human and social development. There has been remarkable progress over the last three decades in reducing preventable maternal mortality and severe morbidity, with a 24% decrease in maternal mortality over the past decade.¹ However, improvements have been uneven. Too many women continue to die in pregnancy and childbirth: nearly 200,000 mothers still die from complications related to pregnancy and childbirth each year¹ (see Table 1, page 4). Table 1. Global statistics on death and disability caused by pregnancy and labor.

Year	Number of women dying as a result of pregnancy or childbirth ¹	New cases of pregnancy complications ³
2007	254,824 deaths	77,084,262 cases
2017	193,639 deaths	79,812,246 cases
Change	24% fewer deaths	4% more cases of complications

over 38,500 mothers could be saved each year



die in low to medium sociodemographic index countries To understand the total impact of poor maternal health outcomes, it is important to take into account not only maternal and child deaths but also the health burden borne by mothers who survive pregnancy-related injuries or complications. One way to understand this impact is through a measure called the disabilityadjusted life year (DALY). Think of one DALY as one lost year of healthy life. For each condition (e.g., type 2 diabetes), DALYs are calculated as the sum of the years of life lost to premature death plus the years lived in less than optimal health. In 2017, nearly 12 million years of healthy motherhood were lost due to pregnancy and childbirth complications² (see Table 2, page 5).

Disability caused during pregnancy and labor can have long term effects on health for the rest of a woman's life. Maternal obstructed labor and uterine rupture is the number one cause of long-term maternal disability worldwide (50%). If these two conditions were avoided, nearly 400,000 years of a pain-free, disability-free life could be returned to mothers.⁴ Maternal hemorrhage is the number one cause of maternal deaths worldwide.⁵ In 2017, 20% of maternal deaths globally were due to hemorrhage. If death from maternal hemorrhage alone can be avoided, over 38,500 mothers could be saved each year. $^{\rm 6}$

The table on the next page shows the number of healthy years of life lost by mothers in 2017 in the countries with the most years of healthy life lost due to poor maternal health outcomes. It displays estimates, based on Global Burden of Disease (GBD) data from 1990-2017, of how many healthy years of life will be lost in 2040, along with a percent change indicating whether there would be an increase or a decrease in years of healthy life lost between 2017 and 2040. The burden of maternal and newborn morbidity and mortality is inequitably distributed within and between countries. Wealthy and highly educated countries with lower birth rates, like Sweden or Germany, have lower rates of maternal death and disability than countries with lower income and education and higher birth rates, like Nigeria or India.

Of the 531 women who die each day from causes related to pregnancy and childbirth, approximately 97% die in low to medium socio-demographic index countries. (continued p. 6)

DALY: disability adjusted life year - think one DALY as one lost year of healthy life

Ethiopia has been tremendously successful at driving down maternal mortality Table 2. Years of healthy life lost due to pregnancy and childbirth complications, by country. Source: Institute for Health Metrics and Evaluation (IHME). Used with permission. All rights reserved.

Top 20 locations in terms of years of healthy motherhood lost	Measure	Mothers' healthy years lost (number, 2017) ²	By 2040, healthy years lost for mothers (number)	% change 2017 to 2040 (healthier mothers or more years of healthy life lost)
India	DALYs	2,475,486	989,246	-150%
Pakistan	DALYs	1,152,610	420,426	-174%
Nigeria	DALYs	1,073,810	838,985	-28%
Democratic Republic of the Congo	DALYs	576,679	642,610	10%
Ethiopia	DALYs	479,795	331,792	-45%
Indonesia	DALYs	376,673	312,662	-20%
Tanzania	DALYs	291,968	283,925	-3%
Bangladesh	DALYs	289,777	92,060	-215%
Kenya	DALYs	245,142	200,696	-22%
Afghanistan	DALYs	235,923	267,885	12%
Niger	DALYs	169,286	189,985	11%
China	DALYs	164,140	36,715	-347%
Chad	DALYs	160,048	172,479	7%
Madagascar	DALYs	159,866	159,774	0%



Top 20 locations in terms of years of healthy motherhood lost	Measure	Mothers' healthy years lost (number, 2017) ²	By 2040, healthy years lost for mothers (number)	% change 2017 to 2040 (healthier mothers or more years of healthy life lost)
Cote d'Ivoire	DALYs	152,779	148,144	-3%
Cameroon	DALYs	152,774	136,140	-12%
Mali	DALYs	151,220	98,115	-54%
Sudan	DALYs	138,578	83,482	-66%
Somalia	DALYs	137,372	177,518	23%
Mozambique	DALYs	134,341	153,935	13%

A Black Mothers

experience a 112-115% higher rate of severe maternal morbidity in the United States (SDI summarizes where a country lies on the spectrum of economic development, expressed on a scale from O-1; it summarizes the averages for income per capita, educational attainment, and birth rates).⁷ Similarly, of the estimated 193,639 maternal deaths that occurred globally in 2017, nearly half occurred in Sub-Saharan Africa and approximately one-third in South Asia.⁸ Furthermore, adolescent mothers, women and children in conflict and humanitarian settings, and those who are most vulnerable and marginalized (based on geographic, ethnic, racial, socio-economic or immigration status) face a higher risk of poor health outcomes.⁹

Some countries have defied these expectations, for better or worse. For example, Ethiopia has been tremendously successful at driving down maternal mortality faster than some of its economic peers, while the United States has performed far worse than most of its wealthy counterparts (see Figure 1), particularly among women who are socially and economically disadvantaged. Women in the United States are more likely to die from childbirth or pregnancy-related causes than women in any other high-income country, and maternal mortality among black women is 3-4 times higher than among their white counterparts.^{10, 11, 12} In fact, maternal mortality levels in the US closely resemble some lower-income countries. The trend in mortality is mirrored in maternal morbidity data as well, which is also inequitably distributed across population groups.

Black mothers experience a 112–115% higher rate of severe maternal morbidity (such as acute renal failure, shock, and sepsis, or procedures including blood transfusion or hysterectomy) than white mothers.¹³ Figure 1: In the United States, mothers are losing more years of healthy life due to pregnancy and childbirth than countries like China and Brazil. Source: Institute for Health Metrics and Evaluation (IHME). Used with permission. All rights reserved.



Pregnancy and childbirth, of course, have a strong effect on mothers' health, but they are also critically important to the health of newborns in the short- and long-term. Short gestation for birth weight and low birth weight for gestation contributed to over 7.2 million years lived with disability worldwide in 2017, due to preterm birth.¹⁴

Babies born before term are at an increased risk of mortality throughout childhood, are more likely to have less than a high school diploma or graduate education, have poorer reproductive health outcomes later in life, and are more likely to have premature babies of their own later in life. 15

Obstetric complications during pregnancy, childbirth, and the immediate postpartum period are not the only causes of poor maternal and newborn health. Gestational diabetes mellitus (GDM), anemia, mental health conditions, overweight and obesity, and hypertension during pregnancy have a significant adverse impact on the health outcomes in both women and their newborns.^{16, 17, 18, 19, 20, 21}

Women in the U.S. are more likely to die from childbirth or pregnancy-related causes than women in any other highincome country



Furthermore, when these conditions are present during the maternal health period, they increase the risk of these conditions becoming chronic in the years following the pregnancy.²² For instance, women who have experienced GDM during pregnancy face a 50% increased risk of type 2 diabetes a few years later in their life course,²³ and depression in the early postpartum period is associated with chronic depression at later time points,²⁴ which, in extreme instances, can lead to self-harm.²⁵

Furthermore, emerging evidence demonstrates that various exposures in utero, as well as during infancy and early childhood periods, increase the risk of adverse health outcomes in the short-term and later in life. Such exposures range from environmental to psychosocial to nutritional.²⁶

For example, suboptimal nutrition, such as lack of folate (during a critical period of neural tube development), iron, and vitamin B12 can lead, respectively, to: neural tube defects, congenital heart disease and oral clefts;²⁷ lower Apgar scores, reduced stores of iron and other nutrients, growth stunting;¹⁵ and poorer memory and attention span and an increased risk for insulin resistance.²⁸ (The important relationship between exposures in early development and health across the life course will be discussed further later in this section.)



Poor Maternal and Child Health: Beyond a Personal Tragedy

Complex social processes determine who survives and who thrives during and after childbirth.²⁹ The implications are interlinked, intergenerational, and extensive, impacting women's health in later stages of the life course, child's survival and development, and the health of the next generation.

The impact of maternal deaths goes beyond the immediate family, affecting the wider community and leading to social and economic breakdown.

The causes and implications of poor pregnancy and birth outcomes are complex. Poor maternal and newborn health in most cases is not an outcome of a single misfortunate episode attributable to an isolated biological or individual risk factor. Rather, it is typically a product and reflection of a range of factors including:

- The health status of girls and women,
- Their access (or lack thereof) to quality and timely health care, and
- Critical social factors that strongly influence health, such as socio-economic status, education, and gender disparity.

A social determinants approach to maternal health has enhanced our understanding of the complex interplay between structural determinants and conditions of daily life that shape health outcomes and produce health inequalities.³⁰ A mother's death and severe disability can devastate livelihoods, quality of life and survival odds of those she leaves behind This approach argues that disparities in people's access to information, decision making and life opportunities, along with political and social structures that distribute power and resources unequally across populations, contribute to ill health and inequitable levels of well-being across population groups.³¹

Figure 2: Structural and social determinants of maternal health.



Individual Attributes of Women

age, parity, knowledge of services, previous obstetric history



Family Charactristics

economic status, access to resources, support from natal and extended family, marital relationship



Applied to the analysis of poor maternal health, the

structural and social determinants (Figure 2): ³²

World Health Organization identifies six categories of

Community Context

rural-urban, class cast, ethnicity, social capital, distance to facilities



Culture and Social Values

women's status, gender norms, religion, health beliefs, social cohesion



Health services

availability of skilled healthcare workforce, acceptability of services, fees and charges for services



Structural Determinants

laws, policies, budgets, education, social protection for promoting health and well-being of women



A holistic approach to understanding and addressing poor maternal health is required to move the needle towards a healthier future

The other side of the story – what happens following a poor pregnancy and childbirth experience – is equally complex, going far beyond a single event or a personal tragedy. A mother's death and severe disability can devastate livelihoods, guality of life and survival odds of those she leaves behind.³³ A nascent but growing body of research points towards the disastrous consequences and ripple effect of maternal mortality and morbidity. The death and severe disease of mothers are linked with infant and child mortality and, beyond this immediate effect, the impacts are intergenerational and multi-sectoral.^{34, 35, 36} In many societies, a woman, especially a mother, plays a critical role for home and social functioning – from providing newborn and infant care, to maintaining social relations, to ensuring proper health, education and socialization of her children.

The loss of a mother is therefore associated with poor growth outcomes for the surviving children, increased risk of disrupted education and school dropouts, early marriage and childbearing of adolescent daughters, and their associated increased risk of maternal mortality and morbidity.^{37, 38, 39}At the societal level, poor birth outcomes are related to loss of economic opportunities and spiraling cycles of poverty for the mothers, children, and their families; such outcomes can also accrue to communities that lose women during childbirth.^{40, 41}

Given the complexity of factors leading up to an adverse maternal and/or newborn outcome at birth and the long-term consequences of such an event on the woman, her child, and community, a holistic approach to understanding and addressing poor maternal health is required to move the needle towards a healthier future.

Providing full access to evidence-based approaches and interventions to all women and children requires an understanding of the context in which those women live and the health systems operate, as well as a sufficient and sustained investment to tackle the complex network of causes culminating in and resulting from poor maternal health.⁴² In the same vein, it is worth noting that investing in improving maternal health is not just intrinsically important but likely to have tremendous returns, considering the lifetime impact of pregnancy and childbirth on the health and well-being of women, newborns and children, and their associated economic and societal impact.⁴³ As such, we emphasize the case for a societal responsibility of improving maternal health.



Advancing the Maternal and Child Health Agenda Through a **Life Course Approach**

A life course approach can help prevent, detect early, and manage causes and consequences of poor maternal and child health outcomes. Taking a life course perspective recognizes the relationship between risk factors and subsequent health outcomes at different stages of life. The five core principles of the life course perspective offer a framework for understanding and addressing both upstream and downstream determinants of poor maternal health:^{44, 45}

- Life span development and timing views health as a lifelong process, meaning that experiences across the person's lifespan must be contextually considered to understand their health.
- Timing of exposures views not only what the exposures are, but when they happen and how they shape health. For example, exposures may have stronger effects if they occur during certain critical or sensitive periods of development where individuals are more vulnerable. The duration of exposures and the order in which they occur also affects outcomes.
- 3. Human agency emphasizes the role of personal control in one's health.
- 4. Linked lives stresses the notion of interdependent lives, suggesting the societal responsibility towards health.
- 5. Historical time and place impact the contextual factors influencing health over an individual's life course.

A life course approach advocates for broadening the scope of maternal and newborn health beyond the narrow period of pregnancy, childbirth and six weeks' postpartum period (the "traditional" maternal health period). That is, it conceptualizes maternal and newborn health as impacted by events before, during, after and outside of the pregnancy and the immediate postpartum period. It also breaks down artificial silos between maternal health and chronic disease that result in poor health outcomes and missed opportunities to tackle the comprehensive health needs of women and children.^{46, 47}It therefore allows viewing maternal health care as an opportunity to assess risks, detect conditions and intervene in a timely fashion, educate and counsel women and families and, consequently, improve women and children's health for the long term.

The life course perspective also recognizes that early development is a critical or sensitive window that has a disproportionate importance on the child's future health. According to the developmental origins of health and disease (DOHaD) paradigm, adverse exposures during early development can contribute to disease later in life,^{26,48} a process referred to as "developmental programming." There are a number of reasons why early development is a particularly susceptible period. Infants and children have an increased hand-to-mouth activity and spend more time on the floor, which can increase their chemical exposure. They consume more air, food, and water relative to their body weight, which increases the relative dose of exposures. Furthermore, during the prenatal, infancy, and early childhood periods, rapid and extensive development of immature organs and systems takes place. The fragility and plasticity of these

Genes do not solely determine our biological fate

The preconception period is a critical window during which exposures experienced by the mother or father can affect the future offspring's development organs and systems leaves them vulnerable to harmful influences and disruptions that may affect their future function.^{49,50} Emerging evidence indicates that even the preconception period is a critical window during which exposures experienced by the mother or father can affect the future offspring's development.^{51,52,53} In particular, developing humans are susceptible to epigenetic effects that contribute to disease later in life.

The field of epigenetics – modifications that can change gene expression without actual DNA changes – has grown significantly in recent years and has altered our understanding of the relationship between our genes and our environment. The epigenome can be thought of as marks or patterns that regulate whether and how the genes encoded in the DNA sequence are expressed. That is, genes do not solely determine our biological fate; rather, they provide the basis for a range of potential outcomes that are determined through interactions with our environments. Epigenetic modifications are in essence a molecular memory left behind by our environments,^{54,55} and early development is a key window when epigenetic modifications occur,⁵⁶ leaving long-lasting impacts of these early environments.

Early epigenetic and developmental origins research focused on the quality and quantity of maternal and infant nutrition, while subsequent research has expanded to examine the environment more broadly. Environmental pollutants and chemicals linked to epigenetic modifications or otherwise linked to the DOHaD paradigm include secondhand smoke, ambient air pollution, endocrine disruptors, and metalloids such as arsenic.^{56,57} Psychosocial factors include prenatal maternal stress, parenting behaviors, lower socioeconomic status, and neighborhood disadvantage (e.g., socioeconomic status or crime).^{26,58,59} Diseases linked to developmental exposures are similarly wide-ranging, including reproductive conditions; certain types of cancer; obesity; cardiovascular disease; asthma; neurodevelopmental problems; psychiatric conditions; and immunological disorders.^{26,48}

Paternal exposures, too, matter, as some epigenetic modifications are potentially inheritable across generations. One long-term study, for example, found that children born to fathers who did not have abundant access to food during pre-puberty had lower rates of cardiovascular disease, whereas children whose paternal grandfathers had plenty of food during that same period and may have overeaten had an increased risk of diabetes.⁶⁰

It is important to note that **different exposures and related health outcomes have different critical windows throughout pregnancy and early childhood.** For example, studies of a European famine (the Dutch Winter Hunger Study) found that children born to mothers who experienced famine in mid- to late pregnancy had significantly lower birth weight and were more likely to develop type 2 diabetes as adults, whereas those whose mothers experienced the famine in early pregnancy were more likely to be obese as adults.⁶¹

Collectively, the principles and overall framework of the life course perspective, applied to the understanding of the causes and consequences of poor maternal and child health, indicate the importance of coupling promotion of healthy pregnancies with attention to women's lifelong health and well-being. Applying the life course perspective creates an opportunity to address both distal and proximate factors that affect maternal and child health (Figure 3, next page). Figure 3: Distal and proximate factors affecting maternal and child health.

PROXIMATE FACTORS	DISTAL FACTORS
Nutrition	Poverty
Timely and competent	Racism
clinical care	Poorly planned urbanization
Supportive and high-quality	Political crises
pregnancy and childbirth	Gender inequality
An enabling environment for	Deficient education
I healthy child development	Gender-based violence
	Environmental crises

For every one year of increase in the education of women of reproductive age, the child mortality decreased by 9.5%

Education, Health and Human Capital

As the social determinants of health and life course model are considered, we can start to examine the role, and measure the impact, of education on the health and economic productivity of a country. As we focus the lens on education of women, research has shown that the educational attainment of women in particular has important implications for health outcomes, including those of their children.

Between 1970 and 2009, with improvements in the educational attainment of young women around the world, global under-5 child mortality rates dramatically improved. Over four million children surviving past the age of 5 can be attributed to better mother's education. Mothering skills in particular can be credited for this progress because the link between mothers' education and childhood survival is stronger for children aged 1–5 years than for younger infants.

As we examine the impact of just one additional year of education, it has been found that for every one year of increase in the education of women of reproductive age, the child mortality decreased by 9.5% (1970-2009).⁶²

Substantial progress in educational attainment for women has been achieved globally; however, the gap between the countries with the highest and lowest educational attainment for women widened between 1970 and 2009 – with a difference of 13.8 years of education for women in 2009. In 17 countries, the mean educational attainment for women was less than two years, and in six of these countries (Afghanistan, Burkina Faso, Chad, Mali, Niger, and Yemen), adult women received less than one year of education.⁶² 195 countries demonstrates that nations failing to invest in health and education are at risk of stagnating economies and lower per capita GDP In addition to the direct link between education and child mortality, a recent study measuring human capital in 195 countries demonstrates that nations failing to invest in health and education are at risk of stagnating economies and lower per capita GDP.⁶³ This link is measured using human capital by looking at attributes of a population – including levels of education, training, skills and health – that, along with physical capital such as buildings, equipment, and other tangible assets, contribute to economic productivity. Human capital (productive years an individual in each country can be expected to work between the ages of 20 to 64, maximum being 45) can help inform a strategy that looks at the overall productivity of a country and provide a mechanism to measure the outcomes related to investments in health and education. Figure 4, below, shows the global variation in human capital across countries.

Figure 4: Map of expected human capital by country in 2016. http://www.healthdata.org/sites/default/files/files/ infographics/Infographic_Human-Capital_2018.pdf. Institute for Health Metrics and Evaluation (IHME), used with permission. All rights reserved.

EACH COUNTRY IS ASSIGNED A HUMAN CAPITAL SCORE RANGING FROM 0 TO 45, measured in units of health-, education-, and learning-adjusted expected years lived between age 20 and 64 years.



Our Environments and Our Health

Our environment plays an important role in determining our health status. Although it is less often thought of as an opportunity for health promotion compared to other determinants such as health services, it is increasingly well understood that our environment has a profound impact on our health and well-being and that it is a critical target for efforts to improve population and individual health. The physical environment is comprised of a wide variety of factors which include natural as well as built environments, air and water quality, among others^{64,65} (Figure 5, below). Our social environment – our relationships, groups, neighborhoods, and workplaces – can also influence health in myriad ways.⁶⁶

Figure 5: Factors included in the physical environment.



Natural environment, such as plants, weather, or climate change



Built environment, such as buildings or transportation



Water and air quality



Worksites, schools, and recreational settings



Housing, homes, and neighborhoods



Exposure to toxic substances and other physical hazards



Physical barriers, especially for people with disabilities



Aesthetic elements, such as good lighting, trees, or benches

Conventional water treatment does not always remove contaminants effectively



100,000 deaths per year are being contributed by air pollution in the US

Clean air is essential for optimal health. Humans breathe more than 15,000 liters (530 ft³) of air every day, consuming approximately four times more air than food and liquid together.⁶⁷ Research is well-established on the detriments of poor air quality – particulate matter pollution, increased levels of carbon dioxide, volatile organic compounds, and other contaminants - which can lead to cardiovascular diseases, diabetes, lower respiratory infections, and respiratory system cancers.¹⁴ Indeed, air pollution is considered one of the greatest killers of our generation.⁶⁸ In the United States alone, air pollution is estimated to contribute to over 100,000 deaths per year,⁶⁹ and is a significant contributor to many noncommunicable diseases.⁷⁰ In 2015, air pollution was responsible for 19% of all cardiovascular deaths, 24% of all deaths caused by ischemic heart disease, 21% of all stroke deaths, and 23% of all lung cancer deaths globally.71

Access to water that is clear of inorganic, organic and biological contaminants is also critical for maintaining optimal health. Humans are mostly made of water in fact, water makes up more than 50% of an adult's body weight.⁷² Humans have developed increasingly sophisticated systems to transport water to our homes. However, even in parts of the world with access to these advanced treatment technologies, it is still challenging to ensure that everyone has access to water that is free of contaminants. Conventional water treatment does not always remove contaminants effectively, and pollutants can also be introduced through water distribution infrastructures. Agricultural contaminants, heavy metals, bacteria, disinfectant by-products and other chemicals can be harmful if they are present in drinking water, leading to diarrheal diseases, developmental delays and disabilities, kidney damage and various cancers.⁷³⁻⁷⁹ To give one specific example, water is a major source of

lead exposure, which is the 2nd leading environmental contributor to heart disease globally⁸⁰ and is responsible for 63% of DALYs due to intellectual disability⁸¹ (in total, including water and other sources).

New ways in which our environment affects our health continue to be discovered. Of note, mounting research evidence indicates that the quality, type, and timing of light exposure can have profound effects on our health, well-being, and performance.⁸² Most mammals, including humans, have an internal clock that keeps the sleep-wake rhythm on a roughly 24-hour cycle. Our bodies are naturally programmed to function on a cycle that matches the solar day.⁸³ Known as the circadian rhythm, this clock is synchronized by light and controls many aspects of our physiology, metabolism, and behavior, including our sleep-wake cycle.⁸⁴

Multiple body functions, including sleep and digestion, are regulated in part by the daily hormonal fluctuations prompted by our internal circadian clocks. These hormones are released by an area in the brain called the hypothalamus.⁸⁵ The timing of hormone release is based on the timing of light exposure, which the brain receives via specialized nerve cells in the eye, called intrinsically photosensitive retinal ganglion cells (ipRGCs). In addition to its effects on the sleep-wake cycle, light also affects many other functions of our body, including alertness,⁸⁶ mood,⁸⁷ cognition,⁸⁶ and metabolism.⁸⁴ Disruption or desynchronization of the circadian rhythm and related hormones (e.g., through exposure to bright light at night) has been linked to obesity, diabetes, depression, metabolic disorders, and breast cancer.⁸⁸⁻⁹³ Furthermore, reduced exposure to daylight is associated with depression, cognitive function impairment, and poorer work performance.94-98



Concentrations of toxins, allergens and other pollutants in the air can be two to five times higher indoors than they are outside Although people often think only of the outdoors when they think of "environments," the indoor environments are also important for our health. For most of human history, people have spent most of their lives outdoors, experiencing both the dangers and benefits of the natural environment.

Today, in contrast, people spend much of their lives indoors – over 90% among Americans.⁹⁹ While our transition to indoor environments has provided us with many advantages – such as protection against the elements – it has also created a fundamental disconnect with the power of nature, and its central impact on our biology.

Furthermore, the indoor environment can fail to provide adequate protection from – or even increase exposure to – key environmental hazards. Research suggests that concentrations of toxins, allergens and other pollutants in the air can be two to five times higher indoors than they are outside.¹⁰⁰ There are several reasons for this increase; for example, indoor air quality is significantly influenced by outdoor air quality due to forced ventilation, infiltration, and window operation. Indoor sources can pose a threat to air quality as well, including building materials and furnishings, gas appliances, solid fuel, pests, pets, and insects.

We can further broaden our understanding of the effects of the "environment" on health by moving beyond the physical environment to the social environment. Interpersonal interactions and community conditions can establish norms that facilitate healthy or unhealthy behaviors, such as smoking, or seeking help when needed. They can expose individuals to harmful experiences, such as discrimination and bullying, or beneficial ones, such as validation and trust. And they can connect people to health-relevant resources, such as jobs, access to health care, or housing.¹⁰¹ Social support is reliably associated with mental and emotional health, and in the long term, with chronic disease and mortality.¹⁰²⁻¹⁰⁴



We have an opportunity to make long-lasting improvements to health across multiple generations

Materno-Toxic Environments

By applying the social determinants of health life course perspective, and environmental influences to maternal and child health, we can develop a more comprehensive approach to creating conditions in which women and newborns thrive. The term "materno-toxic," coined by Humanity 2.0 collaborator Jennie Joseph, describes areas or conditions that are unsafe or lethal for pregnant, postpartum or parenting women, and by extension to their children.

Across the pathways through which the environment affects health, there is clear patterning of risk across the life course: mothers require supportive, healthy environments to experience optimal pregnancies and subsequent health. Meanwhile, the in utero, infancy, and early childhood periods are windows of increased vulnerability to harmful environmental exposures, which may not manifest in disease until adulthood or even old age.

Materno-toxic exposures are not just within the physical or built environment, but are embedded in social and interpersonal environments that contain implicit and explicit biases which are perpetuated by the systemic discrimination based on race, class and gender that plague America and many other countries. That type of toxicity can surround the mother or mother/baby dyad regardless of whether other environmental factors or the institution itself is designed to be safe for maternity care or support.

While a healthy environment is important at every stage of women's and children's life course, it is particularly critical leading up to and during pregnancy, and during infancy and early childhood. As such, creating an optimally healthy environment in the broadest sense of the word should be an urgent priority for improved reproductive outcomes and human development. For example, reproductive health associations including the International Federation of Gynecology and Obstetrics, the American College of Obstetricians and Gynecologists, and the Royal College of Obstetricians and Gynaecologists urge reproductive health professionals "to take timely action to prevent exposure to toxic environmental chemicals," arguing that reducing such exposures "from food, air, water, and other sources of pollution" will contribute to improved maternal and child health.¹⁰⁵

Fortunately, our emerging knowledge of the mechanisms through which the early environment affects health indicates that there is opportunity and reason for hope if we can prevent these harmful exposures. By holistically improving mothers' and babies' environments, we have an opportunity to make long-lasting improvements to health across multiple generations.¹⁰⁶

> The human environment and the natural environment deteriorate together; we cannot adequately combat environmental degradation unless we attend to causes related to human and social degradation. In fact, the deterioration of the environment and of society affects the most vulnerable people on the planet.

- Encyclical Letter Laudato Si' Of The Holy Father Francis On Care For Our Common Home



Opportunities for Alignment with the Catholic Church

over 5300 Catholic hospitals globally

93,000 Catholic elementary schools

9882 Catholic orphanages Improving maternal, newborn and child health is a societal responsibility that requires a well-coordinated and synergistic participation of a wide range of global and national players. Partnerships between public health and faith communities have huge potential to successfully address the challenges that explain poor health outcomes, while creating and seizing opportunities to advance the agenda.

Faith-based platforms offer many capacities that can support population health initiatives, such as scale, influence, and the presence of existing infrastructure.¹⁰⁷ Furthermore, their missions are often well-aligned with health and environmental goals, given shared values related to inclusiveness and justice.¹⁰⁸ They support the health of their communities in direct ways, such as the provision of health care services, as well as less direct ways, such as the development of social capital.¹⁰⁹

The Catholic Church nurtures an incomparable global platform of health care and other social services, influencing the social and built environment of billions of people – from where they receive health care to

where they live, work, and play. It is widely recognized that faith-based organizations deliver a substantial proportion of health care services, particularly in lowincome countries with weaker health systems,^{110,111} and globally, there are over 5300 Catholic hospitals.¹¹² In the United States, Catholic health care organizations represent the country's largest group of not-for-profit health care providers, encompassing 660 hospitals and caring for more than 1 in 7 patients every day.¹¹³ Moreover, there is a vast network of social services operated by or affiliated with the Church. Worldwide there are around 93,000 Catholic elementary schools,¹¹² 43,600 Catholic secondary schools,¹¹² and 1,860 Catholic colleges and universities,¹¹⁴ educating both Catholic and non-Catholic students. The Church and its affiliates also operate 9882 Catholic orphanages.¹¹²

Other types of services provided through the Church and Catholic-identifying organizations include, but are not limited to, assistance enrolling in health insurance, housing and shelter, employment assistance, disaster operations, food banks and pantries, and immigrant and refugee support.¹¹⁵ disseminated through the work of nonprofit organizations, as well as religious institutes and orders, which together have significant reach

The Church's work is

† 700,000 Sisters in 195 countries The Church's work is disseminated through the work of non-profit organizations, as well as religious institutes and orders, which together have significant reach. Caritas International is an umbrella agency for 165 Catholic humanitarian, development, and social service organizations across 200 countries, while in the U.S., Catholic Charities USA and its network provide services to over 8.5 million people annually.¹¹⁵ The International Union of Superiors General (UISG) is one example of a Catholic religious institute; it encompasses 700,000 Sisters in 195 countries, making it the largest organization of Religious Sisters in the world.

The Church's mission and work is fundamentally aligned with the vision of improving human health through better environments. In the words of His Holiness Pope Francis, it is time for humanity to "come together to take charge of this home which has been entrusted to us."¹¹⁶ The recognition of the importance of the environment in shaping our health, and the corresponding urgent need for action, is expressed in His Holiness' landmark encyclical Laudato Si. ¹¹⁶ For example, His Holiness states that "exposure to atmospheric pollutants produces a broad spectrum of health hazards, especially for the poor, and causes millions of premature deaths," yet "frequently no measures are taken until after people's health has been irreversibly affected."116 Similarly, he argues that "access to safe drinkable water is a basic and universal human right, since it is essential to human survival." ¹¹⁶

The Vatican has also been a commendable leader in the expansion of green buildings and environmentallyconscious building practices – for example, in its installation of a solar energy system and broader commitment to renewable energy use.¹¹⁷ Specifically, the massive footprint of the Catholic Church means that it operates many buildings, whose environments could be improved for health and sustainability to the benefit of its occupants and humanity at large.

Collectively, these considerations indicate a scope for meaningful collaboration between the public health and faith communities for promoting maternal and child health through improved environments. The impact of the supportive and nourishing social environment that the Church provides, combined with the impact of the built environment of a healthy building, could exert an amplified and remarkable effect on the health and well-being of those whom the Church serves.



Conclusion

Improved maternal, fetal, and child health is key to better global health and a better future. Pregnancy is a special and crucial time for most women around the world and for the development of a new human being – and the world's future generations – making the physical, social and economic environments to which the mother is exposed to vital for the healthy development of her baby. That includes access to high quality healthcare, education, supportive social environments, good air and water quality, optimal nutrition, access to social services and better maternal leave policies.

While there are significant differences in public health concerns, and different priorities exist across different regions and countries, high-quality global public health data is available to help guide us and prioritize our interventions based on geographically-based population level health concerns to maximize the health benefits for all people.

There is tremendous potential to impact the health of all people in the world through focusing our efforts on advancing women's health throughout the life course and child health outcomes. By re-thinking what a healthy maternal environment is comprised of and what factors contribute to materno-toxic environments as well as how to measure them, and by collaborating with a diverse array of key stakeholders to identify, prioritize, create and deliver the solutions aimed at improving the health of women and their children, we envision creating a healthier world for all.



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References

1.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4rnn.
2.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4rnm.
3.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4s1c.
4.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4rla.
5.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4s1d
6.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4rnk.
7.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4s26
8.	Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4s25.
9.	Graham W, Woodd S, Byass P, et al. Diversity and divergence: the dynamic burden of poor maternal health. <i>Lancet.</i> 2016;388(10056):2164-2175.
10.	Moaddab A, Dildy GA, Brown HL, et al. Health Care Disparity and State-Specific Pregnancy-Related Mortality in the United States, 2005-2014. <i>Obstet Gynecol.</i> 2016;128(4):869-875.
11.	Mann S, Hollier LM, McKay K, Brown H. What We Can Do about Maternal Mortality - And How to Do It Quickly. <i>N Engl J Med.</i> 2018;379(18):1689-1691.
12	Division of Reproductive Health - National Center for Chronic Disease Prevention and Health Promotion

- Division of Reproductive Health National Center for Chronic Disease Prevention and Health Promotion.
 Pregnancy Mortality Surveillance System. 2018; https://www.cdc.gov/reproductivehealth/maternalinfanthealth/
 pregnancy-mortality-surveillance-system.htm. Accessed March 24, 2019.
- Fingar KF (IBM Watson Health), Hambrick MM (AHRQ), Heslin KC (AHRQ), Innovation) MJIfM. Trends and Disparities in Delivery Hospitalizations Involving Severe Maternal Morbidity, 2006-2015. Rockville, MD: Agency for Healthcare Research and Quality;2018.

- 14. Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4rld.
- 15. Swamy GK, Østbye T, Skjærven R. Association of preterm birth with long-term survival, reproduction, and next-generation preterm birth. *Jama.* 2008;299(12):1429-1436.
- 16. Goldenberg RL, McClure EM, Harrison MS, Miodovnik M. Diabetes during Pregnancy in Low- and Middle-Income Countries. *Am J Perinatol.* 2016;33(13):1227-1235.
- Rahman MM, Abe SK, Rahman MS, et al. Maternal anemia and risk of adverse birth and health outcomes in low- and middle-income countries: systematic review and meta-analysis. *Am J Clin Nutr.* 2016;103(2): 495-504.
- Lumbiganon P, Laopaiboon M, Intarut N, et al. Indirect causes of severe adverse maternal outcomes: a sec ondary analysis of the WHO Multicountry Survey on Maternal and Newborn Health. *BJOG*. 2014;121 Suppl 1:32-39.
- 19. Poston L, Caleyachetty R, Cnattingius S, et al. Preconceptional and maternal obesity: epidemiology and health consequences. *Lancet Diabetes Endocrinol.* 2016;4(12):1025-1036.
- 20. Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of maternal obesity on the long-term health of offspring. *Lancet Diabetes Endocrinol.* 2017;5(1):53-64.
- 21. Bilano VL, Ota E, Ganchimeg T, Mori R, Souza JP. Risk factors of pre-eclampsia/eclampsia and its adverse outcomes in low- and middle-income countries: a WHO secondary analysis. *PLoS One.* 2014;9(3):e91198.
- 22. Kapur A. Links between maternal health and NCDs. *Best Pract Res Clin Obstet Gynaecol.* 2015;29(1):32-42.
- 23. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet.* 2009;373(9677):1773-1779.
- 24. Goodman JH. Postpartum depression beyond the early postpartum period. *J Obstet Gynecol Neonatal Nurs.* 2004;33(4):410-420.
- G. B. D. Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for
 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet.* 2017;390(10100):1151-1210.

- 26. Heindel JJ, Balbus J, Birnbaum L, et al. Developmental Origins of Health and Disease: Integrating Environmental Influences. *Endocrinology.* 2016;2016(1):17-22.
- 27. Greenberg JA, Bell SJ, Guan Y, Yu Y-h. Folic acid supplementation and pregnancy: more than just neural tube defect prevention. *Reviews in Obstetrics and Gynecology.* 2011;4(2):52.
- 28. Duggan C, Srinivasan K, Thomas T, et al. Vitamin B-12 supplementation during pregnancy and early lactation increases maternal, breast milk, and infant measures of vitamin B-12 status. *The Journal of nutrition.* 2014;144(5):758-764.
- 29. Wikler D. Personal and social responsibility for health. *Ethics Int Aff.* 2002;16(2):47-55.
- 30. Thaddeus S, Maine D. Too far to walk: maternal mortality in context. Soc Sci Med. 1994;38(8):1091-1110.
- 31. Marmot M, Friel S, Bell R, Houweling TA, Taylor S, Commission on Social Determinants of H. Closing the gap in a generation: health equity through action on the social determinants of health. *Lancet*.2008;372(9650):1661-1669.
- 32. Renu Khanna, Sri BS. Social determinants approach to maternal deaths: *Dead Women Talking Initiative, India. Maternal, newborn, child and adolescent health* 2019; https://www.who.int/maternal_child_adolescent/epidemiology/maternal-death-surveillance/case-studies/india-social-determinants/en/. Accessed March 24, 2019.
- 33. Miller S, Belizan JM. The true cost of maternal death: individual tragedy impacts family, community and nations. *Reprod Health.* 2015;12:56.
- 34. Kusiako T, Ronsmans C, Van der Paal L. Perinatal mortality attributable to complications of childbirth in Matlab, Bangladesh. *Bull World Health Organ.* 2000;78(5):621-627.
- 35. Vogel JP, Souza JP, Mori R, et al. Maternal complications and perinatal mortality: findings of the World Health Organization Multicountry Survey on Maternal and Newborn Health. *BJOG*. 2014;121 Suppl 1:76-88.
- 36. Houle B, Clark SJ, Kahn K, Tollman S, Yamin A. The impacts of maternal mortality and cause of death on children's risk of dying in rural South Africa: evidence from a population based surveillance study (1992-2013). *Reprod Health.* 2015;12 Suppl 1:S7.

- 37. Bazile J, Rigodon J, Berman L, et al. Intergenerational impacts of maternal mortality: Qualitative findings from rural Malawi. *Reprod Health.* 2015;12 Suppl 1:S1.
- 38. Pande R, Ogwang S, Karuga R, et al. Continuing with "...a heavy heart" consequences of maternal death in rural Kenya. *Reprod Health*. 2015;12 Suppl 1:S2.
- Moucheraud C, Worku A, Molla M, Finlay JE, Leaning J, Yamin A. Consequences of maternal mortality on infant and child survival: a 25-year longitudinal analysis in Butajira Ethiopia (1987-2011). *Reprod Health.* 2015;12 Suppl 1:S4.
- 40. Kes A, Ogwang S, Pande R, et al. The economic burden of maternal mortality on households: evidence from three sub-counties in rural western Kenya. *Reprod Health.* 2015;12 Suppl 1:S3.
- 41. Molla M, Mitiku I, Worku A, Yamin A. Impacts of maternal mortality on living children and families: A qualitative study from Butajira, Ethiopia.*Reprod Health.* 2015;12 Suppl 1:S6.
- 42. Azenha GS, Parsons-Perez C, Goltz S, et al. Recommendations towards an integrated, life-course approach to women's health in the post-2015 agenda. *Bull World Health Organ.* 2013;91(9):704-706.
- 43. Susan Foster, Malcolm Bryant, Gampo Dorji, Ehimen Aneni, Olivia Blain, Roxas M. *A Framework for Estimating Benefits of Investing in Maternal, Newborn, and Child Health.* Boston, MA: Partnership for Maternal, Newborn & Child Health;2013.
- 44. Salinas-Miranda AA, King LM, Salihu HM, et al. Exploring the Life Course Perspective in Maternal and Child Health through Community-Based Participatory Focus Groups: Social Risks Assessment. J *Health Dispar Res Pract.* 2017;10(1):143-166.
- 45. Glen H. Elder, Janet Z. Giele. *The Craft of Life Course Research.* New York; London: Guilford Press; 2009.
- 46. Langer A, Meleis A, Knaul FM, et al. Women and Health: the key for sustainable development. *Lancet.* 2015;386(9999):1165-1210.
- 47. Knaul FM, Langer A, Atun R, Rodin D, Frenk J, Bonita R. Rethinking maternal health. *Lancet Glob Health.* 2016;4(4):e227-228.
- 48. Winett L, Wallack L, Richardson D, Boone-Heinonen J, Messer L. A Framework to Address Challenges in Communicating the Developmental Origins of Health and Disease. *Curr Envir Health Rpt.* 2016;3(3):169-177.

- 49. Lanphear BP. The Impact of Toxins on the Developing Brain. *Annual Review of Public Health.* 2015;36(1):211-230.
- 50. Landrigan PJ, Rauh VA, Galvez MP. Environmental Justice and the Health of Children. *Mount Sinai Journal of Medicine: A Journal of Translational and Personalized Medicine.* 2010;77(2):178-187.
- 51. Messerlian C, Bellinger D, Mínguez-Alarcón L, et al. Paternal and maternal preconception urinary phthalate metabolite concentrations and child behavior. *Environmental research*. 2017;158:720-728.
- 52. Messerlian C, Williams PL, Ford JB, et al. The Environment and Reproductive Health (EARTH) Study: a prospective preconception cohort. *Human reproduction open.* 2018;2018(2):hoy001.
- 53. Braun JM, Messerlian C, Hauser R. Fathers matter: why it's time to consider the impact of paternal environmental exposures on children's health. *Curr Epidemiol Rep.* 2017;4(1):46-55.
- 54. Olden K, Olden HA, Lin Y-S. The Role of the Epigenome in Translating Neighborhood Disadvantage Into Health Disparities. *Curr Envir Health Rpt.* 2015;2(2):163-170.
- 55. Thayer ZM, Kuzawa CW. Biological memories of past environments: Epigenetic pathways to health disparities. *Epigenetics*. 2011;6(7):798-803.
- 56. Perera F, Herbstman J. Prenatal environmental exposures, epigenetics, and disease. *Reproductive Toxicology.* 2011;31(3):363-373.
- 57. Baccarelli A, Bollati V. Epigenetics and environmental chemicals. *Current Opinion in Pediatrics.* 2009;21(2):243-251.
- 58. Landecker H, Panofsky A. From Social Structure to Gene Regulation, and Back: A Critical Introduction to Environmental Epigenetics for Sociology. *Annual Review of Sociology.* 2013;39(1):333-357.
- 59. Giurgescu C, Nowak AL, Gillespie S, et al. Neighborhood Environment and DNA Methylation: Implications for Cardiovascular Disease Risk. *J Urban Health.* 2019.
- 60. Kaati G, Bygren LO, Edvinsson S. Cardiovascular and diabetes mortality determined by nutrition during parents' and grandparents' slow growth period. *European journal of human genetics.* 2002;10(11):682.
- 61. Ravelli AC, van der Meulen JH, Michels R, et al. Glucose tolerance in adults after prenatal exposure to

famine. The Lancet. 1998;351(9097):173-177.

- Gakidou E, Cowling K, Lozano R, Murray CJ. Increased educational attainment and its effect on child mortality in 175 countries between 1970 and 2009: a systematic analysis. *The Lancet.* 2010;376(9745):959-974.
- 63. Lim SS, Updike RL, Kaldjian AS, et al. Measuring human capital: a systematic analysis of 195 countries and territories, 1990–2016. *The Lancet.* 2018;392(10154):1217-1234.
- 64. World Health Organization. The determinants of health: Introduction. 2010; https://www.who.int/hia/ evidence/doh/en/.
- 65. U.S. Department of Health and Human Services. Determinants of Health. Healthy People 2020 2019; https://www.healthypeople.gov/2020/about/foundation-health-measures/Determinants-of-Health.
- 66. Yen IH, Syme SL. The social environment and health: a discussion of the epidemiologic literature. *Annual review of public health.* 1999;20(1):287-308.
- 67. McDowell J. Encyclopedia of Human Body Systems. In: Greenwood; 2010.
- 68. Landrigan PJ. Air pollution and health. *The Lancet Public Health.* 2017;2(1).
- 69. Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4p4u.
- 70. Forouzanfar MH, Afshin A, Alexander LT, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet.* 2016;388(10053):1659-1724.
- 71. Wang H, Naghavi M, Allen C, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet.* 2016;388(10053):1459-1544.
- 72. Watson PE, Watson ID, Batt RD. Total body water volumes for adult males and females estimated from simple anthropometric measurements. *The American journal of clinical nutrition.* 1980;33(1):27-39.
- 73. Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/40e0.

- 74. U. S. Environmental Protection Agency. *National Primary Drinking Water Regulations.*
- 75. U.S. Environmental Protection Agency. *Toxicological Review of Dichloroacetic Acid. Washington*, DC2003.
- 76. World Health Organization. Dichloroacetic acid in drinking-water: Background document for development of WHO guidelines for drinking-water quality. 2005.
- 77. Villanueva CM, Cantor KP, Grimalt JO, et al. Bladder cancer and exposure to water disinfection byproducts through ingestion, bathing, showering, and swimming in pools. *American journal of epidemiology.* 2007;165(2):148-156.
- 78. Costet N, Villanueva CM, Jaakkola JJ, et al. Water disinfection by-products and bladder cancer: is there a European specificity? A pooled and meta-analysis of European case-control studies. *Occup Environ Med.* 2011;68(5):379-385.
- 79. *World Health Organization. Trihalomethanes in Drinking-Water. Geneva:* World Health Organization;2004.
- 80. Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4ojy
- 81. Institute for Health Metrics and Evaluation (IHME). GBD Compare. 2018. Available at: http://ihmeuw.org/4nys
- 82. LeGates TA, Fernandez DC, Hattar S. Light as a central modulator of circadian rhythms, sleep and affect. *Nature Reviews Neuroscience.* 2014;15(7):443.
- 83. Reppert SM, Weaver DR. Molecular analysis of mammalian circadian rhythms. *Annual review of physiology.* 2001;63(1):647-676.
- 84. Huang W, Ramsey KM, Marcheva B, Bass J. Circadian rhythms, sleep, and metabolism. *The Journal of clinical investigation. 2011;121(6):2133.*
- 85. Sack RL, Auckley D, Auger RR, et al. Circadian rhythm sleep disorders: part I, basic principles, shift work and jet lag disorders. *Sleep.* 2007;30(11):1460-1483.
- 86. Chellappa SL, Steiner R, Blattner P, Oelhafen P, Götz T, Cajochen C. Non-visual effects of light on melatonin, alertness and cognitive performance: can blue-enriched light keep us alert?

PloS one. 2011;6(1):e16429.

- 87. Hampp G, Ripperger JA, Houben T, et al. Regulation of monoamine oxidase A by circadian-clock components implies clock influence on mood. *Current Biology.* 2008;18(9):678-683.
- 88. Cho Y, Ryu S-H, Lee BR, Kim KH, Lee E, Choi J. Effects of artificial light at night on human health: A literature review of observational and experimental studies applied to exposure assessment. *Chronobiology international.* 2015;32(9):1294-1310.
- 89. Challet E KA. Circadian Rhythms and Metabolism. 2017.
- 90. Plano SA, Casiraghi LP, García Moro P, Paladino N, Golombek DA, Chiesa JJ. Circadian and metabolic effects of light: implications in weight homeostasis and health. *Frontiers in neurology.* 2017;8:558.
- 91. Fonken LK, Nelson RJ. The effects of light at night on circadian clocks and metabolism. *Endocrine reviews.* 2014;35(4):648-670.
- 92. Boyce P, Barriball E. Circadian rhythms and depression. *Australian family physician.* 2010;39(5):307.
- 93. Hurley S, Goldberg D, Nelson D, et al. Light at night and breast cancer risk among California teachers. *Epidemiology (Cambridge, Mass).* 2014;25(5):697.
- 94. Lam RW, Levitt AJ, Levitan RD, et al. Efficacy of bright light treatment, fluoxetine, and the combination in patients with nonseasonal major depressive disorder: a randomized clinical trial. *JAMA psychiatry.* 2016;73(1):56-63.
- 95. Figueiro MG. Disruption of circadian rhythms by light during day and night. *Current sleep medicine reports.* 2017;3(2):76-84.
- 96. Kent ST, McClure LA, Crosson WL, Arnett DK, Wadley VG, Sathiakumar N. Effect of sunlight exposure on cognitive function among depressed and non-depressed participants: a REGARDS cross-sectional study. *Environmental Health.* 2009;8(1):34.
- 97. Ruger M, Gordijn MC, Beersma DG, de Vries B, Daan S. Time-of-day-dependent effects of bright light exposure on human psychophysiology: comparison of daytime and nighttime exposure. *American Journal of Physiology-regulatory, integrative and comparative physiology.* 2006;290(5):R1413-R1420.

- 98. Heschong L. Windows and offices: A study of office worker performance and the indoor environment. *California Energy Commission.* 2003:1-5.
- 99. Klepeis NE, Nelson WC, Ott WR, et al. The National Human Activity Pattern Survey (NHAPS): a resource for assessing exposure to environmental pollutants. *Journal of exposure analysis and environmental epidemiology*. 2001;11(3):231-252.
- 100. Agency USEP. *Targeting Indoor Air Pollution: EPA's Approach and Progress.* 1993.
- 101. Berkman LF, Glass T. Social integration, social networks, social support, and health. *Social epidemiology*. 2000;1:137-173.
- 102. Uchino BN. Social support and health: a review of physiological processes potentially underlying links to disease outcomes. *Journal of behavioral medicine*. 2006;29(4):377-387.
- 103. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. *PLoS medicine*. 2010;7(7):e1000316.
- 104. Valtorta NK, Kanaan M, Gilbody S, Ronzi S, Hanratty B. Loneliness and social isolation as risk factors for coronary heart disease and stroke: systematic review and meta-analysis of longitudinal observational studies. *Heart.* 2016;102(13):1009-1016.
- 105. Di Renzo GC, Conry JA, Blake J, et al. International Federation of Gynecology and Obstetrics opinion on reproductive health impacts of exposure to toxic environmental chemicals. *International Journal of Gynecology & Obstetrics.* 2015;131(3):219-225.
- 106. Wallack L, Thornburg K. Developmental Origins, Epigenetics, and Equity: Moving Upstream. *Matern Child Health J.* 2016;20(5):935-940.
- 107. Duff JF, Buckingham WW. Strengthening of partnerships between the public sector and faith-based groups. *The Lancet.* 2015;386(10005):1786-1794.