The measure of a healthy society

A number of journalistic reports over the last year have drawn attention to dismaying trends in maternal and fetal health in the United States, particularly among African Americans. This public health crisis highlights the need for research into the genetic basis of maternal–fetal health and consideration of the genetic risk factors and exposures of women and children in diverse populations more broadly.

Maternal–fetal health is of central importance to a healthy society, and yet globally, maternal and neonatal mortality remains a widespread issue, even in wealthy and developed nations such as the United States. The genetics and basic research communities should be motivated by the need to address gaps in understanding of the biology of maternal–fetal health and disease, which remains understudied and imprecisely understood. We therefore encourage greater allocation of attention and resources to research that explores the genetic basis of maternal and fetal disease risk and the relationship between genetics, gestational/neonatal phenotypes and long-term health consequences.

Over the last year, excellent long-form reporting from ProPublica (https://www.propublica.org/series/lost-mothers), *The New York Times* (https://www.nytimes.com/2018/04/11/magazine/black-mothers-babies-death-maternal-mortality.html) and others has helped to illuminate public health failings in the area of maternal and fetal health in the United States, and in particular how this crisis is disproportionately impacting African-American communities. In the United States, African-American mothers are roughly three times more likely to die from complications in childbirth than mothers of white European ancestry. African Americans have twice the infant mortality rate and infants are three times more likely to die from complications related to low birth weight as well as those related to the health of their mother (https://www.cdc.gov/nchs/hus/contents2016.htm). It seems clear that these disparities must stem at least partially from poverty and the accompanying lack of access to quality medical care and nutrition. However, infant mortality rates for babies born to African-American mothers who have a professional degree are still higher than those for babies born, for example, to white mothers with only a high school degree, suggesting additional complexities in the causal roots of these trends.

A possible contributing factor is the documented disparities in the ways African Americans are treated as they seek medical care. For instance, African-American patients have been found to be undertreated for pain, both broadly and for specific medical conditions (examples at *Proc. Natl. Acad. Sci. USA* **113**, 4296–4301, 2016 and *JAMA Pediatr.* **169**, 996–1002, 2015). Pain management depends on the patient's self-reporting of severity but also on how the healthcare provider receives the patient's assessment; the subjectivity of this system may render individuals of different ethnicities vulnerable to discriminatory attitudes and subtext. As with the biology of pain, much of the understanding of the biology of maternal–fetal health remains idiopathic. Such ambiguity can only increase the exposure of patients to institutional bias and impedes the progress of women's and children's health outcomes overall.

Achieving a more mechanistic understanding of maternal–fetal health entails specific challenges. In utero, the genetics and physiology of either the mother or fetus contribute directly to fetal phenotypes, yet mother and child have an overlapping genetic makeup. Partitioning genetic risk to maternal and fetal contributions therefore presents a unique methodological challenge. Disentangling these contributions is also necessary to direct functional follow-up research on the relevant tissues and biological processes at play. The placenta has a central role (as acknowledged, for example, by the Human Placenta Project of the US National Institutes of Health), but has been traditionally difficult to study in real time as it develops and executes its critical functions. Integrating genetic datasets with more highly resolved models of the cellular composition and physiology of the placenta should yield specific insights into the basis of major conditions affecting women and their unborn or newborn babies—including preeclampsia, gestational diabetes, preterm birth and low birth weight.

Basic insights into the biology of pregnancy and fetal development have the potential to guide better medical care for all women and their families. But the disparities in society make it imperative that we also focus particular attention on diverse and underserved populations. It seems likely that groups of different ancestry have unique disease architectures owing to differences in their underlying genetics; if so, we need to know this and can only do so through well-powered and thoughtfully designed genetic studies. Another major goal should be to understand how specific environmental exposures act via sets of genetic variants to influence health outcomes among certain populations. Phenotypes like low birth weight are observationally correlated with later-in-life health outcomes such as heart disease. Therefore, longitudinal datasets are needed to develop understanding of the ways in which a woman's genome and her life experience contribute to the long-term health of her children, beyond the gestational and perinatal periods. Ideally, one consequence of this research will be to motivate greater societal investment in preventive and prenatal care for all. ❐

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