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Challenges and opportunities to improving research in maternal cardiovascular health

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Pregnancy is associated with a substantial risk of short-term and long-term cardiovascular diseases. Here we discuss physiological and social factors that affect the risk of pregnancy-related cardiovascular diseases and opportunities to improve outcomes.

Much has been written about the maternal mortality crisis in the United States. More women die as a result of pregnancy than in any other high-income country, and rates have continued to rise in recent years[1]. Cardiovascular conditions are the leading cause of pregnancy-associated deaths, defined as those deaths that occur during pregnancy or within a year of delivery, from any cause related to or exacerbated by pregnancy. Cardiomyopathy is the most common cause of death after delivery, whereas coronary heart disease, congenital heart disease and other cardiovascular diseases are the leading causes during pregnancy[2]. More than 60% of cardiovascular deaths are considered preventable and occur as a result of provider and health system factors.

For an even larger number of women, pregnancy complications impact cardiovascular health during pregnancy and in the years following delivery. Hypertensive disorders of pregnancy (HDP) such as preeclampsia and gestational hypertension affect up to 15% of pregnancies and are associated with an almost twofold higher risk of coronary heart disease, stroke and heart failure in the decades following delivery[3]. The excess cardiovascular risk during pregnancy is partially explained by a higher burden of traditional cardiovascular risk factors, such as hypertension and obesity, which highlights the importance of early risk factor control and prevention[4]. In short, pregnancy is associated with substantial short-term and long-term cardiovascular risk. Opportunities to understand maternal cardiovascular disease and improve outcomes are thus critically important to public health.

Physiological changes in pregnancy increase cardiac demand and may exacerbate or unmask previously undiagnosed cardiovascular disease. Pregnancy may also be associated with changes in vessel wall architecture, leading to a 3–4-fold increase in the risk of myocardial infarction and aortic dissection. Why some women have a maladaptive response to the hemodynamic and hormonal changes of pregnancy is not well understood and requires further research. Preeclampsia leads to the release of antiangiogenic markers from the placenta, such as soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng), which cause endothelial dysfunction, vasoconstriction and immune dysregulation, which leads to clinical manifestations later in pregnancy. The link between HDP and later cardiovascular outcomes has been well established, though how and why some women develop accelerated cardiovascular disease is not clear. Some studies suggest that the endothelial dysfunction that is caused by preeclampsia triggers ongoing vascular damage, which results in long-term vasoconstriction, left ventricular remodeling and premature vascular aging. The use of aspirin has been shown to prevent the early onset of preeclampsia in high-risk women but whether this intervention reduces long-term cardiovascular disease risk needs to be evaluated in clinical trials. Ongoing clinical trials are evaluating pravastatin, a hydrophilic statin, in early pregnancy for preeclampsia prevention via anti-inflammatory mechanisms and the potential to restore angiogenic balance.

The etiology of peripartum cardiomyopathy (PPCM) is likely multifactorial but preeclampsia is an important risk factor and these conditions share some mechanistic pathways. Animal models implicate the vasculotoxic role of a 16-kDa prolactin fragment in the pathogenesis of PPCM, a process that can be inhibited by bromocriptine, a dopamine agonist that suppresses prolactin release. Clinical trials are ongoing to evaluate bromocriptine for the treatment of PPCM[5]. An alternate animal model of PPCM also implicates excess levels of sFlt-1 leading to decreased availability of VEGF[6]. Genetic predisposition may also play a role, as up to 15% of patients with PPCM have a truncating mutation in genes that are implicated in dilated cardiomyopathy[7], but further work is needed to determine the genetic risk, if any, in the remaining 85%.

The racial disparities that are observed in maternal cardiovascular health necessitate special consideration. Black and Native American women are three times more likely to die as a result of pregnancy compared with white women in the United States[8]. Black women have a twofold higher risk of preeclampsia and a fourfold higher risk of PPCM compared with white women, and have higher risk of complications and death from these conditions[9]. The higher prevalence and risk of adverse outcomes is largely caused by social determinants of health, including where people live, and structural racism, which impact access to and quality of care[10]. Studies that examine how social determinants interact with clinical risk factors to cause cardiovascular disease are not well understood; a deeper understanding of these pathways has the potential to prevent disease, improve clinical outcomes and reduce racial disparities.

Biomedical research has historically excluded sex as a biological variable in the study of cardiovascular disease, with broad impact on understanding sex-based differences in pathophysiology, disease manifestations and treatment[11]. Women make up 38% of participants in contemporary cardiovascular clinical trials, although pregnant women are almost always excluded even when no biological basis exists to do so. This 'protection by exclusion' approach leads to limited understanding and uptake of potentially life-saving treatments in pregnant individuals, such as the COVID-19 vaccine. Opportunities to improve maternal cardiovascular outcomes and to reduce disparities exist across the spectrum of basic and translational science, clinical research and population health studies, but must include a sex-specific biological lens and account for the contribution of sex steroid changes over the lifespan.

Interventions that are focused on standardizing and improving quality of care could significantly impact maternal cardiovascular outcomes and reduce disparities. Black women in New York City deliver in hospitals with higher risk-adjusted severe maternal morbidity rates; delivering in similar hospitals as white women could reduce severe maternal morbidity by one-third[12]. Collaborative quality improvement efforts in California have improved statewide maternal mortality outcomes using data integration and patient safety bundles[13]. Cardiovascular screening tools have been proposed but validation and implementation in diverse health systems have not yet been conducted. Creating and adapting strategies to improve quality of care throughout the pregnancy and postpartum period and targeted to diverse healthcare providers and health systems is key, especially when implemented as part of broader policy changes.

Digital interventions, such as remote blood pressure monitoring following a hypertensive pregnancy, have improved rates of blood pressure screening and treatment, especially among Black women[14]. Digital interventions that promote physical activity and weight loss have also been successful in the postpartum period to improve cardiovascular health metrics[15]. Digital tools that promote cardiovascular health that can be incorporated within health systems or community organizations have the greatest potential to become standard of care and reach the majority of patients. Such interventions may focus on optimal blood pressure management strategies, education and early detection of symptoms through apps or automated text messages, recognition of hemodynamic changes that may be a precursor to disease such as heart rate variability through wearable devices, or on physical activity or weight loss programs to promote cardiovascular health. Machine learning methodologies are increasingly applied to data from electronic health records to identify and predict uncommon diseases; pooling clinical and biobank data across clinical sites could facilitate algorithms to identify women at risk of cardiovascular complications.

Finally, community-based interventions and policy changes offer the potential to address social determinants of health and reduce disparities by addressing structural racism and improving access to high-quality care. Compared to white women, Black women are more likely to report that their concerns are disregarded by healthcare providers[16]. Care provided by a more diverse workforce may better address patients' needs and preferences. Community-based staff, such as midwives and doulas, who provide emotional support and postpartum care, help serve as patient advocates, connect parents to additional resources, and can improve infant and maternal outcomes. Implementation and evaluation of care models using diverse maternity care providers is needed to understand how best to incorporate these providers into care teams to improve patient outcomes.

In summary, advancing science in maternal cardiovascular health has the potential to improve health over the lifespan with long-lasting repercussions for children and families.

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Competing interests

The author declares no competing interests.