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Pregnancy and SARS-CoV-2: an opportunity to systematically study the complexity of maternal health

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Despite a worldwide, strategic, rapid, multi-pronged approach to developing viral-specific testing, therapeutics, and vaccines as the SARS-CoV-2 pandemic unfolded and its pathobiology became understood, the scientifically complex population of pregnant people were routinely excluded from these clinical trials.[1] Nearly 2 years later, an information gap on pregnancy-specific therapeutics or vaccines for SARS-CoV-2 persists. Using electronic health records, Samantha Piekos and colleagues[2] contribute to the evolving knowledge on birth outcomes modified by the pregnancy trimester in which the infection occurred. Comparing pregnant people who had undergone testing and adjusting for common covariates impacting birth outcomes, those with mild or moderate SARS-CoV-2 infections in the first and second trimester had an increased risk of preterm birth and stillbirth.

In their study,[2] details about treatments and management during pregnancy are largely unknown. No one was vaccinated. One could speculate that symptomatic people infected in the first or second trimester of pregnancy received anticoagulation to mitigate the thrombotic risk. As of December, 2021, therapies administered during pregnancy for SARS-COV-2 infection, like most other therapies, are extrapolated from studies of non-pregnant people due largely to barriers excluding women and pregnant people from clinical research.[1,3] If treatment lessened their risk of thrombotic or microvascular placental disease, their risk of preterm birth or stillbirth might be decreased compared with asymptomatic pregnant people without such treatment.

Worldwide, symptomatic pregnant people experienced a higher risk for intensive care, mechanical ventilation, and death accompanied by the suggestion of increased rates of preterm birth.[1,3] Other respiratory infectious diseases also disproportionately affect pregnant people and neonates albeit at higher rates and virus-specific vaccination improves their outcomes.[1] The effect of specific SARS-CoV-2 treatments or vaccination on pregnancy outcome remain unknown. Furthermore, women constitute a higher proportion of those with post-acute sequelae of SARS-CoV-2, yet descriptions of their maternal or pregnancy outcomes are similarly unknown.

For pregnant people in the USA, the SARS-CoV-2 pandemic has been a collision of crises.[3] To date, studies show differences in risk and outcomes across multiple axes, including sex, gender, race, and age and a disproportionate physical, psychological, and an economic toll on Black, Indigenous, People of colour communities, people living at, near, and below the poverty line, and women.[4,5] Notably, after adjusting for these sociodemographic factors, the authors report an increased risk of preterm birth and stillbirth in those with less severe SARS-CoV-2 infections acquired early in pregnancy.[2]

Thus, at the heart of the scientific response to SARS-CoV-2, is the question—how can research answer crucial questions fast enough to alleviate suffering, save lives, and ensure that findings are relevant and of benefit for all, including pregnant people? The pandemic revealed an unprecedented opportunity to ensure, even during a crisis, that research is both scientifically rigorous and equitable—concepts that are mutually reinforcing. The complexity of pregnancy with its distinct susceptibilities and physiologies offers a vitally important opportunity to generate much needed evidence through responsible inclusion of pregnant people in research. Contemporary research on the developmental origins of disease has shown that social and structural determinants of health inequities embed themselves epigenetically.[3,6]

In recognition of the opportunity to incorporate an equity lens and support meaningful integration of sex and gender considerations into SARS-CoV-2 research, the National Institute for Health (NIH) Office of Research on Women's Health (ORWH) developed a set of guiding principles: first, multidimensional approaches to the health of women including pregnancy; second, inclusion across the life course; third, consideration of sex as a biological variable; fourth, assessment of COVID-19's impact on careers; and fifth, purposeful study of understudied, under-represented, and under-reported populations of women.[7] The current NIH Strategic Plan for Women's Health Research and the NIH-Wide Strategic Plan for COVID-19 Research identify pregnancy, maternal health, and prevention of severe morbidity as key areas of focus.[8,9] The Task Force on Research Specific

to Pregnant Women and Lactating Women promulgated implementation plans that could guide inclusion of this vulnerable population in research.[10]

Maternal health disparities in the USA can no longer be ignored, nor can we ignore disparities associated with SARS-CoV-2. It has dramatically illuminated both persistent health inequities and the failure of research, clinical care, and medical education to address the social and structural factors that generate and perpetuate these inequities among those at greatest risk of adverse pregnancy outcome. For populations of women already burdened by historical marginalisation and health impacts of social inequality, the consequences of SARS-CoV-2 are staggering. Internationally, the Venice Forum of researchers and economists argued that sustainable recovery from COVID-19 will require investment in maternal, neonatal, and child health.[6] Intentional consideration of the NIH ORWH guiding principles offers a way to both inspire a more inclusive body of research and encourage a crucial dialogue on the importance of maternal health care and infectious disease prevention in improving the health of women.[7] Piekos and colleagues' recommendation to closely monitor preganant people who have had a SARS-CoV-2 infection during the first or second trimester of pregnancy is an essential beginning.

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See Online for appendix

The acknowledgments are available in the appendix.

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