SARS-CoV-2 infection is associated with enhanced disease severity in pregnant women. Despite the potential of COVID-19 vaccines to reduce severe disease, vaccine uptake remained relatively low among pregnant women. Just as coordinated messaging from the Centers for Disease Control and Prevention and leading obstetrics organizations began to increase vaccine confidence in this vulnerable group, the evolution of SARS-CoV-2 variants of concerns, including the Omicron variant, raised new concerns about vaccine efficacy because of their ability to escape vaccine-induced neutralizing antibodies. Early data point to a milder disease course following infection with the Omicron variant in vaccinated individuals. Thus, these data suggest that alternate vaccine-induced immunity beyond neutralization may continue to attenuate Omicron variant—induced disease, such as Fc-mediated antibody activity.

Objective
This study aimed to test whether vaccine-induced antibodies raised during pregnancy continue to bind to and leverage Fc receptors to protect against variants of concern including the Omicron variant.

Study Design
The receptor binding domain or whole spike-specific antibody isotype binding titers and Fc gamma receptor binding directed toward variants of concern, including the Omicron variant, were analyzed in pregnant women after receiving the full dose regimen of either the Pfizer/BioNTech BNT62b2 (n=10) or Moderna messenger RNA-1273 (n=10) vaccination using a multiplexing Luminex assay.

Results
Reduced isotype recognition of the Omicron receptor binding domain was observed following administration of either vaccine with relatively preserved, albeit reduced, recognition of the whole Omicron spike by immunoglobulin M and G antibodies (Figure). Despite the near complete loss of Fc receptor binding to the Omicron receptor binding domain, Fc receptor binding to the Omicron spike was more variable but largely preserved.

Conclusion
Reduced binding titers to the Omicron receptor binding domain aligns with the observed loss of neutralizing activity. Despite the loss of neutralization, preserved, albeit reduced, Omicron spike recognition and Fc receptor binding potentially continue to attenuate disease severity in pregnant women.

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This study was funded by the National Institutes of Health (NIH) under grants 3R37AI080289-11S1, R01AI146785, U19AI42790-01, U19AI135995-02, 1U01CA260476-01, and CIVIC75N93019C00052, and by the Bill and Melinda Gates Foundation: Global Health Vaccine Accelerator Platform under grants OPP1146996 and INV-001650. A.G.E. received funding from the NIH under grant R01HD100022-S2 and from the March of Dimes Foundation under grant 6-FY-20-223 to support sample collection.


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Supporting material appears on the next page
Compromised RBD, but not spike-specific Omicron recognition in pregnant individuals

Pregnant individuals received either the full dose regimen of the BNT162b2 (n = 10) or the mRNA-1273 (n = 10) vaccination. Samples were taken at peak immunogenicity 2 to 4 weeks after the last dose. IgM, IgA1, and IgG1 binding titers to D614G (wild-type [WT]; blue), Alpha (B.1.1.17; yellow), Beta (B.1.351; purple), Delta (B.1.617.2; orange), and Omicron (B.1.529; red) variants of concern RBD (A) or whole spike (B) were measured by Luminex. Background corrected data are shown, and negative values were set to 100 for graphing purposes. A Kruskal-Wallis test with a Benjamini-Hochberg posttest correcting for multiple comparisons was used to test for statistical differences between WT variant and Omicron variant titers. P values for significantly different features are shown above and the fold-change reduction in Omicron titer compared with WT titer is given below each data set.

Ig, immunoglobulin; mRNA, messenger RNA; RBD, receptor binding domain.