



## COVID-19 vaccination is effective at preventing severe illness and complications during pregnancy



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Pregnancy increases the risk of severe illness and death from COVID-19; moreover, SARS-CoV-2 infection during pregnancy is associated with increased risk for adverse pregnancy and neonatal outcomes, such as preterm birth, stillbirth, and neonatal death.<sup>1</sup> COVID-19 vaccination is the most effective strategy to prevent severe COVID-19.<sup>2,3</sup> Although pregnant women were excluded from COVID-19 vaccine clinical trials, limiting initial data on effectiveness in pregnancy,<sup>4</sup> other studies have shown that mRNA COVID-19 vaccines are effective in pregnant women.<sup>2,3</sup> Three studies of pregnant women, published in 2022, have assessed disease severity<sup>5</sup> and vaccine effectiveness<sup>2,6</sup> during the period of omicron variant predominance. Using population-level data among women from Scotland with SARS-CoV-2 infection during pregnancy, authors found that, compared with the period of delta variant predominance, the omicron period was associated with significantly lower risk of preterm birth and severe illness during pregnancy.<sup>5</sup> In studies from the USA and Israel, monovalent mRNA COVID-19 vaccination was less effective during the omicron period than the delta period and effectiveness waned over time, particularly during the omicron period in pregnant women who had not received a COVID-19 booster vaccination.<sup>2,6</sup>

In *The Lancet*, José Villar and colleagues report findings from a prospective cohort study assessing disease severity and vaccine effectiveness among pregnant women in 18 countries during the omicron period. The authors compared 1545 pregnant women with laboratory-confirmed SARS-CoV-2 infection with 3073 unmatched controls recruited consecutively from the same hospital. Pregnant women with COVID-19 were at moderately increased risk for maternal morbidity (adjusted relative risk [aRR] 1.16 [95% CI 1.03–1.31]) and perinatal morbidity (aRR 1.21 [95% CI 1.00–1.46]). The authors did not find an increased risk in neonatal morbidity (aRR 1.23 [95% CI 0.88–1.71]).<sup>7</sup> Consistent with studies among the general population, the risk of severe disease was lower compared with studies done before the omicron variant predominated.<sup>1,8</sup> This finding might be due to the intrinsic lower severity of the SARS-CoV-2 omicron

variant than previous variants, population-level immunity from vaccination and previous infection, or both.<sup>8</sup> This study also reports protective effects of vaccination against severe maternal complications during the omicron period, building on scarce evidence to date.<sup>7</sup> COVID-19 vaccine effectiveness against severe complications (severe symptoms, referral to a higher level of care, ICU admission, and death), during the omicron period, was 48% (95% CI 22–65) after primary series and increased to 76% (47–89) with a booster dose. Notably, the effectiveness against progression to severe complications among women with SARS-CoV-2 infection was 74% (48–87) after primary series and 91% (65–98) after a booster dose. Receipt of a monovalent mRNA booster was 81% (95% CI 47–94) effective at preventing severe complications from COVID-19 among all women and 94% (56–99) effective at preventing progression to severe complications among those with SARS-CoV-2 infection.

Although protection against severe complications was high, receipt of a primary vaccine series was not effective against SARS-CoV-2 infection or moderate symptoms. Even after a booster dose, protection against infection was just 30% (95% CI 19–39) and against moderate symptoms was 48% (32–61). Strengths of this study include the large, multinational sample size. A key limitation of the study is that most pregnant women were infected in the third trimester (median gestational age 36.7 weeks), which might indicate ascertainment bias and limits the generalisability of the findings to women infected in the first and second trimesters of pregnancy. Additionally, although the authors assessed cumulative incidence of SARS-CoV-2 infection among those vaccinated over time, they did not account for time since vaccination or waning immunity in their vaccine effectiveness estimates. Therefore, the increased effectiveness of a booster dose against severe complications is probably due, at least in part, to immunity waning of the primary vaccine series, further highlighting the importance of booster doses after completing primary COVID-19 vaccination.<sup>7</sup>

Although this study reported outcomes only up until the delivery hospitalisation, current evidence shows

that maternal COVID-19 vaccination protects against severe illness both among pregnant women and their infants up to 6 months of age who are too young to be vaccinated.<sup>2,3,7,9</sup> During the omicron period, it remains crucial to convey that COVID-19 vaccination primarily prevents severe illness, including hospitalisation and death, in the general population; Villar and colleagues show this is also true for pregnant women.<sup>7</sup> COVID-19 vaccination among pregnant women is effective against severe illness and complications during the omicron period, but immunity wanes over time.<sup>2</sup> Receipt of a booster regardless of the type of primary series received was highly effective.<sup>7</sup> Additionally, a recent 2022 study among the general US population showed that bivalent mRNA boosters (containing components both from the ancestral SARS-CoV-2 strain and omicron sublineages) provide significant additional protection against symptomatic SARS-CoV-2 infection compared with receipt of monovalent mRNA boosters.<sup>10</sup> To prevent adverse outcomes associated with SARS-CoV-2 infection during pregnancy, pregnant women should stay up to date with recommended COVID-19 vaccines, including, if available, a bivalent mRNA booster when they are eligible.<sup>10,11</sup>

We declare no competing interests. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention.

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## New medications to mitigate attacks of hereditary angioedema: does one size fit all?



Hereditary angioedema has received renewed attention in the past two decades, with the elucidation of the biochemical pathways resulting in bradykinin overproduction in patients with congenital C1esterase inhibitor (C1INH) deficiency, leading to recurrent attacks of tissue swelling due to uncontrolled vascular permeability.<sup>1</sup> Oedema attacks affecting the lingual or laryngeal area can become lethal as a result of asphyxiation.<sup>2</sup> Several new treatments have emerged, 143 years after Quincke's first description of hereditary angioedema and 15 years after the introduction of the first specific bradykinin B2 receptor inhibitor

(icatibant). These drugs specifically target crucial steps in the kallikrein-kinin (contact) cascade downstream of bradykinin production.<sup>3</sup> Many of these agents have shown their efficacy and safety in acute (on-demand) treatment and prophylaxis of hereditary angioedema attacks, saving lives and revolutionising patients' quality of life.<sup>4</sup> These modalities fit well into the modern paradigm in hereditary angioedema treatment, supporting patients' autonomy, recommending self-administration, and reducing reliance on hospital emergency rooms, health-care providers, and medical points of care.<sup>5</sup>



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