typically take 2–4 days to start making neutralising antibodies,[5] people who are more susceptible to severe disease need the earlier protection afforded by high antibody levels.

Although the CDC has opted for a simple message across all age groups, data-driven recommendations will increase trust, especially given that only 71% of the population in the USA older than 65 years had received a single booster as of Oct 12, 2022.[6] If we clarify the goals of our booster strategy to prevent severe disease[7] (as recommended by WHO), the annual booster campaign that the FDA has stated is the new strategy going forward will probably only be needed for people who are at highest risk (as defined by age, comorbidities, and whether they are immunocompromised). In fact, once a year might not be enough for some risk groups.

As for timing, we agree with the Canadian National Advisory Committee on Immunization to recommend the updated vaccine at an interval of 6 months after previous vaccination or infection. Antibody levels stabilise 6–9 months after vaccination for individuals with and those without previous infection.[8] Giving a booster too soon (within 60 days) after a recent infection interferes with effective B-cell responses,[9] and extended intervals between vaccine doses increase both neutralising antibodies and memory B cells.[8] If one of the aims of omicron-specific boosters is to increase antibodies and prevent even mild infections, the antibody level plateau at the 6-month mark would signal an ideal time to boost with a variant-focused vaccine.[8]

We are excited about the ability of the mRNA vaccines to be updated as new variants emerge. However, focusing our booster recommendations on those most clinically vulnerable to severe disease first, and timing vaccine administration to optimise the immune response, is a good public health strategy.

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Effectiveness of BNT162b2 booster after CoronaVac primary regimen in pregnant people during omicron period in Brazil

Infection with SARS-CoV-2 during pregnancy increases the risk of severe negative maternal and foetal clinical outcomes.[1] In the general population, the SARS-CoV-2 B.1.1.529 (omicron) variant can evade both natural and vaccine-induced protection,[2] highlighting the importance of booster doses.[3] However, little is known about the vaccine effectiveness of a booster dose against COVID-19 in pregnant people, and no data have been published for those with a primary series of CoronaVac (inactivated-virus vaccine).[4,5] In this study, we investigated the vaccine effectiveness in pregnant people who received two doses of CoronaVac to estimate the additional protection provided by a booster dose with BNT162b2 (mRNA vaccine) during the omicron period.

We conducted a test-negative design study on pregnant people who had a SARS-CoV-2 RT–PCR or an antigen test aged 15–49 years in Brazil, from Jan 1 to April 30, 2022 (appendix pp 2–4).[6,7] Pregnancy information was abstracted from COVID-19 notifications from the national surveillance system for RT-PCR and antigen tests for COVID-19 infection (e-SUS Notifica) and the information system for severe acute respiratory illness (SIVEP-Gripe). Inclusion and exclusion criteria are described in the appendix (pp 2–4). Briefly, cases consisted of symptomatic pregnant people with a positive test (SARS-CoV-2 RT–PCR or antigen), and controls were pregnant individuals with a negative SARS-CoV-2 RT–PCR or antigen test. Individuals who were hospitalised or died from COVID-19 infection were classified as severe COVID-19. To attribute the death or hospitalisation to COVID-19, the hospitalisation had to have occurred 3 days before or 14 days after the positive test, and the death within 28 days of the positive test. Logistic regression was used to estimate the vaccine effectiveness of a booster dose compared with two doses of CoronaVac, both at 14 days or more after the last vaccination. The following confounders were included

See Online for appendix

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	Tested positive (n=6280)	Severe cases* (n=434)	Tested negative (n=4506)	Vaccine effectiveness for symptomatic infection (95% CI)	Vaccine effectiveness for severe cases (95% CI)
Two doses of CoronaVac only					
≥14 days	5036 (80·2%)	381 (87·8%)	3156 (70·0%)	Reference	Reference
BNT162b2 booster dose					
0–13 days	194 (3·1%)	16 (3·7%)	188 (4·2%)	46·4% (33·2–57·0%)	43·2% (1·7–67·2%)
≥14 days	1050 (16·7%)	37 (8·5%)	1162 (25·8%)	37·7% (28·9–45·3%)	68·4% (52·6–78·9%)

The reference group were pregnant people vaccinated with two doses of CoronaVac at 14 days or less. *Severe cases include hospitalisations and deaths.

Table: **Adjusted vaccine effectiveness against symptomatic infection and severe cases for pregnant people receiving a BNT162b2 booster dose (two doses of CoronaVac plus BNT162b2) at days 0–13 and 14 days or more**

in the model: age, ethnicity, week of infection, the month when the second dose was received, region of residence, socioeconomic status, previous SARS-CoV-2 infection, and the presence of comorbidities. Detailed methods can be found in the appendix (p 2).

A total of 10 786 tests were included, with 6280 (58·2%) testing positive (cases) and 4506 (41·8%) testing negative (controls; appendix p 4). Among the cases, 434 met the criteria for severity. Cases and controls had similar characteristics (appendix p 5). The adjusted vaccine effectiveness for a booster compared with primary complete vaccination in pregnant people was 37·7% (95% CI 28·9–45·3) against symptomatic COVID-19 and 68·4% (52·6–78·9%) against severe COVID-19 (table). Crude and adjusted odds ratios can be found in the appendix (p 6). Furthermore, the vaccine effectiveness was similar at 7 days or more compared to 14 days and more after the booster dose (appendix p 6).

The data collected in Brazil are from high-quality national databases, increasing their statistical power.[6,7] The test-negative design is used to minimise bias related to access to health care, the occurrence of symptoms, and health-seeking behaviour. The primary assumption of the test-negative design is that people seeking and getting tested would be influenced by similar pressures, regardless of their vaccination status,[8] and a limitation is the absence of information of pregnancy status at the time of vaccination and the precise gestational age at the time of testing.

Our findings strongly support the importance of a booster dose for pregnant people, because they provide additional maternal protection against mild and severe COVID-19 during the omicron period. Further studies are needed to assess the protection afforded by a booster dose in preventing negative foetal outcomes of COVID-19 for BNT162b2 and other COVID-19 vaccine regimens.

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