Effectiveness of mRNA booster doses against the omicron variant

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Since its emergence in November, 2021, the omicron (B.1.1.529) variant of SARS-CoV-2 has rapidly spread and quickly overtaken the delta (B.1.617.2) variant as the most common cause of infection.[1] Due to numerous spike mutations, the omicron variant showed increased transmissibility and reduced neutralisation by antibodies from prior infections compared with the wild-type virus and other variants of concern. Concurrently, breakthrough infections surged in populations with high vaccination rates, which expedited efforts to scale up booster vaccination.[1]

In *The Lancet Infectious Diseases*, Susana Monge and colleagues[2] report on the effectiveness of mRNA vaccine boosters against SARS-CoV-2 infection in Spain during the era of omicron predominance. In this nationwide representative study, data for 3 111 159 matched pairs of vaccinated individuals with a median age of 53 years (IQR 50–57) were retrieved from three nationwide population registries. These registeries tracked COVID-19 vaccine doses, date, and result of SARS-CoV-2 tests (done by health-care providers or self-administered) for all registered individuals, along with their demographic data. Both cohorts (booster group and no booster group) included people aged 40 years or older, who completed their primary vaccination schdules at least 3 months before the study start date, with no history of SARS-CoV-2 infection. Each day between Jan 1, and Feb 6, 2022, matched individuals from each cohort of the same sex, age group, postal code, type of primary vaccination (BNT162b2 [Pfizer–BioNTech], mRNA-1273 [Moderna], ChAdOx1 nCoV19 [Oxford–AstraZenica], or Ad26.COV2.S [Janssen]), time since primary vaccination, and number of previous tests, were assessed for laboratory-confirmed SARS-CoV-2 infection to estimate vaccine effectiveness. Follow-up started on the day of booster dose administration and lasted 34 days.

The study reported a 51·3% (95% CI 50·2–52·4) estimated overall effectiveness for mRNA boosters in preventing SARS-CoV-2 infection up to 34 days after administration. Higher effectiveness was observed in females (52·6% [51·1–54·1]) compared with males (49·8% [48·1–51·5]) and individuals aged 60–79 years (58·0% [55·8–60·4]) compared with 40–59-year-olds (49·9% [48·6–51·3]) and individuals ages 80 years or older (53·5% [43·9–63·3]). Other nationwide studies done in Qatar (49%),[3] Scotland (57%),[4] the USA (66%),[5] and Canada (37%)[6] also showed substantially lower booster effectiveness against the omicron variant compared with other variants of concern. Similar reductions in neutralising activity against the omicron variant were reported using sera derived from cohorts boosted with mRNA vaccines.

Despite the waning effectiveness of booster vaccines against the omicron variant, a third dose vaccine dose with mRNA-1273 was found to provide higher effectiveness (52·5% [95% CI 51·3–53·7]) than a BNT162b2 booster (46.2% [43·5–48·7]), which was highest in individuals boosted 7 months after completion of primary vaccination. These data are consistent with other studies, which report a 20-times higher neutralisation titers after boosting with mRNA-1273 against the omicron variant, irrespective of primary vaccination type.[8]

Of note, higher effectiveness was seen in individuals primed with ChAdOx1 nCov-19 (58·6% [95% CI 55·5–61·6]) or mRNA-1273 (55·3% [52·3–58·2]) compared with those primed with BNT162b2 (49·7% [48·3–51·1]) or Ad26.COV2.S (48·0% [42·5–53·7]) vaccine. Although there are no current reports regarding vaccine effectiveness following heterologous boosting of Ad26.COV2.S with mRNA vaccines, the lower effectiveness for BNT162b2 compared with ChAdOx1 nCoV-19 and mRNA-1273 vaccines seems to be inconsistent with other studies and merits replication in other countries.[9]

Although the optimal interval between primary vaccination completion and booster administration has not been established, Monge and colleagues[2] showed the highest effectiveness for boosters administered after the longest time interval in this study. However, due to the surge in omicron variant infections, this interval might be justified to mitigate the epidemic. Regardless, more studies are needed to evaluate and model when to administer a booster dose. On the basis of existing evidence, it seems that longer intervals (>7 months) are preferable.

This study is important because it provides an estimation of mRNA booster effectiveness after primary immunisation with several COVID-19 vaccines in a nationwide setting during the omicron peak. Vaccines were shown to differ in effectiveness against the omicron variant, with mRNA-1273 booster showing the highest effectiveness, perhaps owing to its large dose. The study had some limitations, including the possible existence of confounding variables that could affect the diagnostic intensity in assessed cohorts. Also, not all self-administered tests were recorded in the national registry, which could affect the estimated effectiveness. Another caveat is that the study did not assess booster effectiveness against severe disease and death. However, on the basis of the knowledge obtained from previous studies during the era of other variants of concern, boosters are likely to offer higher levels of protection against severe and fatal diseases.[10]

Moreover, despite showing the important role of boosters as an effective strategy to limit the health effects of the omicron pandemic, certain concerns remain, especially that vaccine effectiveness was considerably lower than for earlier variants even in the first few months after a booster dose when protection is presumed to be highest. Hence, effectiveness studies evaluating the protection from and waning immunity of mRNA boosters are needed to generate robust recommendations, especially in the context of variants of concern.

We declare no competing interests.

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