

# Number needed to vaccinate for COVID-19 booster doses: a valuable metric to inform vaccination strategies

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Three and a half years after it first emerged, SARS-CoV-2 continues to cause infections, hospitalizations and deaths globally. SARS-CoV-2 vaccines are the most effective tool for reducing disease burden in the ongoing post-pandemic phase. In the context of waning immunity after primary vaccination series and the emergence of new variants, the importance of booster doses in maintaining a higher level of individual and population immunity against severe disease cannot be over-emphasised.<sup>1</sup> Countries have adopted varying policies for booster doses, considering factors such as prioritised populations, dosing regimens, and timing.

Among the first booster vaccines administered, mRNA vaccines—notably BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna)—have been most widely administered in middle- and high-income countries. Currently, the United States Centers for Disease Control and Prevention recommends that individuals aged 6 months and older receive at least one dose of a bivalent mRNA COVID-19 vaccine.<sup>2</sup> In addition, individuals  $\geq 65$  years of age have the option to receive a second bivalent mRNA vaccine dose. Such policies underscore the important role of booster vaccinations. However, the average severity of infections has been declining over time. This is because vaccinated individuals have long-term reductions in the risk of severe disease even if vaccines only provide transient protection against infection,<sup>3</sup> and immunity following natural infections might also protect some individuals from severe disease when reinfecting even if a booster vaccination is not received. In this context of increasing levels of population immunity against severe disease, the optimal strategy and target group for booster doses remains to be elucidated.

Adams et al. carried out a retrospective cohort study to evaluate the performance of a third dose vaccine during the Omicron BA.1 predominant period between

December 2021 and February 2022, focusing on immunocompetent adults in four U.S. states.<sup>4</sup> They estimated the Number Needed to Vaccinate (NNV) to describe the potential impact of a booster dose. The NNV is an estimate of the average number of people that should be vaccinated in order to prevent one disease event, for example if the specified outcome is hospitalizations an NNV of 100 means that on average 100 people should be vaccinated to prevent one hospitalization due to SARS-CoV-2. Adams et al. analysed data from over a million patient records, with 37.2% of these individuals having received a third dose, while the others received only two doses. The median estimated NNV for a booster dose was 205 to prevent one hospitalisation, and was 156 to prevent one emergency department visit. The authors conducted subgroup analyses by various characteristics such as age groups, underlying conditions, and study sites. The findings showed that the NNV varied substantially by clinical setting, population characteristics and sites, ranging approximately from 40 for older individuals to 600 for younger individuals, to prevent one hospitalization or emergency department visit. The estimated NNV to prevent one hospitalization was much lower for high-risk individuals, including those at least 65 years of age or with at least one underlying medical condition, supporting booster strategies that prioritise these high-risk groups. Importantly, variations in the NNV to prevent hospitalisation were observed across three study periods, with values ranging from 46 to 110 among individuals aged 65 years or older. This highlights the role of timely assessment and continuous monitoring of NNV to guide vaccination strategy, because the NNV is not likely to remain constant.

The results reported by Adams et al. support the use of booster doses in late 2021 and early 2022. However, they may not be able to inform booster dose policies in the evolving landscape of SARS-CoV-2 Omicron subvariants. Values of the NNV may have increased, reducing the cost-effectiveness of booster doses in lower-risk individuals. Given that SARS-CoV-2 infections continue to cause hospitalizations in older individuals<sup>5</sup> and given that booster doses protect against hospitalization with the latest Omicron subvariants,<sup>6,7</sup> it



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is likely that booster doses will continue to be recommended for high-risk individuals. Updated data from studies like the one by Adams et al. would be valuable to indicate whether booster doses continue to provide a cost-effective strategy for the prevention of COVID-19 in younger and lower-risk individuals.

## Contributors

SF was responsible for the conceptualisation and wrote original draft. All authors contributed to “writing—review & editing”, and approved the final version of the manuscript.

## Declaration of interests

SF contributed to COVID-19 vaccine intellectual property licensed by Oxford University Innovation to AstraZeneca. BJC received consulting fees from AstraZeneca, Fosun Pharma, GlaxoSmithKline, Haleon, Moderna, Pfizer, Roche, and Sanofi Pasteur.

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## References

- 1 Ferdinands JM, Rao S, Dixon BE, et al. Waning 2-dose and 3-dose effectiveness of mRNA vaccines against COVID-19-associated

emergency department and urgent care encounters and hospitalizations among adults during periods of delta and Omicron variant predominance—VISION network, 10 states, August 2021–January 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71(7):255–263.

- 2 Lin DY, Xu Y, Gu Y, Zeng D, Sunny SK, Moore Z. Durability of bivalent boosters against Omicron subvariants. *N Engl J Med.* 2023;388(19):1818–1820.
- 3 Andrews N, Tessier E, Stowe J, et al. Duration of protection against mild and severe disease by covid-19 vaccines. *N Engl J Med.* 2022;386(4):340–350.
- 4 Adams K, Riddles JJ, Rowley EAK, et al. Number needed to vaccinate with a COVID-19 booster to prevent a COVID-19-associated hospitalization during SARS-CoV-2 Omicron BA.1 variant predominance, December 2021–February 2022, VISION Network: a retrospective cohort study. *Lancet Reg Health Am.* 2023;23:100530.
- 5 Wee LE, Pang D, Chiew C, et al. Long-term real-world protection afforded by third mRNA doses against symptomatic SARS-CoV-2 infections, COVID-19-related emergency attendances and hospitalizations amongst older Singaporeans during an Omicron XBB wave. *Clin Infect Dis.* 2023. <https://doi.org/10.1093/cid/ciad345>.
- 6 Link-Gelles R, Weber ZA, Reese SE, et al. Estimates of bivalent mRNA vaccine durability in preventing COVID-19-associated hospitalization and critical illness among adults with and without immunocompromising conditions—VISION network, september 2022–April 2023. *MMWR Morb Mortal Wkly Rep.* 2023;72(21):579–588.
- 7 Muhsen K, Maimon N, Mizrahi AY, et al. Association of receipt of the fourth BNT162b2 dose with Omicron infection and COVID-19 hospitalizations among residents of long-term care facilities. *JAMA Intern Med.* 2022;182(8):859–867.