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## Why older adults can continue to benefit from covid-19 boosters

Newly published studies show that mRNA covid-19 boosters, including those updated against newer variants, are effective and safe in protecting older adults from severe covid-19, but what does that mean for healthcare providers and patients? Kristine Macartney and Bette Liu discuss

Despite the covid-19 global health emergency being officially over, timely evidence is still needed on the safety and effectiveness of covid-19 vaccines. Most countries continue to recommend covid-19 vaccination for older adults to reduce the risk of severe disease.<sup>1</sup> Despite much of the population having “hybrid immunity,”<sup>2</sup> derived from both vaccination and infection, covid-19 is still responsible for many hospital admissions and deaths among older people.<sup>3</sup> Data on the impact of additional vaccine doses, including those specifically designed to protect against new variants, is needed by policy makers, governments, and individuals to inform ongoing decision making. Uptake has declined recently, owing to complacency about the need for vaccines,<sup>4</sup> distrust fuelled by misinformation, concerns about safety, and the rolling back of delivery programmes.

### Real world evidence

The three studies by Andersson and colleagues using linked data from Denmark, Finland, Norway, and Sweden provide important real world evidence of the effectiveness and safety of mRNA covid-19 vaccines.<sup>5-7</sup>

The first study (doi:10.1136/bmj-2022-074325) included 3.6 million adults aged 18 and older and compared those who received differing brands (heterologous schedule) of covid-19 vaccines for their first three doses with people who had received the same brand (homologous schedule) or no booster during the omicron period (December 2021 to December 2022).<sup>5</sup> All mRNA booster schedules were effective against severe covid-19 compared with primary vaccination only, but heterologous boosters were slightly more effective than homologous boosters at preventing covid-19 related hospital admissions. No study participants received a booster using an Oxford-AstraZeneca (ChAdOx1) vaccine, meaning the effectiveness of this brand could not be assessed. As found in studies of hybrid immunity,<sup>2</sup> the cumulative incidence of infection was lowest for people who had been previously infected and received a booster dose.

The second study (doi:10.1136/bmj-2023-075015), in adults aged 50 and older, estimated the incidence of 27 prespecified adverse events in the 28 days after immunisation in 1.7 million recipients of a bivalent mRNA booster.<sup>6</sup> The authors observed no excess risk of neurological, cardiovascular, autoimmune, and other serious conditions in the 28 days after vaccination overall, or when stratified by age group, sex, or booster type.

A post hoc analysis found no increase in incidence of cerebrovascular infarction associated with vaccination but did find a higher incidence of myocarditis among women that was statistically

significant, based on a small number of events. However, the estimated absolute attributable risk was only about two to three additional cases per million booster doses. This risk is much lower than that of developing severe covid-19 in the absence of a booster or the risk of myocarditis resulting from covid-19.<sup>8</sup> In other safety studies, myocarditis, although still rare, mostly occurred after mRNA vaccination in male participants aged 12-39 years, and after the second dose.<sup>8,9</sup>

The third study (doi:10.1136/bmj-2022-075286) compared the effectiveness of a fourth dose of the new mRNA bivalent covid-19 vaccines with a third dose only.<sup>7</sup> The analysis, involving 2.5 million booster recipients aged 50 years and older, estimated a 65-70% relative reduction in risk of covid-19 associated hospital admission or death in the three months after the bivalent booster. This translated to an absolute reduction of 92-113 hospital admissions and 34-39 deaths for every 100 000 booster recipients. No substantive difference was found in effectiveness between the BA.1 and BA.5 bivalent mRNA vaccines.

### Practical implications

What are the practical implications of these findings for patients, clinicians, and policy makers? Firstly, together with other large observational studies<sup>10-13</sup> that use linked registry data or other digital health records and take account of hybrid immunity, these findings confirm that mRNA vaccines, particularly those adapted to recent SARS-CoV-2 variants, work well as boosters to protect older people from severe covid-19. This should build confidence in healthcare providers, policy makers, and the public as to the value of continuing to promote and take up vaccination.

Secondly, Andersson and colleagues' findings provide reassurance that updated covid-19 vaccines continue to have an excellent safety profile. Globally, vaccination has been critical in protecting people and populations against the ongoing effects of the pandemic, and serious vaccine attributable risks are rare. Repeated and robust epidemiological as well as mechanistic studies continue to be important in determining whether and how vaccines increase the risk of certain medical conditions.<sup>14</sup>

Collectively, Andersson and colleagues' studies show that when used as recommended, the new bivalent mRNA covid-19 vaccines are safe and provide considerable benefit for older adults. Our ongoing challenge is to ensure this information helps to increase vaccine uptake in this important age group.

Finally, SARS-CoV-2 continues to evolve. Having a durable protective response against this pathogen,

after vaccination, previous infection, or both, continues to be a challenge in those with the highest risk of severe outcomes. Recommendations for regular vaccination of older adults from the World Health Organization and others, preferably with updated vaccines, will likely see monovalent covid-19 vaccines targeted towards the XBB lineage of the omicron variant available in the coming months.<sup>15 16</sup> We need to ensure that robust studies continue to provide timely evidence on the real world impact of updated vaccines.

Competing interests: The authors declare the following interests: BL holds shares in Fisher and Paykel Healthcare and Resmed.

Further details of The BMJ policy on financial interests is here: <https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf>.

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