Rapid Reviews COVID-19 •

Review 2: "Protection Across Age Groups of BNT162b2 Vaccine Booster against Covid-19"

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RR:C19 Evidence Scale rating by reviewer:

- **Reliable.** The main study claims are generally justified by its methods and data. The results and conclusions are likely to be similar to the hypothetical ideal study. There are some minor caveats or limitations, but they would/do not change the major claims of the study. The study provides sufficient strength of evidence on its own that its main claims should be considered actionable, with some room for future revision.

Review:

Bar-On et al. have published an updated follow-up study to their recent NEJM paper (N Engl J Med. 2021 Oct 7;385(15):1393-1400). The researchers analyzed the effect of booster vaccination (three doses) versus two doses with BNT162b2 (Pfizer) in people +60 years of age and younger age groups in Israel. The methods are robust, and they perform sensitivity analysis, thus confirming their claims. The authors prove that booster vaccination with BNT162b2 confers improved protection against infection for at least two months post-booster date. The effect was sustained in all age groups. The manuscript also claims reductions in severe disease; however, the frequency of severe disease was low, making their conclusions on disease severity slightly less robust. Lastly, they could not assess mortality because of very low numbers (a win of vaccination, boosted or not!). There has been criticism regarding the definition of severe disease in Israel. Since severity is defined freely by front-line providers and because WHO's definitions changed during the pandemic (decreasing oxygen requirements from 93% to 90% to be considered severe), the data on severity may have more bias than the data on infections. The implications of this study are debatable (not because of the quality of the paper, but because implications depend on resource availability, ethics, and overall intent of a country's public health response). Some will see this paper as supporting evidence for widespread utilization of boosters, while others may want to see longer-term data and more data on safety. It is likely unquestionable that boosters decrease the likelihood of infection. However, the long-term durability of the added protection against infection is not evident yet and may well be temporary. The effects on severity and mortality are likely lower, especially in younger fully vaccinated age groups. All in all, this is a critical study that deserves publication after peer-review. This manuscript will inform policy, but policy, as always, should and will consider other factors such as vaccine availability and global supply and coherence with other local and global public health measures implemented.