

## Review of: "Measuring the efficacy of a vaccine during an epidemic"

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Potential competing interests: No potential competing interests to declare.

This is a well written piece. However, it should be noted that vaccines have both specific and nonspecific effects. Strictly speaking your paper is addressing the specific effects of COVID-19 vaccination and does not address the nonspecific effects which can be inferred from a study of all-cause mortality.

We have just submitted a comprehensive study on the nonspecific effects of COVID-19 vaccination regarding monthly measurement of the change in all-cause mortality following vaccination. The outcome is highly dependent on combinations of age/sex/vaccine history/COVID variant and the month in which the person dies. During the Omicron variant the all-cause mortality outcomes are mostly negative, i.e., all-cause mortality was increased relative to the unvaccinated. Roles for small noncoding RNAs were implicated.

The effect of month more or less tallies with your observations.

Hence, there is no problem with your estimates regarding the specific effects of mRNA vaccination - however the efficacy against all-cause mortality can be an entirely different matter.

As a starting point can I recommend the following study: Benn, C.; Schaltz-Buchholzer, F.; Nielsen, S.; Netea, M.; Aaby, P. Randomised clinical trials of COVID–19 vaccines: Do adenovirus-vector vaccines have beneficial non-specific effects? Available at: SSRN: <a href="https://ssrn.com/abstract=4072489">https://ssrn.com/abstract=4072489</a> or <a href="http://dx.doi.org/10.2139/ssrn.4072489">https://ssrn.com/abstract=4072489</a> or <a href="http://dx.doi.org/10.2139/ssrn.4072489">https://ssrn.doi.org/10.2139/ssrn.4072489</a>

This particular group has done a lot of work investigating the nonspecific effects of vaccines.

I hope that these thoughts are helpful.

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