Title: Higher contact among vaccinated can be a mechanism for negative vaccine effectiveness

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Summary

Why did we conduct this study?

In December 2021 when Omicron arrived, early observational studies suggested that vaccine effectiveness – a measurement of how well vaccines work in the real world – was "negative", meaning that vaccinated individuals were becoming infected at higher rates than unvaccinated individuals. We questioned the validity of this "negative" result and hypothesized that it could be due to a type of bias related to different contact patterns among vaccinated vs unvaccinated.

What did we do?

We developed a transmission model and simulated epidemics with an efficacious vaccine (which means that it protects against infection and against passing infection on to others). We used the simulations to test whether increased contact among vaccinated persons (which could have arisen due to to vaccine mandates) could produce "negative" measurements even when a vaccine was beneficial.

What did we find?

Our simulations showed that the following conditions could create a perfect storm for observing "negative" vaccine effectiveness even when a vaccine was efficacious:

- 1) when vaccinated persons have more contacts with other vaccinated (e.g. because of a policy like a vaccine mandate); and
- 2) when underlying vaccine benefits are lower but not negative (e.g. which could happen with new variants such as Omicron); and
- 3) when vaccine effectiveness is measured when an epidemic is growing (e.g. with the emergence of a new variant).

What do these findings mean for public health?

- 1. Even if vaccines work, increased contact among vaccinated persons can lead to the appearance of the vaccine not working.
- 2. A clue that this bias is present is the observation of "negative" vaccine effectiveness when the epidemic is growing.
- 3. Our findings can assist future empirical studies to recognize this bias and highlight the importance of accounting for different contact patterns when measuring vaccine effectiveness to avoid misinterpretation and prevent vaccine mistrust.

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