Estimating the indirect effects of COVID-19 vaccination against the Omicron variant of SARS-CoV-2 in California state prisons

Pre-analysis Plan
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Objective: Estimate the indirect protection of COVID-19 vaccination against the Omicron variant conferred to unvaccinated persons in California state prisons.

Hypothesis: Unvaccinated persons in California state prisons are less likely to be infected by the Omicron SARS-CoV-2 variant if they reside with other vaccinated residents.

Study outcome: SARS-CoV-2 infection in an unvaccinated resident

Statistical analysis:

Inclusion criteria

- Residents that stay in rooms with exactly one other resident for at least 14 days at any point during the Omicron wave (December 15, 2021 – December 15, 2022)
- Both residents must have resided in California state prisons beginning in March 2020 to ensure more complete reporting of prior SARS-CoV-2 infection
- Both residents have not had a prior SARS-CoV-2 infection (positive SARS-CoV-2 test) within the 90 days prior to co-residence in the unit
- At least one resident must be unvaccinated during co-residence (i.e., if a room initially has one unvaccinated and one vaccinated resident and the unvaccinated resident receives a COVID-19 vaccine, the room would be excluded after onset of vaccine protection (14 days after first dose))
- At least one unvaccinated resident must have continuous biweekly (rolling 2-week window) testing data during co-residence

Matching

We will refer to a room over a continuous period of time that meets inclusion criteria as a unit. All analysis is retrospective and no interventions are prospectively assigned. We will refer to units where both residents are unvaccinated as control units and units where one resident is vaccinated as treatment units. Within both types of units, we will assign residents to be either primary or secondary residents. In treatment units, we will assign the unvaccinated resident as the primary resident and the vaccinated resident as the secondary resident. The primary resident must have SARS-CoV-2 testing data that meets the study criteria. In control units, the primary resident will be assigned to maximize observation time of testing data during co-residence; if both residents have the same observation time of testing data, a primary resident will be chosen at random. The second unvaccinated resident in the room will be referred to as the secondary resident.

We will perform optimal matching of control and treatment units by building, prior infection status of the primary resident, and time. We will exclude the first 5 days of co-residence of each unit from matching to minimize potential confounding from previous housing environments. There must be at least 7 days of overlap between matched units. We will only include overlapping time in the final matches. Matches will be made to maximize number of control units included in the final sample and maximize total observation time across matches. We will additionally consider k:1 matching based on sample size considerations.

Time-to-event regression modeling
The primary statistical analysis will use a frailty (mixed effects) Cox model to predict the risk of infection in primary residents (time to event outcome) by vaccine status of secondary resident (exposure). The frailty model was chosen to account for correlation within a match and repeated use of control unit over different observation periods. We will assess the relationship of vaccination status of the secondary resident on the hazard rate of SARS-CoV-2 infection in the primary resident. Within the regression model, we will control for the following covariates: institution, building, prior infection in both residents, vaccination status of secondary resident (binary or categorical: unvaccinated, primary series, booster). Alternatively, we will perform the analysis using a simple stratified analysis.

Our sample size calculations suggest the analysis is powered to detect an effect size of approximately a 35% reduction in hazard. We will perform a sensitivity analysis that relaxes inclusion criteria to increase the sample size if the findings suggest the analysis is underpowered, which will include removal of requirement to be incarcerated over entire pandemic period. We will perform at least two additional sensitivity analyses to examine using work activity as a covariate for exposure risk and relaxing the testing requirement.

Additional related planned analyses
We will plan to perform at least two additional analyses. First, we will investigate the indirect effects of recent COVID-19 vaccination. We will repeat the proposed analysis where a treatment unit is defined by a secondary resident with recent COVID-19 vaccination (within 3-6 months). Second, we will investigate whether indirect effects are present at a larger spatial scale, such as floor or cell block.

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