Estimating the infectiousness of SARS-CoV-2 infections due to the Omicron variant in vaccinated persons in California state prisons

Pre-analysis Plan
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Objective: Estimate the relative infectiousness of SARS-CoV-2 infections due to the Omicron variant in unvaccinated and vaccinated persons in California state prisons from December 15, 2021, to March 25, 2022

Hypothesis: SARS-CoV-2 infections due to the Omicron variant in unvaccinated individuals are more infectious than infections in vaccinated individuals.

Study outcome: Risk of transmission of SARS-CoV-2 infection among close contacts of an index case

Important definitions:

Index case

Inclusion	Exclusion
- Residents with any positive SARS-CoV-2 test and - Residents with a negative PCR SARS-CoV-2 test in the 8 days* prior to first positive test and - Residents that stay in rooms with solid doors*** at the start of their infectious period** and - Residents with valid close contacts	- Residents with prior infection in the last 90 days, unless negative PCR in the interim or - Residents that have a negative PCR SARS-CoV-2 test during the 5-day infectious period** or - Residents with no housing data over entire infectious period or - Residents with any contact that has a concurrent infection (first positive test within 2 days of first exposure)

*We chose 8 days to account for variability in the timing and cadence in testing (e.g., approximately weekly testing), with consideration to maximize sample size.
**Infectious period: 5 days starting the day of first positive SARS-CoV-2 test. If a resident has a negative antigen test during 5-day infectious period, infectious period is truncated
***We will include residents that stayed in 180 cells (room type 1), 270 cells (room type 2), or other cells (room type 4) with solid doors during their infectious period in this analysis. Figure 1 below is a bar chart showing distribution of movement during an index case's infectious period. Each number in the label of the bin represents the room type in which an infectious resident stayed (e.g., bar labeled '1' means that 1000 index cases stayed in room type 1 (180 cell) for their entire infectious period, and bar labeled '325' means that a few index cases started their infectious period in room type 3 (270 dorm), and were moved to type 2 (270 cell) then 5 (dorm) during their infectious period).

Circled in green are potential index cases that meet inclusion criteria – circled in yellow are potential index cases we include only if the facility was built after 1980 (cells have solid doors).

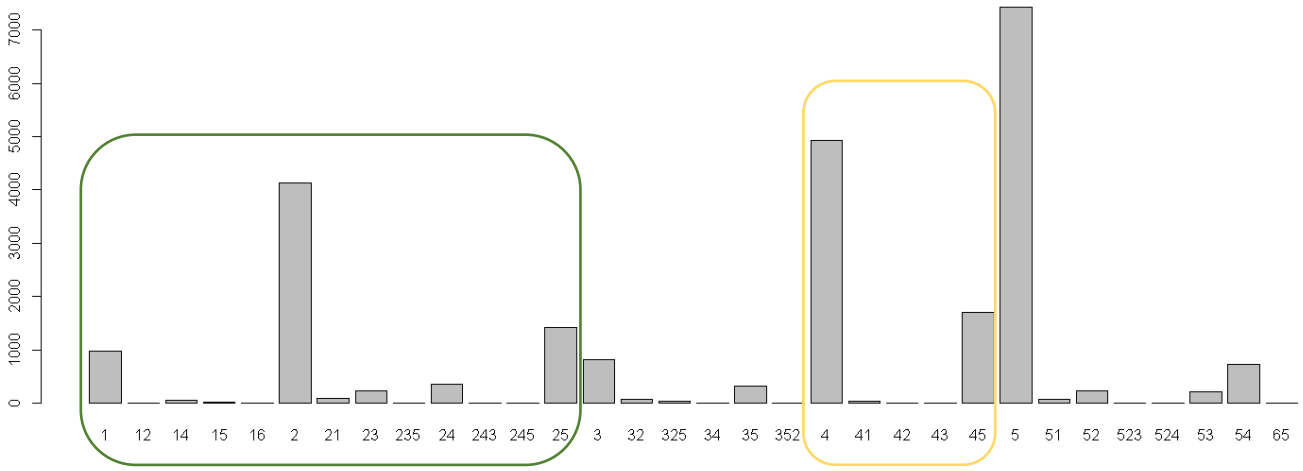

Figure 1. Histogram of room type over the infectious period of the index case.

Close contact

Inclusion	Exclusion
- Residents that share a room (with solid doors) with an index case during their infectious period and - Residents that have a negative SARS-CoV-2 test within 2 days (+/-) of first exposure and - Residents that have SARS-CoV-2 testing data between 3 days after first exposure and 14 days after last exposure*	- Residents with no housing data or - Residents with prior infection in the last 90 days, unless negative PCR in the interim

*Secondary case: A valid close contact that tests positive between 3 days after first exposure and 14 days after last exposure

Statistical analysis:

We will estimate the risk of transmission of SARS-CoV-2 infection due to the Omicron variant under different vaccine statuses. We will include index cases that meet study inclusion criteria and occur on or after December 15, 2021 to reflect the spread of the Omicron variant in California state prisons based on genomic surveillance data. We will perform 1:*k* matching without replacement to match unvaccinated and vaccinated index cases by time and facility using the MatchIt package. We will include matches that occur in the same facility and within 30 days of each other, and *k* will be chosen as 3 to maximize sample size.

We will fit robust Poisson regression models that use the vaccination status of index cases (unvaccinated v. vaccinated) as the key exposure variable to predict infection among close contacts (outcome variable). The regression models will incorporate the matching results and include a random effect for the index case to capture heterogeneity of transmission across cases. The coefficient of interest will estimate the comparative infectiousness of index cases that are unvaccinated and vaccinated. To account for possible confounding variables, including variability across different California prison facilities, SARS-CoV-2 variants, and natural immunity, we will adjust for covariates related to index cases and their close contacts. We will assess covariates for collinearity and association with the outcome of interest. A list of covariates is as follows:

- Incidence in the facility in the 7 days leading up to infection in the index case (continuous, defined as number of cases divided by the total population in the facility)
- Facility (categorical)
- Index case
    - prior vaccination (binary, defined as 0 if index case is unvaccinated or <14 days after receipt of first dose of any COVID-19 vaccine or 1 if ≥14 days after receipt of any dose of a COVID-19 vaccine)
    - prior infection (binary, defined as any positive SARS-CoV-2 test based on prior testing data)
- Close contact
    - prior vaccination (numerical, defined as total number of doses of COVID-19 vaccines received ≥14 days ago with maximum of 4 doses)
    - prior infection (binary, defined as any positive SARS-CoV-2 test based on prior testing data)

The Poisson regression model is as follows:

infection in close contact ~ vaccination status of index case + prior infection in index case + prior vaccination in close contact + prior infection in close contact + facility + incidence + random effect for index case + weights from matching

Sensitivity analysis and contingency:

We will conduct additional analyses with a more parsimonious model depending on sample size considerations and variability in covariates. We will consider varying the vaccine status definition in the index and close contact (e.g., aggregating number of vaccine doses received in close contact). We will consider using logistic regression models to estimate study outcomes.

We will relax assumptions in the inclusion and exclusion criteria in the study design, including the start and duration of the infectious period. We will test the following scenarios:

- Infectious period begins 2 days prior to first positive test
    - with an infectious period of 5 days
    - with an infectious period of 7 days

- Removing requirement for a negative test in the index case and close contacts

We will perform analyses with alternative definitions of vaccination in both the index case and close contact to account for partial vaccination, booster doses, and time since vaccination. This will also consider non-linear increases in protection with each dose of vaccination, and consideration of protection from time since last dose.

This document was written prior to generation of any results pertaining to the study hypothesis.

Signatures:

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