Title: Infectiousness of SARS-CoV-2 breakthrough infections and reinfections during the Omicron wave

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Abstract:

With more recent SARS-CoV-2 variants, breakthrough infections in vaccinated individuals and reinfections among previously infected individuals are increasingly common, especially during the Omicron wave. Such infections have led to concerns about controlling transmission and underscore a broader need to understand the contribution of vaccination, including booster doses, and natural immunity to the infectiousness of persons with SARS-CoV-2 infections, especially in high-risk populations with intense transmission such as prisons. Here, we show that both vaccine-derived and naturally acquired immunity independently reduce the infectiousness of persons with Omicron variant SARS-CoV-2 infections in a prison setting. Analyzing data from system-wide SARS-CoV-2 surveillance across 35 California state prisons, we estimate that Omicron variant infections among unvaccinated cases had a 36% (95% confidence interval (CI): 31-42%) risk of transmitting to close contacts, as compared to 28% (25-31%) risk among vaccinated cases. In adjusted analyses, we estimated that any vaccination, prior infection alone, and both vaccination and prior infection reduced an index case's risk of transmitting to close contacts by 22% (6-36%), 23% (3-39%) and 40% (20-55%), respectively. Receipt of booster doses and more recent vaccination further reduced infectiousness among vaccinated cases. These findings suggest that although vaccinated and/or previously infected individuals remain highly infectious upon SARS-CoV-2 infection in this prison setting, their infectiousness is reduced compared to individuals without any history of vaccination or infection.

Main Text:

Transmission dynamics of SARS-CoV-2 have shifted over the course of the pandemic due to widespread vaccination, natural infection, and emergence of novel variants *(1).* While the early pandemic was characterized by infections in susceptible individuals, SARS-CoV-2 breakthrough infections among vaccinated individuals and reinfections among previously infected individuals are now increasingly common *(2–4)*. Following the emergence of the highly infectious Omicron variant in December 2021, the United States observed the largest surge in COVID-19 cases to date *(5)*. Determining the impact of vaccination, including booster doses, and prior infection on the infectiousness of persons with Omicron variant infections remains necessary to understand transmission dynamics of this variant.

There is limited data on the infectiousness of breakthrough SARS-CoV-2 infections in vaccinated persons and reinfections with the Omicron variant. Available data on the infectiousness of SARS-CoV-2 breakthrough infections in vaccinated individuals is mixed, with most data reported during the Delta variant wave or earlier, among persons immunized only with primary series doses *(6–11).*

Studying the transmission dynamics of the SARS-CoV-2 Omicron variant and the impact of vaccination and prior infection is especially important in vulnerable, high-risk populations with intense ongoing transmission, such as the incarcerated population. The COVID-19 pandemic has disproportionately affected incarcerated individuals *(12,13)*, as transmission of SARS-CoV-2 remains high in prison settings, fueled in part by overcrowding, poor or lack of ventilation, and introduction from community sources *(12,14–19*). In this study, we report on the infectiousness

of SARS-CoV-2 infections occurring in vaccinated persons and/or those with prior infection relative to unvaccinated and previously uninfected individuals who are incarcerated in a U.S. state prison system during the Omicron wave. The study aims to have broad implications to public health policy and particular relevance to incarcerated populations and other high-density congregate living environments.

Results

SARS-CoV-2 infections and testing within the study population

We analyzed detailed records of SARS-CoV-2 infection and housing data from all 35 adult institutions in California's state prison system during periods of high-volume testing, assessing risk of transmission between individuals sharing a cell with solid doors and walls. We aimed to assess the infectiousness of Omicron variant SARS-CoV-2 infections in confirmed index cases, stratified by their vaccine status and prior infection history. We analyzed data during a 5-month period (December 15, 2021 - May 23, 2022) of widespread circulation of the Omicron variant, during periods of both systematic and reactive SARS-CoV-2 testing. In total, there were 22,334 confirmed SARS-CoV-2 infections and 31 hospitalizations due to COVID-19 in the study population (N=111,687) during the Omicron wave (Figures 1 and S1). During the study period, residents in the study population were tested on average 8.1 times (interquartile range (IQR): 4-11) for SARS-CoV-2. The average time between tests in the study population was 11.7 days (IQR: 4-10) (see Appendix, Figure A1). We identified 1,226 index cases over the study period based on the inclusion criteria of having a positive SARS-CoV-2 diagnostic test (without a prior positive test in preceding 90 days), continuous incarceration beginning prior to April 1, 2020 (to ensure reliable reporting of prior SARS-CoV-2 infection), and a valid close contact in a shared,

closed-door cell (Figures 1 and S1). We defined close contacts of the index case as residents who shared a cell with an index case for at least one night while the index case was infectious (assuming a 5-day infectious period following a positive test *(20)*); we required the close contact to have a negative SARS-CoV-2 test within 2 days of first exposure as well as follow up testing data within 14 days after last exposure. Each index case was assigned a single close contact at random if multiple contacts were identified (<0.1% of cases). Further description of inclusion criteria, exclusion criteria, and matching that was needed to address concerns for confounding and misclassification is available in the Methods and Appendix (Figure S1). We matched unvaccinated index cases (n=273) and vaccinated index cases (n=953) by institution (exactly) and time (within 30 days) and by a propensity score (for receipt of vaccination), excluding cases without eligible matches (Figure S1). We matched an average of 3.5 (interquartile range: 2-4) vaccinated index cases to each unvaccinated index case (see Appendix, Figure A4). The mean duration of exposure of close contacts to index cases was 2.4 days for unvaccinated index cases and 2.2 days for vaccinated index cases (see Appendix, Figure A3). The average duration from a close contact's first exposure to subsequent testing for contacts exposed to a vaccinated and unvaccinated index was both 6.2 days, and the mean duration of last eligible follow up testing in close contacts occurred at day 10 after first exposure for unvaccinated index cases and 10.6 days for vaccinated index cases (see Appendix, Figure A6). The distribution of secondary cases from time since exposure was similar between vaccinated and unvaccinated index cases (6.7 versus 5.7 days, see Figure A2). Descriptive data on the study population's demographics, vaccine uptake, and prior infections are shown in Table 1, Table S1, and in the Appendix.

Relative infectiousness of SARS-CoV-2 breakthrough infections and reinfections

Over an average 2.3 days of exposure to the index case, the unadjusted risk of transmission to all close contacts of index cases was 30% (95% CI: 27-32%). Unvaccinated index cases had a 36% (31-42%) risk of transmitting to close contacts, while vaccinated index cases had a 28% (25-31%) risk of transmitting to close contacts (Figure 2). Index cases with a history of prior SARS-CoV-2 infection (i.e., reinfection) had a lower risk of transmitting to close contacts [23% (19-27%)] than index cases with no history of prior infection [33% (30-37%)]; reduced risk of transmission from index cases who were previously infected was apparent in strata of index cases who had or had not been vaccinated, and who did or did not receive a booster dose (Figure 2 and Table S2).

Adjusting for duration of exposure between index cases and close contacts, close contacts' history of vaccination and prior infection, and facility effects and background SARS-CoV-2 incidence via a robust Poisson regression model, we estimated that index cases who had received ≥1 COVID-19 vaccine doses had 22% (6-36%) lower risk of transmitting infection than unvaccinated index cases. In analyses that further accounted for the number of vaccine doses received by an index case, each additional dose was associated with an average 11% reduction (5-17%) in risk of transmission to the close contact (Figure 3 and Tables S3-5). Prior SARS-CoV-2 infection was similarly associated with a 23% reduction (3-39%) in risk of transmission from the index case. Having both prior vaccination and SARS-CoV-2 infection was associated with a 40% (20-55%) reduction risk of transmission by the index case, based on a linear combination of regression coefficients (Figure 3); we did not identify evidence of interaction between history of vaccination and natural infection associated with transmission risk (Table S6).

We assessed the relationship between time since last vaccine dose and/or natural infection on infectiousness of a SARS-CoV-2 infection and found that time since last dose of a COVID-19 vaccine (as a continuous variable) was associated with increased infectiousness of SARS-CoV-2 infections; for every 5 additional weeks since last vaccine dose, SARS-CoV-2 breakthrough infections were 6% (2-11%) more likely to transmit infection to close contacts. We did not observe a statistically significant relationship between time since last SARS-CoV-2 infection and risk of transmission (Table S7 and Figure S2).

We conducted a number of sensitivity and additional model analyses to evaluate the robustness of the study findings. We evaluated primary study outcomes when relaxing exclusion criteria for close contacts; any prior COVID-19 vaccination was associated with 23% (8-35%) reduction in attack rate when we included close contacts that tested positive within two days of exposure to the first index case and 19% (3-33%) reduction when removed the requirement of a negative test in close contacts within two days of first exposure to an index case (Table S8). Study findings were also similar across changes in the matching process (Table S9). Varying definitions of the start and duration of the infectious period attenuated some of the findings (Table S10). We found excluding index cases that received the *Ad26.COV2* vaccine led to similar results (Table S11). We repeated the primary adjusted analysis using a logistic regression model and found that both prior vaccination [odds ratio (OR) 0.66 (0.48-0.91)] and prior infection [OR 0.68 (0.49-0.95)] were associated with reduced odds of infection in close contacts (Table S12). Additional details on sensitivity analyses are available in the Appendix.

Transmission attributable to primary infections, breakthrough infections, and reinfections

We estimated that primary infections (15% of index cases) contributed to 20% (16-25%) of transmission to secondary cases, breakthrough infections (49% of index cases) contributed to 52% (47-57%) of transmission to secondary cases, reinfections (7% of index cases) contributed to 7% (5-10%) of transmission to secondary cases, and breakthrough infections in previously infected residents (29% of index cases) contributed to 21% (17-26%) of transmission to secondary cases in the study population. We observed similar results over the entire study period (Table S13).

Discussion

Using detailed epidemiologic data from SARS-CoV-2 surveillance within the California state prison system, we found that vaccination and prior infection reduced the infectiousness of Omicron variant SARS-CoV-2 infections. Vaccination and prior infection were each associated with comparable reductions in infectiousness during SARS-CoV-2 infection, and notably, additional doses of vaccination (e.g., booster doses) against SARS-CoV-2 and more recent vaccination led to greater reductions in infectiousness. Of note, reductions in transmission risk associated with prior vaccination and infection were found to be additive, indicating an incremental benefit of vaccination for reducing cases' infectiousness even after prior infection. Irrespective of vaccination and/or prior natural infection, SARS-CoV-2 breakthrough infections and reinfections remained highly infectious and were responsible for 80% of transmission observed in the study population, which has high levels of both prior infection and vaccination. This observation underscores that vaccination and prevalent naturally acquired immunity alone

will not eliminate risk of SARS-CoV-2 infection, especially in higher risk settings such as prisons.

Prior studies during the Delta variant wave and prior to widespread booster vaccination are mixed on whether SARS-CoV-2 breakthrough infections in vaccinated persons are potentially less infectious *(6–9)* or equally infectious *(10,11)* to primary infections. In this study, we find consistent >20% reductions in infectiousness from either vaccination or prior natural infection and 40% reduction from both vaccination and infection (based on a linear combination of coefficients). Several factors may have enhanced our ability to observe statistically meaningful findings in the present study. The risk of transmission among close contacts in the prison setting and consistency in contact structure, especially in light of increased transmissibility of the Omicron SARS-CoV-2 variant, may have enhanced statistical power in our sample. Relatedly, a higher proportion of index cases in our sample were previously vaccinated or infected, further enhancing the opportunity to compare transmission risk from vaccinated or unvaccinated index cases, and from those who were previously infected or previously uninfected.

A key finding is that the vaccine-mediated reduction in infectiousness of SARS-CoV-2 breakthrough infections appears to be dose dependent. In the adjusted analysis, each dose of the vaccine provided an additional average 11% relative reduction in infectiousness, which was mostly driven by residents with a booster dose. The findings of this study support the indirect effects of COVID-19 vaccination (especially booster doses) to slow transmission of SARS-CoV-2 and build on evidence of the direct effects of COVID-19 vaccination *(21)* to emphasize the overall importance of COVID-19 vaccination. The public health implication of these findings is

further support for existing policy using booster doses of vaccination *(22)* to achieve the goal of lowering population level transmission. The impact of additional booster doses, which are currently recommended for older adults and high-risk individuals to prevent severe disease *(22)*, on transmission should be a priority for further study. Additional considerations about the timeliness of vaccine doses are also necessary as we found that index cases with more distant history of COVID-19 vaccination had higher risk of transmission of infection to close contacts. Given this finding of more recent vaccination reducing infectiousness, this study raises the possibility of timed mass vaccination in incarcerated settings during surges to slow transmission.

The findings from this study have direct implications in addressing COVID-19 inequities in the incarcerated population through additional vaccination. In California state prisons, although 81% of residents and 73% of staff have completed a primary vaccination series, only 59% of residents and 41% of staff have received the number of vaccination doses recommended by the Centers for Disease Control and Prevention based on their age and comorbid medical conditions *(23).* Our findings also provide a basis for additional considerations for housing situations of cases based on prior vaccination and infection history in future surges and can be used alongside other measures, such as depopulation and ventilation interventions, to protect incarcerated populations.

However, this study also underscores the persisting vulnerability to COVID-19 among residents and staff in correctional settings despite widespread vaccination, natural immunity, and use of non-pharmaceutical interventions. The overall attack rate of SARS-CoV-2 among cellmates in the study population (who were generally moved into isolation following symptoms or a positive test) was 30%, and index cases with breakthrough infections or reinfections remained highly

infectious. While our study demonstrates that vaccination and boosting can slow transmission, this study's findings call into question the ability of high vaccination rates alone to prevent all SARS-CoV-2 transmission in correctional settings. In the United States, which incarcerates more residents per capita than any other country in the world *(23)* and has a quarter of the world's incarcerated population, correctional settings are characterized by poorly ventilated facilities, populations with increased rates of comorbid health conditions, high-risk dormitory housing, and overcrowding *(16,24–26).* Given the inability of current efforts to reduce transmission of SARS-CoV-2, decarceration efforts are the most likely to have substantial effects on reducing cases.

The secondary attack rate in this study was on the lower end of published estimates from household studies. Of note, the secondary attack rate of the SARS-CoV-2 Omicron variant in recent household studies ranges from 29-63% (*27–29*), in contrast to a 30% attack rate in this study. The dense living environment increases the likelihood of transmission in the prison environment compared to a household, while the frequent asymptomatic testing (with isolation of positive cases) in the prisons likely reduced the exposure time and subsequent transmission risk compared to households. The transmission of the prison cell is also likely more uniform than a household.

Strengths of this study include access to detailed records of all residents in the California state prison system, encompassing individuals' prior COVID-19 vaccine receipt and prior natural infection history (based on frequent testing throughout the pandemic), as well as social network given record of where residents slept each night over the study period. We use a consistent definition of social contact between the index case of COVID-19 and close contact based on the

uniformity of cell type. The frequent testing occurring during the study period ensures early identification of infections and systematic capture of asymptomatic and symptomatic infections to avoid bias by participants' immune status (which could affect temporal onset of symptoms). The risk of misclassification of close contacts is low given most follow up testing in close contacts occurred well after first exposure to an index case (see Appendix). The large sample size facilitates analyses of the contribution of combinations of prior vaccination statuses and natural infection on risk of transmission, including analyses examining the impact of booster doses.

Limitations should also be considered. We cannot exclude the possibility of some residual confounding (e.g., behavioral differences that affect risk of transmission) between persons who were vaccinated against SARS-CoV-2 and those who were unvaccinated. There is a possibility that close contacts who test positive for SARS-CoV-2 were not infected by their assigned index case but instead by interaction with infectious individuals outside of their cell. However, this misattribution would be expected to dampen apparent associations of transmission risk with index cases' vaccination status and infection history, but not bias the relative estimates. To further address the risk of misattribution, we adjust for background SARS-CoV-2 incidence and match contact pairs by facility and time. Our study population is a subset of the entire incarcerated population in California and may not represent all incarcerated settings. Given limited SARS-CoV-2 testing capacity early in the pandemic and some residents' decision to decline testing, it is possible infections among some residents may not have been captured, although such misclassification would be expected to bias our findings to the null. SARS-CoV-2 testing was variable over time in the prison system, with periods of routine weekly testing and

other periods of reactive testing; however, periods without reactive testing align with times during which SARS-CoV-2 was unlikely to be circulating at high levels within the facilities, suggesting this is unlikely to bias results substantially. The study findings on boosters may also be related to recent vaccination effects. This study design did not provide a basis for identifying effects of vaccination and prior infection on risk of acquiring SARS-CoV-2 among close contacts, although we did adjust for prior infection and vaccination in close contacts in the primary analysis. Of note, vaccine effectiveness against infection among incarcerated persons has been reported within this population during earlier periods (*30,31*). We do not have a detailed record of person-level masking, symptoms, cycle thresholds for polymerase chain reaction testing, or serologic testing.

This study demonstrates that breakthrough COVID-19 infections with the Omicron variant remain highly infectious, but that both vaccination and natural infection confer reductions in transmission, with benefit of additional vaccine doses. As SARS-CoV-2 breakthrough infections and reinfections become the predominant COVID-19 case, this study supports the importance of booster doses in reducing population level transmission with consideration of mass timed vaccination during surges, with particular relevance in vulnerable, high-density congregate settings.

Materials and Methods

Data

We used data from the California Correctional Health Care Services (CCHCS), which included anonymized person-level data on SARS-CoV-2 testing, COVID-19 vaccination, and nightly

resident housing for incarcerated persons in the California state prison system from March 1, 2020, to May 20, 2022. The objective of the study was to study the relative infectiousness of Omicron SARS-CoV-2 breakthrough infections and reinfections. This project was approved by the institutional review board at the University of California, San Francisco.

COVID-19 index case definition and infectious period

The inclusion and exclusion criteria for an index case of COVID-19 for the study are shown in Figure S1. We defined an index case as a resident with a positive SARS-CoV-2 diagnostic test. The majority of tests (83%) were polymerase chain reaction. We excluded index cases with a prior positive test within the preceding 90 days (see Appendix), as well as those with a false positive or inconclusive result. We defined the period of the Omicron variant wave as between December 15, 2021, and May 20, 2022, based on genomic surveillance data from the California prison system. We included only infections that occurred in residents who were incarcerated continuously beginning prior to April 1, 2020, to ensure consistent reporting of prior SARS-CoV-2 infection given that these data are not available from recently incarcerated residents. We classified index cases based on their COVID-19 vaccination status and prior natural infection history. We defined SARS-CoV-2 breakthrough infections as a positive SARS-CoV-2 diagnostic test occurring in persons at least 14 days after their first dose of vaccine, as long as that person did not have a prior positive diagnostic test in the preceding 90 days. We defined reinfection as a positive SARS-CoV-2 diagnostic test occurring in persons with a prior laboratory-confirmed natural infection provided that at least 90 days had elapsed since the first infection.

For a conservative measure of the time each index case was infectious, we counted from the date of an index case's first positive SARS-CoV-2 test through 5 days thereafter *(20,32,33*). We varied the start and the duration of the infectious period in sensitivity analyses. Isolation and quarantine protocols in the prison system are described in the Appendix.

Close contacts of COVID-19 index case

We defined a close contact of a COVID-19 index case as any resident who shared a cell with an index case while the index case was considered infectious, per the above definition. We further required a close contact to test negative for SARS-CoV-2 within 2 days before or after first exposure to an index case (to reduce the chance they were already infected by another resident) and to have follow up testing within 3 to 14 days after last exposure (see Appendix). We defined first exposure as the first day that the index case and close contact shared a room during the index case's infectious period (based on a positive test in the index case). To limit misattribution of secondary cases and close contacts, we only included contacts that shared a solid-door cell with fewer than 10 total residents during the index case's infectious period (>95% of index cases had 3 or fewer persons per cell). We defined secondary SARS-CoV-2 infection as close contacts who tested positive for SARS-CoV-2 between 3 days after first exposure and 14 days after last exposure to the index case. We excluded close contacts that were secondary cases for multiple index cases (only 1 close contact). After other inclusion and exclusion criteria were applied to close contacts, if index cases had more than one valid close contact (<0.1% of index cases and index cases had no more than 3 valid close contacts), we randomly selected a single contact to include in the analysis.

Statistical analysis

We performed matching of unvaccinated index cases and vaccinated index cases to limit confounding and to account for heterogeneity of SARS-CoV-2 epidemiology across institutions and over time. We first estimated the propensity for index cases to receive vaccination based on their age, prior history of SARS-CoV-2 infection, and COVID-19 risk score (see Appendix) (*34*). We then applied 1:10 nearest matching on institution (exact), time (< 30 days), and propensity score (caliper choice of 0.1) without replacement (see Appendix for distribution of number of matches). We excluded any index cases without matches. We estimated unadjusted attack rates, defined as the proportion of close contacts who tested positive between 3 days after initial exposure and 14 days after last exposure with an index case, and computed associated 95% binomial confidence intervals (95% CI). We estimated attack rates by number of vaccine doses and prior natural infection.

To estimate the relative infectiousness of SARS-CoV-2 breakthrough infections and/or SARS-CoV-2 reinfections, we fit a Poisson regression model with robust errors to account for key variables in an adjusted analysis (*35*). The primary study outcome was binary, the SARS-CoV-2 infection outcome in the close contact. The exposure of interest was the vaccine status (primary analysis with binary vaccine status, alternative analysis with number of vaccine doses) of the index case, which can be interpreted as the relative change in attack rate in the close contact based on the index cases' vaccine status. We also adjusted for index case's prior SARS-CoV-2 infection history, duration of exposure between index case and close contact, close contact's vaccine status (number of doses) and prior natural infection, institution, and institution-specific SARS-CoV-2 incidence in the 7 days leading up to infection in the index case. The regression

model accounted for matching weights and cluster-robust standard errors based on matching group membership. We did not use repeated measured data.

We classified secondary infections (N=363) among close contacts by index cases' prior vaccination and/or infection history and estimated the crude fraction of secondary infections that were attributable to different index cases as well as their respective 95% binomial confidence intervals. We additionally estimated the attributable fraction of transmission among all SARS-CoV-2 infections in the study period. We first estimated the adjusted attack rate of SARS-CoV-2 infection by a case's prior vaccination and/or infection history using estimates of the relative reduction in infectiousness. We then applied the attack rates to the observed number of infections to estimate the attributable fraction of transmission by prior vaccination and prior infection status.

We conducted an alternative analysis where we examined the relationship between number of vaccine doses in index cases and infectiousness (see Appendix). We further examined the relationships between prior vaccination, prior infection, and infectiousness of an index case by testing a formal interaction between prior vaccination and prior natural infection and evaluating the relationship between the time since most recent exposure (as continuous variable) to either COVID-19 vaccination or SARS-CoV-2 infection. We varied definitions of COVID-19 vaccine status in close contacts in sensitivity analyses. We assessed impact of relaxing different exclusion criteria for index cases and close contacts on study results. We varied the start and duration of the infectious period in sensitivity analyses. To assess model robustness, we evaluated study outcomes under different matching specifications and when using a logistic

regression model. Given the lower vaccine effectiveness of the *Ad26.COV2* vaccine, we conducted a sensitivity analysis removing index cases that received the *Ad26.COV2* vaccine. Further details can be found in the Appendix. The pre-analysis plan and all analytic code is publicly available, with further description in the appendix *(36)*. Analyses were conducted in R (version 4.1.1). Data requests may be made to CCHCS and are subject to controlled access due to requirements to enhance protection of this vulnerable incarcerated population.

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Study concept and design: JAL, IRB, DS, NCL

Statistical analysis: STT, IRB, NCL

Acquisition, analysis, or interpretation of data: All authors

First draft of the manuscript: STT, NCL

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Data and materials availability: Data requests may be made to CCHCS and are subject to controlled access. All analytic code is publicly available *(31)*.

Tables and Figures

Table 1: Characteristics of study population of COVID-19 index cases and close contacts in California prisons.

	Index cases (N=1226) (N (%) or mean (SD))		Close contacts (N=1226) (N (%) or mean (SD))	
	No COVID-19 vaccination (N=273)	Any COVID-19 vaccination (N=953)	No COVID-19 vaccination (N=173)	Any COVID-19 vaccination (N=1053)
Sex				
Female	8 (3%)	30 (3%)	7 (4%)	31 (3%)
Male	265 (97%)	923 (97%)	166 (96%)	1022 (97%)
Age (years)	36.3 (10)	39 (10.7)	35.9 (10.1)	39.6 (11.1)
Race				
American Indian/Alaskan Native	0 (0%)	11 (1%)	1 (1%)	10 (1%)
Asian or Pacific Islander	4 (2%)	12 (1%)	0 (%)	10 (1%)
Black	89 (33%)	221 (23%)	56 (32%)	244 (23%)
Hispanic	121 (44%)	402 (42%)	71 (41%)	440 (42%)
Mexican	24 (9%)	146 (15%)	17 (10%)	159 (15%)
White	7 (3%)	25 (3%)	5 (3%)	35 (3%)
Other	28 (10%)	136 (14%)	23 (13%)	155 (15%)
COVID-19 risk score (range 0-12)*	0.7 (1.3)	1 (1.4)	0.7 (1)	1.1 (1.5)
Number of days of exposure between index case and close contact	2.4 (1.2)	2.2 (1.1)	2.4 (1.2)	2.3 (1.1)
Prior infection	84 (31%)	356 (37%)	59 (34%)	448 (43%)
Vaccination status				
Unvaccinated	273 (100%)	-	173 (100%)	-
Ad26.COV2	-	113 (12%)	-	152 (15%)
Completed only primary series	-	58 (51%)	-	70 (46%)
Received booster or additional doses	-	55 (49%)	-	82 (54%)
BNT162b2	-	188 (20%)	-	193 (18%)
Received 1 dose of primary series	-	5 (3%)	-	3 (2%)
Completed only primary series	-	55 (29%)	-	43 (22%)
Received booster or additional doses	-	128 (68%)	-	147 (76%)
mRNA-1273	-	652 (68%)	-	708 (67%)
Received 1 dose of primary series	-	13 (2%)	-	25 (4%)
Completed only primary series	-	229 (35%)	-	223 (31%)
Received booster or additional doses	-	412 (63%)	-	462 (65%)

History of prior natural infection and vaccination status reflect the index case and close contact's vaccination and natural infection status on the day of first positive test (for index cases) or first exposure to an infectious index case (for close contacts)
*COVID-19 risk score was estimated by California Correctional Health Care Services as weighted sum of different comorbidities most associated with severe COVID-19 complications (*34*)

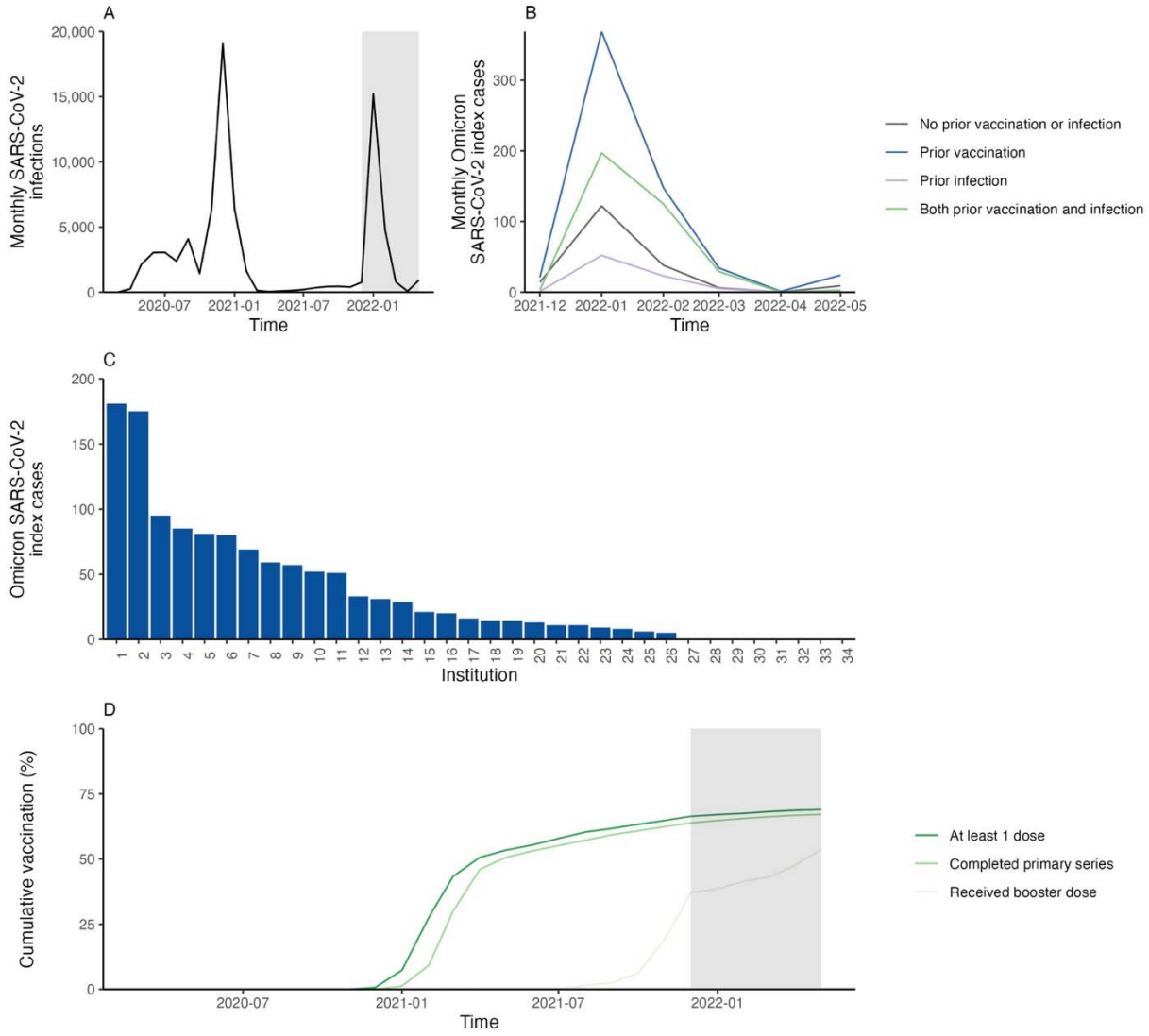

Figure 1: SARS-CoV-2 infections and vaccination over time in the study population in California state prisons. We obtained data on SARS-CoV-2 infections, vaccination, and contact history for residents incarcerated in the California state prison system from March 1, 2020, to May 20, 2022. Panel A shows the number of SARS-CoV-2 infections over time in the study population. Panel B shows the number of SARS-CoV-2 index cases included in the analysis over time, stratified by history of prior natural infection and vaccination. Panel C shows the number of SARS-CoV-2 index cases by institution during the Omicron wave (December 15, 2021, to May 20, 2022) included in the analysis. Panel D shows the COVID-19 vaccine coverage over time for residents in the California state prison system by primary series and booster dose. The shaded region in panels A and D corresponds with the Omicron variant wave.

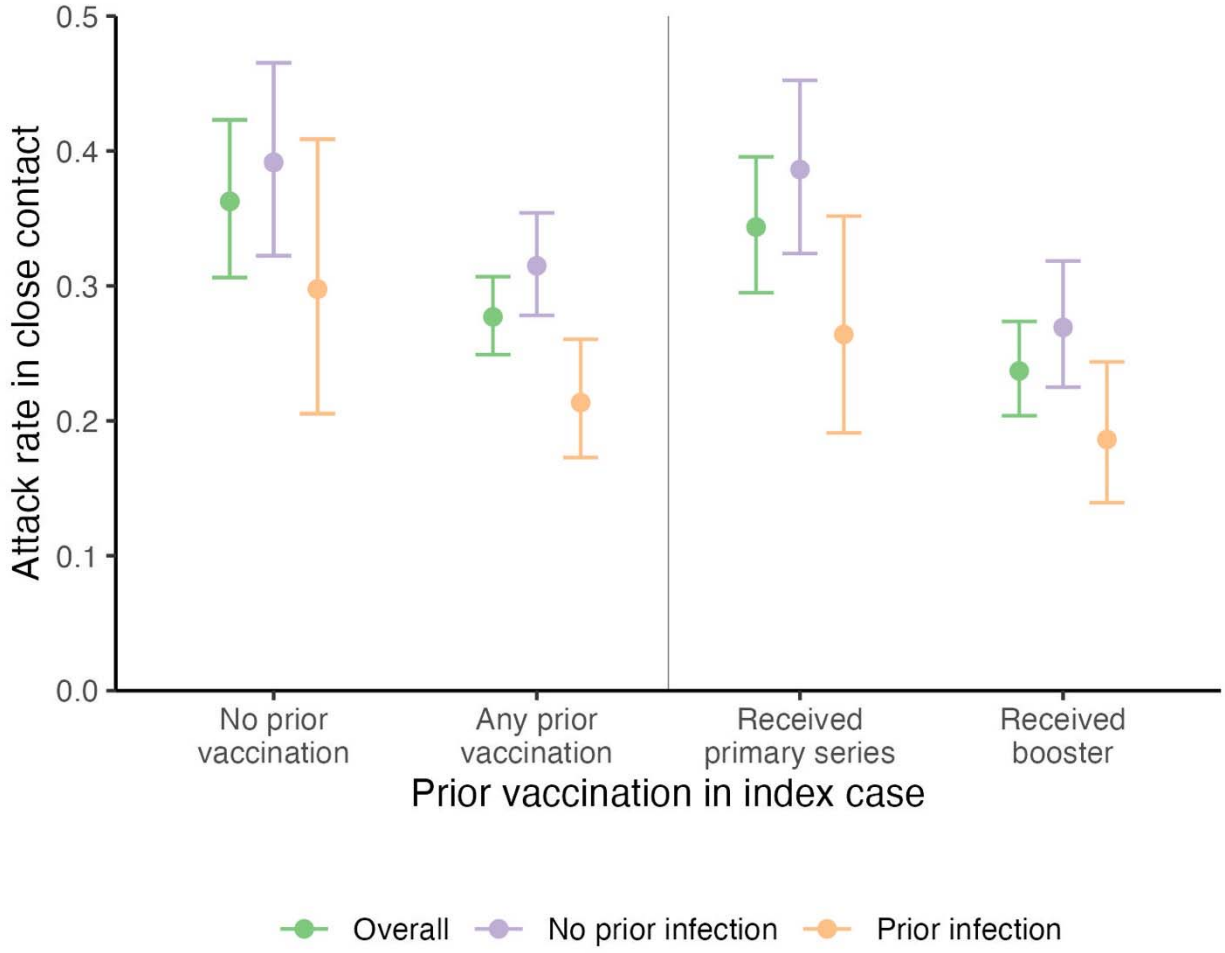

Figure 2: Unadjusted Omicron SARS-CoV-2 attack rate in close contact based on index cases' vaccine and prior natural infection status. We identified index cases of SARS-CoV-2 infections in residents of the California state prison system who were in close contact with another resident who was confirmed negative for SARS-CoV-2 at the time of contact. We estimated the outcome of subsequent SARS-CoV-2 infection in the close contact under different immune conditions of the index case, with a composite study outcome of attack rate. The attack rate is the probability of infection in the close contact given exposure to an index case. We estimated the unadjusted attack rate (and 95% confidence intervals) of SARS-CoV-2 in the close contact stratified by the index cases' overall vaccine status, the number of vaccine doses in the index case, and index cases' history of natural infection.

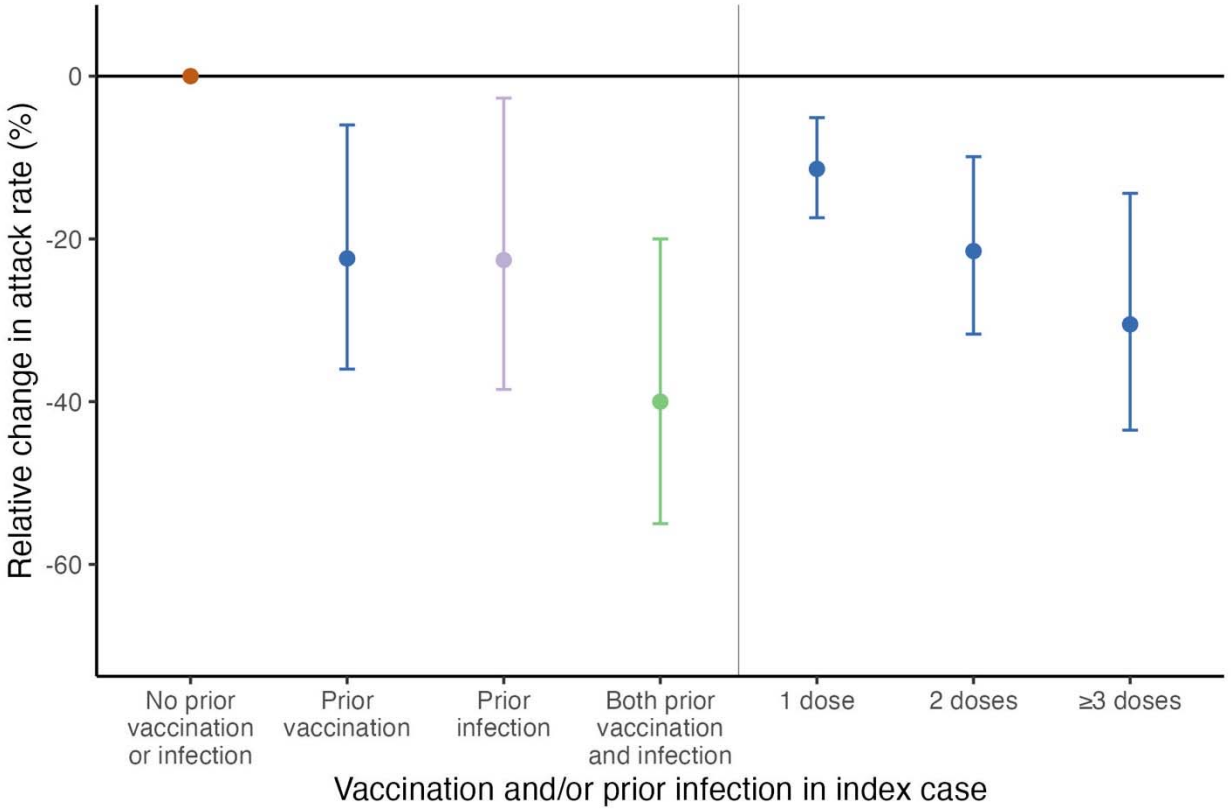

Figure 3: Relative change in Omicron SARS-CoV-2 attack rate in close contacts based on index cases' vaccine and prior natural infection status in an adjusted model. We applied a robust Poisson regression model to estimate the relationship between vaccination and natural immunity in index cases on their risk of SARS-CoV-2 transmission in close contacts. This analysis focused on SARS-CoV-2 breakthrough infections and reinfections. We plotted the adjusted relative reduction in infectiousness of index cases, as measured via attack rate in close contacts, conferred by vaccination alone, prior infection alone, and both prior vaccination and infection. The estimate for both prior vaccination and infection is based on a linear combination of regression coefficients, given lack of formal statistical interaction between vaccination and prior infection. We conducted a separate regression analysis (right side of graph) that was stratified based on the number of vaccine doses received by the index case. We plotted cluster-robust 95% confidence intervals.