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

Authors: Sophia T. Tan BA¹, Ada T. Kwan PhD MHS²,³, Isabel Rodriguez-Barraquer MD PhD¹,³, Benjamin J. Singer PhD¹, Hailey J. Park BA¹, Joseph A. Lewnard PhD⁵-⁷, David Sears MD³,⁴, and Nathan C. Lo MD PhD¹,³*

Affiliations:

¹Division of HIV, Infectious Diseases, and Global Medicine, University of California, San Francisco, San Francisco, CA, USA
²Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, San Francisco, CA, USA
³Department of Medicine, University of California, San Francisco, San Francisco, CA, USA
⁴Division of Infectious Diseases, University of California, San Francisco, San Francisco, CA, USA
⁵Division of Epidemiology and Biostatistics, School of Public Health, University of California, Berkeley, Berkeley, CA, USA
⁶Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley, Berkeley, CA, USA
⁷Center for Computational Biology, College of Engineering, University of California, Berkeley, Berkeley, CA, USA

*Corresponding author:
Nathan C. Lo, MD PhD
Division of HIV, Infectious Diseases, and Global Medicine
Department of Medicine
University of California, San Francisco
San Francisco, CA, USA 94110
Nathan.Lo@ucsf.edu

Abstract Word Count: 125
Main Text Word Count: 3608
Figures: 3
Tables: 1

Keywords: COVID-19, SARS-CoV-2, Omicron, vaccination, epidemiology, transmission, attack rate, correctional health

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
Abstract: Breakthrough infections in vaccinated individuals and reinfections among previously infected individuals are increasingly prevalent, especially during the Omicron wave. Here, we analyze data from SARS-CoV-2 surveillance across 35 California prisons to understand the impact of vaccination and prior infection on infectiousness of individuals with SARS-CoV-2 Omicron infections in prison settings. We estimate that vaccination, prior infection, and both vaccination and prior infection reduced an index case’s risk of transmitting to close contacts by 24% (9-37%), 21% (4-36%) and 41% (23-54%), respectively. Booster vaccine doses and more recent vaccination further reduced infectiousness. These findings suggest that although vaccinated and/or previously infected individuals remain infectious upon SARS-CoV-2 Omicron infection in this prison setting, their infectiousness is reduced compared to individuals without any history of vaccination or infection.

One Sentence Summary: Vaccine-derived and naturally acquired immunity independently reduce the infectiousness of persons with Omicron SARS-CoV-2 infections.
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 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 1,261 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. 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=276) and vaccinated index cases (n=985) by institution (exactly) and time (within 30 days), excluding cases without eligible matches (Figure S1). We matched an average of 3.6 (interquartile range: 2-4) vaccinated index cases to each unvaccinated index case (see Appendix, Figure A3). The mean duration of exposure of close contacts to index cases was 2.3 days (see Appendix, Figure A2). Descriptive data on the study population’s demographics, vaccine uptake, and prior infections are shown in Table 1.

**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 29% (95% CI: 26-31%). Unvaccinated index cases had a 36% (30-42%) risk of transmitting to close contacts, while vaccinated index cases had a 27% (24-30%) 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 [22% (18-27%)] than index cases with no history of prior infection [30% (26-34%)]; 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 S1).

Adjusting for close contacts’ history of vaccination and prior infection as well as 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 24% (9-37%) 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 12% reduction (6-17%) in risk of transmission to the close contact (Figure 3 and Tables S2-S3). Prior SARS-CoV-2 infection was similarly associated with a 22% reduction (4-36%) in risk of transmission from the index case. Having both prior vaccination and SARS-CoV-2 infection was associated with a 41% (23-54%) 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 as determinants of transmission risk (Table S4).

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 COVID-19 vaccine was inversely associated with infectiousness of SARS-CoV-2 infections; for every 5 additional weeks since last vaccine dose, SARS-CoV-2 breakthrough infections were 6% (2-10.2%) 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 S5 and Figure S2).
We conducted a number of sensitivity and additional model analyses to evaluate the robustness of the study findings. We observed similar reductions in the attack rate of index cases with different matching specifications; any prior COVID-19 vaccination was associated with a 22% reduction (6-35%) in attack rate under 1:10 matching within 15 days, 23% reduction (7-36%) under 1:4 matching within 30 days, and 25% reduction (10-38%) without matching (Table S6 and Figure S3). Varying definitions of the start and duration of the infectious period also yielded similar results (Table S7 and Figure S4). We repeated the primary adjusted analysis using a logistic regression model and found that both prior vaccination [0.65 odds ratio (OR) (0.48-0.88)] and prior infection [0.7 OR (0.52-0.95)] were associated with lower odds of infection in close contacts (Table S8).

Transmission attributable to primary infections, breakthrough infections, and reinfections

We estimated that primary infections (15% of index cases), breakthrough infections (49% of index cases), reinfections (7% of index cases), and breakthrough infections in previously infected residents (29% of index cases) contributed to 20% (16-25%), 50% (45-56%), 7% (5-10%), and 22% (18-27%) of transmission to secondary cases in the study population, respectively, with similar results over the entire study period (Table S9).

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 may 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% reductions from both vaccination and infection. 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 12% 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.

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 29%, 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.

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 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. 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 vaccine effectiveness against infection among incarcerated persons has been reported within this population during earlier periods (27). We do not have a detailed record of person-level masking, symptoms, or cycle thresholds for polymerase chain reaction 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 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. 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 (20,28,29). 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 and to have follow up testing within 3 to 14 days after last exposure (see Appendix). 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. If index cases had more than one valid close contact (<0.1% of index cases), 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 account for heterogeneity of SARS-CoV-2 epidemiology across institutions and over time. We applied 1:10 nearest matching on institution (exact) and time (within 30 days) to maximize sample size, excluding any index cases without matches (see Appendix for distribution of number of 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 rate stratified 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 (30). 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 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, 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. These variables were pre-specified. 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 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 to either COVID-19 vaccination or SARS-CoV-2 infection. We varied definitions of COVID-19 vaccine status in both index cases and close contacts in sensitivity analyses, including by number of vaccine doses. To assess model robustness, we evaluated study outcomes under different matching specifications and when using a logistic regression model. 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 (31). 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.
References and Notes

1. Koelle K, Martin MA, Antia R, Lopman B, Dean NE. The changing epidemiology of SARS-CoV-2. *Science*. 2022;375(6585):1116-1121. doi:10.1126/science.abm4915

2. Pulliam JRC, van Schalkwyk C, Govender N, et al. Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa. *Science*. 2022;376(6593):eabn4947. doi:10.1126/science.abn4947

3. Altarawneh HN, Chemaitelly H, Hasan MR, et al. Protection against the Omicron Variant from Previous SARS-CoV-2 Infection. *N Engl J Med*. 2022;386(13):1288-1290. doi:10.1056/NEJMc2200133

4. Chaguza C, Coppi A, Earnest R, et al. Rapid emergence of SARS-CoV-2 Omicron variant is associated with an infection advantage over Delta in vaccinated persons. *Med*. 2022;3(5):325-334.e4. doi:10.1016/j.medj.2022.03.010

5. CDC. COVID Data Tracker. Centers for Disease Control and Prevention. Published March 28, 2020. Accessed June 9, 2022. https://covid.cdc.gov/covid-data-tracker

6. Prunas O, Warren JL, Crawford FW, et al. Vaccination with BNT162b2 reduces transmission of SARS-CoV-2 to household contacts in Israel. *Science*. 2022;375(6585):1151-1154. doi:10.1126/science.abl4292

7. Jung J, Kim JY, Park H, et al. Transmission and Infectious SARS-CoV-2 Shedding Kinetics in Vaccinated and Unvaccinated Individuals. *JAMA Netw Open*. 2022;5(5):e2213606. doi:10.1001/jamanetworkopen.2022.13606

8. Puhach O, Adea K, Hulo N, et al. Infectious viral load in unvaccinated and vaccinated individuals infected with ancestral, Delta or Omicron SARS-CoV-2. *Nat Med*. Published online April 8, 2022:1-10. doi:10.1038/s41591-022-01816-0
9. Abu-Raddad LJ, Chemaitelly H, Ayoub HH, et al. Relative infectiousness of SARS-CoV-2 vaccine breakthrough infections, reinfections, and primary infections. *Nat Commun.* 2022;13(1):532. doi:10.1038/s41467-022-28199-7

10. Singanayagam A, Hakki S, Dunning J, et al. Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK: a prospective, longitudinal, cohort study. *Lancet Infect Dis.* 2022;22(2):183-195. doi:10.1016/S1473-3099(21)00648-4

11. Kissler SM, Fauver JR, Mack C, et al. Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Persons. *N Engl J Med.* 2021;385(26):2489-2491. doi:10.1056/NEJMc2102507

12. *Decarcerating Correctional Facilities during COVID-19: Advancing Health, Equity, and Safety.* National Academies of Sciences, Engineering, and Medicine.

13. Burkhalter E, Colón I, Derr B, et al. Incarcerated and Infected: How the Virus Tore Through the U.S. Prison System. *The New York Times.*

https://www.nytimes.com/interactive/2021/04/10/us/covid-prison-outbreak.html. Published April 10, 2021. Accessed July 1, 2022.

14. Saloner B, Parish K, Ward JA, DiLaura G, Dolovich S. COVID-19 Cases and Deaths in Federal and State Prisons. *JAMA.* 2020;324(6):602-603. doi:10.1001/jama.2020.12528

15. UCLA Law COVID Behind Bars Data Project. Accessed June 30, 2022.

https://uclacovidbehindbars.org/

16. Montoya-Barthelemy AG, Lee CD, Cundiff DR, Smith EB. COVID-19 and the Correctional Environment: The American Prison as a Focal Point for Public Health. *Am J Prev Med.* 2020;58(6):888-891. doi:10.1016/j.amepre.2020.04.001
17. Chin ET, Ryckman T, Prince L, et al. COVID-19 in the California State Prison System: an Observational Study of Decarceration, Ongoing Risks, and Risk Factors. *J Gen Intern Med.* 2021;36(10):3096-3102. doi:10.1007/s11606-021-07022-x

18. LeMasters K, Ranapurwala S, Maner M, Nowotny KM, Peterson M, Brinkley-Rubinstein L. COVID-19 community spread and consequences for prison case rates. *PLOS ONE.* 2022;17(4):e0266772. doi:10.1371/journal.pone.0266772

19. Kwan, A., Sklar, R., Cameron, D.B., Schell, R.C., Bertozzi, S.M., McCoy, S.I., Williams, B. and Sears, D.A. Respiratory pandemic preparedness learnings from the June 2020 COVID-19 outbreak at San Quentin California State Prison. *Int J Prison Health.* 2022;ahead-of-print(ahead-of-print).

20. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med.* 2020;26(5):672-675. doi:10.1038/s41591-020-0869-5

21. Altarawneh HN, Chemaitelly H, Ayoub HH, et al. Effects of Previous Infection and Vaccination on Symptomatic Omicron Infections. *N Engl J Med.* 2022;0(0):null. doi:10.1056/NEJMoa2203965

22. Coronavirus Disease 2019. Centers for Disease Control and Prevention. Published May 19, 2022. Accessed July 1, 2022. https://www.cdc.gov/media/releases/2022/s0519-covid-booster-acip.html

23. Population COVID-19 Tracking. COVID-19 Information. Accessed June 30, 2022. https://www.cdcr.ca.gov/covid19/population-status-tracking/

24. Greene M, Ahalt C, Stijacic-Cenzer I, Metzger L, Williams B. Older adults in jail: high rates and early onset of geriatric conditions. *Health Justice.* 2018;6(1):3. doi:10.1186/s40352-018-0062-9
25. Population Reports. Office of Research. Accessed June 30, 2022.
   https://www.cdcr.ca.gov/research/population-reports-2/

26. Leibowitz AI, Siedner MJ, Tsai AC, Mohareb AM. Association Between Prison Crowding and COVID-19 Incidence Rates in Massachusetts Prisons, April 2020-January 2021. JAMA Intern Med. 2021;181(10):1315-1321. doi:10.1001/jamainternmed.2021.4392

27. Chin ET, Leidner D, Zhang Y, et al. Effectiveness of the mRNA-1273 Vaccine during a SARS-CoV-2 Delta Outbreak in a Prison. N Engl J Med. 2021;385(24):2300-2301. doi:10.1056/NEJMc2114089

28. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. Ann Intern Med. 2021;174(1):69-79. doi:10.7326/M20-5008

29. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). Accessed June 28, 2022.
   https://www.science.org/doi/10.1126/science.abb3221

30. Zou G. A Modified Poisson Regression Approach to Prospective Studies with Binary Data. Am J Epidemiol. 2004;159(7):702-706. doi:10.1093/aje/kwh090

31. sophttan/CDCR-CalProtect. GitHub. Accessed June 9, 2022.
   https://github.com/sophttan/CDCR-CalProtect

32. Introduction. Accessed June 9, 2022. https://cran.r-project.org/web/packages/MatchIt/vignettes/MatchIt.html
Acknowledgments:

We thank the individuals at the Office of the California Prison Health Care Receivership and California Correctional Health Care Services, as well as all those involved in the ongoing response to the COVID-19 pandemic in California.

Funding: University of California, San Francisco Department of Medicine (NCL)

Author contributions: Ms. Sophia Tan and Dr. Nathan Lo had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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

Critical revision of the manuscript: All authors

Contributed intellectual material and approved final draft: All authors

Competing interests: JAL has received grants, honoraria, and speaker fees from Pfizer; grants and honoraria from Merck, Sharp, & Dohme; and honoraria from VaxCyte; all unrelated to the subject of this work. ATK and DS received funding from California Prison Health Care Receivership. The remaining authors have no disclosures.

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

List of Supplementary materials:

Technical Appendix

Tables S1-S9
Figures S1-S4

References (32)
# Tables and Figures

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

|                      | Index cases (N=1261) (N (%) or mean (SD)) | Close contacts (N=1261) (N (%) or mean (SD)) |
|----------------------|-------------------------------------------|----------------------------------------------|
| **Sex**              |                                           |                                              |
| Female               | 40 (3%)                                   | 40 (3%)                                      |
| Male                 | 1221 (97%)                                | 1221 (97%)                                   |
| **Age (years)**      | 39 (11.1)                                 | 39 (11.2)                                    |
| **Race**             |                                           |                                              |
| American Indian/Alaskan Native | 11 (0.9%)                           | 11 (0.9%)                                   |
| Asian or Pacific Islander | 17 (1.4%)                           | 10 (0.8%)                                   |
| Black                | 320 (25%)                                 | 305 (24%)                                   |
| Hispanic             | 530 (42%)                                 | 527 (42%)                                   |
| Mexican              | 173 (14%)                                 | 180 (14%)                                   |
| White                | 177 (14%)                                 | 186 (15%)                                   |
| Other                | 33 (2.6%)                                 | 42 (3.3%)                                   |
| **Prior natural infection** | 455 (36%)                        | 517 (41%)                                   |
| **Vaccination status** |                                           |                                              |
| Unvaccinated         | 276 (22%)                                 | 175 (14%)                                   |
| Ad26.COV2            | 114 (9%)                                  | 153 (12%)                                   |
| Completed only primary series | 60 (53%)                           | 70 (46%)                                    |
| Received booster or additional doses | 54 (47%)                           | 83 (54%)                                    |
| BNT162b2             | 192 (15%)                                 | 194 (15%)                                   |
| Received 1 dose of primary series | 5 (2.6%)                            | 3 (1.5%)                                    |
| Completed only primary series | 54 (28%)                            | 45 (23%)                                    |
| Received booster or additional doses | 133 (69%)                           | 146 (75%)                                   |
| mRNA-1273            | 679 (54%)                                 | 739 (59%)                                   |
| Received 1 dose of primary series | 13 (1.9%)                            | 28 (3.8%)                                   |
| Completed only primary series | 232 (34%)                           | 229 (31%)                                   |
| Received booster or additional doses | 434 (64%)                           | 482 (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)
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, either prior vaccination or infection, and both prior vaccination and infection. The estimate for both prior vaccination and infection is based on a linear combination of regression coefficients. 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.