

Reinfection with SARS-CoV-2 among previously infected healthcare personnel and first responders

Lara J. Akinbami^{1,2}, Brad J. Biggerstaff³, Philip A. Chan⁴, Emily McGibbon⁵, Preeti Pathela⁵, Lyle R. Petersen³

1. National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, Maryland, 20782 USA

2. U.S. Public Health Service, Rockville, Maryland, 20852 USA

3. Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado, 80521 USA

4. Rhode Island Department of Health, Providence, Rhode Island, 02908, USA

5. New York City Department of Health and Mental Hygiene, Queens, New York, USA

Corresponding author: Lara Akinbami, MD, 3311 Toledo Road, Hyattsville, MD USA 20782, 301-458-4306, lea8@cdc.gov

Summary: SARS-CoV-2 reinfection was uncommon among first responders and healthcare personnel before widespread variant circulation. Seropositivity was protective against reinfection. Exposure to household member(s) with COVID-19 prior to serology testing was protective, likely due to decreased household transmission after initial infection.

Abstract

Background: SARS-CoV-2 virus testing among first responders and healthcare personnel who participated in a May-August 2020 serosurvey which assessed spike protein antibodies (S1 region) provided an opportunity to assess reinfection.

Methods: Serology survey data were merged with virus testing results from Rhode Island (March 1, 2020-February 17, 2021) and New York City (March 10-December 14, 2020). Participants with a positive virus test ≥ 14 days before their serology test were included. Reinfection was defined as a second positive SARS-CoV-2 test result ≥ 90 days after the first positive test. The association between serostatus and reinfection was assessed with a proportional hazards model adjusting for demographics, exposures, and virus testing frequency.

Results: Among 1,572 previously infected persons, 40 (2.5%) were reinfected. Reinfection differed by serostatus: 8.4% among seronegative versus 1.9% among seropositive participants ($p < 0.0001$). Most reinfections occurred among Rhode Island nursing home and corrections (RINHC) personnel ($n=30$) who were most frequently tested (mean 30.3 tests versus 4.6 for other Rhode Island and 2.3 for New York City participants). The adjusted hazard ratio (aHR) for reinfection in seropositive versus seronegative persons was 0.41 (95% CI 0.20, 0.81). Exposure to a household member with COVID-19 before the serosurvey was also protective (aHR 0.34, 95% CI 0.13, 0.89).

Conclusions: Reinfections were uncommon among previously infected persons over a 9-month period that preceded widespread variant circulation. Seropositivity decreased reinfection risk. Lower reinfection risk associated with exposure to a household member with COVID-19 before the serosurvey may reflect subsequently reduced household transmission among members of previously infected households.

Keywords: SARS-CoV-2, reinfection, antibody, healthcare personnel, first responders

Introduction

Studies are needed to build the evidence base about the frequency of and risk factors for reinfection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Most definitively, documented reinfection has occurred among persons infected with a genetically different variant than the primary infection [1, 2]. However, few persons have stored samples to make this determination. Probable reinfections have also been described among persons with two positive virus detection tests (antigen or viral nucleic acid amplification test [NAAT]) separated by long intervals. In the absence of genomic sequencing, a 90-day timeframe is used to determine a reinfection for surveillance purposes [3]. Uncertainty regarding the duration of detection of viral nucleic acid due to shedding following infection previously limited this approach. However, NAAT testing data among frequently tested cohorts suggest that the duration of viral shedding is <90 days in immunocompetent persons [4-6].

Observational studies and data from serially tested cohorts suggest that previous infection confers some degree of immunity, at least for several months. Among staff and residents of two British nursing homes, seropositive persons were 96% less likely to become infected during a second outbreak four months later [7]. In a British prospective cohort study which observed persons with and without SARS-CoV-2 antibodies for seven months, seropositivity was associated with an 84% lower risk of infection [8]. Another British cohort study found an 83% reduction in the incidence of SARS-CoV-2 infection over a five-month period among seropositive persons or those with prior infection documented by NAATs [9]. A large U.S. study that linked commercial laboratory results with medical claims data and electronic medical records found a 90% reduction in infection (measured ≥ 90 days after baseline antibody testing) among seropositive compared to seronegative persons [10]. A French study of healthcare workers found an 85% reduction in infection for seropositive versus seronegative persons after a 6-month observation period [11]. A study of long-term care facility (LTCF) residents and workers in England with periodic serology testing and weekly

virus testing found that seropositivity reduced risk of reinfection by 85% in residents aged ≥ 65 years and by 61% in staff members over a 10-month observation period [12]. Finally, a South African community study found an 84% reduction in reinfection when initial infection was defined by positive NAAT or serology test [13].

These studies defined prior infection using positive serology status; thus, persons who were previously infected but did not develop antibodies could thereby have been misclassified. Prior studies have shown that among persons known to have been infected, a sizeable minority remain seronegative [14, 15]. Although seropositive persons appear to be protected from reinfection compared to initial infection among seronegative persons, the risk of reinfection among infected persons who do not seroconvert has not previously been assessed. To identify frequency and risk factors for SARS-CoV-2 reinfection among seropositive and seronegative persons with previous SARS-CoV-2 infection based on virus testing, we merged NAAT or antigen test results from population-based surveillance systems with study data for health care workers and first responders who participated in SARS-CoV-2 serology surveys in Rhode Island and New York City [16, 17].

Methods

Serology surveys focused on first responder and healthcare personnel in Rhode Island during July-August 2020 and in New York City during May-July 2020 as previously described [16, 17]. In both settings, the serology survey occurred between two waves of transmission (Supplemental Figure 1). Antibody testing was performed using the ORTHO Clinical Diagnostics VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG test directed at the S1 domain of the spike protein (<https://www.orthoclinicaldiagnostics.com>)[16, 17].

Beginning in March 2020, all diagnostic laboratories were required to report SARS-CoV-2 laboratory test results (virus and serology) for state residents to the Rhode Island State Department of Health (RIDOH). The Centers for Medicare & Medicaid Services mandated routine periodic testing for

nursing home personnel. RIDOH also conducted frequent testing among correctional facility personnel due to the increased risk of outbreaks in this congregate setting. As a result, workers in these two settings were tested with greater frequency compared to participants at other Rhode Island sites. RIDOH matched all participants in the serosurvey (n=11,978) with state diagnostic testing results. The five boroughs under the jurisdiction of the New York City Department of Health and Mental Hygiene (DOHMH) reported testing results to DOHMH. Although increased testing frequency was mandated in New York skilled nursing facilities, nursing home personnel were not included in the New York City serosurvey. Of the 24,648 New York City serosurvey participants, 15,180 were New York City residents and had virus test results reported to DOHMH.

CDC received de-identified virus test results for the time periods for which data were available from each jurisdiction, from March 1, 2020, through February 17, 2021, for Rhode Island participants and from March 10, 2020, through December 14, 2020, for New York City participants. Although vaccinations started on December 14th in both jurisdictions, no vaccination status data were available at the time of data transfer. Additionally, no symptom data associated with virus testing were available. The combined study population of Rhode Island and New York City healthcare workers and first responders was linked with serology survey data using unique identification numbers. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy, and was considered to be public health surveillance by RIDOH and DOHMH Institutional Review Boards.

Only participants with an initial positive virus test result (defined below) ≥ 14 days before their serology test were included. Those with no positive virus test results were excluded because they were presumed never infected and therefore were not at risk for reinfection. Those with a first positive virus test result after their serology test were also excluded because the association between serology status and reinfection could not be assessed. The final sample included 373 Rhode Island participants and 1,199 New York City participants (Supplemental Figure 2).

Outcome and main exposure

SARS-CoV-2 testing data included the date and result of each virus test performed. The study outcome, reinfection with SARS-CoV-2, was defined as a positive virus test (either NAAT or antigen test) collected ≥ 90 days after an initial positive test [3]. Participants who had two positive tests ≥ 90 days apart were considered to have an observed reinfection. Serology status (positive or negative) was the primary factor of interest in assessing risk of reinfection.

Covariates

Serology survey participants reported their primary work agency, age, sex, race/ethnicity, underlying medical conditions and date of symptom onset. Primary workplace agency was categorized dichotomously as Rhode Island nursing home or corrections facilities (RINHC) versus all other agencies for the following reasons: nursing homes and corrections facilities were congregate settings in which personnel underwent more frequent testing than those in other workplaces; additionally, some workplace agencies had low sample sizes, which precluded robust statistical analysis; and finally, reporting frequencies for workplaces with small sample sizes could pose a disclosure risk. Participants were asked to report an exposure to anyone known to have COVID-19, with an exposure defined as >10 minutes within 6 feet of a person with COVID-19 per the April 2020 Council of State and Territorial Epidemiologists case definition [18] prior to survey participation. Frequency of virus testing was calculated by summing reported test results and was incorporated into statistical modeling to provide adjustment for serology status to account for factors beyond those provided by adjusting for workplace agency type.

Statistical analysis

Demographic and workplace characteristics were calculated overall and for subgroups. Differences were assessed using Fisher's exact test with the mid-p correction with significance level of 0.05. Cumulative incidence of reinfection was assessed among previously infected seropositive and seronegative persons. Direct bivariate comparisons of reinfection risk by characteristic were not performed because individual differences in follow-up times could not be accounted for. Kaplan-Meier curves were generated to show the cumulative probability of a subsequent positive virus test by antibody status. To allow for varying individual follow-up times and right-censored observations, a multivariable Cox proportional hazards regression (CPHR) was used to assess associations of covariates with reinfection risk. Exploratory analyses were used to assess the proportional hazards assumption and model selection was based on likelihood ratio tests. Estimates of hazard ratios and 95% confidence intervals (CI) were calculated. Length of follow-up was defined as the interval from the first positive virus test to either a subsequent positive virus test that occurred ≥ 90 days later, or to the last negative virus test that occurred ≥ 90 days later for those with no subsequent positive virus test, or to the end of the virus test reporting period for those with neither of these two occurrences.

Results

The study included 1,572 persons, 373 from Rhode Island and 1,199 from New York City who tested positive for the presence of SARS-CoV-2 RNA ≥ 14 days prior to collection of a serum sample. Demographic characteristics varied by study location. RINHC personnel underwent the most frequent testing (mean 30.3 tests per individual) compared to other Rhode Island (mean 4.6 tests per individual) and New York City (mean 2.3 tests per individual) personnel. Rhode Island personnel were more likely to be seronegative after infection versus New York City personnel (Rhode Island 19.8%, and New York City 6.7%) (Table 1). Overall, 2.5% (n=40) were reinfected, that is, had two positive virus tests ≥ 90 days apart (Table 2). The mean interval between infection and reinfection

was 216.0 (95% CI 198.8, 233.1) days. The primary risk factor of interest was serostatus: 8.4% of seronegative persons were reinfected during the time of observation versus 1.9% of seropositive persons (difference 6.5% [95% CI 3.0-12.0%]). Reinfection was more frequent among seronegative versus seropositive personnel among most subgroups (Table 2).

Figure 1 shows Kaplan-Meier survival curves by serology status for RINHC personnel (30 reinfections) and personnel from all other agencies (10 reinfections). Incidence of SARS-CoV-2 reinfection increased more slowly among seropositive compared to seronegative persons in both groups. The last reinfection observed during the study was in mid-January 2021 in the Rhode Island cohort and 13 of the 30 reinfections in Rhode Island occurred after December 14th, the last observation day in New York City. However, the longer observation period in Rhode Island was not the sole factor in the greater number of reinfections observed in this site: cumulative incidence of reinfection for the period before December 14th was 0.5% for New York City versus 7.2% for Rhode Island.

Preliminary analyses indicated the proportional hazards assumption was tenuous by workplace agency (RINHC versus other), so we conservatively included this variable in CPHR analyses as a stratification variable. We evaluated testing frequency by including it in preliminary CPHR models as a penalized spline (degree 3) term, separately for each dichotomous workplace group to evaluate the functional shape of the resulting curves, as numerical instability precluded using spline fits interacted with the dichotomous workplace agency variable. Fitted spline curves appeared well-approximated by linear and quadratic functions of virus testing frequency for RINHC and other workplace groups, respectively. We therefore included terms for serology status and linear and quadratic terms for testing frequency, each interacted with workplace agency, and then evaluated other covariates for model inclusion (Table 3). The final model selected using likelihood ratio tests contained serology status, exposure to COVID-19 positive household members, and main effects and interaction terms for testing frequency and workplace agency dichotomy. From this model fit, the resulting estimated adjusted hazard ratio for serostatus was 0.41 (95% CI 0.20, 0.81). Exposure to a

household member with COVID-19 prior to the serology survey was also inversely associated with reinfection (aHR 0.34, 95% CI 0.13, 0.89).

Discussion:

This is among the first studies to evaluate the risk of reinfection by antibody status among previously infected individuals. Reinfection with SARS-CoV-2 was uncommon (2.5%) in this large cohort of first responders and healthcare workers in Rhode Island and New York City, and occurred less frequently in seropositive versus seronegative persons. The 9- to 11-month observation period included the summer months of 2020 when community transmission was low, as well as the fall and early winter months when the rates of community transmission were similar to or greater than the early pandemic period. This observation period also preceded widespread full vaccination with mRNA vaccines, especially for New York City given the shorter observation period in this site. These results agree with prior studies that showed reinfection was uncommon and provided additional evidence that even in those with NAAT-confirmed re-infections, seropositivity is associated with lower risk of reinfection [19].

Previous studies that assessed cumulative risk of infection among seropositive versus seronegative persons observed between 83% and 96% reduction in reinfection risk [7, 9, 12, 19], higher than the 59% reduction observed in this study. This lower risk reduction could be due to several factors. First, the impact of serology status on reinfection risk was assessed among persons with a positive virus test rather than a positive serology test, and thus included seropositive and seronegative persons with known prior infection. Most prior studies compared infection rates among seropositive versus seronegative persons at baseline with the assumption that seronegative persons had not been previously infected. These studies all found antibodies were associated with reduced risk of

reinfection among seropositive persons [7-9, 11, 12, 20] but in comparison to initial infection rates among presumably never infected persons. If initial infection is determined by virus testing rather than serology testing, a lower protective effect of seropositivity is plausible. That is, compared to a seronegative group that includes persons never infected, a seronegative group with documented positive virus tests may have some immunity, including cellular immunity [21]. Second, reinfection was most frequently observed in the cohort that underwent frequent testing (RINHC personnel). Asymptomatic reinfections may have been more likely to be detected with mandated testing at frequent intervals as opposed to testing indicated by symptoms or suspected/known exposures. Lower protection of seropositivity could be observed if serum antibodies are less effective in preventing asymptomatic infection. Third, this study had a long observation period (9-11 months) compared to some previous studies that ranged from 4 months to just under 8 months [7-9, 19]. A study of LTCF staff and residents with a similar follow-up period (up to 10 months) found a similar level of protection of antibodies among LTCF staff (61%) to our study [12].

Reinfection was less likely among persons with reported exposure to a household member with COVID-19 prior to participation in the serology survey but was not associated with other potential risk factors in adjusted models, including the presence of chronic health conditions. Studies of healthcare personnel have found that community transmission was a strong risk factor for initial infection [17, 22-27]. Persons initially infected in their households may have a lower risk of subsequent household infection if household members also developed immunity. Household exposure may also be more easily identified compared to exposure to other persons with COVID-19.

The main limitation of this study was lack of clinical data associated with subsequent positive virus tests. Thus, we could not assess clinical severity of reinfections. One study that obtained paired genomic sequences to determine reinfection observed that among those with antibodies, reinfections were less severe than primary infections [19]. A prospective study of LTCF staff and

residents identified 14 reinfections during a 10-month period, of which 11 were symptomatic but none required hospitalization [12]. Given that most reinfections occurred in RINHC personnel and may have been detected in the workplace after symptom-based screening, it is likely that many of the reinfections detected were not clinically severe or even symptomatic. Our study population included only working adults. Thus, risk factors for severe symptomatic SARS-CoV-2 reinfection among unvaccinated individuals observed in a nationwide study in Mexico[28]—severe initial infection, older age, and comorbid conditions—were less likely to be present in this study cohort than in the general population. Another limitation is lack of data of vaccination status. COVID-19 vaccinations began in both sites in mid-December. While full immunity would not have been achieved until up to 5 weeks later among the first to be vaccinated (2 weeks after the second dose), vaccine-derived immunity may have impacted observed results in Rhode Island, which had a longer observation period. Next, a higher percentage of previously infected Rhode Island staff were seronegative, which could raise the possibility of false positive NAATs. However, viral tests generally have high specificity (above 98%) [29]. Additionally, previous studies have shown up to 16% of previously infected persons are seronegative, even in study populations with few immunocompromised persons [14, 15]. In other words, failure to develop detectable antibodies after SARS-CoV-2 infection may not be a rare phenomenon. The differences in testing frequency between sites could also have resulted in fewer primary infections being identified in setting where testing availability was limited, especially early in the pandemic. Because our study population was a healthy, younger working population with few immunocompromising conditions, results may not be generalizable. The study period preceded widespread transmission of variants of concern or interest, for which observed protection afforded by antibodies acquired after infection may differ from that of earlier circulating viral strains. It is unknown to what extent asymptomatic reinfections pose transmission risk, but previous studies found the mean cycle threshold value was lower among persons with symptomatic reinfection versus all reinfection [9] and among primary infections versus reinfections [12].

Strengths of our study included a large study cohort with information on demographics, workplace, and exposures during the first wave of the pandemic. Additionally, participants had known first positive NAAT and serology dates. This permitted inclusion criteria to specify a 2-week period between NAAT and serology testing. Current CDC guidance notes seroconversion may take up to 3 weeks [30]. However, all 8 participants with <21-day interval between the initial positive NAAT and serology testing were seropositive. Combining a cross sectional serology survey with longitudinal SARS-CoV-2 test results to examine reinfection extended the utility of the original serology survey and is a novel approach to assessing protection of seropositivity among previously infected persons. This study of a large cohort of previously infected persons (based on an initial positive NAAT test) found that protection from reinfection was associated with seropositivity.

Accepted Manuscript

NOTES

Acknowledgements: The authors would like to thank the members of the CDC Epidemiology Task Force First Responder Serosurvey Team for their invaluable contributions to the serology surveys that made this work possible: Craig Hales, Maryann Ingratta, Susan Lukacs, Lisa Mackey, Samira Sami, and Nga Vuong. Kushal Modi of the Rhode Island Department of Health and Addie Crawley of the New York City Department of Health and Mental Hygiene provided vital support with data matching between virus testing results and serology data.

Funding: Data and specimen collection activities and specimen testing was supported by a US Health and Human Services Contract (75P00120C00036).

Declarations of interest: None of the authors have any conflicts of interest to declare.

The findings and conclusions in this paper are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention. PAC reports receiving grant funding from the NIH, CDC, SAMHSA which did NOT fund this study.

Accepted Manuscript

References

1. Selhorst P, Van Ierssel S, Michiels J, et al. Symptomatic SARS-CoV-2 reinfection of a health care worker in a Belgian nosocomial outbreak despite primary neutralizing antibody response. *Clin Infect Dis* **2020**. epub ahead of print.
2. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. *Lancet Infect Dis* **2020**; 20(5): 565-74.
3. Council of State and Territorial Epidemiologists. 21-ID-01: Update to the standardized surveillance case definition and national notification for 2019 novel coronavirus disease (COVID-19). Available at: https://cdn.ymaws.com/www.cste.org/resource/resmgr/ps/ps2021/21-ID-01_COVID-19.pdf. Accessed 07/29/2021.
4. Zhou B, She J, Wang Y, Ma X. Duration of viral shedding of discharged patients with severe COVID-19. *Clin Infect Dis* **2020**; 71(16): 2240-2.
5. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* **2020**; 395(10229): 1054-62.
6. Phillips SP, Wei X, Kwong JC, et al. Duration of SARS-CoV-2 shedding: A population-based, Canadian study. *PLoS One* **2021**; 16(6): e0252217.
7. Jeffery-Smith A, Iyanger N, Williams SV, et al. Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020. *Euro Surveill* **2021**; 26(5).
8. Lumley SF, O'Donnell D, Stoesser NE, et al. Antibody status and incidence of SARS-CoV-2 infection in health care workers. *N Engl J Med* **2021**; 384(6): 533-40.

9. Hall VJ, Foulkes S, Charlett A, et al. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). *Lancet* **2021**; 397(10283): 1459-69.
10. Harvey RA, Rassen JA, Kabelac CA, et al. Association of SARS-CoV-2 seropositive antibody test with risk of future infection. *JAMA Intern Med* **2021**; 181(5): 672-9.
11. Dimeglio C, Herin F, Miedouge M, Martin-Blondel G, Soulat JM, Izopet J. Protection of healthcare workers against SARS-CoV-2 reinfection. *Clin Infect Dis* **2021**. epub ahead of print.
12. Krutikov M, Palmer T, Tut G, et al. Incidence of SARS-CoV-2 infection according to baseline antibody status in staff and residents of 100 long-term care facilities (VIVALDI): a prospective cohort study. *Lancet Healthy Longev* **2021**; 2(6): e362-e70.
13. Cohen C, Kleynhans J, von Gottberg A, et al. SARS-CoV-2 incidence, transmission and reinfection in a rural and an urban setting: results of the PHIRST-C cohort study, South Africa, 2020-2021. *medRxiv* **2021**: 2021.07.20.21260855.
14. Petersen LR, Sami S, Vuong N, et al. Lack of antibodies to SARS-CoV-2 in a large cohort of previously infected persons. *Clin Infect Dis* **2020**. epub ahead of print.
15. Gudbjartsson DF, Norddahl GL, Melsted P, et al. Humoral immune response to SARS-CoV-2 in Iceland. *N Engl J Med* **2020**. epub ahead of print.
16. Akinbami LJ, Chan PA, Vuong N, et al. Severe Acute Respiratory Syndrome Coronavirus 2 seropositivity among healthcare personnel in hospitals and nursing homes, Rhode Island, USA, July-August 2020. *Emerg Infect Dis* **2021**; 27(3): 823-34.
17. Sami S, Akinbami L, Petersen L, et al. Prevalence of SARS-CoV-2 antibodies in first responders and public safety personnel — New York City, May–July 2020. *Emerg Infect Dis* **2020**; 27(2).
18. Epidemiologists CoSaT. Coronavirus Disease 2019 (COVID-19) 2020 interim case definition, approved April 5, 2020: CSTE position statement Interim-20-ID-01 Available at:

<https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2020/>. Accessed August 25, 2021.

19. Abu-Raddad LJ, Chemaitelly H, Coyle P, et al. SARS-CoV-2 antibody-positivity protects against reinfection for at least seven months with 95% efficacy. *EClinicalMedicine* **2021**; 35: 100861.
20. Harvey RA, Rassen JA, Kabelac CA, et al. Real-world data suggest antibody positivity to SARS-CoV-2 is associated with a decreased risk of future infection. *medRxiv* **2020**.
21. Gallais F, Velay A, Nazon C, et al. Intrafamilial Exposure to SARS-CoV-2 Associated with Cellular Immune Response without Seroconversion, France. *Emerg Infect Dis* **2021**; 27(1).
22. Akinbami LJ, Vuong N, Petersen LR, et al. SARS-CoV-2 seroprevalence among healthcare, first response, and public safety personnel, Detroit metropolitan area, Michigan, USA, May–June 2020. *Emerging Infectious Diseases* **2020**; 26(12): 2863-71.
23. Barry M, Robert AA, Temsah MH, et al. COVID-19 community transmission among healthcare workers at a tertiary care cardiac center. *Med Sci (Basel)* **2021**; 9(3).
24. Schwartz KL, Achonu C, Buchan SA, et al. Epidemiology, clinical characteristics, household transmission, and lethality of severe acute respiratory syndrome coronavirus-2 infection among healthcare workers in Ontario, Canada. *PLoS One* **2020**; 15(12): e0244477.
25. Lai X, Wang M, Qin C, et al. Coronavirus disease 2019 (COVID-2019) infection among health care workers and implications for prevention measures in a tertiary hospital in Wuhan, China. *JAMA Netw Open* **2020**; 3(5): e209666.
26. Hunter E, Price DA, Murphy E, et al. First experience of COVID-19 screening of health-care workers in England. *Lancet* **2020**; 395(10234): e77-e8.
27. Steensels D, Oris E, Coninx L, et al. Hospital-wide SARS-CoV-2 antibody screening in 3056 staff in a tertiary center in Belgium. *JAMA* **2020**; 324(2): 3.

28. Murillo-Zamora E, Mendoza-Cano O, Delgado-Enciso I, Hernandez-Suarez CM. Predictors of severe symptomatic laboratory-confirmed SARS-CoV-2 reinfection. *Public Health* **2021**; 193: 113-5.
29. Mustafa Hellou M, Górska A, Mazzaferri F, et al. Nucleic acid amplification tests on respiratory samples for the diagnosis of coronavirus infections: a systematic review and meta-analysis. *Clin Microbiol Infect* **2021**; 27(3): 341-51.
30. Prevention CfDCa. Test for Past Infection. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/testing/serology-overview.html>. Accessed 8/25/2021.

Accepted Manuscript

Table 1. Characteristics of previously infected healthcare and first responder personnel per serology survey responses, New York City (May-July 2020) and Rhode Island (July-August 2020)

Characteristic	Sample n (%)			p-value	
	Total	NYC	RI		
Total	1572 (100.0)	1199 (100.0)	373 (100.0)		
Serology status	Negative	154 (9.8)	80 (6.7)	74 (19.8)	<.000 1
	Positive	1418 (90.2)	1119 (93.3)	299 (80.2)	
Sex	Male	872 (55.5)	789 (65.8)	83 (22.3)	<.000 1
	Female	700 (44.4)	410 (34.2)	290 (77.8)	
Race/ ethnicity	NH white	579 (36.8)	326 (27.2)	253 (67.8)	<.000 1
	NH black	241 (15.3)	205 (17.1)	36 (9.7)	
	NH other	272 (17.3)	236 (19.7)	36 (9.7)	
	Hispanic	480 (30.5)	432 (36.0)	48 (12.9)	
Age group	18-34 years	554 (35.2)	450 (37.5)	104 (27.9)	<.000 1
	35-59 years	924 (58.8)	696 (58.1)	228	

				(61.1)	
	60+ years	94 (6.0)	53 (4.4)	41 (11.0)	
Weight status	Under/nor			110	<.000
	mal	348 (22.1)	238 (19.9)	(29.5)	1
	Overweight			110	
		640 (40.7)	530 (44.2)	(29.5)	
	Obesity			153	
		584 (37.2)	431 (36.0)	(41.0)	
Chronic condition	No			236	
		886 (56.4)	650 (54.2)	(63.3)	0.002
	Yes			137	
		686 (43.6)	549 (45.8)	(36.7)	
Immunosuppressive medications	No	1560	1191	369	
		(99.2)	(99.3)	(98.9)	0.49
	Yes	12 (0.8)	8 (0.7)	4 (1.1)	
Exposed to COVID-19+ person prior to serology survey ^a	Coworker	1080		204	<.000
		(68.7)	876 (73.1)	(54.7)	1
	Household			106	
	member	497 (31.6)	391 (32.6)	(28.4)	0.13
	Patient			177	<.000
		177 (11.3)	0 (0.0)	(47.5)	1
	Other			116	<.000
	person	678 (43.1)	562 (46.9)	(31.1)	1

Agency				
	NY			<.000
		105 (6.7)	105 (8.8)	
	Corrections			1
	NY Fire	404 (31.6)	404 (33.7)	
	NY Law			
	Enforcement	524 (33.3)	524 (43.7)	
	NY Other ^b	166 (10.6)	166 (13.8)	
	RI Nursing			177
	homes & Corrections	177 (11.3)		(46.1)
	RI Other ^c			196
		196 (12.5)		(52.6)

^a Exposure since March 1 to time of serology survey for >10 minutes within 6 feet. Only exposed categories shown; categories not mutually exclusive

^b Includes NYC hospitals, Office of Chief Medical Examiner, Regional Enrichment Centers (childcare providers for first responders)

^c Includes Rhode Island (RI) Hospitals, EMS, Fire, Law Enforcement, and RI National Guard

Note: NH=non-Hispanic; weight status defined as BMI<25 (under/normal weight), BMI≥25 and <30 (overweight), and BMI≥30 (obesity). Chronic conditions included diabetes, hypertension, heart disease, kidney disease, liver disease, asthma, and chronic obstructive pulmonary disease.

Table 2. Observed reinfection and characteristics of previously infected healthcare and first responder personnel in New York City (March – December 2020) and Rhode Island (March 2020 – February 2021), by serology status

		Seropositive		Seronegative	
		Total	Reinfected	Total	Reinfected
		n	n (%)	n	n (%)
Total		1,418	27 (1.9)	154	13 (8.4)
Sex	Male	809	6 (0.7)	63	2 (3.2)
	Female	609	21 (3.5)	91	11 (12.1)
Race/ ethnicity	NH White	495	11 (2.2)	84	10 (11.9)
	NH Black	231	6 (2.6)	10	1 (10.0)
	NH other	258	2 (0.8)	14	1 (7.1)
	Hispanic	434	8 (1.8)	46	1 (2.2)
Age group	18-34 years	499	8 (1.6)	55	3 (5.5)
	35-59 years	836	17 (2.0)	88	10 (11.4)
	60+ years	83	2 (2.4)	11	0 (0.0)
Weight status	Under/normal	295	5 (1.7)	53	3 (5.7)
	Overweight	590	10 (1.7)	50	2 (4.0)
	Obesity	533	12 (2.3)	51	8 (15.7)
Chronic condition	No	795	17 (2.1)	91	10 (11.0)
	Yes	623	10 (1.6)	63	3 (4.8)

Immunosuppressive medications	No	1408	27 (1.9)	152	13 (8.6)
	Yes	10	0 (0.0)	2	0 (0.0)
Exposed to COVID-19+ person prior to serology survey ^a	Coworker	983	15 (1.5)	97	8 (8.3)
	HH member	466	4 (0.9)	31	1 (3.2)
	Patient	151	12 (8.0)	26	4 (15.4)
	Other person	617	11 (1.8)	61	3 (4.9)
	Agency	NYC Other ^b	1119	5 (0.0)	80
	RI Nursing homes & Corrections	144	21 (14.6)	33	9 (27.3)
	RI Other ^c	155	1 (0.7)	41	3 (7.3)

^a Exposure since March 1 to time of serology survey for >10 minutes within 6 feet. Only exposed categories shown; categories not mutually exclusive

^b Includes NYC corrections, fire, law enforcement, hospitals, Office of Chief Medical Examiner, Regional Enrichment Centers (childcare providers for first responders)

^c Includes Rhode Island hospitals, emergency medical services, fire, law enforcement, and RI National Guard

Note: NH=non-Hispanic; weight status defined as BMI<25 (under/normal weight), BMI≥25 and <30 (overweight), and BMI≥30 (obesity). Chronic conditions included diabetes, hypertension, heart disease, kidney disease, liver disease, asthma, and chronic obstructive pulmonary disease.

Table 3: Adjusted hazard ratios for SARS-CoV-2 reinfection for healthcare and first responder personnel in New York City (March – December 2020) and Rhode Island (March 2020 – February 2021)

Covariate	Levels	Likelihood Ratio Test p-value ^a	Hazard Ratio (95% CI)
Sex	female vs. male	0.38	1.43 (0.63, 3.22)
Age group	35-59 vs 18-34 years	0.75	1.11 (0.54, 2.27)
	60+ vs. 18-34 years		0.66 (0.14, 3.06)
Race/ethnicity	Hispanic vs. NH White	0.42	1.34 (0.56, 3.20)
	NH Black vs. NH White		1.80 (0.78, 4.11)
	NH other vs. NH White		0.70 (0.20, 2.39)
Weight status	Obesity vs. under/normal weight	0.47	1.64 (0.70, 3.82)
	Overweight vs. under/normal weight		1.58 (0.64, 3.95)
Chronic condition	Any vs. none	0.37	0.74 (0.38, 1.45)
Exposed to COVID-19+ person prior to serology Survey ^b	Coworker (vs. not exposed)	0.75	1.11 (0.58, 2.12)
	Patient (vs. not exposed)	0.77	0.91 (0.46, 1.77)
	Household member (vs. not exposed)	0.01	0.34 (0.13, 0.89)
Workplace agency (dichotomized) ^c	Other person (vs. not exposed)	0.97	0.97 (0.49, 2.89)
	RI Nursing home/Corrections vs. other	<0.0001	14.00 (6.75, 29.35)
Serology Status	Positive vs. negative	0.02 ^d	0.41 (0.20, 0.81)

^a Test of 0 effect when serology status testing frequency (linear and quadratic terms), and testing frequency (linear and quadratic terms)-Workplace agency interaction in the model

^b Exposure since March 1 to time of serology survey for more than 10 minutes within 6 feet. Categories shown are not mutually exclusive.

^c Dichotomized to RINHC versus all other agencies (RI Other and NYC Other from Table 2), when evaluated in the model alone (and without stratification)

^d P-value for test of interaction between serology status and workplace agency equal to "other workplace agency"

Note: NH = non-Hispanic; weight status defined as BMI < 25 (under/normal weight), BMI ≥ 25 and < 30 (overweight), and BMI ≥ 30 (obesity). Chronic conditions included diabetes, hypertension, heart disease, kidney disease, liver disease, asthma, and chronic obstructive pulmonary disease.

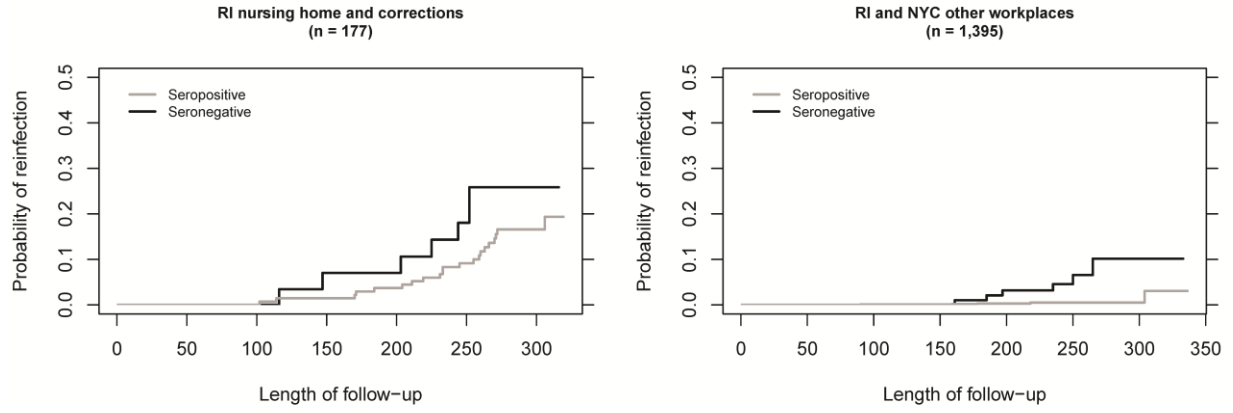
Accepted Manuscript

Figure 1

Kaplan-Meier curves among previously infected (based on positive antigen and NAAT results) healthcare and first responder personnel, by workplace agency (RI Nursing Home and Corrections and RI and NYC other workplaces) and serology status.

Accepted Manuscript

Figure 1



Accepted Manuscript