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Pfizer-BioNTech Coronavirus Disease 2019 Vaccine Effectiveness Against Severe Acute Respiratory Syndrome Coronavirus 2 Infection Among Long-term Care Facility Staff With and Without Prior Infection in New York City, January–June 2021

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Background. Evidence is accumulating of coronavirus disease 2019 (COVID-19) vaccine effectiveness among persons with prior severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Methods. We evaluated the effect against incident SARS-CoV-2 infection of (1) prior infection without vaccination, (2) vaccination (2 doses of Pfizer-BioNTech COVID-19 vaccine) without prior infection, and (3) vaccination after prior infection, all compared with unvaccinated persons without prior infection. We included long-term care facility staff in New York City aged <65 years with weekly SARS-CoV-2 testing from 21 January to 5 June 2021. Test results were obtained from state-mandated laboratory reporting. Vaccination status was obtained from the Citywide Immunization Registry. Cox proportional hazards models adjusted for confounding with inverse probability of treatment weights.

Results. Compared with unvaccinated persons without prior infection, incident SARS-CoV-2 infection risk was lower in all groups: 54.6% (95% confidence interval, 38.0%–66.8%) lower among unvaccinated, previously infected persons; 80.0% (67.6%–87.7%) lower among fully vaccinated persons without prior infection; and 82.4% (70.8%–89.3%) lower among persons fully vaccinated after prior infection.

Conclusions. Two doses of Pfizer-BioNTech COVID-19 vaccine reduced SARS-CoV-2 infection risk by ≥80% and, for those with prior infection, increased protection from prior infection alone. These findings support recommendations that all eligible persons, regardless of prior infection, be vaccinated against COVID-19.

Keywords. COVID-19 vaccine effectiveness; SARS-CoV-2 reinfection; long-term care facilities.

Real-world evaluations have demonstrated high effectiveness of coronavirus disease 2019 (COVID-19) vaccines authorized for use in the United States against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1]. Epidemiologic evidence of vaccine effectiveness (VE) among previously infected persons is accumulating. Three previous studies estimated that vaccination following prior infection increases protection relative to prior infection alone, with full vaccination associated with a >2-fold reduction in the odds of reinfection [2, 3] and 1 dose associated with a 1.9-fold reduction [4]. However, these studies relied on surveillance data from people tested for SARS-CoV-2 nonsystematically; study results therefore may have been biased by differential testing behaviors among vaccinated and unvaccinated individuals. Robust evidence of any incremental benefit of vaccination beyond that provided by prior infection alone is needed to guide the vaccination decisions of previously infected persons and to inform policy decisions.

The incidence of SARS-CoV-2 in New York City (NYC) was high in the first wave of the COVID-19 pandemic, with nearly

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one-quarter of adults infected [5]. SARS-CoV-2 exposure among employees of long-term care (ie, skilled nursing and adult care) facilities (LTCFs) was likely higher than among the general population owing to the high number of infections in congregate settings [6] and the lack of high-quality personal protective equipment [7]. From 15 May 2020 through 10 June 2021, all LTCF employees in New York State were required to be tested for SARS-CoV-2 at least once per week [8]. Frequent, periodic SARS-CoV-2 diagnostic testing among this group, as well as high rates of infection before vaccine availability, provide a unique opportunity to evaluate the protective effect of prior infection and vaccination alone and in combination against symptomatic, asymptomatic, and any SARS-CoV-2 infection.

METHODS

Study Population

We conducted a retrospective cohort study of LTCF NYC resident employees from 21 December 2020 through 5 June 2021. We identified LTCF staff as persons (1) <65 years of age, (2) with SARS-CoV-2 laboratory-based polymerase chain reaction (PCR) test frequency every ≤10 days in the New York State Electronic Clinical Laboratory Reporting System (ECLRS), (3) with a facility name or geocoded address in ECLRS or NYC Citywide Immunization Registry (CIR) records that corresponded to any of the 245 LTCFs within NYC, and (4) with a home address in NYC that did not correspond to an LTCF (to distinguish staff from residents). Laboratories are mandated to report all SARS-CoV-2 test results to ECLRS [9]. Pfizer-BioNTech COVID-19 vaccination was offered to LTCF employees and residents through the Centers for Disease Control and Prevention's (CDC's) Pharmacy Partnership for Long-Term Care Program [10]; LTCF employees and residents were among the first groups to have access to COVID-19 vaccination [11].

On-site vaccination clinics began on 21 December 2020, and all LTCFs hosted ≥1 on-site vaccination clinic by 28 February 2021. COVID-19 vaccine availability in general public settings was limited during this time [12], so the majority of LTCF staff vaccinated during the study period received the Pfizer-BioNTech vaccine offered through the federal Pharmacy Partnership program. Vaccine providers are required to report COVID-19 vaccinations administered in NYC to the CIR, and data exchanges with New York State and New Jersey capture vaccinations administered to NYC residents in these locations. Test records in ECLRS were probabilistically matched with CIR immunization records (Supplementary Materials). We classified records with a match probability ≤70% as nonmatches (ie, unvaccinated) and records with a match probability >90% as matches (ie, vaccinated). Persons with testing and immunization records with a match probability >70% or ≤90% were excluded, because probabilities in this range indicated uncertainty in the match, and thus vaccination status. Following the match, we also excluded individuals who received Moderna or Janssen COVID-19 vaccines (owing to the small number of persons who received these vaccines); those who received 2 doses of the Pfizer-BioNTech vaccine <17 days apart [13]; those with >2 recorded doses, doses from >1 manufacturer, or any doses reported without manufacturer listed; and those whose ECLRS and CIR records did not have complete covariate data, including a geocodable home address and sex. Figure 1 details all exclusions in a CONSORT (Consolidated Standards of Reporting Trials) flow diagram.

Study Design

In our primary analysis, we compared the time to SARS-CoV-2 infection among unvaccinated persons without prior infection (reference group) relative to that in exposure groups of individuals who were (1) unvaccinated and previously infected, (2) fully vaccinated without prior infection, or (3) fully vaccinated after prior infection. Full vaccination was defined as ≥14 days after receipt of a second dose of Pfizer-BioNTech COVID-19 vaccine (ie, completion of the primary series). Person-time for fully vaccinated persons therefore began 14 days after receipt of the second vaccine dose, and person-time for unvaccinated persons began on the earliest date that the person could have been fully vaccinated (ie, 35 days after the first on-site vaccination clinic at any of the LTCFs where the person worked, accounting for 21 days for the Pfizer-BioNTech primary series schedule plus 14 days). In this analysis, the earliest person-time start date is 21 January 2021.

In a secondary analysis, we used a counting process to allow a person's vaccination status over the course of follow-up to change from unvaccinated to vaccinated with 1 dose (categorized as 1–13 days since receipt of the first dose or ≥14 days from receipt of the first dose to receipt of the second dose) and to vaccinated with 2 doses (categorized as 1–13 days since receipt of the second dose or fully vaccinated). Person-time for all individuals in this analysis began on the date of the first on-site vaccination clinic at any of the LTCFs at which a person worked (ie, the earliest date when a person could have received a first vaccine dose), with the earliest person-time start date being 21 December 2020. While our primary analysis is comparable to the primary analysis of the Pfizer-BioNTech clinical trial [14], this secondary analysis reduces potential selection bias that could occur in the primary analysis, which restricts the analytic population to persons who remained uncensored until at least the start date of their primary analysis person-time. The secondary analysis also allows for estimation of the protective effect of a single vaccine dose against SARS-CoV-2 infection among those with or without prior infection, again compared with unvaccinated persons without prior infection. We defined single-dose vaccination as ≥14 days after receipt of the first dose to receipt of the second dose.

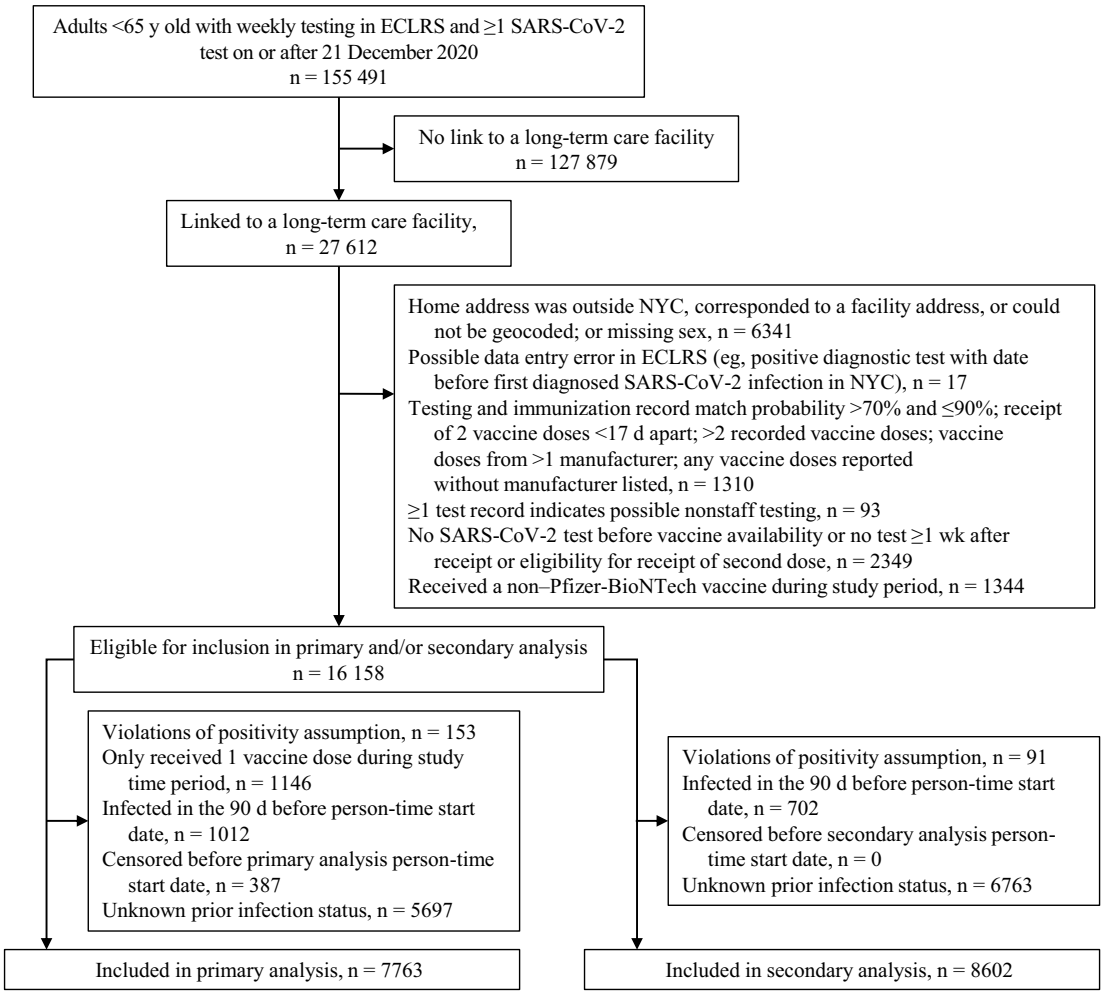

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram showing initial eligible population, exclusion criteria, and final analytic samples for primary and secondary analyses. The positivity assumption was violated if there were not exposed and unexposed persons in each confounder stratum. Abbreviations: ECLRS, New York State Electronic Clinical Laboratory Reporting System; NYC, New York City; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

In the primary and secondary analyses, prior infection was defined as having a positive diagnostic test result (laboratory-based PCR, point-of-care PCR, or antigen tests reported via ECLRS) or a positive serology test result before the start of on-study person-time and, among vaccinated persons in the primary analysis, before receipt of the first vaccine dose. Absence of a prior infection was defined as having a negative immunoglobulin G or total antibody serology test before 15 June 2020 (ie, within approximately 3 months of onset of the first wave, when the vast majority of previously infected individuals would have detectable antibodies [15]) and no positive diagnostic or positive serology test result before on-study person-time started. Persons without a positive diagnostic result before the start of on-study person-time and no serology test before 15 June 2020 to indicate infection or lack thereof during the first wave were considered to have unknown prior infection status and were excluded.

Finally, we evaluated the effectiveness of full vaccination against symptomatic [16] and asymptomatic SARS-CoV-2 infection among persons without a prior infection. Symptom status was ascertained in daily symptom monitoring performed by the NYC Test & Trace Corps. Persons with reinfections were not routinely contacted for case interviews, precluding estimation of VE by symptom status among those with a prior infection. Persons with an incident infection for which symptom status was unknown were excluded from analyses of VE against symptomatic and asymptomatic infection. In all analyses, we excluded individuals with a positive laboratory-based PCR test within 90 days before the beginning of their person-time start date to reduce the possibility of misclassification of persistent viral shedding as an incident infection [17].

Statistical Analysis

We used Cox proportional hazards models to compare time to incident SARS-CoV-2 infection detected by laboratory-based

PCR test between exposure groups defined by vaccination status and prior infection. From January through May 2021, sampled positive specimens were predominantly viral variants neither of concern nor of interest or Iota or Alpha variants. The Delta variant increased rapidly thereafter in 2021, from 8% of sampled positive specimens on 5 June to 28% by 12 June 2021 [18]. Prior literature suggests similar VE against Iota, Alpha, and viral variants not of concern or interest [19, 20], while VE against the Delta variant is lower [21]. Because the weekly testing mandate ended for vaccinated LTCF staff on 10 June 2021 [8] and to include a variant distribution that was similar with respect to VE, analyses include data through 5 June 2021.

To control for potential confounding, we constructed stabilized inverse probability of treatment weights [22] (IPTWs) to balance exposed and reference groups with respect to age, sex, race/ethnicity, neighborhood poverty [23], borough of residence, neighborhood political affiliation [24–26], calendar week, and the LTCF where a person was primarily employed. We calculated IPTWs separately for each exposure of interest and evaluated balance achieved by IPTWs by comparing the standardized difference in covariates between the exposed and reference groups before and after application of IPTW [22]. Standardized differences <0.1 after IPTW application were considered acceptable [22]. We also assessed the positivity assumption (ie, that there were exposed and unexposed persons in each confounder stratum) by calculating the mean, minimum, and maximum of the stabilized IPTW, and we excluded individuals with covariate values that produced violations of the positivity assumption [22].

Age, sex, race/ethnicity, borough, and the employing LTCF were obtained directly from ECLRS, CIR, or patient interviews. Race/ethnicity was obtained first from patient interviews, then ECLRS, and finally from CIR if missing from both interview and ECLRS records. For other potential confounders, we obtained residential census tract and election district by geocoding the home address included in ECLRS and CIR records. These were then linked to data on the census tract–level proportion of households below the federal poverty level [23] and the proportion of Democratic votes in the 2020 presidential election [24] (as a proxy for political affiliation). In addition, where missing, we imputed race/ethnicity with the Bayesian Improved Surname Geocoding method [27], using census tract-level race/ethnicity population proportions [28] and the 2010 census surname file [29]. Missing race/ethnicity was imputed in 50 data sets. Analyses were performed on each data set, and we used Rubin's rules [30] to calculate pooled effect estimates and standard errors. We evaluated the proportionality of hazards assumption for each model and calculated E-values to estimate the minimum strength of association of unmeasured confounders that could nullify the lower bound and point estimates of exposure-outcome relationships [31]. All analyses were performed with R software, version 3.5.2 (R Foundation for Statistical Computing).

The NYC Department of Health and Mental Hygiene Institutional Review Board reviewed and approved study procedures. This activity was also reviewed by the CDC and was conducted consistent with applicable federal law and CDC policy (see, eg, 45 CFR part 46, 21 CFR part 56, 42 USC §241(d), 5 USC §552a, and 44 USC §3501 et seq).

RESULTS

Our primary analysis included 7763 persons employed at 179 of 245 LTCFs (73.1%) (Supplementary Materials). A majority (n = 4905 [63%]) were aged 45–64 years, and approximately three-quarters (n = 5728 [74%]) were women (Table 1). Most individuals lived in neighborhoods with a low (n = 2458 [32%]) or medium (n = 2786 [36%]) proportion of households below the federal poverty level. Averaged across 50 imputed data sets, 41% of persons (n = 3186) were non-Hispanic Black/African American, followed by non-Hispanic White (n = 1534 [20%]), Hispanic (n = 1144 [15%]), multiracial or another race/ethnicity (n = 1201 [15%]), and Asian or Pacific Islander (n = 698 [9%]). Demographic characteristics of the secondary analysis population were similar (Supplementary Table 1). Among the approximately half of persons in the primary analysis with documented race/ethnicity, the correlation of documented race/ethnicity values with race/ethnicity probabilities calculated with the Bayesian Improved Surname Geocoding method was moderate for all race/ethnicity groups, except for the group of persons who were multiracial or another race/ethnicity, for whom correlation was low (Supplementary Table 2).

Among individuals included in the primary or secondary analyses, the proportion of persons vaccinated increased rapidly in the first weeks of vaccine availability, rising from 19.2% receiving ≥1 dose in the week of the first facility-based vaccination clinics to 53.0% by 31 January 2021. The proportion of persons vaccinated in the study population increased more slowly thereafter, reaching 66.0% by the final week of the study period (Supplementary Figure 1*A*). More than half of all persons in the primary analysis (n = 4462 [57.5%]) were fully vaccinated by the end of the study period (Supplementary Figure 1*B*), with the second dose administered a median of 21 days after the first dose; 90% of second doses were administered 20–25 days after receipt of the first dose.

In the primary analysis, 69.6% of persons (n = 5400) had a documented prior infection (Supplementary Materials). At least 85.0% of prior infections occurred during the first wave of the pandemic (ie, before 1 July 2020); 8.3% of individuals with a prior infection had a positive serologic test result on or after 1 July 2020 with no documented positive diagnostic test, so it is therefore unknown whether their prior infection occurred during or after the first wave.

Table 1. Characteristics of Long-term Care Facility Staff Overall and by Vaccination and Prior Infection Status, New York City, January–June 2021

Characteristic	LTCF Staff, No. (Column %)				
		No Prior SARS-CoV-2 Infection (n = 2363)		Previous SARS-CoV-2 Infection (n = 5400)	
	Full Cohort (N = 7763)	Unvaccinated[a] (n = 958)	Fully Vaccinated[a] (n = 1405)	Unvaccinated[a] (n = 2343)	Fully Vaccinated[a] (n = 3057)
Age, y					
18–24	200 (3)	44 (5)	25 (2)	80 (3)	51 (2)
25–44	2658 (34)	451 (47)	473 (34)	957 (41)	777 (25)
45–64	4905 (63)	463 (48)	907 (65)	1306 (56)	2229 (73)
Sex					
Female	5728 (74)	701 (73)	1008 (72)	1818 (78)	2201 (72)
Male	2035 (26)	257 (27)	397 (28)	525 (22)	856 (28)
Race and ethnicity[b]					
Asian or Pacific Islander	698 (9)	54 (6)	203 (14)	114 (5)	327 (11)
Non-Hispanic Black	3186 (41)	403 (42)	389 (28)	1219 (52)	1176 (38)
Hispanic	1144 (15)	178 (19)	223 (16)	354 (15)	389 (13)
Non-Hispanic White	1534 (20)	265 (28)	311 (22)	508 (22)	450 (15)
Multiracial or other	1201 (15)	58 (6)	278 (20)	149 (6)	716 (23)
Proportion of households below federal poverty level[c]					
Low (0% to <10%)	2458 (32)	296 (31)	494 (35)	706 (30)	962 (31)
Medium (10% to <20%)	2786 (36)	327 (34)	519 (37)	850 (36)	1090 (36)
High (20% to <30%)	1427 (18)	188 (20)	212 (15)	432 (18)	595 (19)
Very high (≥30%)	1092 (14)	147 (15)	180 (13)	355 (15)	410 (13)
Borough of residence					
The Bronx	1888 (24)	221 (23)	318 (23)	590 (25)	759 (25)
Brooklyn	2322 (30)	291 (30)	324 (23)	880 (38)	827 (27)
Manhattan	366 (5)	55 (6)	93 (7)	78 (3)	140 (5)
Queens	2167 (28)	244 (25)	442 (31)	554 (24)	927 (30)
Staten Island	1020 (13)	147 (15)	228 (16)	241 (10)	404 (13)

Abbreviations: LTCF, long-term care facility; SARS-CoV-2, severe acute respiratory syndrome coronavirus.

[a]Unvaccinated was defined as having received zero doses of any coronavirus disease 2019 (COVID-19) vaccine and fully vaccinated defined as ≥14 days since receipt of the second dose of Pfizer-BioNTech COVID-19 vaccine.

[b]Race and ethnicity are imputed for 4136 persons (53.3%) with the Bayesian Improved Surname Geocoding method. Numbers and percentages in this table are the means across 50 data sets with imputed race and ethnicity.

[c]Households within a census tract that have income <100% of the federal poverty level, as measured in the American Community Survey, 2015–2019 [23].

Over a median follow-up period of 99 days (range, 1–133 days) in our primary analysis, there were 286 incident SARS-CoV-2 infections, for an incidence rate in the full cohort of 0.44 (95% confidence interval [CI], .39–.49) per 1000 person-days. The incidence was highest among unvaccinated persons without prior infection at 1.17 (95% CI, .95–1.44) per 1000 person-days, followed by 0.51 (95% CI, .42–.62) per 1000 person-days among unvaccinated and previously infected persons (Table 2). The incidence was lowest among fully vaccinated persons and was similar among those fully vaccinated with or without prior infection (0.21 [95% CI, .16–.28] and 0.26 [95% CI, .17–.37] per 1000 person-days, respectively). In adjusted analyses, compared with unvaccinated persons without a prior infection, the risk of an incident SARS-CoV-2 infection was lower in all groups: 54.6% (95% CI. 38.0%–66.8%) lower among unvaccinated and previously infected persons, 80.0% (67.6%–87.7%) lower among fully vaccinated persons without prior infection, and 82.4% (70.8%– 89.3%) lower among fully vaccinated and previously infected persons (Table 2). IPTW achieved acceptable balance in covariates (Supplementary Figure 2*A*–2*C*).

In our secondary analysis, in which vaccination status was time varying, the incidence among unvaccinated persons without prior infection was 1.70 (95% CI, 1.50–1.92) per 1000 person-days; this was higher than the incidence among the same group in the primary analysis because earlier person-time start dates in the secondary analysis included a period with higher citywide incidence. The incidence was 0.63 (95% CI, .33–1.07) per 1000 person-days among those with single-dose vaccination and no prior infection and 0.45 (95% CI, .27–.71) per 1000 person-days among those with single-dose vaccination who were previously infected. The incidence was lowest among fully vaccinated persons and similar between those fully vaccinated with or without prior infection (0.20 [95% CI, .14–.26] and 0.24 [95% CI, .16–.35] per 1000 person-days, respectively). In adjusted analyses, single-dose vaccination reduced the risk

Table 2. Relative Risk of Severe Acute Respiratory Syndrome Coronavirus 2 Infection: Unvaccinated Persons With No Prior Infection Versus Persons in Other Vaccination/Infection Categories

Vaccination and Prior SARS-CoV-2 Infection Status[a]	Persons, No.	Person-days	Infections, No.[b]	Incidence Rate (95% CI), Infections per 1000 Person-Days	Crude Risk Reduction (95% CI), %[c]	*P* Value	Adjusted Risk Reduction (95% CI), %[c,d]	*P* Value
Unvaccinated with no prior infection	958	80 112	94	1.17 (.95–1.44)	Reference	…	Reference	…
Unvaccinated and previously infected	2343	214 907	110	0.51 (.42 –.62)	55.0 (40.7–65.9)	<.001	54.6 (38.0–66.8)	<.001
Fully vaccinated with no prior infection	1405	116 018	30	0.26 (0.17, 0.37)	78.5 (67.6–85.8)	<.001	80.0 (67.6–87.7)	<.001
Fully vaccinated and previously infected	3057	244 164	52	0.21 (.16–.28)	82.5 (75.4–87.5)	<.001	82.4 (70.8–89.3)	<.001

Abbreviations: CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Unvaccinated was defined as having received zero doses of any coronavirus disease 2019 (COVID-19) vaccine and fully vaccinated as ≥14 days after receipt of the second dose of Pfizer-BioNTech COVID-19 vaccine.

[b]Infection was defined as a positive result of a laboratory-based polymerase chain reaction test.

[c]Percentages were calculated as (1 − hazard ratio) × 100.

[d]A priori selected variables anticipated to be confounders (including age, sex, race and ethnicity, borough, neighborhood poverty, neighborhood political affiliation, calendar week, and the primary long-term care facility where an individual worked) were used to construct inverse probability of treatment weights. Race and ethnicity are imputed for 4136 (53.3%) missing observations. The adjusted percentage reduction in risk and 95% confidence intervals were pooled from 50 imputed data sets.

of infection by 73.8% (95% CI, 49.8%–86.4%) among those without prior infection and by 79.6% (95% CI, 61.8%–89.1%) among previously infected persons, both compared with unvaccinated persons without prior infection. Estimates of the effect of full vaccination among those with or without prior infection were similar in the secondary and primary analyses (Table 3 and Figure 2). IPTW achieved acceptable balance in most covariates in secondary analyses, although the standardized difference remained >0.1 for some covariates (Supplementary Figure 3*A*–3*C*).

Among persons without prior infection, symptom status was known for 94 of 124 (75.8%) incident SARS-CoV-2 infections. Symptom status was known for a similar proportion of infections among vaccinated and unvaccinated persons (76.7% and 75.5%, respectively). The effectiveness of full vaccination against symptomatic infection was 87.5% (95% CI, 73.2%–94.1%) in unadjusted analyses and equivalent in adjusted analyses (87.5% [69.4%–94.9%]). The effectiveness of full vaccination against asymptomatic infection was 65.2% (95% CI, 35.2%–81.3%) in unadjusted analyses and 68.9% (36.0%–84.9%) in adjusted analyses. IPTW achieved acceptable balance in covariates (Supplementary Figure 4). E-values for all analyses are shown in Supplementary Figure 5*A*–5*C* and indicate that unmeasured confounders would need to be strongly associated with the exposure and outcome to nullify findings.

DISCUSSION

In this cohort of LTCF staff with weekly SARS-CoV-2 testing, full vaccination after prior infection increased the protection against SARS-CoV-2 infection afforded by prior infection alone, from 55% to 82%, similar to the VE against infection among those without prior infection. These findings strengthen a growing body of epidemiologic evidence [2–4] that full vaccination for previously infected individuals increases protection against reinfection. Two previous studies estimated that, among previously infected persons, unvaccinated individuals were approximately 2.3-fold more likely to be reinfected than fully vaccinated persons [2, 3]. Similarly, among previously infected persons in our study, those who were unvaccinated had a 2.6-fold increased risk of reinfection compared with fully vaccinated persons, based on the difference in risk reduction (55% and 82%, respectively) between these 2 groups.

In addition, these analyses corroborate other real-world analyses of Pfizer-BioNTech VE, demonstrating that it was highly effective in our cohort against infection, including symptomatic and asymptomatic infection, for a median of 3 months and up to a maximum follow-up period of 4.4 months after full vaccination. However, these analyses cover a period in NYC during which Delta variant infections were rare and before emergence of the Omicron variant. Previously published literature shows reduced ability of vaccines to prevent Delta variant infections [21], with even greater reductions in the effectiveness of 2-dose vaccination against Omicron variant infection [32]. Determining the role of vaccine boosters and inclusion of additional vaccine antigenic targets to restore and sustain high levels of protection against SARS-CoV-2 infection will be important decisions for the next phase of the pandemic.

Estimates of the protective effect of prior infection suggest that risk of reinfection is reduced by >80% for up to 7 months following an initial infection [33–35], with protection waning to 69% >1 year after infection [36]. Among previously infected persons in our cohort, the vast majority experienced a first infection during the first wave of the pandemic. Although we

Table 3. Relative Risk of Severe Acute Respiratory Syndrome Coronavirus 2 Infection: Unvaccinated Persons Without Prior Infection Versus Persons With or Without Prior Infection by Time-Varying Vaccination Status

Vaccination History by Prior SARS-CoV-2 Infection Status[a]	Persons, No.[b]	Person-Days	Infections, No.[c]	Incidence Rate (95% CI), Infections per 1000 Person-Days	Crude % Risk Reduction (95% CI), %[d]	*P* Value	Adjusted Risk (95% CI), % Reduction[d,e]	*P* Value
No prior infection								
Unvaccinated	2126	158 061	269	1.70 (1.50–1.92)	Reference	…	Reference	…
1–13 d since receipt of 1st dose	1697	21 836	39	1.79 (1.27–2.44)	16.2 (−19.9 to 41.4)	.334	40.9 (10.9–60.9)	.0112
≥14 d after 1st dose to receipt of 2nd dose	1620	20 701	13	0.63 (.33–1.07)	64.8 (37.8–80.1)	<.001	73.8 (49.8–86.4)	<.001
1–13 d since receipt of 2nd dose	1486	19 115	12	0.63 (.32–1.10)	59.9 (26.4–78.1)	.003	72.2 (45.3–85.9)	<.001
Fully vaccinated	1399	116 174	28	0.24 (.16–.35)	79.3 (69.0–86.1)	<.001	83.9 (74.4–89.9)	<.001
Previously infected								
Unvaccinated	4447	375 642	198	0.53 (.46–.61)	68.0 (61.5–73.4)	<.001	64.2 (41.5–78.0)	<.001
1–13 d since receipt of 1st dose	3379	43 635	45	1.03 (.75–1.38)	49.2 (29.5–63.5)	<.001	67.6 (37.3–83.2)	.001
≥14 d after 1st dose to receipt of 2nd dose	3229	41 975	19	0.45 (.27–.71)	74.0 (58.0–84.0)	<.001	79.6 (61.8–89.1)	<.001
1–13 d since receipt of 2nd dose	2956	38 269	19	0.50 (.30–.78)	71.2 (53.2–82.3)	<.001	81.7 (58.0–92.0)	<.001
Fully vaccinated	2801	232 666	46	0.20 (.14–.26)	81.5 (74.4–86.7)	<.001	85.0 (76.9–90.2)	<.001

Abbreviations: CI, confidence interval; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Unvaccinated was defined as having received zero doses of any coronavirus disease 2019 (COVID-19) vaccine; fully vaccinated, as ≥14 days after receipt of the second dose of Pfizer-BioNTech COVID-19 vaccine.

[b]Because vaccination status is time varying, sample sizes for each vaccination status are not mutually exclusive.

[c]Infection was defined as a positive result of a laboratory-based polymerase chain reaction test.

[d]Percentages were calculated as (1 − hazard ratio) × 100.

[e]A priori selected variables anticipated to be confounders (including age, sex, race and ethnicity, borough, neighborhood poverty, neighborhood political affiliation, calendar week, and the primary long-term care facility where an individual worked) were used to construct inverse probability of treatment weights. Race and ethnicity are imputed for 4295 (49.9%) missing observations. The adjusted percentage reduction in risk and 95% confidence intervals were pooled from 50 imputed data sets.

were unable to determine dates of prior infection using antibody test results, most infections in our cohort likely occurred in March and April 2020 since most first-wave cases in the NYC general population occurred during these months [37]; this suggests that most prior infections in our cohort occurred 10–11 months before the median person-time start date in the primary analysis and 9–10 months before the median person-time start date in the secondary analysis. These individuals were 55% and 64% less likely in primary and secondary analyses, respectively, to have an incident infection over the subsequent 3–5 months of the study period if they remained unvaccinated. However, this protection increased to >80% after vaccination, emphasizing the importance of vaccination for maintaining protection against reinfection.

The current study has several strengths. Routine weekly testing among all cohort members reduced potential biases from differential testing behaviors among exposure groups by ensuring equal opportunities for detection of infection across groups. Furthermore, high uptake of serologic testing in our cohort as the first wave of the pandemic in NYC subsided allowed us to identify individuals with or without infection before vaccine availability, despite limited diagnostic testing during the first wave.

However, these data also have limitations. There may be residual confounding, particularly owing to imperfect imputation of race/ethnicity among persons for whom these data were missing and remaining imbalance between covariates across exposure groups in some data sets, although E-values indicate that this was unlikely to nullify findings. In addition, there may be mislinkage across testing and vaccination records, leading to misclassification of vaccination status or incident SARS-CoV-2 infection. To reduce the risk of misclassifying vaccination status, we used a high (>90%) match threshold between testing and vaccination records and excluded persons with match probabilities indicating uncertainty in true vaccination status. Any remaining misclassification would likely bias estimates toward the null; our estimates may therefore be conservative. To reduce the risk of misclassifying incident infection, we manually reviewed a random sample of 880 persons for overmatching (ie, 2 people linked under a single unique identifier) within ECLRS and identified 2 (0.2%) instances of overmatching, neither of which resulted in a misclassified outcome.

Our analyses were also limited by the time frame in which weekly testing was required for LTCF staff, which ended before

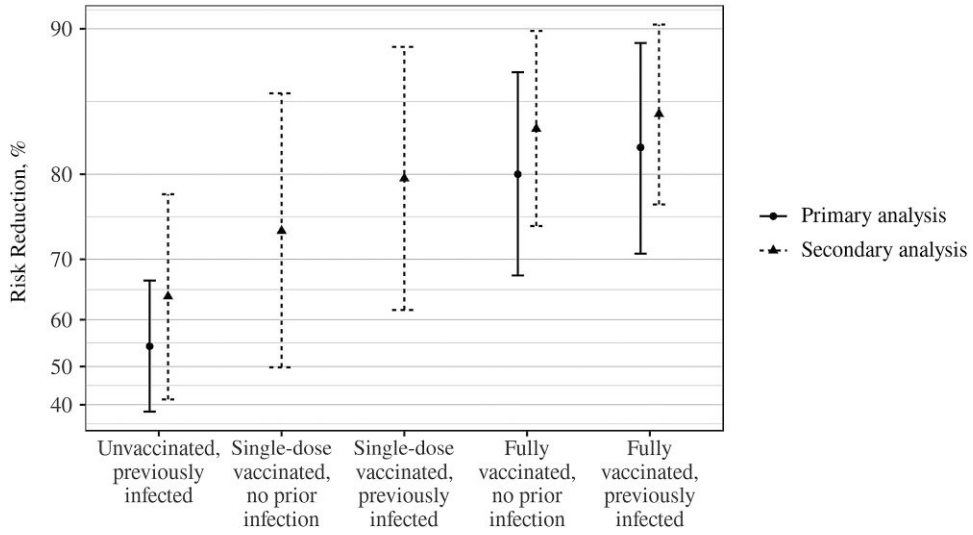

Figure 2. Percentage reduction in risk of severe acute respiratory syndrome coronavirus 2 infection, compared with unvaccinated persons without prior infection, by vaccination and prior infection status. Study population included long-term care facility staff in New York City from December 2020 to June 2021. Percentages were calculated as (1 − hazard ratio) × 100 and are shown on a log scale. Unvaccinated was defined as having received zero doses of any coronavirus disease 2019 (COVID-19) vaccine; single-dose vaccinated, as ≥14 days after receipt of the first dose of Pfizer-BioNTech COVID-19 vaccine until receipt of the second dose; and fully vaccinated, as ≥14 days after receipt of the second dose of Pfizer-BioNTech COVID-19 vaccine. In the primary analysis, person-time for vaccinated persons began ≥14 days after receipt of the second dose, and person-time for unvaccinated persons began on the earliest date when persons could have been fully vaccinated. In the secondary analysis, person-time began for all individuals on the date of the first on-site vaccination clinic held at any of the long-term care facilities where they worked.

the predominance of Delta and Omicron variant infections. As a result, it is unknown whether our findings can be generalized to currently circulating strains. While other analyses demonstrate that full vaccination after infection provides better protection against Delta variant infections than prior infection alone [3, 4], future research should continue to evaluate whether full vaccination provides additional protection beyond prior infection against emerging variants. We were also unable to evaluate whether the duration of vaccine-induced protection differed by prior infection status.

In conclusion, full vaccination reduced SARS-CoV-2 infection risk by ≥80% among all persons and increased the protection conferred by prior infection alone among those with a prior infection. These findings support recommendations that all eligible persons, regardless of prior infection, be vaccinated against COVID-19.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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