Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: White EM, Yang X, Blackman C, et al. Incident SARS-CoV-2 infection among mRNA-vaccinated and unvaccinated nursing home residents. N Engl J Med 2021;385:474-6. DOI: 10.1056/NEJMc2104849

SUPPLEMENTARY APPENDIX

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Supplementary Methods

This supplementary appendix provides additional details on the data sources and methods used to examine incident SARS-CoV-2 infections following mRNA vaccination in a large population of nursing home residents. Genesis Healthcare is the largest long-term care provider in the U.S. and, since March 2020, has transferred detailed clinical data to Brown University nightly under an IRB-approved Data Use Agreement. These data have been used in multiple prior analyses to characterize SARS-CoV-2 infections and outcomes in nursing home residents.[1-4]

Data Sources

Genesis data include the Electronic Health Record (EHR), Minimum Data Set (MDS), and a database used by the organization to track the vaccination clinics. All EHR and MDS data are available from January 2020 onward, covering the duration of the pandemic. All data files include unique de-identified resident study IDs and facility IDs that allow for linkage. In addition to the Genesis data, we obtained county SARS-CoV-2 prevalence data from the Johns Hopkins Coronavirus Resource Center. Each data source is described below.

Electronic Health Record. Genesis centrally hosts its own EHR, PointClickCare. The following EHR elements were used in the analysis:

(1) ***Daily census.*** Person-day level file that provides each resident's disposition on a given day and captures transfers, discharges, and deaths.
(2) ***Immunization records.*** Dates and descriptions of immunization administrations and consents. Records include vaccine manufacturer.
(3) ***SARS-CoV-2 test records.*** Polymerase chain reaction and antigen test dates and results. These include tests done in-house and by outside labs.
(4) ***Nursing change in condition notes.*** Licensed nurses assess all residents and check vital signs at least once daily. Any new symptoms are documented in structured chain in condition notes that include vital signs and checkboxes for symptoms. From these notes, we flag the following as SARS-CoV-2 related signs and symptoms: cough, hypoxia, fever, chills, dyspnea, tachycardia, nausea, vomiting, diarrhea, chest congestion, altered mental status, rhinorrhea, nasal congestion, sore throat, malaise, taste changes, headache, loss of appetite, respiratory arrest, and respiratory infection. Nursing notes are reviewed regularly by nursing supervisors

[1] White EM, et al. Asymptomatic and Presymptomatic Severe Acute Respiratory Syndrome Coronavirus 2 Infection Rates in a Multistate Sample of Skilled Nursing Facilities. JAMA Intern Med. 2020 Dec 1;180(12):1709-1711. doi: 10.1001/jamainternmed.2020.5664.
[2] Panagiotou OA, et al. Risk Factors Associated With All-Cause 30-Day Mortality in Nursing Home Residents With COVID-19. JAMA Intern Med. 2021 Jan 4:e207968. doi: 10.1001/jamainternmed.2020.7968. [Epub ahead of print.]
[3] White EM, et al. SARS-CoV-2 antibody detection in skilled nursing facility residents. J Am Geriatr Soc. 2021 Feb 5. doi: 10.1111/jgs.17061. [Epub ahead of print]
[4] Kosar, CM, et al. COVID-19 Mortality Rates Among Nursing Home Residents Declined From March to November 2020. Health Affairs. 2021 Mar 11; 40(4):655-663. doi: 10.1377/hlthaff.2020.02191

and managers within facilities, and also undergo periodic quality control checks at the organizational level.

Minimum Data Set. The MDS is a federally-mandated clinical assessment tool completed on admission and quarterly thereafter for all residents of Medicaid- and Medicare-certified nursing homes. The MDS includes resident demographics, validated measures of cognitive and physical function, diagnoses, and other clinical indicators.

Genesis vaccination tracker. Genesis coordinated its SARS-CoV-2 vaccinations through the federal Pharmacy Partnership for Long Term Care Program, which provided each facility with three clinics to vaccinate both staff and residents. In our analysis, we included vaccinations administered between the first and second clinics, which began December 18, 2020 and completed February 15, 2021. Genesis maintains a daily vaccination tracker which includes clinic dates, and number and rates of staff and residents who were eligible and vaccinated at each clinic.

Johns Hopkins Coronavirus Resource Center.[5] Publicly-available daily county SARS-CoV-2 incidence and prevalence data which we link to the Genesis data based on the county in which a nursing home is located.

Study Participants

Using the immunization records, we identified two groups of vaccinated residents:

(1) Residents who received at least one mRNA vaccine dose as of February 15, 2021;
(2) Residents who received both mRNA vaccine doses as of February 15, 2021. All residents in this category are included in the first category.

Individuals with incident SARS-CoV-2 infection (a new positive test) in the 90 days prior to dose 1 were excluded from analysis. Those who tested positive between doses 1 and 2 were included in the first category, but excluded from the second category.

We identified a third group of unvaccinated residents, defined as:

(3) Residents who were present in the nursing home on the day of their facility's first vaccination clinic, but as of March 31, 2021, were not vaccinated. We identified clinic dates from the Genesis vaccination tracker and used the daily census to determine that residents were alive in the nursing home on the clinic 1 date.

For this group, individuals who had incident SARS-CoV-2 infection in the 90 days prior to the clinic 1 date were excluded from analysis.

Though we excluded residents with recent incident infection from the study sample, we did include them in our supplementary analyses to compare baseline infection rates between unvaccinated and vaccinated residents in the month before the vaccination clinics started (November 17, 2020 to December 17, 2020).

[5] Johns Hopkins Coronavirus Resource Center; 2021. https://coronavirus.jhu.edu/ Accessed April 16, 2021

Identification and Classification of Incident SARS-CoV-2 Cases

Testing frequency. Genesis operates under a testing policy consistent with Centers for Disease Control and Prevention guidance. Weekly, they classify all of their nursing homes into risk categories based on county incidence and test positivity rates, and whether the facility has a current outbreak (i.e. any new staff or resident cases in the prior 14 days). During an outbreak, both residents and staff undergo surveillance testing every 3 to 7 days. Additionally, regardless of outbreak status, residents are tested on admission to the facility, if they develop any new SARS-CoV-2-related signs or symptoms, or if they have a potential exposure. In the absence of an outbreak, only staff undergo routine surveillance testing, which varies in frequency from twice weekly up to once a month depending on the community risk level.

Incident SARS-CoV-2 cases. For vaccinated residents, we counted the number who newly tested positive after each vaccine dose. For unvaccinated residents, we anchored the observation window for incident cases to the date of the first vaccine clinic in the resident's facility. We did this to have a comparable period that paralleled when the majority of vaccinated residents in the facility were receiving their first and second doses.

Symptom classification. We classified residents with incident infection as symptomatic if the nursing notes documented new SARS-CoV-2 symptoms occurring from 5 days before up to 14 days after their positive test. If no new symptoms were documented in this time window, we classified the resident as asymptomatic. As a quality check, a medical director completed full chart reviews on the fully vaccinated residents who developed incident symptomatic infection and confirmed the findings.

Supplementary Analyses

Summary

Table S1 compares demographic and clinical characteristics of vaccinated and unvaccinated residents in the study sample. Compared to vaccinated residents, unvaccinated residents were on average younger, and more likely to be male and Black. Additionally, unvaccinated residents had lower rates of advanced cognitive impairment, coronary artery disease, heart failure, chronic obstructive pulmonary disease, and hypertension compared to vaccinated residents; but higher rates of chronic kidney disease. Baseline infection rates from November 17-December 17, 2020 for the full population (study sample plus residents who were excluded due to recent infection) were similar for vaccinated and unvaccinated residents, though unvaccinated residents were more likely to be hospitalized.

Table S2 presents the data from the main analysis, stratifying residents based on whether they lived in nursing homes located in counties with low, moderate, or high county SARS-CoV-2 incidence during the vaccination period. Incident infections were slightly more frequent among vaccinated residents living in nursing homes in the highest risk counties compared to those in low and moderate risk counties, particularly in earlier weeks. Still, even in the highest risk counties, post-vaccination incident infection rates dropped to 14/3,449 (0.4%) for fully vaccinated residents and 92.9% of those were asymptomatic. The highest incident infection rates were seen among unvaccinated residents in the highest risk counties in the initial 14 days after the first vaccine clinic, in which 75/977 residents (7.7%) were infected. As with vaccinated residents, infection rates declined substantially over time among unvaccinated individuals, even in the highest risk counties.

Table S3 presents the same information as Table 2 but in this case stratifies residents based on staff vaccination rates in the nursing home where they lived. Staff were vaccinated during the same clinics as residents, and vaccination rates were pulled from the Genesis vaccination tracker. We did not observe consistent patterns in resident incident infections relative to staff vaccination rates, except for noting that a slightly higher proportion of residents infected post-dose 2 in nursing homes with moderate to high staff vaccination rates were asymptomatic compared to residents in nursing homes with low vaccination rates. Still, by the time most residents were fully vaccinated, incident infection rates were extremely low across nursing homes.

Figure S1 shows incident SARS-CoV-2 cases by day and symptom status, illustrating the preponderance of asymptomatic cases, particularly among vaccinated residents. For vaccinated residents, incident cases declined steadily from 15 days post-dose 1 onward. Nineteen of the 38 cases that occurred more than 14 days after dose 2 occurred between days 15-21, suggesting that those residents may have been infected before they reached full immunity. For both vaccinated and unvaccinated residents, cases in later weeks are sparse and isolated events.

Table S1. Resident characteristics

	Received at least dose 1	Unvaccinated
Study sample, n	**18242**	**3990**
Female, n (%)	11248 (61.7%)	2264 (56.7%)
Age, median (IQR)	78.0 (68.2, 86.7)	75.9 (66.9, 84.8)
Race/ethnicity, n (%)		
Black	2270 (12.4%)	805 (20.2%)
Hispanic/Latino	774 (4.2%)	181 (4.5%)
White	14348 (78.7%)	2699 (67.6%)
Other	419 (2.3%)	90 (2.3%)
Unknown	431 (2.4%)	215 (5.4%)
Advanced cognitive impairment,[1] n (%)	6361 (34.9%)	1060 (26.6%)
Advanced functional impairment,[2] n (%)	9174 (50.3%)	1939 (48.6%)
Advanced CHESS score,[3] n (%)	3717 (20.4%)	805 (20.2%)
Diagnoses, n (%)		
Coronary artery disease	4400 (24.1%)	849 (21.3%)
Heart failure	3985 (21.8%)	762 (19.1%)
Chronic obstructive pulmonary disease	4487 (24.6%)	879 (22.0%)
Diabetes	6863 (37.6%)	1477 (37.0%)
Hypertension	13813 (75.7%)	2874 (72.0%)
Chronic kidney disease	4315 (23.7%)	1014 (25.4%)
Study sample plus residents with incident SARS-CoV-2 infection in the 90 days prior to study window,[4] n	**21620**	**4860**
SARS-CoV-2 outcomes, November 17, 2020 – December 17, 2020		
Incident infection, n (%)	1741 (8.1%)	385 (7.9%)
Hospitalized within 30 days of diagnosis, n (%)	239 (1.1%)	81 (1.7%)

Abbreviations: IQR, interquartile range; CHESS, Changes in Health, End-Stage Disease and Symptoms and Signs Scale

Notes*:* Resident characteristics derived from the electronic health record and Minimum Data Set (MDS). Vaccination status is as of February 15, 2021.

[1] MDS Cognitive Function Scale of 3 or 4.

[2] MDS Activities of Daily Living score of 19 or higher.

[3] The MDS CHESS score incorporates functional, clinical, and prognostic indicators to identify advanced illness (higher scores). We identified advanced CHESS scores as 2 or higher.

[4] Because residents are excluded from the study sample if they had incident SARS-CoV-2 infection in the 90 days prior to dose 1 (for vaccinated residents) or the first vaccine clinic date (for unvaccinated residents), we report incident SARS-CoV-2 infection and hospitalization rates for the entire resident population (study sample plus those who were excluded). Rates reported for the month prior to the first date of the vaccine clinics for Genesis nursing homes (December 18, 2020).

Table S2. Incident SARS-CoV-2 infections in residents living in nursing homes located in counties with low, moderate, and high county SARS-CoV-2 incidence rates during the vaccination period

	Low county incidence (Less than 250 cases per 10,000 population)		Moderate county incidence (251-337 cases per 10,000 population)		High county incidence (338-529 cases per 10,000 population)	
	Total	**Percent (%) asymptomatic**	**Total**	**Percent (%) asymptomatic**	**Total**	**Percent (%) asymptomatic**
Residents vaccinated with at least dose 1, n	**5940**		**7268**		**5034**	
Tested positive 0-14 days after dose 1, n(%)	245 (4.1%)	70.2%	229 (3.2%)	71.2%	348 (6.9%)	72.4%
Tested positive 15-28 days after dose 1, n(%)	70 (1.2%)	67.1%	71 (1.0%)	70.4%	109 (2.2%)	75.2%
Residents vaccinated with doses 1 & 2, n	**4142**		**5457**		**3449**	
Tested positive 0-14 days after dose 2, n(%)	29 (0.7%)	86.2%	52 (1.0%)	76.9%	49 (1.4%)	91.8%
Tested positive >14 days after dose 2, n(%)	10 (0.2%)	50.0%	14 (0.3%)	78.6%	14 (0.4%)	92.9%
Unvaccinated residents	**1388**		**1625**		**977**	
Tested positive 0-14 days after clinic 1 held, n(%)	51 (3.7%)	66.7%	47 (2.9%)	72.3%	75 (7.7%)	62.7%
Tested positive 15-28 days after clinic 1 held, n(%)	10 (0.7%)	70.0%	39 (2.4%)	74.4%	20 (2.0%)	30.0%
Tested positive 29-42 days after clinic 1 held, n(%)	5 (0.4%)	80.0%	7 (0.4%)	71.4%	4 (0.4%)	100.0%
Tested positive >42 days after clinic 1 held, n(%)	3 (0.2%)	66.7%	7 (0.4%)	85.7%	2 (0.2%)	100.0%

Notes: Nursing homes tertiled by county incidence rates, i.e. incident SARS-CoV-2 cases per 10,000 population in the county during the vaccination period, December 18, 2020 to February 15, 2021. County data from the Johns Hopkins Coronavirus Resource Center.

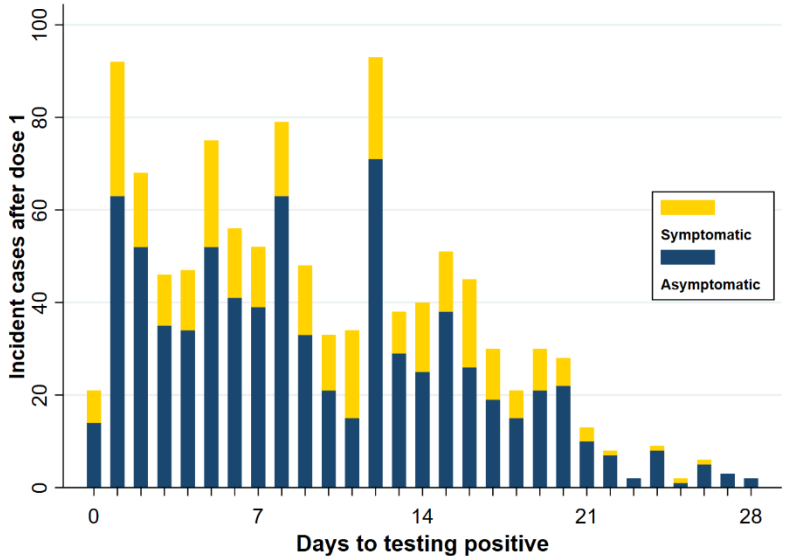
Table S3. Incident SARS-CoV-2 infections in residents living in nursing homes with low, moderate, and high staff vaccination rates

	Low staff vaccination (Less than 58.7% of staff vaccinated)		Moderate staff vaccination (58.7 - 69.2% of staff vaccinated)		High staff vaccination (69.3 - 95.7% of staff vaccinated)	
	Total	**Percent (%) asymptomatic**	**Total**	**Percent (%) asymptomatic**	**Total**	**Percent (%) asymptomatic**
Residents vaccinated with at least dose 1, n	**5691**		**6291**		**6260**	
Tested positive 0-14 days after dose 1, n(%)	266 (4.7%)	71.1%	267 (4.2%)	74.2%	289 (4.6%)	69.2%
Tested positive 15-28 days after dose 1, n(%)	83 (1.5%)	75.9%	50 (0.8%)	62.0%	117 (1.9%)	72.6%
Residents vaccinated with doses 1 & 2, n	**4001**		**4579**		**4468**	
Tested positive 0-14 days after dose 2, n(%)	46 (1.1%)	80.4%	32 (0.7%)	87.5%	52 (1.2%)	86.5%
Tested positive >14 days after dose 2, n(%)	18 (0.4%)	72.2%	8 (0.2%)	75.0%	12 (0.3%)	83.3%
Unvaccinated residents	**1629**		**1296**		**1065**	
Tested positive 0-14 days after clinic 1 held, n(%)	73 (4.5%)	65.8%	65 (5.0%)	66.2%	35 (3.3%)	68.6%
Tested positive 15-28 days after clinic 1 held, n(%)	31 (1.9%)	64.5%	15 (1.2%)	46.7%	23 (2.2%)	65.2%
Tested positive 29-42 days after clinic 1 held, n(%)	6 (0.4%)	83.3%	4 (0.3%)	75.0%	6 (0.6%)	83.3%
Tested positive >42 days after clinic 1 held, n(%)	6 (0.4%)	83.3%	3 (0.2%)	66.7%	3 (0.3%)	100.0%

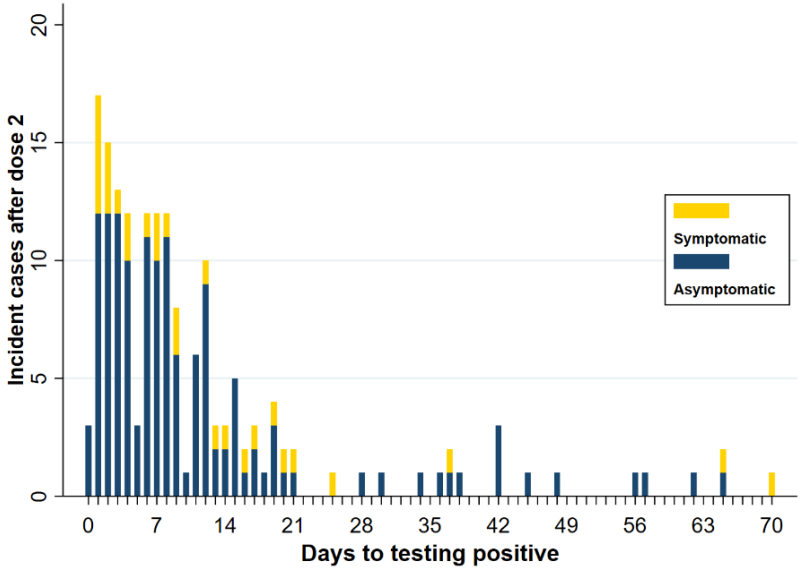
Notes. Nursing homes stratified by tertiles of staff vaccination rates as of February 17, 2021. Staff vaccinations occurred simultaneously with resident vaccinations and rates were tracked by the organization.

Figure S1. Incident SARS-CoV-2 cases by day and symptom status for nursing home residents who were (A) vaccinated with at least dose 1, (B) vaccinated with doses 1 and 2, and (C) unvaccinated

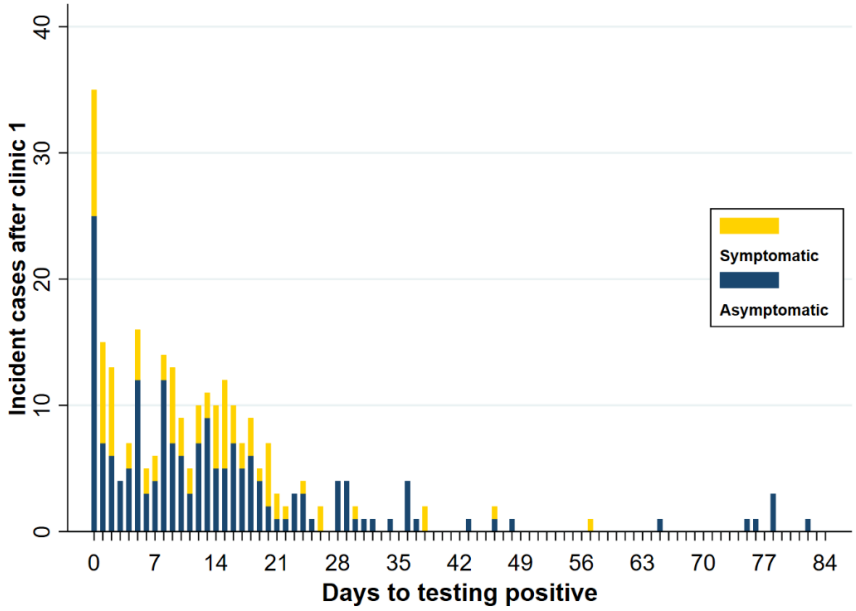
(A) Vaccinated residents: Incident cases after dose 1



(B) Vaccinated residents: Incident cases after dose 2



(C) Unvaccinated residents: Incident cases after first vaccine clinic held



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