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Kinetics of SARS-CoV-2 Shedding in Nursing Home Residents and Staff

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Abstract

Background: Nursing homes (NHs) were disproportionately affected by the COVID-19 pandemic. However, little is known regarding the kinetics of SARS-CoV-2 shedding in NH residents and staff, which could inform treatment and infection prevention.

Methods: We enrolled NH residents and staff in eight US states from April to November 2023 and analyzed the kinetics of SARS-CoV-2 using serial antigen and molecular (RT-PCR) tests, whole genome sequencing, and viral culture (VC). Symptoms, vaccination, and treatment were collected via interviews and chart review. Viral load trajectories were modeled with gamma distribution functional forms. Antigen and VC test positivity over time were assessed using a Chi-squared test.

Results: Of the 587 enrolled participants, 86 tested positive and 73 underwent testing for ≥ 10 days; most residents (78%) and staff (87%) had ≥ 3 COVID-19 vaccine doses. The modeled SARS-CoV-2 proliferation period (period prior to reaching peak viral load) had ended for 48% (14/29) of residents and 56% (9/16) of staff when they took the initial RT-PCR test. Both antigen and VC showed higher positivity rates early in the course of disease (Days 0–5 vs. Days ≥ 6) (antigen: $p < 0.001$, VC: $p < 0.001$). VC positivity was 15% after Day 5 (14/96); two participants were VC positive after Day 10.

Conclusions: Peak viral load occurs early in the disease, suggesting asymptomatic and presymptomatic transmission may be a significant driver of transmission. Only two participants had a positive VC after Day 10, supporting current isolation and return to work recommendations.

Keywords

COVID-19; kinetics; nursing home; SARS-CoV-2; shedding

1 | Introduction

The COVID-19 pandemic caused over two million SARS-CoV-2 cases in nursing home (NH) residents and staff and over 172,000 residents and 3000 staff deaths in the United States as of July 2024 [1]. Infection prevention and control (IPC) policies like isolation and quarantine of infected or exposed residents and exclusion of infected staff can reduce transmission. However, these policies can negatively impact resident well-being, be costly for NHs, and exacerbate staff shortages [2]. Despite the implementation of IPC policies, many facilities struggle with outbreaks and uncertainty regarding appropriate testing methods, isolation periods, and contact tracing for both residents and staff. Improved understanding of viral kinetics in NH residents and staff can help enhance IPC recommendations.

To date, studies on viral kinetics of SARS-CoV-2 have pre-dominantly focused on community-dwelling adults [3–5]. However, since viral kinetics, its association with infectiousness, and immune response may vary depending on host factors, including age, underlying comorbidities, prior COVID-19 vaccination and/or infection, and immune status [6, 7], results from community-dwelling adults may not generalize to NH residents. Additionally, evidence suggests that older adults may clear SARS-CoV-2 slower than

younger adults, potentially prolonging transmission in NHs [8] where transmission remains poorly understood. We prospectively enrolled NH residents and staff across 24 NHs from April 2023 to November 2023 and examined the kinetics of SARS-CoV-2 shedding using serial antigen tests, molecular reverse transcription polymerase chain reaction (RT-PCR) tests, whole genome sequencing (WGS), and viral culture (VC).

2 | Methods

2.1 | Study Design

This study was conducted through the Nursing Home Public Health Response Network, a collaborative of eight academic institutions across the United States (see Supporting Information), approximately 50 NHs, a central coordinating center, and a central laboratory that collects and shares real-time data with the Centers for Disease Control and Prevention (CDC) to aid in response to emerging infectious diseases in NHs. From April to November 2023, 24 NH infection preventionists (IPs) performed surveillance per CDC guidance [9] and their facility protocols and notified the academic study team within 24 h of identifying a resident or staff member positive for SARS-CoV-2.

There were two pathways for adult resident and adult staff enrollment, prospectively or after the identification of a positive SARS-CoV-2 test. Residents and staff, regardless of enrollment status, were identified as positive for SARS-CoV-2 by routine testing and public health surveillance, which included exposure testing with both antigen and RT-PCR on Days 1, 3, and 5 per public health recommendations [10]. If prospectively enrolled, roommates of infected residents received more frequent testing on Days 1–7 after exposure. Potential participants were excluded if they had impaired decision-making capacity and no legally authorized representative (LAR) or were unable to communicate in English. Study staff followed enrolled individuals who tested positive for SARS-CoV-2 (“cases”) for 14 days from the first positive test. During each daily testing, two anterior or mid-turbinate nasal swabs were collected using standard methods. One swab was used to conduct on-site antigen testing (CLINITEST or Quidel) per the manufacturer’s instructions. The second swab was shipped to a central laboratory (Marshfield Clinical Research Institute) for further testing (described below). Study staff obtained information on symptoms and antiviral treatment at each testing event via resident interview and/or chart review. Enrolled NH staff self-collected their swabs and directly entered survey responses documenting symptoms, antiviral treatment, and antigen results in a REDCap survey. Participants were allowed to remain in the study if a testing day was skipped.

Study staff abstracted demographic and clinical information (i.e., comorbid conditions, COVID-19 vaccination history, and SARS-CoV-2 infection and treatment history) from resident NH records of enrollees. Information not available from the record was collected through discussion with the resident or their LAR. NH staff enrollees received a questionnaire via email or text to self-complete. Data collection for all sites used standard forms in a centralized REDCap (Research Electronic Data Capture) managed by Abt Global and housed at Vanderbilt University. Participants were compensated for completing milestones of study participation.

All study sites used a common protocol, data collection tools, and standard operating procedures. Abt served as a central Institutional Review Board (IRB) with reliance from each site's IRB. The Abt IRB determined that the study presented no greater than minimal risk per 45CFR46 and approved the request for a waiver of written informed consent per 45CFR46.117(c)(1)(ii) though some site IRBs required written consent (JHU, UoP) [11]. This study was funded by the US CDC. This study was reviewed and approved by the Abt, Brown University, Case Western Reserve University, Emory University, Johns Hopkins University, Oregon State University, University of Michigan, University of Pittsburgh, and University of Wisconsin IRBs.¹

2.2 | Measurement of SARS-CoV-2 by RT-PCR, WGS, and Viral Culture

All swabs sent to Marshfield were tested by qualitative RT-PCR using the TaqPath COVID-19, FluA, FluB Combo Kit on QuantStudio 7 Pro. The qualitative RT-PCR returned cycle threshold (Ct) values, which are inversely correlated with the viral RNA copy number (load) in a sample. Those that tested positive ($Ct \leq 37.0$) underwent quantitative RT-PCR testing using the CDC Influenza SARS-CoV-2 (Flu SC2) Multiplex Assay. All Ct values were calculated by Marshfield, which verified a direct association with the log viral load (quantitative result) through a standard curve generated from synthetic SARS-CoV-2 RNA [12]. VC and WGS were performed on a participants' first test specimen with a $Ct < 30$; this cutoff was selected based on previous work conducted by Marshfield [12]. WGS was performed by Marshfield. VC was performed by St. Jude Children's Research Hospital on one qualitative RT-PCR specimen with $Ct < 30$ collected during each of the following intervals for each participant: Days 1–2, 3–5, 6–8, 9–11, and 12–14. If multiple samples had $Ct < 30$ in an interval, VC was performed on the specimen with the lowest Ct value. Infectious virus particles were quantified using an immune-staining-based TCID₅₀ in which nasal samples were titrated and incubated for 4–5 days on Vero cells ectopically expressing TMPRSS2 and human ACE2. Infected cell monolayers were stained, and virus-positive cells were identified by two-fold increase in optical density compared to the mean value of negative wells.

2.3 | Data Analyses

Descriptive analyses were conducted to describe enrolled participants and cases. We reported demographic data and WGS on all cases, but restricted statistical analysis to cases with ≥ 10 days of testing of any test type to limit the effect of loss to follow-up. A Chi-squared test was used to compare the proportion of antigen and VC positives during early illness (Days 0–5) compared to later illness (Day ≥ 6) and for $Ct < 25$ compared to $Ct \geq 25$. Resident's and staff's duration of shedding was compared using Kaplan–Meier survival analysis on time from first positive to first negative test result for RT-PCR and antigen testing, restricted to patients who had at least 10 days of follow-up after first positive test of given type. Similar analyses were conducted for symptomatic vs. asymptomatic cases with the addition of time to first $Ct > 30$. Log-rank tests were used to compare survival curves.

¹See 45 C.F.R. part 46.101(c); 21 C.F.R. part 56 and 45 CFR 46.102(a) HHS/OHRP 2008 Engagement Guidance at III B(1–11).

To estimate the viral load within an individual over time (i.e., viral trajectory), gamma distribution functional forms were fitted to Ct values [13, 14]. For each participant, we used a likelihood-based approach to calculate optimal gamma distribution parameters (shape, scale, and location) and a scaling coefficient. This produced an estimated viral trajectory for all participants. Participant viral trajectories were aligned by their estimated peak viral load, then the data from individuals were used to fit a new population-level gamma distribution functional form for staff and residents separately. Participants with no measured Ct value before estimated peak viral load were excluded from population-level fitting. From these estimated population trajectories, we calculated proxies for the proliferation period (time from passing the RT-PCR positivity threshold [$Ct \leq 37$] to the peak Ct value) and decay period (time from peak Ct to passing the RT-PCR positivity threshold) with non-parametric 95% confidence intervals (CIs). Participants with fewer than five measured Ct values < 43.64 were excluded from individual functional form fitting, as this was deemed insufficient to fit the viral trajectory. Participants treated with antivirals were also excluded from individual functional form fitting because antivirals alter the viral trajectory. See Supporting Information for details.

Descriptive analyses of viral load rebound were conducted for all participants regardless of antiviral treatment. Rebound was defined as a 10-fold increase where the amount of increase was at or above five log copies per milliliter after the completion of SARS-CoV-2 antiviral treatment, or if the participant was untreated, 7 days after the initial positive test [15]. Duration of antiviral treatment was assumed to be 5 days [16] unless a longer treatment course was documented.

2.4 | Role of the Funding Source

CDC staff were involved in the study design, in the writing of the report, and in the decision to submit the paper for publication.

3 | Results

Across the 24 NHs in eight states, 587 participants (275 residents, 312 staff) were enrolled (Table S3). One hundred and thirty-five residents and 48 staff tested positive during the study period, and 86 of these (“cases”) agreed to enroll (63/135 residents, 23/48 staff) (Table 1). Of the 86 enrolled cases, 73 (85%; 51/63 residents, 22/23 staff) were tested for ≥ 10 days after an initial positive test (Figure 1). Twenty-four of the 73 cases were the index case for an outbreak in the facility.

Sixty-eight percent (59/86) of cases were 60 years or older (Table 1). Thirty-eight percent (33/86) of cases reported never having a previous SARS-CoV-2 infection; 27% (23/86) reported one previous infection, and 12% (10/86) reported having two or more infections (Table S1). Most resident cases (78%) and staff cases (87%) had received at least three COVID-19 vaccine doses prior to entering the study; 6/86 cases (7%; three residents, three staff) had been vaccinated in the 6 months prior to testing positive, with half (3/6) having been vaccinated less than 2 weeks prior to testing positive.

Most resident cases did not receive antivirals; 59% (37/63) received no treatment, 11% (7/63) were treated with nirmatrelvir–ritonavir, and 25% (16/63) were treated with molnupiravir. There was no treatment data for 3/63 residents. Seventy-eight percent of staff (18/23) were untreated, and 13% (3/23) received nirmatrelvir–ritonavir. There was no treatment data for 2/23 staff (Table S1).

Among the 86 cases, 70 (81%; 61 residents, 9 staff) had documented pre-existing comorbid conditions. Resident cases most frequently reported a history of hypertension (75%, 46/61), diabetes (34%, 21/61), or cerebrovascular disease (31%, 19/61). Staff cases most frequently reported diabetes (67%, 6/9) and hypertension (33%, 3/9) (Table S2). During the study, one resident and zero staff were hospitalized, and no deaths were reported.

All identified SARS-CoV-2 variants were Omicron sublineages; the most common lineages were XBB.1.16 ($n = 14$), HV.1 ($n = 12$), EG 5.1.1 ($n = 12$), XBB.1.16.6 ($n = 8$), and FL.1.5.1 ($n = 8$) (Figure S1).

3.1 | Duration of Shedding

Residents tested positive by both antigen and RT-PCR for longer than staff. However, this result was only statistically significant for RT-PCR results ($p = 0.007$) (Figure 2). Five days after the first positive test, 29/51 of residents (57%) and 13/21 of staff (62%) remained antigen positive, and 37/42 (88%) and 16/20 (80%), respectively, remained RT-PCR positive. Ten days after the first positive test, 10/51 of residents (20%) and 1/21 of staff (5%) remained antigen positive, and 24/42 (57%) and 4/20 (20%), respectively, remained RT-PCR positive. The median duration of antigen positivity was 6 days in both residents and staff. The median duration of RT-PCR positivity was 11 days for residents and 8 days for staff.

Nine participants (eight residents, one staff) were considered asymptomatic (no symptoms reported during 14-day survey period). Symptomatic participants (i.e., those with at least 1 day of reported symptoms) experienced a longer time to reach their first negative antigen test (median 7 vs. 4 days, $p < 0.001$) and Ct > 30 (median 7 vs. 4 days, $p = 0.013$). All asymptomatic participants tested antigen negative by day 6 and reached a Ct > 30 by Day 7 (Figure S2).

3.2 | Test Agreement

Of 218 RT-PCR-positive specimens that underwent VC, 68 (31%) were VC positive. Antigen tests were sensitive to VC positivity (96%) but not specific (28%). Both antigen and VC were more likely to be positive early (Days 0–5) (antigen: 82% [296/361] vs. 23% [113/500] $p < 0.001$, VC: 44% [54/122] vs. 15% [14/96] $p < 0.001$) and at lower Ct values (Ct < 25) (antigen: 90% [234/261] vs. 21% [109/528] $p < 0.001$, VC: 42% [66/157] vs. 3% [2/61] $p < 0.001$) by a Chi-squared test (Figures 3, 4).

Positive VC that occurred after Day 10 belonged to two participants who were treated with antivirals, were concurrently antigen positive, and experienced laboratory-defined rebound in viral shedding.

3.3 | Modeling Viral Kinetics With Gamma Distribution Functional Forms

Of the 29 residents and 16 staff who met criteria for fitting individual gamma distribution function forms (i.e., ≥ 5 Ct values < 43.64 and no antivirals), only 15 (52%) residents and seven (44%) staff had at least one measured Ct value preceding the model estimated peak Ct value. This implied that the peak Ct value was missed for 48% of residents and 56% of staff.

At the population level, the functional form approximated proliferation period was 4.70 (95% CI 3.94, 7.27) days for residents and 3.35 (95% CI 1.84, 5.43) days for staff. The decay period was 10.83 (95% CI 9.71, 12.14) days for residents and 8.66 (95% CI 7.86, 9.67) days for staff (Figures S11, S12).

3.4 | Rebound

Nine residents and three staff in the study met criteria for rebound [15]. Three were treated with molnupiravir, four were treated with nirmatrelvir—ritonavir, four were untreated, and one had no treatment data. Of those who experienced rebound, 11 had specimens that were tested for VC during the rebound period and 55% (6/11) were positive (Figure S4).

4 | Discussion

The COVID-19 pandemic significantly impacted NH residents and staff underscoring the need to better understand the viral dynamics within these populations and this unique setting [18]. To our knowledge, this is the largest cohort of NH residents with longitudinal data on the kinetics of SARS-CoV-2 shedding to date. We found that despite active surveillance, approximately half of residents and staff were past peak viral load at the time regular testing began, residents experienced higher viral loads longer than staff, and most participants were VC negative after Day 10.

Based on the estimated viral trajectory, approximately half of residents and staff were past their peak viral load before RT-PCR testing began, despite performing proactive contact testing. This is a particular challenge in congregate living settings with large numbers of contacts, as substantial transmission can occur prior to identifying an initial positive case in a facility. Previous modeling in community settings suggests that up to 59% of cases may come from asymptomatic or pre-symptomatic transmission [13], and these numbers may be even higher in a congregate living setting. This makes implementation of IPC policies challenging and may support recommendations for universal masking, environmental testing such as wastewater surveillance, or regular test-based screening of staff members when SARS-CoV-2 indicators are high.

In our study, residents were typically RT-PCR positive longer than staff, which is consistent with other studies showing that older adults shed virus for longer than their younger counterparts [19, 20]. Our findings also suggest that symptomatic persons shed virus for longer than asymptomatic persons, which could be driven by a shorter infection duration in asymptomatic individuals or late identification of infection due to lack of symptoms. This is consistent with other studies comparing viral kinetics across a variety of clinical presentations, with more severe cases generally shedding virus for longer [20–22].

In healthcare settings, according to current guidance [9, 23], CDC recommends NH residents and staff with mild to moderate illness isolate for 10 days from initial positive test or symptom onset, assuming fever resolution and symptom improvement. Staff could return to work earlier if certain criteria, including negative viral testing, are met [23]. In this cohort of NH residents and staff with mild–moderate SARS-CoV-2 infection, replication competent virus was only isolated beyond Day 10 in individuals who experienced rebound, supporting current CDC recommendations. Additionally, most staff tested antigen-negative on or before Day 10; this, in addition to the high sensitivity of antigen test outcome and VC positivity, supports test-based strategies for early return to work.

In this prospective investigation, we also observed that despite access to antiviral therapy, treatment was under-utilized; 59% of residents received no treatment. The resident population included in this study was at higher risk for severe outcomes from SARS-CoV-2; 92% were 60 years or older, and of those who reported medical conditions, 34% had diabetes and 31% had cerebrovascular disease [24]. Underutilization of treatment is consistent with findings of larger cohorts [25] and shows that increasing access to antivirals and education about the benefits of treatment for preventing severe disease, death, and long COVID may be needed. Our study was not sufficiently powered to address the effect of treatment on the risk of viral rebound, but our limited data showed that rebound could occur in both treated and untreated individuals and was not associated with severe symptoms, hospitalization, or death in any subjects who met criteria, consistent with prior research [26]. Finally, while NH residents often suffer the most severe outcomes from COVID-19, our cohort presented with mild disease, low hospitalization rates, and no mortality across the cohort. This may have been due to high vaccination rates, hybrid immunity from previous vaccinations and natural infection, and circulating variants at the time of the investigation. Notably, only 3/86 (3%) cases who had been vaccinated within the past 6 months and were 2 weeks past their most recent vaccination tested positive for SARS-CoV-2 during the study period. Most cases in this cohort occurred prior to the rollout of the 2023–2024 COVID-19 boosters; therefore, we were not able to adequately assess the impact of the updated boosters on shedding. However, this low percentage suggests that vaccination within the past 6 months was largely protective. Previous analyses of community-dwelling adults have shown a reduced infectious period in individuals who were up to date on vaccination [27], and further support the benefits of regular vaccination for reducing transmission rates.

4.1 | Limitations and Strengths

Due to potential discomfort and the need to obtain two swabs for both antigen and RT-PCR tests, we used anterior nasal samples rather than nasopharyngeal samples, which may have resulted in lower detection of viral material and could have affected our assessment of viral load or antigen positivity. Our sample size was too small to determine significant differences in terms of clinical comorbidities, vaccination status, or symptoms; however, trends were consistent with previously published data. While nine residents appeared to exhibit rebound viral load, these data cannot be used to compare treatment types due to the low sample size and few patients who received treatment across the cohort. Finally, the study design relied on NH site IPs to notify the study team of new positive cases in the facility. There were instances when this notification process was delayed, leading to a lag in testing and

symptom assessment that reduced our ability to track the full viral trajectory of shedding among all enrolled individuals; we attempted to mitigate this limitation by having study staff on site in the facility and ensuring regular communication with the NHs.

This study had several strengths. By prospectively assisting with outbreak investigations and sampling exposed participants prior to symptoms, we were able to obtain a more complete view of viral shedding to visualize the peak of viral load, something that is often missed in studies which enroll participants days after an initial positive test or the development of symptoms. We were also able to identify individuals who tested positive but never developed symptoms and compare kinetics in asymptomatic and symptomatic individuals. Further, because all samples were processed in a central laboratory, we could reliably compare Ct values, VC, and viral loads across the study participants, a limitation of other multi-center studies relying on several laboratories.

5 | Conclusion

Following the COVID-19 public health emergency NHs continue to struggle with staff shortages, fatigue, and isolation for residents. Understanding how to balance these challenges with IPC and safety of the residents and staff can be informed by understanding viral kinetics in this population. As new variants of SARS-CoV-2 continue to emerge, viral kinetics studies are crucial to evaluate test concordance with infectivity, duration of viral shedding, and host factors which may impact transmissibility. Peak viral load occurs early and often before or upon symptom onset in NHs, suggesting asymptomatic and presymptomatic transmission of SARS-CoV-2 may be the most significant drivers of continued outbreaks. These findings highlight the importance of surveillance and source control during periods of increased transmission, and support current isolation recommendations for persons with COVID-19 in healthcare facilities [9, 23]. Ct values and the likelihood of having a negative antigen test increased after Day 5 supporting current guidance that begins testing staff on Day 5 for test-based return to work strategies [23]. Finally, our results emphasize the importance of preventing severe COVID-19 and other adverse outcomes in NH residents through regular vaccination (including second vaccinations in the season when recommended by age or comorbidity criteria, such as for the past 2023–2024 season) and treatment when indicated.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Centers for Medicare & Medicaid Services, "COVID-19 Nursing Home Data," accessed July 11, 2024, <https://data.cms.gov/covid-19/covid-19-nursing-home-data>.
- McGarry BE, Grabowski DC, and Barnett ML, "Severe Staffing and Personal Protective Equipment Shortages Faced by Nursing Homes During the COVID-19 Pandemic," *Health Affairs* 39, no. 10 (2020): 1812–1821, 10.1377/hlthaff.2020.01269, Epub August 20, 2020, [PubMed: 32816600]
- Kissler SM, Fauver JR, Mack C, et al. , "Viral Dynamics of Acute SARS-CoV-2 Infection and Applications to Diagnostic and Public Health Strategies," *PLoS Biology* 19, no. 7 (2021): e3001333. [PubMed: 34252080]
- Vetter P, Eberhardt CS, Meyer B, et al. , "Daily Viral Kinetics and Innate and Adaptive Immune Response Assessment in COVID-19: A Case Series," *mSphere* 5, no. 6 (2020): e00827–20, 10.1128/mSphere.00827-20.
- Killingley B, Mann AJ, Kalinova M, et al. , "Safety, Tolerability and Viral Kinetics During SARS-CoV-2 Human Challenge in Young Adults," *Nature Medicine* 28, no. 5 (2022): 1031–1041, 10.1038/s41591-022-01780-9, Epub March 31, 2022.
- Chisty ZA, Li DD, Haile M, et al. , "Immune Response Kinetics to SARS-CoV-2 Infection and COVID-19 Vaccination Among Nursing Home Residents—Georgia, October 2020–July 2022," *PLoS One* 19, no. 4 (2024): e0301367, 10.1371/journal.pone.0301367. [PubMed: 38625908]
- Puhach O, Meyer B, and Eckerle I, "SARS-CoV-2 Viral Load and Shedding Kinetics," *Nature Reviews Microbiology* 21, no. 3 (2023): 147–161, 10.1038/s41579-022-00822-w. [PubMed: 36460930]
- Hafez W, "COVID-19 Patient Characteristics and Time to Viral Clearance: A Retrospective Observational Study in a Multiethnic Population (United Arab Emirates)," *Journal of Clinical Virology* 157 (2022): 1–8, 10.1016/j.jcv.2022.105297.
- CDC, "Infection Control Guidance: SARS-CoV-2," accessed August 29, 2024, <https://www.cdc.gov/covid/hcp/infection-control/index.html>.
- CDC, "Testing and Management Considerations for Nursing Home Residents With Acute Respiratory Illness Symptoms When SARS-CoV-2 and Influenza Viruses Are Co-Circulating," accessed May 10, 2024, <https://www.cdc.gov/flu/professionals/diagnosis/testing-management-considerations-nursinghomes.htm>.
- Office for Human Research Protections, "45 CFR 46," 2016, accessed August 29, 2024, <https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html>.
- Joseph G, Barnes J, Azziz-Baumgartner E, et al. , "Association of mRNA Vaccination With Clinical and Virologic Features of COVID-19 Among US Essential and Frontline Workers," *Journal of the American Medical Association* 328, no. 15 (2022): 1523–1533. [PubMed: 36255426]

13. Johansson MA, Quandelacy TM, Kada S, et al. , “SARS-CoV-2 Transmission From People Without COVID-19 Symptoms,” *JAMA Network Open* 4, no. 1 (2021): e2035057, 10.1001/jamanetworkopen.2020.35057. [PubMed: 33410879]
14. Zipfel CM, Paul P, Gowler CD, et al. , “Modeling the Effectiveness of Healthcare Personnel Reactive Testing and Screening for the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Omicron Variant Within Nursing Homes,” *Clinical Infectious Diseases* 75, no. 2 (2022): S225–S230, 10.1093/cid/ciac505. [PubMed: 35724112]
15. Smith-Jeffcoat SE, Biddle JE, Talbot HK, et al. , “Symptoms, Viral Loads, and Rebound Among Coronavirus Disease 2019 (COVID-19) Outpatients Treated With Nirmatrelvir/Ritonavir Compared With Propensity Score-Matched Untreated Individuals,” *Clinical Infectious Diseases* 78, no. 5 (2024): 1175–1184, 10.1093/cid/ciad696. [PubMed: 37963102]
16. Soriano V, de-Mendoza C, Edagwa B, et al. , “Oral Antivirals for the Prevention and Treatment of SARS-CoV-2 Infection,” *AIDS Reviews* 24, no. 1 (2022): 41–49, 10.24875/AIDSRev.22000001. [PubMed: 35073629]
17. Sundararajan V, Henderson T, Perry C, Muggivan A, Quan H, and Ghali WA, “New ICD-10 Version of the Charlson Comorbidity Index Predicted In-Hospital Mortality,” *Journal of Clinical Epidemiology* 57, no. 12 (2004): 1288–1294, 10.1016/j.jclinepi.2004.03.012. [PubMed: 15617955]
18. Ouslander JG and Grabowski DC, “COVID-19 in Nursing Homes: Calming the Perfect Storm,” *Journal of the American Geriatrics Society* 68, no. 10 (2020): 2153–2162. [PubMed: 32735036]
19. Caputo V, Termine A, Fabrizio C, et al. , “Age and Sex Modulate SARS-CoV-2 Viral Load Kinetics: A Longitudinal Analysis of 1735 Subjects,” *Journal of Personalized Medicine* 11, no. 9 (2021): 882, 10.3390/jpm11090882.
20. Lin Y, Wu P, Tsang TK, et al. , “Viral Kinetics of SARS-CoV-2 Following Onset of COVID-19 in Symptomatic Patients Infected With the Ancestral Strain and Omicron BA.2 in Hong Kong: A Retrospective Observational Study,” *Lancet Microbe* 4, no. 9 (2023): e722–e731, 10.1016/S2666-5247(23)00146-5. [PubMed: 37659420]
21. Jang S, Rhee JY, Wi YM, and Jung BK, “Viral Kinetics of SARS-CoV-2 Over the Preclinical, Clinical, and Postclinical Period,” *International Journal of Infectious Diseases* 102 (2021): 561–565, 10.1016/j.ijid.2020.10.099, Epub November 5, 2020, [PubMed: 33160066]
22. Radulescu A, Istrate A, Flonta M, and Lupse M, “Antibody and Viral RNA Kinetics in SARS-CoV2 Infected Patients Admitted to a Romanian University Hospital of Infectious Diseases,” *International Journal of Infectious Diseases* 107 (2021): 205–211, 10.1016/j.ijid.2021.04.067, Epub April 24, 2021. [PubMed: 33901653]
23. CDC, “Interim Guidance for Managing Healthcare Personnel With SARS-CoV-2 Infection or Exposure to SARS-CoV-2,” accessed August 22, 2024, https://www.cdc.gov/covid/hcp/infection-control/guidance-risk-assessment-hcp.html?CDC_AAref_Val=https://www.cdc.gov/coronavirus/2019-ncov/hcp/guidance-risk-assessment-hcp.html.
24. CDC, “People With Certain Medical Conditions and COVID-19 Risk Factors,” accessed August 29, 2024, https://www.cdc.gov/covid/risk-factors/?s_cid=SEM.MS:PAI:RG_AO_MS_TM_A18_C-CVD-Safet y-Brd:covid%20vaccine%20safety:SEM00058&utm_id=SEM.MS:PAI:RG_AO_MS_TM_A18_C-CVD-Safety-Brd:covid%20vaccine%20safety:SEM00058.
25. McGarry BE, Sommers BD, Wilcock AD, Grabowski DC, and Barnett ML, “Monoclonal Antibody and Oral Antiviral Treatment of SARS-CoV-2 Infection in US Nursing Homes,” *Journal of the American Medical Association* 330, no. 6 (2023): 561–563, 10.1001/jama.2023.12945. [PubMed: 37450293]
26. Smith DJ, Lambrou A, and Patel P, “SARS-CoV-2 Rebound With and Without Use of COVID-19 Oral Antivirals,” *MMWR. Morbidity and Mortality Weekly Report* 72 (2023): 1357–1364. [PubMed: 38127665]
27. Kissler SM, Fauver JR, Mack C, et al. , “Viral Dynamics of SARS-CoV-2 Variants in Vaccinated and Unvaccinated Persons,” *New England Journal of Medicine* 385, no. 26 (2021): 2489–2491. [PubMed: 34941024]

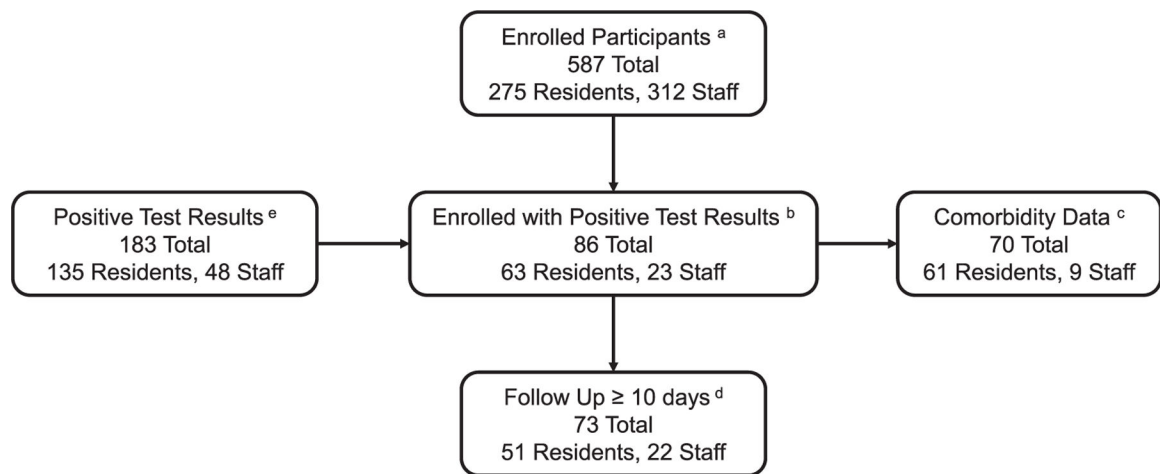
Summary

Key points

- Peak viral load for SARS-CoV-2 occurs early in the course of disease, often before symptoms are identified, which may be a significant driver of continued outbreaks in nursing homes.
- Nursing home residents test positive for SARS-CoV-2 for longer than nursing home staff.
- Replication competent virus was only isolated beyond Day 10 in individuals who experienced rebound, supporting current CDC isolation recommendations for residents in nursing homes.

Why does this paper matter?

- This prospective trial followed residents and staff in nursing homes who tested positive for SARS-COV-2 with daily antigen and RT-PCR tests for 14 days, with paired viral culture and whole genome sequencing on positive tests, allowing us to assess test concordance and duration of shedding of infectious virus.
- Only two participants had a positive viral culture after Day 10, supporting current isolation and return to work recommendations.



^a Data used to generate Supplementary Tables 3, 4, 6.

^b Data used to generate Table 1, Supplementary Tables 1,5, and Supplementary Figure 1.

^c Data used to generate Supplementary Table 2.

^d Data used to generate Figures 2-4 and Supplementary Figures 2-13.

^e Results identified through routine public health surveillance include enrolled and unenrolled persons.

FIGURE 1 |.

Consort diagram, April–November 2023. This diagram describes enrolled participants, cases, cases with 10 or more days of follow-up, and unenrolled cases who were identified through routine health surveillance.

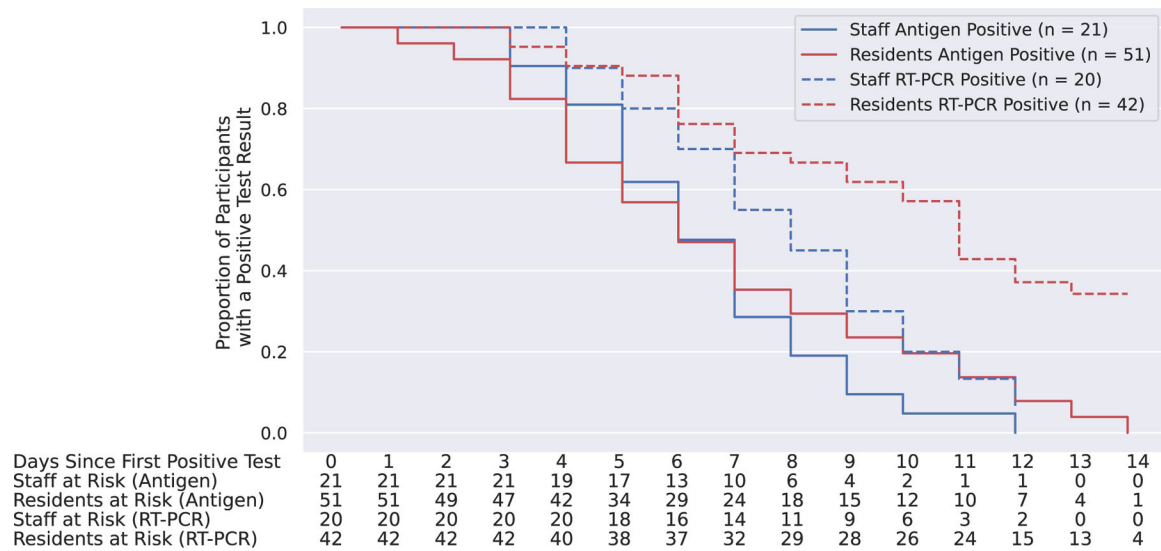


FIGURE 2 |.

Kaplan–Meier analysis of the time to first negative for both antigen and RT-PCR test results among residents and staff, April– November 2023. Differences in the survival curves between residents and staff were significant for RT-PCR ($p = 0.007$) but not antigen ($p = 0.425$) by the log rank test. There are 10 fewer participants (one staff and nine residents) for the RT-PCR curve because five participants never tested RT-PCR positive and five participants did not have the required 10 days follow-up after initial RT-PCR positive.

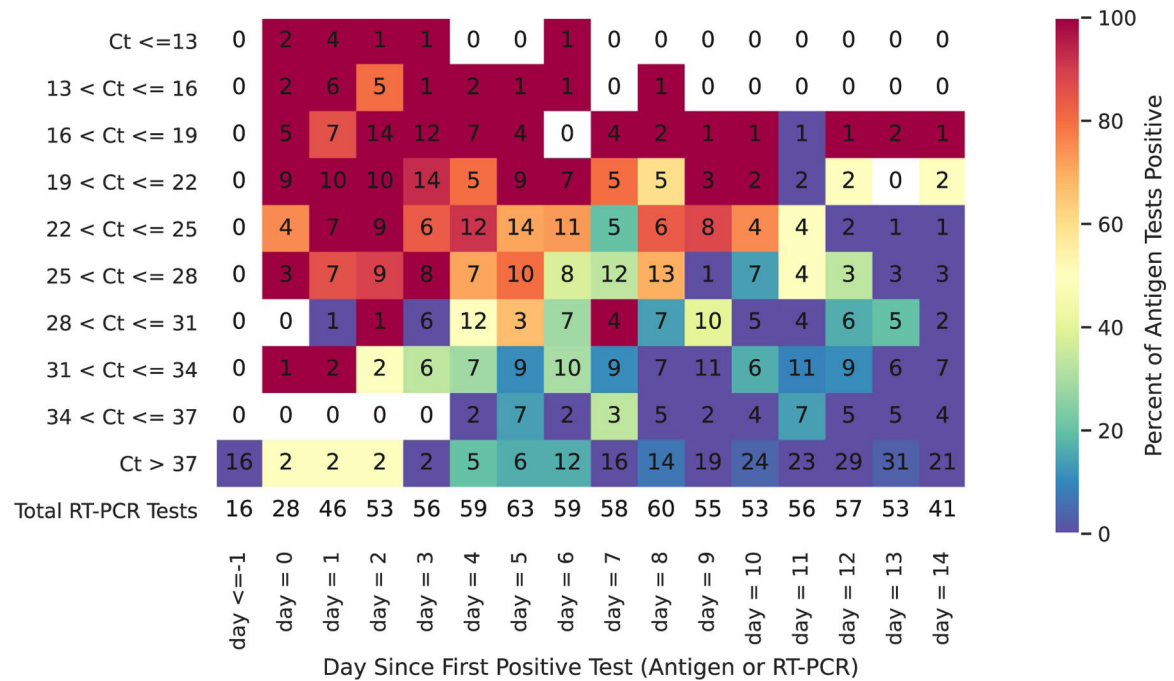


FIGURE 3 |.

Percentage of antigen tests results that were positive for a RT-PCR Ct value range-day pair, April–November 2023. The black text is the number of antigen tests that occurred on a given day that corresponded to a RT-PCR Ct value in the given range. Dark red denotes that all antigen results were positive and purple denotes all antigen tests were negative. Early infection and at low Ct values a majority of antigen test are positive. Later in the infection and at higher Ct values a majority of antigen tests are negative. There is a small subset of antigen tests that were positive when the RT-PCR test results were negative. These results belong to three participants, one tested antigen positive and RT-PCR negative on Days 0, 1, 2, 3, 6, 7, 10, and 13 while the other two each tested antigen positive and RT-PCR negative once on Days 4 and 6.

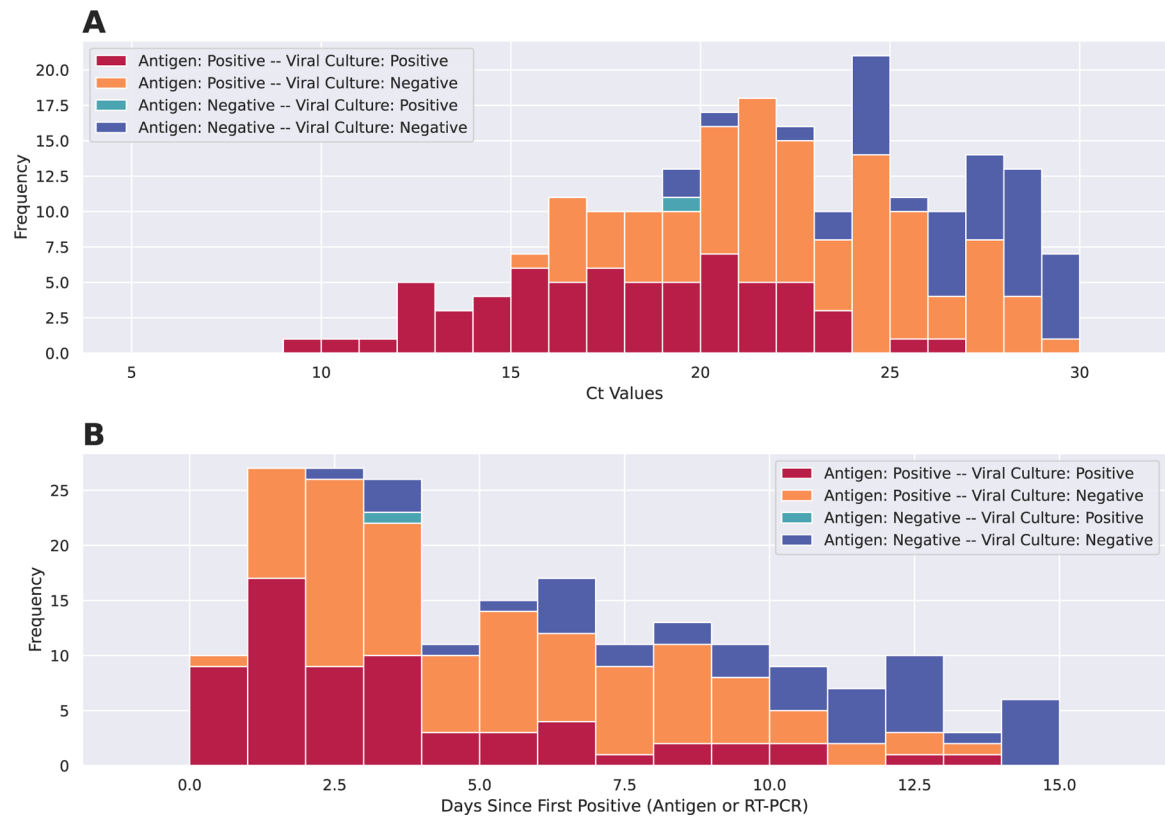


FIGURE 4 |

Concordance between viral culture and antigen results by (A) Ct value and (B) time, April–November 2023. Dark red denotes both antigen and viral culture results are positive while purple denotes that both antigen and viral culture results are negative. Most viral culture positives occur when Ct < 24. The two viral culture positives after day 10 were participants who experienced rebound.

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TABLE 1 |
Demographic information for all SARS-CoV-2 cases enrolled across 24 US nursing homes, April–November 2023.

	Resident (N = 63)	Staff (N = 23)	Overall (N = 86)
Age (years)			
18–39	0 (0%)	6 (26%)	6 (7%)
40–59	3 (5%)	15 (65%)	18 (21%)
60–79	29 (46%)	1 (4%)	30 (35%)
≥ 80	29 (46%)	0 (0%)	29 (34%)
Missing	2 (3%)	1 (4%)	3 (4%)
Sex			
Female	42 (67%)	18 (78%)	60 (70%)
Male	19 (30%)	4 (17%)	23 (27%)
Missing	2 (3%)	1 (4%)	3 (4%)
Race			
American Indian or Alaska Native	1 (2%)	2 (9%)	3 (3%)
Black or African American	10 (16%)	5 (22%)	15 (17%)
Native Hawaiian or Other Pacific Islander	0 (0%)	1 (4%)	1 (1%)
White	50 (79%)	12 (52%)	62 (72%)
Other	0 (0%)	2 (9%)	2 (2%)
Missing	2 (3%)	1 (4%)	3 (4%)
Ethnicity			
Hispanic	2 (3%)	4 (17%)	6 (7%)
Non-Hispanic	57 (90%)	17 (74%)	74 (86%)
Unknown	2 (3%)	0 (0%)	2 (2%)
Missing	2 (3%)	2 (9%)	4 (5%)
Charlson Comorbidity Index (CCI) [17]			
Mean (SD)	5.46 (2.30)	0.909 (0.868)	4.25 (2.85)
Median [min, max]	5.00 [2.00, 13.0]	1.00 [0, 3.00]	4.00 [0, 13.0]
Missing	2 (3%)	1 (4%)	3 (4%)

Abbreviations: max, maximum; min, minimum; SD, standard deviation.