Dementia prevalence, a contextual factor associated with SARS-CoV-2 in veterans affairs community living centers

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Abstract

Background: Alzheimer’s disease and related dementias (ADRD) impact the diagnosis and infection control of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in nursing homes (NH) by influencing the behavior of residents and their caregivers. Health system data show an association between ADRD and SARS-CoV-2. Whether this association is present in NH populations remains unknown. How increased SARS-CoV-2 risk among residents with ADRD impacts the greater NH population also remains unknown.

Methods: This retrospective cohort study used electronic health record data on Veterans residing in 133 Veterans Affairs Community Living Centers (CLC) and 15 spinal cord injury units from March 1, 2020 to December 13, 2020. We measured ADRD using diagnostic codes 12 months before an index SARS-CoV-2 test date for each resident. We used Poisson regression to determine the relative risk of SARS-CoV-2 for the highest quartile of facility ADRD prevalence versus the lowest, stratifying by individual ADRD status, and adjusting for covariates, with and without a random intercept to account for facility clustering.

Results: Across the study period, 15,043 residents resided in CLCs, 1952 (13.0%) had SARS-CoV-2, and 8067 (53.6%) had ADRD. There was an estimated 60% increased risk of SARS-CoV-2 in facilities with highest dementia prevalence versus lowest (relative risk, 1.6 [95% confidence interval 0.95, 2.7]).

Conclusions: CLC residents had a greater likelihood of SARS-CoV-2 infection in facilities with greater ADRD prevalence. Facility characteristics other than ADRD prevalence may account for this association.

Keywords
dementia, nursing home, SARS-CoV-2
INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has devastated nursing home (NH) residents: 5% of the overall cases and 31% of the total Coronavirus Disease 2019 (COVID-19) deaths in the United States have occurred in NH as of June 30, 2021.1 Retrospective studies of hospitalized older adults with COVID-19 and Alzheimer’s disease and related dementias (ADRD) report alterations in cognition or functional status as the most common symptoms.2–4 Furthermore, ADRD reduces adherence to infection control measures in NH such as testing, masking and physical distancing.5–7 Through these multiple mechanisms, the contextual factor of ADRD prevalence could lead to increased risk of SARS-CoV-2 in a NH.

Prior work shows a network-level effect of NH ADRD prevalence on SARS-CoV-2 mitigation efforts. In Massachusetts nursing homes, adherence to infection control practices correlated with reductions in SARS-CoV-2 infection and mortality, even when accounting for county SARS-CoV-2 prevalence.8 In facilities with higher dementia prevalence, infection rate decreased more for each 1-unit increase in infection control adherence score.9 Analysis of association between facility dementia prevalence and SARS-CoV-2 infection rate will add to this emerging body of knowledge.

The 133 Veterans Affairs (VA) Health System Community Living Centers (CLCs), functionally equivalent to NHs, provide short term rehabilitation and long-term care of residents with complex medical or functional assistance needs. From March through December 2020, CLCs tested residents for SARS-CoV-2 due to clinical suspicion of COVID-19 and systematically for infection control purposes. We sought to investigate the influence of ADRD prevalence on rates of SARS-CoV-2 infection in CLCs. Using retrospective observational methods, we tested the hypothesis that risk of SARS-CoV-2 was greater among residents in the highest quartile of ADRD prevalence at the site and time of a test: overall and separately in residents with and without ADRD.

METHODS

This retrospective cohort study used electronic health record data from VA CLCs. The study was approved by the Providence VA Medical Center’s Institutional Review Board.

Cohort

This analysis included individuals who stayed in a CLC for at least 1 day between March 1, 2020 and December 13, 2020, and who were tested for SARS-CoV-2. It assigned to each resident an index test date: the date of the first positive test for residents who had SARS-CoV-2, and the date of the last negative test for residents who did not. Several other publications report on data from this cohort.10–14 Analysis included 133 unique CLCs and 15 spinal cord injury units, comprising 148 total sites of care (Figure S1). From the electronic health record, we obtained demographic characteristics and information about comorbid medical diagnoses. We also calculated the average daily census during the study period for the site of care of each resident’s index test as a resident-level variable.

Exposure

For each resident, review of ICD-10-CM codes from the 12 months before the study period identified ADRD diagnosis.15,16 Use of a 12-month reference period for ADRD diagnoses provided greater diagnostic specificity than a 3-year reference period, and was more appropriate to the higher intensity of care delivered in CLCs compared with a community-dwelling population.

The total residents in a single site on a single day comprise one site-day in this analysis. By dividing the number of residents with ADRD by the total number of residents, we assigned each site-day an ADRD site prevalence.

Key points

- Settings of higher dementia prevalence were associated with higher likelihood of developing a SARS-CoV-2 infection in residents with and without dementia.
- Dementia prevalence is a contextual factor associated with SARS-CoV-2 in Veterans Affairs Community Living Centers.

Why does this paper matter?

Prevalence of dementia in congregate living settings such as nursing homes and veterans affairs communities is associated with SARS-CoV-2 infection. Clinicians, administrators, and policymakers should recognize this important contextual risk factor when assessing residents and designing infection control procedures.
The other outcome was the proportion of residents with SARS-CoV-2 per ADRD site prevalence quartile over the entire study period.

Next, we used Poisson regression to determine the risk ratio of SARS-CoV-2 in (with 95% confidence interval) the 2nd, 3rd, and 4th quartiles compared with the 1st quartile. After completing this for the overall cohort, we analyzed the stratum of individuals with diagnosed ADRD separately from the stratum without diagnosed ADRD.

Based on literature review and clinical experience, we selected variables for a multivariate model representing known and suspected confounders and predictors of the outcome. We included variables which differed between the highest and lowest ADRD prevalence quartiles with \( p \) values of less than 0.05. The model included age, race, diabetes mellitus (with and without complications), depression, long stay, ADRD, DM, HTN, DM with complications, HTN with complications, ADRD history, history of alcohol or drug abuse, anemia, depression, cancer, psychosis, and history of TBI.

### Table 1: Demographics and comorbidities

|                      | Overall \( n \), Mean (SD) \( n = 15,041 \) | Lowest quartile ADRD site prevalence, \( n \), Mean (SD) \( n = 2955 \) | Highest quartile ADRD site prevalence, \( n \), Mean (SD) \( n = 3586 \) | \( p \) value$^a$ |
|----------------------|---------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|-------------|
| Age, years (SD)      | 72.7 (11.6)                                | 69.1 (12.5)                                                     | 74.8 (10.6)                                                     | <0.001      |
| Male, no. (%)        | 14,395 (95.7)                              | 2810 (95.1)                                                    | 3454 (96.3)                                                    | 0.017       |
| Race, white, no. (%) | 10,619 (70.6)                              | 2140 (72.4%)                                                   | 2465 (68.7)                                                    | 0.001       |
| Race, black, no. (%) | 3259 (21.7)                                | 537 (18.2%)                                                    | 893 (24.9)                                                     | <0.001      |
| Race, other, no. (%) | 1163 (7.7)                                 | 278 (9.4%)                                                     | 228 (6.4)                                                      | <0.001      |
| Long stay,$^b$ proportion (SD) | 0.69 (0.17)                                   | 0.57 (0.14)                                                   | 0.78 (0.15)                                                    | <0.001      |
| Number of tests,$^c$ no. (%) | 4.4 (5.3)                                      | 3.9 (4.5)                                                     | 5.1 (6.5)                                                      | <0.001      |
| ADRD, no. (%)        | 8065 (53.6)                                | 798 (27.0%)                                                    | 2890 (80.6)                                                    | <0.001      |
| DM,$^d$ no. (%)      | 6039 (40.2)                                | 1060 (35.9%)                                                   | 1463 (40.8)                                                    | 0.001       |
| DM with complications, no. (%) | 6352 (42.2)                                    | 1117 (37.8%)                                                  | 1600 (44.6)                                                    | <0.001      |
| HTN,$^e$ no. (%)     | 11,033 (73.4)                              | 2083 (70.5%)                                                   | 2749 (76.7)                                                    | <0.001      |
| HTN with complications, no. (%) | 5748 (38.2)                                    | 1037 (35.1%)                                                  | 1407 (39.3)                                                    | <0.001      |
| Heart failure, no. (%) | 4589 (30.5)                                      | 866 (29.3%)                                                   | 1137 (31.7)                                                    | 0.039       |
| Pulmonary disease, no. (%) | 5743 (38.2)                                    | 1056 (35.8%)                                                  | 1455 (40.6)                                                    | <0.001      |
| Body mass index, mean (SD) | 28.2 (7.3)                                      | 28.7 (7.6)                                                   | 27.9 (7.4)                                                     | 0.725       |
| Valvular heart disease, no. (%) | 1742 (11.6)                                     | 336 (11.4%)                                                  | 407 (11.4)                                                     | 0.999       |
| History of alcohol abuse, no. (%) | 2307 (15.3)                                     | 445 (15.1%)                                                  | 545 (15.2)                                                     | 0.904       |
| History of drug abuse, no. (%) | 1757 (11.7)                                     | 418 (14.2%)                                                  | 331 (9.2)                                                      | <0.001      |
| Anemia, no. (%)      | 7392 (49.2)                                 | 1514 (51.3%)                                                   | 1802 (50.3)                                                    | 0.441       |
| Depression, no. (%)  | 7100 (47.2)                                 | 1334 (45.2%)                                                   | 1833 (51.1)                                                    | <0.001      |
| Cancer, no. (%)      | 2876 (19.1)                                 | 549 (18.6%)                                                   | 667 (18.6)                                                     | 0.999       |
| Psychosis, no. (%)   | 4172 (27.7)                                 | 558 (18.9%)                                                   | 1250 (34.9)                                                    | <0.001      |
| History of TBI, no. (%) | 942 (6.3)                                         | 220 (7.5%)                                                  | 209 (5.8)                                                      | 0.010       |
| Average census,$^f$ mean (SD) | 71.0 (42.8)                                       | 43.4 (27.5)                                                  | 73.4 (35.3)                                                    | <0.001      |

Abbreviations: ADRD, Alzheimer's disease and related dementias; HTN, hypertension; DM, diabetes mellitus; TBI, traumatic brain injury.

$p$ values compare highest to lowest quartile only.

$^a$Proportion of long stay (>100 days) at each resident's site on the day of their index test, averaged across each quartile.

$^b$Number of SARS-CoV-2 tests during the Community Living Center stay before the index test.

$^c$Excludes hypertension with complications.

$^d$Excludes diabetes mellitus with complications.

$^e$Average daily census at the site of care of the index test during the study period.
We also estimated dementia prevalence compared with the first quartile was 28.2 (SD 7.3). A total of 1952 (13.0%) residents had SARS-CoV-2, and 8067 (53.6%) met the ADRD definition. Final analysis included 117,455 site-days. The average daily census of the site of care in the lowest quartile of ADRD prevalence versus the lowest was 1.6 (95% CI 0.9, 2.6). The highest quartile was associated with an adjusted risk ratio of 1.2 (95% CI 0.9, 1.5) for SARS-CoV-2 compared with testing in a site of care in the lowest quartile (Table 1). Comorbidities were prevalent: for example, diabetes with complications was present in 42.4% (6352). The mean body mass index was 28.2 (SD = 7.3). A total of 1952 (13.0%) residents had SARS-CoV-2, and 8067 (53.6%) met the ADRD definition. Final analysis included 117,455 site-days. The daily census per site averaged across residents throughout the study duration was 71.0 (SD = 42.8).

For the highest quartile of ADRD prevalence within the site of care, the residents were older (74.8 vs. 69.1, \( p < 0.001 \)) and more racially diverse (24.9% black vs. 18.7%, \( p < 0.001 \)) than the lowest quartile. They also had a higher proportion of long stays (0.78 vs. 0.57, \( p < 0.001 \)) and number of SARS-CoV-2 tests (5.12 vs. 4.4, \( p < 0.001 \)). The average daily census of the site of care per resident at the time of their index test was higher among residents in the highest quartile of ADRD site prevalence compared with those in the lowest quartile (73.4 vs. 43.4, \( p < 0.001 \)).

Residents tested at a higher ADRD site prevalence tended to have a higher proportion of SARS-CoV-2 (Figure 1). Site of care in the highest quartile of ADRD prevalence was associated with a risk ratio of 2.0 (95% CI 1.7, 2.3) for SARS-CoV-2 compared with testing in a site of care in the lowest quartile (Table 2). The highest quartile was associated with a risk ratio of 1.5 (95% CI 1.3, 2.0) in residents with ADRD and 1.6 (95% CI 1.3, 2.1) in residents without ADRD.

RESULTS

This NH population (\( n = 15,041 \)) was predominantly white (\( n = 10,620; 70.6% \)) and male (\( n = 14,397; 95.7% \)) with a mean age of 72.7 (SD = 11.6) (Table 1). Comorbidities were prevalent: for example, diabetes with complications was present in 42.4% (6352). The mean body mass index was 28.2 (SD = 7.3). A total of 1952 (13.0%) residents had SARS-CoV-2, and 8067 (53.6%) met the ADRD definition. Final analysis included 117,455 site-days. The daily census per site averaged across residents throughout the study duration was 71.0 (SD = 42.8).

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| Relative Risk | Unadjusted | Adjusted | Random Effect Adjusted |
|---------------|------------|----------|------------------------|
| Q4            | 2.0 [1.7, 2.3] | 1.6 [1.3, 1.9] | 1.6 [0.95, 2.7] |
| Q3            | 1.9 [1.6, 2.2] | 1.3 [1.1, 1.6] | 1.3 [0.8, 2.0] |
| Q2            | 1.2 [1.1, 1.5] | 1.0 [0.9, 1.2] | 1.2 [0.9, 1.6] |

The adjusted risk ratio without random intercept for facility clustering for residents in the highest quartile of ADRD site prevalence versus the lowest was 1.6 (95% CI 1.3, 1.9). The model met the goodness of fit Hosmer-Lemeshow test (\( p = 0.19 \)). The highest quartile was associated with an adjusted risk ratio of 1.2 (95% CI 0.9, 1.5) in residents with ADRD and 1.7 (95% CI 1.2, 2.4) in residents without ADRD. A model including variables for both individual ADRD diagnosis and site prevalence was favored over a model with individual diagnosis alone (\( p \) value <0.001). Variance inflation factor maximum was 1.88 and average was 1.27 (Figure S2).

In the model including random intercepts for facility clustering, the adjusted risk ratio for residents in the highest quartile of ADRD site prevalence versus the lowest was 1.6 (95% CI 0.95, 2.7). The highest quartile was associated with an adjusted risk ratio of 1.3 (95% CI 0.7, 2.3), and the lowest quartile was associated with an adjusted risk ratio of 1.3 (95% CI 0.7, 2.6).

In the sensitivity analysis, after excluding residents in spinal cord injury units, the adjusted risk ratio (95% CI) of SARS-CoV-2 in the highest quartile of ADRD prevalence compared to the lowest was 1.6 (95% CI 0.9, 2.6).
DISCUSSION

This retrospective analysis found that VA CLC residents with and without ADRD tended to have a higher rate of SARS-CoV-2 infection when tested at a higher ADRD site prevalence. The point estimates of effect size were similar across the strata of residents with ADRD and without ADRD, implying that the observed association is not due to the effect of ADRD at the individual level. Adjustment for facility-level effects using a random intercept increased the variance estimate of this association such that the confidence interval included a risk ratio of 1 as well as risk ratios slightly less than 1. This finding suggests that facility-level characteristics other than ADRD prevalence accounted for some of the observed association. The sensitivity analysis excluding spinal cord injury units did not meaningfully change the effect estimate or confidence interval. Examination of ADRD prevalence as a contextual factor adds to the current understanding of SARS-CoV-2 risk in NH.

The relationship between ADRD and increased infection risk is likely multifactorial due to the behavior of NH residents living with dementia and staff resources required to provide effective dementia care. We expect that residents with ADRD generally present with less specific symptoms of COVID-19 than those without ADRD. This could obscure clinical detection and delay diagnosis, resulting in potential exposure of more staff and residents to SARS-CoV-2. Our findings demonstrate the critical importance of infection control and underscore the importance of viral testing and vital signs monitoring, especially in facilities with high ADRD prevalence.

Despite investigations of related questions, the association of ADRD prevalence with SARS-CoV-2 in NH was previously unknown. Analysis of pooled nationwide data from multiple health systems showed an association between diagnosed dementia and SARS-CoV-2. A study of NH data associated mild to moderate impairment on the cognitive function scale (CFS) with increased risk of SARS-CoV-2 infection. Our study examines diagnosed dementia and related dementias to understand the association with SARS-CoV-2 infection in NH.

Note: Site-days were quartiled by prevalence of ADRD, and include all residents whose index tests fall on the corresponding site-day. Adjusted model variables were age, race, diabetes mellitus, diabetes mellitus with complications, hypertension, hypertension with complications, heart failure, pulmonary disease, history of drug abuse, depression, psychosis, and average census.

Abbreviations: ADRD, Alzheimer’s disease and related dementias; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; RR, relative risk.
dementia, which overlaps with but differs from impairment on CFS.\textsuperscript{21,22} Our work builds on a prior report that in NHs with higher ADRD prevalence, infection control measures appear to more effective.\textsuperscript{9} We develop that concept by analyzing ADRD prevalence as a time-varying rather than fixed attribute and by reporting on the outcome of SARS-CoV-2.

This study’s other strengths include the availability of systematically applied longitudinal viral testing data for a large cohort of NH residents and comprehensive coding data for ADRD. Unlike seasonal influenza outbreaks, the SARS-CoV-2 pandemic has prompted frequent asymptomatic testing of NH residents, allowing for the assessment of ADRD prevalence as a contextual risk factor for infection. This study also includes data from multiple sites within a national system where the prevalence of SARS-CoV-2 varied over time, adding to the generalizability of the findings.

Limitations of this study include the use of dementia diagnosis rather than more direct measurements of the behaviors and practices hypothesized to cause increased SARS-CoV-2. Our model of dementia could be confounded by associated conditions in older people with dementia such as frailty, and functional decline, and we are unable to adjust for all of these. Staffing patterns and physical layouts of individual CLCs, which could confound the result, are also absent from our model. The model includes variables such as age, depression, and history of alcohol abuse which may have collinearity with dementia. Because the study uses data from VA CLCs, the cohort is mostly composed of male veterans, and staffing patterns differ from those in community NH, limiting generalizability of the findings. Also, the study uses data from before SARS-CoV-2 vaccination was available, and from before known circulation of the delta variant, both of which conditions may limit the generalizability of these data to future management of SARS-CoV-2 in NH. Finally, the association observed by comparison of quartiles of residents may not generalize to all individuals within the quartile.

Residents tested for SARS-CoV-2 at times and places of higher dementia prevalence tend to have a higher proportion of positive tests, and facility characteristics other than ADRD prevalence may account for some or all of this association. Dementia prevalence within a site of NH care may increase the transmission of respiratory viral illnesses through resident and staff behavior, and through diagnostic and infection control challenges. Medical directors, policy makers, and infection control specialists need guidance defining the appropriate use of medications, seclusion, and physical restraint for infection control purposes.\textsuperscript{23} SARS-CoV-2 has required NH care to navigate a tradeoff between the need to protect all residents and staff from SARS-CoV-2, and the imperative to honor the dignity and autonomy of residents with dementia. All NH stakeholders would benefit from evidence-based guidelines for achieving effective infection control in residents with dementia.

**AUTHOR CONTRIBUTIONS**

Thomas Bayer: literature search, study design, interpretation, writing. Ashna Rajan, Salah Elhamamsy, Marilyne Cadieux, Mriganka Singh, Moniyka Sachar, Aman Nanda: study design, data interpretation, and writing. Frank Devone, Chris Halladay, and Kevin McConeghy: study design, data analysis, interpretation, writing. Stefan Graveinstein, James Rudolph: literature search, study design, data analysis, interpretation, writing. All persons with significant contributions meritng authorship are listed as authors of this work.

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**CONFLICT OF INTEREST**

The authors report no conflicts of interest.

**SPONSOR’S ROLE**

The sponsors had no role in the design of this study.

**ETHICS STATEMENT**

This study was approved by the Providence VAMC Institutional Review Board.

**FINANCIAL DISCLOSURE**

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

Figure S1: Flow diagram illustrating cohort selection and analysis.

Figure S2: Correlation matrix of variables in adjustment model.

Methods: R software session output.