Received: 6 June 2021 | Revised: 23 July 2021 | Accepted: 31 July 2021

DOI: 10.1111/jgs.17415

Journal of the
American Geriatrics Society

Impact of fever thresholds in detection of COVID-19 in Department of Veterans Affairs Community Living Center residents

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Funding information
U.S. Department of Veterans Affairs

Abstract

Background: Among nursing home residents, for whom age and frailty can blunt febrile responses to illness, the temperature used to define fever can influence the clinical recognition of COVID-19 symptoms. To assess the potential for differences in the definition of fever to characterize nursing home residents with COVID-19 infections as symptomatic, pre-symptomatic, or asymptomatic, we conducted a retrospective study on a national cohort of Department of Veterans Affairs (VA) Community Living Center (CLC) residents tested for SARS-CoV-2.

Methods: Residents with positive SARS-CoV-2 tests were classified as asymptomatic if they did not experience any symptoms, and as symptomatic or pre-symptomatic if the experienced a fever (>100.4°F) before or following a positive SARS-CoV-2 test, respectively. All-cause 30-day mortality was assessed as was the influence of a lower temperature threshold (>99.0°F) on classification of residents with positive SARS-CoV-2 tests.

Results: From March 2020 through November 2020, VA CLCs tested 11,908 residents for SARS-CoV-2 using RT-PCR, with a positivity of rate of 13% (1557). Among residents with positive tests and using >100.4°F, 321 (21%) were symptomatic, 425 (27%) were pre-symptomatic, and 811 (52%) were asymptomatic. All-cause 30-day mortality among residents with symptomatic and pre-symptomatic COVID-19 infections was 24% and 26%, respectively, while those with an asymptomatic infection had mortality rates similar to residents with negative SAR-CoV-2 tests (10% and 5%, respectively). Using >99.0°F would have increased the number of residents categorized as symptomatic at the time of testing from 321 to 773.

Conclusions: All-cause 30-day mortality was similar among VA CLC residents with symptomatic or pre-symptomatic COVID-19 infection, and lower

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than rates reported in non-VA nursing homes. A lower temperature threshold would increase the number of residents recognized as having symptomatic infection, potentially leading to earlier detection and more rapid implementation of therapeutic interventions and infection prevention and control measures.

KEYWORDS
Community Living Centers, fever, long term care, SARS-CoV-2

Key Points

- Mortality among VA nursing home residents with COVID-19 infection was ~25%.
- Defining fever as >99.0°F increased the sensitivity to detect residents with symptomatic COVID-19 infection.

Why Does this Paper Matter?

Earlier recognition of residents with COVID-19 infection can hasten treatment and infection prevention.

INTRODUCTION

The pandemic caused by SARS-CoV-2 disproportionately affects nursing home residents. Although only 4% of COVID-19 cases in the United States occurred among nursing home residents and the staff who care for them, as of February 2021, this group accounted for 32% of COVID-19 related deaths in the country.[1] Age, comorbid illness, and inherent frailty likely explain the high mortality rates observed among nursing home residents. Especially early in the pandemic, additional factors that contributed to poor outcomes in this vulnerable population including limitations in the supply of personal protective equipment (PPE) and delays in the availability of SARS-CoV-2 testing and test results. Compounding these factors are age-related physiologic changes that can obscure or blunt signs and symptoms of infection, leading to delays in recognizing residents with COVID-19 infections. In particular, the use of a temperature threshold of 100.4°F may not be sensitive enough to detect nursing home residents with fever as a symptom of COVID-19 and who should undergo further assessment and testing for SARS-CoV-2.[2]

Early descriptions of COVID-19 infection in community nursing homes characterized residents as either symptomatic or asymptomatic at the time of testing, with >50% of those with RT-PCR tests that were positive for SARS-CoV-2 in the latter category.[3,4] Within days of a positive test, however, most individuals who were initially asymptomatic went on to develop symptoms that included fever (>100.0°F), malaise, and cough. A subsequent evaluation of COVID-19 infections among residents of a large academic nursing home reported similar findings.[5] Overall, the majority of residents who were asymptomatic at the time of testing eventually developed symptoms and thus were deemed as pre-symptomatic; less than 15% of residents with a positive SARS-CoV-2 test remained asymptomatic.[3–5]

A lower temperature threshold to define a fever may improve recognition of nursing home residents as having symptoms of COVID-19 infection. Screening criteria described early in the pandemic suggested using a temperature of 99.5°F to assess for fever among frail elders living in congregate care settings.[6,7] Based in part on data describing residents of Department of Veterans Affairs (VA) nursing homes, commonly termed Community Living Centers (CLCs), from March 1 through May 14, 2020, McConeghy et al. proposed using a temperature threshold of 99.0°F to define fever when screening for SARS-CoV-2 among nursing home residents.[8] Here, we compare using a temperature of >100.4°F compared to assess the >99.0°F when screening for COVID-19 infections among a national cohort of VA CLC residents during the first 9 months of the pandemic.

METHODS

Study design, setting, and data sources

We conducted a retrospective cohort study of residents living in any of 134 VA CLCs between March 1 and November 30, 2020. On March 17, 2020 the VA issued a memorandum requiring daily screening of residents for temperature >100.4°F, cough, shortness of breath, or sore throat. Screening residents for signs and symptoms of COVID-19 infection continued throughout the study period; providers were notified of residents with a positive screen and could choose to order a SARS-CoV-2

diagnostic test as clinically appropriate. A memorandum issued on April 14, 2020 called for widespread baseline testing of all CLC residents for SARS-CoV-2. On June 11, in alignment with guidance issued by the Centers for Medicare and Medicaid Services (CMS), the VA issued a memorandum for CLCs to test residents for COVID-19 within 48 h of admission, following detection of a new confirmed case in the CLC, and weekly thereafter until no new cases were identified and at least 14 days passed since the most recent positive test.[9]

We used the Department of Veterans Affairs Informatics and Computing Infrastructure to access clinical databases from the U.S. Veterans Healthcare Administration (VHA). Data were extracted from the VHA's Corporate Data Warehouse, the VHA's Vital Status File, and the VA COVID-19 Shared Data Resource. The Institutional Review Board at the VA Northeast Ohio Healthcare System approved the study protocol.

Case ascertainment and clinical characteristics

The cohort studies included all VA CLC residents tested for SARS-CoV-2 using an RT-PCR-based assay. If residents had a temperature of >100.4°F on the day of or within the 14 days before a positive SARS-CoV-2 test, they were considered symptomatic. If their temperature was >100.4°F in the 14 days following a positive SARS-CoV-2 tests, residents were considered pre-symptomatic

TABLE 1 Characteristics of CLC residents screened for SARS-CoV-2, according to test result and clinical symptoms

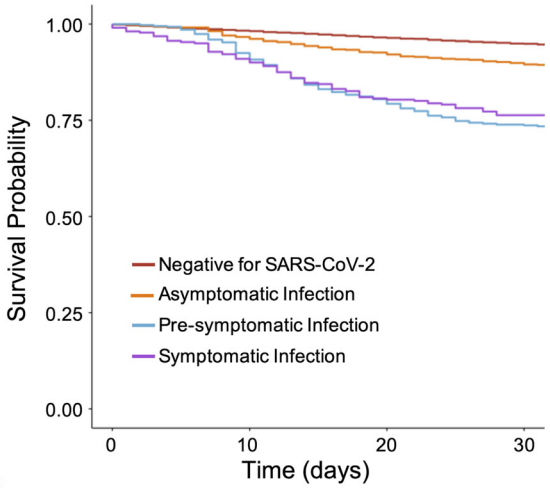
Characteristics	All ($n = 11{,}908$)	Positive SARS-CoV-2 test			Negative SARS-CoV-2 test ($n = 10{,}351$)
		Asymptomatic ($n = 811$)	Pre-symptomatic ($n = 425$)	Symptomatic ($n = 321$)	
Male sex, no. (%)[a]	11,434 (96%)	788 (97%)	418 (98%)	313 (98%)	9915 (96%)
Age, mean (± SD)[b]	74.1 ± 10.7	74.9 ± 11	76.3 ± 9.9	74.3 ± 10.3	73.9 ± 10.8
Race					
White	8373 (70%)	555 (68%)	258 (61%)	205 (64%)	7355 (71%)
Black	2617 (22%)	192 (24%)	132 (31%)	95 (30%)	2198 (21%)
Other[c]	910 (8%)	64 (8%)	34 (5%)	20 (7%)	792 (8%)
Ethnicity					
Non-Latinx	10,881 (91%)	749 (92%)	395 (93%)	291 (91%)	9446 (91%)
Latinx	595 (5%)	41 (5%)	15 (4%)	21 (7%)	518 (5%)
Other[c]	432 (4%)	21 (3%)	15 (4%)	9 (3%)	387 (4%)
Charlson comorbidity index, mean (± SD)[b]	4.85 ± 3.4	4.96 ± 3.3	4.76 ± 3.3	4.80 ± 3.1	4.85 ± 3.4
Comorbid conditions	6063 (51%)	432 (53%)	208 (49%)	180 (56%)	5243 (51%)
Diabetes mellitus, type II	4596 (39%)	317 (39%)	156 (37%)	112 (35%)	4011 (39%)
Pulmonary disease	3958 (33%)	278 (34%)	139 (33%)	89 (28%)	3452 (33%)
Stroke	3733 (31%)	263 (32%)	136 (32%)	113 (35%)	3221 (31%)
Heart disease	3611 (30%)	258 (32%)	139 (33%)	87 (27%)	3127 (30%)
Peripheral vascular disease	3507 (29%)	239 (29%)	116 (27%)	88 (27%)	3064 (30%)
Renal disease	2928 (25%)	178 (22%)	95 (22%)	64 (20%)	2591 (25%)
Cancer	2304 (25%)	30 (17%)	10 (11%)	120 (26%)	2144 (26%)
Liver disease	1645 (14%)	126 (16%)	58 (14%)	35 (11%)	1426 (14%)
HIV	97 (1%)	4 (0%)	8 (2%)	6 (2%)	79 (1%)
Assessment for fever					
>100.4°F	856 (7%)	0 (0%)	0 (0%)	321 (100%)	535 (5%)
>99.0°F	3242 (27%)	257 (32%)	195 (46%)	321 (100%)	2469 (24%)

[a]All values written as no. (%) unless otherwise indicated.
[b]SD, standard deviation.
[c]For race includes American Indian, Alaska Native, Asian, Native Hawaiian or Pacific Islander and unknown; for ethnicity includes unknown.

at the time of testing. Asymptomatic residents had a temperature of ≤100.4°F in the 2 weeks before and after a positive SARS-CoV-2 test. In accordance with the recognition that nursing home residents may have a blunted febrile response, we also conducted analyses using >99.0°F as the temperature threshold for fever.[10,11] To asses for sensitivity and specificity, we considered all tests performed in CLC residents, excluding tests following first positive result in residents who tested positive in between March 1, 2020 and November 30, 2020. Additionally, we assessed age, gender, self-reported race and ethnicity, underlying comorbid conditions, and the Charlson comorbidity index (CCI) based on *International Classification of Diseases* (*ICD*) codes.[12] For residents with a positive SARS-CoV-2 test, all-cause mortality was evaluated at 30 days following their first positive test. For those with only negative test results, the date of the SARS-CoV-2 test closest to the start of the study period was used.

Statistical methods

Differences in continuous values across patient groups were assessed using *F*-tests, and post-hoc pairwise tests of differences are presented with Tukey-adjusted *p*-values. Kaplan–Meier survival curves were estimated for CLC residents based on their categorization as being asymptomatic, pre-symptomatic, or asymptomatic at the time of their first positive SARS-CoV-2 test as well as for those with negative SARS-CoV-2 tests. Time at risk for residents who were negative for SARS-CoV-2 during the study period (March–November) and who later tested positive was censored at the date of the positive test. The survival curves were compared using an omnibus log-rank test and post-hoc pairwise comparisons with *p*-values adjusted using the Holm method. Statistical analyses were performed using R (version 3.5.1; Vienna, Austria)[13] including functions from additional packages.[14–18] Diagnostic test evaluations were performed using MedCalc (Ostend, Belgium).[19]



Number at risk

Negative for SARS-CoV-2	10,351	10,177	9994	9831
Asymptomatic Infection	811	784	751	729
Pre-symptomatic Infection	425	393	342	314
Symptomatic Infection	321	292	259	245

FIGURE 1 Kaplan–Meier curves of time to death among all Community Living Center residents screened for SARS-CoV-2, stratified by test results and symptoms based on a fever threshold of >100.4°F

RESULTS

Between March 1 and November 30 2020, 10,351 of 11,908 (87%) CLC residents tested for SARS-CoV-2 had negative results (Table 1). The positivity rate was 13% or 130.8 cases per 1000 residents. Most of the residents were male (96%) with a mean age of 74.1 (±10.7) years and a high burden of chronic medical conditions with a mean CCI of 4.85 (±3.4). Of the 1557 who tested positive, 321 (21%) were symptomatic, 425 (27%) were pre-symptomatic, and 811 (52%) remained asymptomatic. All of the 425 residents who were pre-symptomatic at the time of testing went on to develop a temperature of >100.4°F. Statistical analysis did not detect differences among the CCI for CLC residents with a negative SARS-CoV-2 test and those with symptomatic, pre-symptomatic, and asymptomatic COVID-19 infection.

Overall, COVID-19 infection resulted in 22.6 deaths per 1000 residents at VA CLCs. All-cause mortality at 30 days was highest among CLC residents with pre-symptomatic infections (26%), followed by those with symptomatic infections (24%), without a statistically significant difference between the survival curves for these two groups (Figure 1). Those with asymptomatic infections had a higher survival rate, with a 30-day mortality of 10%, compared with 5% observed among residents with a negative SARS-CoV-2 test ($p < 0.001$).

Using the lower temperature threshold (>99.0°F) to assess fever at the time of testing would have changed the categorization of 46% (195/425) of pre-symptomatic and 32% (257/811) of asymptomatic residents to symptomatic. This would have increased the number of residents recognized as symptomatic at the time of their positive SARS-CoV-2 test from 321 to 773. The number of residents with a negative SARS-CoV-2 test deemed to have a fever would have also increased, from 535 (with >100.4°F) to 2469 (with >99.0°F). All-cause mortality was similar among groups when residents were categorized using the lower temperature threshold. Mortality remained the highest for those who would have been symptomatic (20%), followed by pre-symptomatic (18%), and asymptomatic (8%). In our cohort of CLC residents, a temperature of >100.4°F as a threshold to consider

(A)

Temperature	RT-PCR test for SARS-CoV-2 Positive	Negative	
> 100.4°F	321	5343	5664
≤ 100.4°F	1236	76,781	78,017
	1557	82,124	83,681
	Sensitivity	21%	
	Specificity	94%	

(B)

Temperature	RT-PCR test for SARS-CoV-2 Positive	Negative	
> 99.0°F	773	22,747	23,520
≤ 99.0°F	784	59,377	60,161
	1557	82,124	83,681
	Sensitivity	50%	
	Specificity	72%	

FIGURE 2 Influence of temperature thresholds when screening Community Living Center residents for COVID-19 infection. Two-by-two contingency tables and resulting sensitivity and specificity when using a temperature of >100.4°F (panel A) or >99.0°F (panel B) to prompt consideration for SARS-CoV-2 testing

testing for SARS-CoV-2 resulted in a sensitivity and specificity of 21% and 93%, respectively (Figure 2). Lowering the temperature threshold to >99.0°F changed the sensitivity and specificity to 50% and 72%, respectively.

DISCUSSION

In our national cohort of CLC residents assessed over 9 months of the COVID-19 pandemic, decreasing the criteria for fever from >100.4 to >99.0°F would have increased the number of residents considered symptomatic at the time of their positive test for SARS-CoV-2 by more than 2-fold. While increasing sensitivity, the lower temperature threshold would also have increased the number of residents needing additional assessment for a possible COVID-19 infection by over 4.5-fold. Although the potential increase in labor and costs associated with a lower specificity when using >99.0°F as part of screening criteria are not trivial, the potential benefits outweigh the potential risks. First, using a temperature of >99.0°F to test for SARS-CoV-2 would permit diagnosing a larger proportion of residents with COVID-19 infection based on symptoms rather than on facility-wide screening. Second, it would help identify nursing home residents with COVID-19 infections earlier in the course of their illness. This, in turn, would result in more rapid initiation of infection prevention and control measures that remain the cornerstone of our response to this pandemic. Third, early recognition of COVID-19 infection can lead to increased vigilance for signs of clinical deterioration. This is an important consideration for nursing home residents who are typically frail with multi-morbid medical conditions; early detection of a change in condition can hasten initiation of supportive care, such as fluids and repositioning to improve breathing, and, if needed, transfer to an acute care setting. Finally, early detection of infection may also allow for more timely initiation of medical therapy that is effective against SARS-CoV-2.

Fever is among the most common signs of COVID-19 infection yet detecting fever in older adults is challenging due to lower baseline body temperatures and blunted temperature changes in response to infection. Clinical practice guidelines defining fever in older adults have included both a >2.0°F change from baseline, any temperature greater than 100.0°F, or repeated temperatures of >99.0°F.[10,11] Rudolph et al. reported that only 27% of Veterans with a positive SARS-CoV-2 test had a temperature ≥100.4°F.[2] They also noted that most CLC residents with a COVID-19 infection had at least 2 deviations in temperature that were ≥0.9°F above baseline. Shi et al. used a temperature of >100.0°F to assess residents of a large academic nursing home for signs and symptoms of a COVID-19 infection; even with this lower threshold, fewer than 25% of the residents with a positive SARS-CoV-2 test met criteria for having a fever.[5] A report describing 231 older adults in three nursing homes in Italy found that even when using a temperature threshold of >99.5°F, less than 2% of their residents were recognized as febrile.[20] Using a larger cohort and longer study period, our results support the recommendations made by McConeghy et al. to use a temperature of >99.0°F when screening nursing home residents for COVID-19 infection.[8] A single temperature threshold also makes recognition of fever easier for frontline staff who check vitals and initiate a clinical response.

The CMS has compiled data pertaining to COVID-19 infections from over 15,000 nursing in weekly internals.[21] Between May 18, 2020, the earliest date national data was available, and November 29, 2020, CMS data indicated an average of 183.4 confirmed COVID-19 cases per 1000 residents and an average of 30.5 deaths per 1000 residents with confirmed COVID-19 infection in community nursing homes. Over a comparable time period, from March 1 to November 30, 2020, our study found a lower rate of COVID-19 infections and 30-day all-cause mortality among CLC residents with COVID-19 infections. VA CLCs are integrated within the large and well-resourced VHA healthcare system. As such, VA CLCs were generally less affected by limitations in personnel, PPE, and access to SARS-CoV-2 tests that affected non-VA nursing homes. CLCs are usually in close proximity to VA medical centers where acute care services are readily available. These conditions may have contributed to the comparatively lower rates of infection and mortality observed among residents of VA CLCs compared with those in community nursing homes.

Our results indicated higher survival among CLC residents with asymptomatic infections, without obvious difference among these individuals compared with those who

were symptomatic or pre-symptomatic at the time of testing. This result is consistent with previous reports of residents with asymptomatic COVID-19 infections.[22] One reason for this difference may relate to the amount of viral shedding. Previous reports have not found statistically significant differences in the viral load of individuals with symptomatic compared with asymptomatic COVID-19 infections.[23] Correlation between viral loads associated with the positive tests and the symptoms manifested by CLC residents was beyond the scope of this study.

In addition to not assessing viral loads, our study has additional limitations. First, VA healthcare users are predominantly white and non-Latinx males and have a higher burden of chronic medical conditions than the rest of the U.S. population,[24,25] which may limit the generalizability of these results. The findings of high rates of mortality as well as a notable proportion of residents who were asymptomatic at the time of testing within the VA CLC cohort are consistent with previous reports among nursing home residents from both the United States and Canada.[3–5,26–29] Second, we relied upon administrative data to assess the results of RT-PCR tests for SARS-CoV-2. While VA Medical Centers as well as VA COVID-19 Shared Data Resource made efforts to mitigate these false positives and the local and national level, some of the RT-PCR results may have been false positives among individuals with a previous COVID-19 infection that continued to shed non-replicative SARS-CoV-2 RNA.[30] Third, our study period is limited to 9 months. To avoid the potential for fevers as a side effect of the mRNA vaccines confounding the data, we chose to examine the period before the Food and Drug Administration issued emergency use authorization for COVID-19 vaccines.

In conclusion, our analysis suggests that using a lower temperature threshold (>99.0°F) to prompt testing may facilitate early detection of COVID-19 infections, thus limiting the time during which residents thought to be asymptomatic might shed and transmit SARS-CoV-2 to other residents and healthcare personnel within the same congregate care setting. Even nursing home residents who are fully vaccinated may still develop symptomatic COVID-19 infections.[31] Modifying COVID-19 screening protocols in nursing homes so that fever is defined as a temperature >99.0°F will support earlier recognition and testing of infected residents which in turn leads to earlier initiation of supportive care, therapeutic interventions, and, crucially, accelerate the infection prevention and control measures that are central to reducing the spread of SARS-CoV-2.

CONFLICT OF INTEREST

None of the authors have relevant conflicts of interest to disclose. Curtis J. Donskey has received research funding from Pfizer, PDI, and Clorox. Federico Perez and Robin L. P. Jump have received research funding from Pfizer, Merck, and Accelerate. Robin L. P. Jump has participated in advisory boards for Pfizer and Merck.

AUTHOR CONTRIBUTIONS

Study conception and design: Taissa Bej, Brigid M. Wilson, Curtis J. Donskey, Federico Perez, Robin L. P. Jump. *Data generation*: Taissa Bej, Janet M. Briggs, Sunah Song, Brigid M. Wilson, Richard E. Banks. *Data analysis and interpretation*: Taissa Bej, Sonya Kothadia, Brigid M. Wilson, Robin L. P. Jump. *Preparation and critical revision of the manuscript*: all authors.

SPONSOR'S ROLE

This study was supported using data from the VA COVID-19 Shared Data Resource and by resources and facilities of the Department of Veterans Affairs (VA) Informatics and Computing Infrastructure (VINCI), VA HSE RES 13-457. These entities had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

FINANCIAL DISCLOSURE

This was an unfunded study supported in part by funds and facilities provided by the Cleveland Geriatric Research Education and Clinical Center (GRECC) at the VA Northeast Ohio Healthcare System.

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How to cite this article: Bej T, Kothadia S, Wilson BM, et al. Impact of fever thresholds in detection of COVID-19 in Department of Veterans Affairs Community Living Center residents. *J Am Geriatr Soc*. 2021;69(11):3044-3050. doi: 10.1111/jgs.17415