Can we use temperature measurements to identify pre-symptomatic SARS-CoV-2 infection in nursing home residents?

Salaheldin Elhamamsy MD | Frank DeVone ScM | Thomas Bayer MD | Chris Halladay ScM | Marilyne Cadieux DO | Kevin McConeghy PharmD
Ashna Rajan MD | Monyka Sachar MD | Nadia Mujahid MD | Mriganka Singh MD | Aman Nanda MD | Lynn McNicoll MD
James L. Rudolph MD | Stefan Gravenstein MD, MPH

Abstract
Background: COVID-19 has had a severe impact on morbidity and mortality among nursing home (NH) residents. Earlier detection of SARS-CoV-2 may position us to better mitigate the risk of spread. Both asymptomatic and pre-symptomatic transmission are common in outbreaks, and threshold temperatures, such as 38°C, for screening for infection could miss timely detection in the majority of residents. We hypothesized that in long-term care residents, temperature trends with SARS-CoV-2 infection could identify infection in pre-symptomatic individuals earlier than standard screening.

Methods: We conducted a retrospective cohort study using electronic health records in 6176 residents of the VA NHs who underwent SARS-CoV-2 testing triggered by symptoms. We collected information about age and other demographics, baseline temperature, and specific comorbidities. We created standardized definitions, and a hypothetical model to test measures of temperature variation and compare outcomes to the VA standard of care.

Results: We showed that a change from baseline of 0.4°C identified 47% of NH residents who became SARS-CoV-2 positive, earlier than standard testing by an average of 42.2 h. Temperature variability of 0.5°C over 3 days when paired with a 37.2°C temperature cutoff identified 55% of NH residents who became SARS-CoV-2 positive earlier than the standard of care testing by an average of 44.4 h. A change from baseline temperature of 0.4°C when combined with temperature variability of 0.7°C over 3 days identified 52% of NH residents who became SARS-CoV-2 positive, earlier than standard testing by an average of 40 h, and by more than 3 days in 22% of the residents. This earlier detection comes at the expense of triggering 57,793 tests, as compared to the number of trigger tests ordered in the VA system of 40,691.

This study was presented as a poster at the meeting of the American Geriatrics Society, 2021.
Conclusions: Our model suggests that early temperature trends with SARS-CoV-2 infection may identify infection in pre-symptomatic long-term care residents.

KEYWORDS
early detection, nursing home, SARS-CoV-2, temperature

INTRODUCTION

Early SARS-CoV-2 detection followed by earlier interventions can reduce disease severity and transmission, especially in nursing homes (NHs). Current early-detection strategies include systematic temperature and symptom screening. However, because pre-symptomatic transmission in NHs is common, clinical screening can miss early cases that risk transmission. Thus, states and individual NHs with high SARS-CoV-2 infection rates have required the strategy of systematic facility-wide or sweep testing of employees and residents as often as twice weekly. A more systematic approach to the interpretation of vital signs could improve the detection of SARS-CoV-2 and reduce the need for sweep testing.

Like most NHs in the United States, Veterans Health Administration (VA) NHs mandated daily clinical and temperature screening of all residents beginning March 1, 2020. The VA required all its NH residents to be Sweep-tested starting April 10th, 2020. These data, captured in the VA’s electronic medical records (EMRs), allowed for evaluation of temperature trends in those with and without SARS-CoV-2 infection.

Building on the common practice of daily temperature monitoring to screen NH residents for SARS-CoV-2 infection, we hypothesize that early temperature trends in the course of SARS-CoV-2 infection could identify pre-symptomatic individuals in the NH setting.

METHODS

Study design

The study used administrative data from the VA’s 133 NHs, housed in the VA’s computerized patient record system (CPRS). The NHs admitted 15,043 residents during the study period between March 1 and December 13, 2020. We evaluated a subset of 6176 residents who underwent SARS-CoV-2 testing, had documented temperatures and who were last tested by symptomatic testing. The temperature was determined using standard equipment.

We created hypothetical screening scenarios that modeled what would have happened if different metrics were used to screen residents for SARS-CoV-2. We compared this to what actually occurred in the VA NHs.

Key points

- Asymptomatic and pre-symptomatic transmission is common with SARS-CoV-2 infection in the Nursing home
- Our model suggests that screening may be improved by a patient-derived baseline temperature or temperature variability

Why does this paper matter?

This paper matters because it may show a path to simplify the tedious screening process medical staff must do for SARS-CoV-2 case-finding. Over 1 million nursing home residents get symptom screening, daily for a condition that remains asymptomatic 40% of the time in unvaccinated residents and over 80% of the time in those with breakthrough infection. We model a method that uses a single daily measurement of temperature as a tool to identify who to screen and test for infection and provides the opportunity for earlier detection.

Measurements and variables

VA standard-of-care, or VA SOC: What actually occurred in the VA NHs.

SARS-CoV-2 Date: The date of a resident’s positive polymerase chain reaction (PCR) test from a certified laboratory or, if they never had a positive test in the study period, the sampling date of their last negative test.

SARS-CoV-2 Period: 14 days before and after the SARS-CoV-2 Date.

Baseline Temperature: The mean of the last five temperatures recorded before the SARS-CoV-2 Period, using the first daily temperature after 4 a.m.
We further defined three metrics that would trigger a SARS-CoV-2 test in a resident:

**Simple T-Max Cutoff:** One-time temperature exceeds a specific value.

**Elevation From Baseline Cutoff:** Temperature exceeds the Baseline Temperature by a specific amount; and,

**Temperature Variability:** The difference between the maximum and minimum temperatures within a three-day period that exceeds a threshold value.

## DATA ANALYSIS

To determine the performance of our model, we used the following metrics:

**Earlier Detection:** The average number of hours a resident was detected earlier using this metric.

**Infected Identified Early:** The percentage of positive cases detected early using this metric.

**Total Days Earlier Detection:** The total time of earlier detection using a particular metric.

**Tests Triggered:** Total number of tests triggered using these metrics.

Once a resident triggered a SARS-CoV-2 test with negative results, they could not be tested again for 7 days. We assumed that a resident could not be positive twice within the study period. Any resident with a temperature of >38°C triggered a test. We used these metrics to see if we could determine SARS-CoV-2 positivity prior to VA SOC’s early detection.

We used standard deviation, \( p \)-value (with an alpha set at 0.05), and confidence intervals to compare groups.

We performed statistical analyses using Microsoft SQL Server 2017 and R statistical software (Version R 4.0.2).

For the demographics table, continuous variables were confirmed with an ANOVA test; categorical variables were compared with \( \chi^2 \).

## RESULTS

During the study period, the total number of SARS-CoV-2 tests (Sweep Testing and Symptomatic Testing) among our cohort was 40,691. We collected data on age and other demographics, Baseline Temperature, and specific comorbidities (Table 1).

Temperatures with SARS-CoV-2-confirmed infections began rising as early as 7 days before testing and remained elevated as late as the 14-day follow-up. Among

### TABLE 1

We collected data on age and other demographics, Baseline Temperature, and specific comorbidities.

|                  | Total | COV+ | COV- | \( p \)-Value |
|------------------|-------|------|------|--------------|
| \( N \)          | 6176  | 914  | 5262 |              |
| Age (years)      |       |      |      |              |
|                  | 71.82 (11.6) | 74.27 (10.87) | 71.40 (11.66) | <0.01 |
| Male (%)         |       |      |      |              |
|                  | 5913 (95.74%) | 888 (97.16%) | 5025 (95.50%) | 0.03 |
| Race: White (%)  |       |      |      |              |
|                  | 4391 (71.10%) | 616 (67.40%) | 3775 (71.74%) | 0.01 |
| Race: Black (%)  |       |      |      |              |
|                  | 1330 (21.53%) | 225 (24.62%) | 1105 (21.00%) | 0.02 |
| Race: Other (%)  |       |      |      |              |
|                  | 455 (7.37%) | 73 (7.99%) | 382 (7.26%) | 0.48 |
| Diabetes Mellitus (DM) (%) | 2621 (42.45%) | 395 (43.22%) | 2226 (42.31%) | 0.64 |
| DMcx (%)         |       |      |      |              |
|                  | 2779 (45.00%) | 398 (43.54%) | 2381 (45.26%) | 0.36 |
| Hypertension (HTN) (%) | 4719 (76.42%) | 693 (75.82%) | 4026 (76.53%) | 0.67 |
| HTNcx (%)        |       |      |      |              |
|                  | 2673 (43.29%) | 364 (39.82%) | 2309 (43.89%) | 0.02 |
| Congestive heart failure (%) | 2138 (34.62%) | 286 (31.29%) | 1852 (35.20%) | 0.02 |
| Pulmonary (%)    |       |      |      |              |
|                  | 2567 (41.57%) | 363 (39.72%) | 2204 (41.89%) | 0.23 |
| BMI (kg/m²)      | 28.27 (7.37) | 28.24 (7.33) | 28.28 (7.37) | 0.45 |
| Valvular (%)     |       |      |      |              |
|                  | 845 (13.68%) | 93 (10.18%) | 752 (14.29%) | <0.01 |
| Alcohol (%)      |       |      |      |              |
|                  | 1107 (17.93%) | 146 (15.97%) | 961 (18.27%) | 0.1 |
| Drugs (%)        |       |      |      |              |
|                  | 882 (14.28%) | 114 (12.47%) | 768 (14.60%) | 0.1 |
| Anemia (%)       |       |      |      |              |
|                  | 3270 (52.96%) | 430 (47.05%) | 2840 (53.98%) | 0.001 |
| Depression (%)   |       |      |      |              |
|                  | 3007 (48.70%) | 426 (46.61%) | 2581 (49.06%) | 0.18 |
| Tumor (%)        |       |      |      |              |
|                  | 1244 (20.15%) | 152 (16.63%) | 1092 (20.76%) | 0.01 |
| Psychoses (%)    |       |      |      |              |
|                  | 1613 (26.12%) | 339 (37.09%) | 1274 (24.22%) | <0.001 |
| TBI (%)          |       |      |      |              |
|                  | 403 (6.53%) | 62 (6.78%) | 341 (6.48%) | 0.79 |
| Baseline temperature | 36.59 (0.24) | 36.58 (0.22) | 36.59 (0.24) | 0.99 |
those residents with SARS-CoV-2, only 47.7% eventually met the fever threshold of 38.0°C.

Table 2 contains possible SARS-CoV-2 detection methods.

Using the temperature threshold of 38.0°C to trigger Screening Tests for SARS-CoV-2 in NH residents, we identified 3575 tests, or 39% of the cases, and detected individual cases, on average 3.6 h later per resident, compared to actual VA SOC testing. Using the lower temperature threshold of 37.2°C, we detected 33% of the SARS-CoV-2-infected residents, on average, 14.4 h earlier.

Temperature elevation of >0.4°C from baseline resulted in the early identification of 47% of SARS-CoV-2-infected residents by an approximate average of 42 h per resident.

Using Temperature Variability to select who to test resulted in the early identification of 55% of SARS-CoV-2 infected residents. When paired with a simple 37.2°C cutoff, early detection improved, on average, by 44.4 h per resident. This temperature cutoff triggered 65,802 tests. With a variability of 0.5°C, we identified 55% of those infected early, and achieved earlier identification of who to test by an average of 42 h per resident. This triggered 64,298 tests. Temperature elevation >0.4°C from baseline, combined with a 0.7°C range, detected 52% of the SARS-CoV-2-infected residents early by 40 h on average and triggered 57,793 tests. Using this method, when we looked at residents whose SARS-CoV-2 infections were detected earlier by 24-h or more, compared to VA SOC, we found that 50% were detected one calendar day or more earlier (see Figure 1); >25% were detected four or more days earlier; and, 11.5% were detected six or more days earlier.

| Temperature criteria to trigger test | Total days earlier detected | Earlier detection per resident (h) | Tests triggered | Infected identified early (%) |
|--------------------------------------|-------------------------------|-----------------------------------|----------------|-------------------------------|
| Tmax >37.2°C                         | 544                           | 14.4                              | 19,203         | 33                            |
| Tmax >38°C                           | 0                             | 0                                 | 3560           | 0                             |
| 0.4°C rise from baseline             | 1215                          | 42.2                              | 45,445         | 47                            |
| Range 0.5°C                         | 1608                          | 42.2                              | 64,298         | 55                            |
| Range 0.5°C or Tmax >37.2°C         | 1690                          | 44.4                              | 65,802         | 55                            |
| Range 0.7 or 0.4°C rise from baseline | 1530                         | 40.1                              | 57,793         | 52                            |

The change in temperature definition denotes the hypothetical trigger threshold that would generate an order for a SARS-CoV-2 diagnostic test. This includes reaching a maximum temperature of 37.2 or 38°C; having a temperature elevate at least 0.4°C above baseline; having a temperature range of at least 0.4, 0.5, or 0.7°C around baseline; or, a combination thereof. The temperature range criterion evaluates the range of temperatures over a consecutive three-day period. Earlier in column two and three means earlier than the VA standard of care.

**FIGURE 1** Cumulative number (%) of individuals identified for potential SARS-CoV-2 screening by two different temperature criteria as compared to the VA standard of care. According to our model: Using a cutoff of 37.2°C, 33% of the cases can be identified for screening one calendar day or more earlier, 16% 3 days or more earlier, and 11% 4 days or more earlier. Using a temperature elevation >0.4°C from baseline combined with a 0.7°C range, 52% of the cases can be identified for screening one calendar day or more earlier, 26% 4 days or more earlier, and 12% 6 days or more earlier than the VA standard of care approach to screening.
DISCUSSION

Our data show that screening of SARS-CoV-2 infection in NHs may be improved using only individual or combined measures of temperature variability. Compared to VA SOC using both clinical and temperature measures, a prospective study to test the prediction of the model is needed.

Implementing our hypothetical model, using a 0.7°C-range temperature variability paired with a 0.4°C-increase-from-baseline-temperature threshold, predicted an average advantage of 40-h in identifying those with SARS-CoV-2 infection for screening. With 52% early detection, and triggered 57,793 tests. According to our model, this approach would identify over half of those infected with SARS-CoV-2 one calendar day or more earlier than SOC (see Figure 1), but also >25.7% were detected four or more days earlier, and 11.5% were detected six or more days earlier than VA SOC.

Using a 37.2°C temperature cutoff threshold instead of the 38°C VA SOC could identify individuals with SARS-CoV-2 for screening 14.4 h earlier on average.

Individual temperatures provide incomplete clinical information and context. Our method leverages information in the medical record to improve its utility for clinical decision-making. If automated in the EMR, it could flag outliers and help identify high-risk individuals who could benefit from SARS-CoV-2 testing.

Older residents tend to have lower baseline temperatures, limiting the utility of a simple temperature cutoff. Investigations of temperature in older adults and NH residents have shown absolute thresholds, such as 38°C, as insensitive. Additionally, NH residents can have atypical physiological responses to infection, and might not be able to report symptoms if they have dementia.

SARS-CoV-2 infection can spread from residents who are presymptomatic or asymptomatic, thus limiting the effectiveness of clinical screening. Early in the pandemic, as in our sample, clinical screening in NHs did not always identify SARS-CoV-2 infection or contain the spread. The consequent sweep testing strategy included weekly and sometimes bi-weekly testing of NH residents and staff, which was expensive, invasive, and used up valuable human and PPE resources.

Deriving a baseline temperature by averaging the first daily temperatures over a three-to-five-day period, is a person-centered approach that is less-invasive, less-costly, and can be used for other infectious diseases once validated.

Temperature monitoring is an inexpensive intervention that NH staff are well-trained for. Understanding early temperature trends with SARS-CoV-2 infection allows NHs to transition away from mass testing. Using a multiple-reading threshold increase from baseline offers a favorable balance of sensitivity and specificity relative to a single reading.

Implementing our model in a clinical setting would require several temperature readings (at minimum, one temperature per day over 3 days) to calculate the temperature range and a documented measure of baseline temperature, to calculate change-from-baseline.

The scale provided by the VA data, allows us to perform these statistical analyses and better study the earlier detection of SARS-CoV-2 in an NH setting than has previously been possible. The strength of our analysis includes a large NH sample, frequent temperature monitoring documented in the EMR, and constant monitoring of COVID-19. The study population includes immune senescent adults living in NHs, who are not often included in medical research.

Study limitations included: point-estimate temperature, as opposed to continuous temperature monitoring, is less ideal to better understand the effect of SARS-CoV-2 on temperature over time; as a hypothetical model, our scenario did not allow for us to perform more traditional statistical tests on the results, compelling us to create the measures as a best-substitute for more traditional sensitivity and specificity analysis; and, our older cohort (predominantly male and white) was relatively homogenous and did not include demographic variations that can affect temperature; Additionally, NHs typically do not define or document baseline temperatures for their residents. To do so, they would need to program the EMR to establish and track baseline temperatures using existing data and create a notification to alert baseline changes. Because records did not distinguish if clinical symptoms triggered a SARS-CoV-2 test, we relied on a conservative Trigger Test definition that limited our sample size by more than half. Had this information been available, we likely would have had a larger portion of our sample available for the analysis. Finally, a prospective study to test the prediction of the model is needed.

CONCLUSIONS AND IMPLICATIONS

Our model suggests that clinical screening for SARS-CoV-2 in NHs may be improved by using a resident-derived baseline temperature with a 0.4°C relative elevation, or temperature variability of 0.7°C thresholds to trigger SARS-CoV2 testing. This approach may potentially lead to better infection control and reduce the need for sweep Testing in NHs. These data can be used for creating early detection algorithms that will be significantly more effective when continuous temperature monitoring is available to high-risk NH residents.
AUTHOR CONTRIBUTIONS
Salaheldin Elhamamsy authored the article. Frank Devone conceived the main analytical approach, and performed the primary analysis for the community nursing homes. Kevin McConeghy and Christopher Halladay assisted with programming and analysis. Stefan Gravenstein assisted with study design, interpretation of results, and co-authored the article. Thomas Bayer, Ashna Rajan, Marilyne Cadieux, Moniyka Sachar, Christopher Halladay, Nadia Mujahid, Mriganka Singh, Aman Nanda, Lynn McNicoll, MD, James Rudolph, and Christopher Halladay assisted with data evaluation and manuscript review.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.

SPONSOR’S ROLE
The study was approved by the Providence VAMC Institutional Review Board. Christopher Halladay and James L. Rudolph provided the primary results for the Veterans Affairs nursing homes.

ORCID
Kevin McConeghy https://orcid.org/0000-0002-5056-0431

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

Appendix S1. Graphical representation of the relationship of temperature criteria used to flag patients for screening and the number of tests that would be triggered as a result of using this temperature criterion. Bars show the percent of individuals that would be flagged for screening using a trigger threshold the dots show the number of tests that would be triggered using the same threshold.

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