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Fevers Are Rarest in the Morning: Could We Be Missing Infectious Disease Cases by Screening for Fever Then?

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Fevers Are Rarest in the Morning: Could We Be Missing Infectious Disease Cases by Screening for Fever Then?

Summary: Body temperatures are less likely to reach the fever range in the morning,[1,2] but it is unknown how this affects practice during disease outbreaks. We retrospectively investigated fever-range temperatures (≥100.4°F, ≥38.0°C) during seasonal influenza outbreaks and the 2009 H1N1 (swine flu) pandemic, which have recently been used as preparatory models for coronavirus disease 2019 (COVID-19). Our analyses included a nationally representative sample of records from adult visits to US emergency departments (*n*=202,181) and data from a Boston emergency department (*n*=93,225). Fever-range temperatures were about half as common in the morning as in the evening, suggesting that morning temperatures can be much less diagnostic, and that revisions may be needed to the practice of once-daily temperature screens at morning arrival to workplaces and schools. Twice-daily screens could be a simple solution, but similar research is still needed on fevers in COVID-19 itself.

Methods: Temperatures (*n*=115,149) were collected during triages at a Boston adult emergency department to monitor outbreaks (September 2009–March 2012).[2,3] We also investigated adult triage temperatures (*n*=218,574) from a nationally representative study of US emergency department visits (December 2002–December 2010).[4] The thermometer types used were temporal artery (Boston) and a nationally representative sample (national). We excluded records missing temperature or time (Boston=1.0%, national=7.5%), or indicating repeated or accidental measurement (repeated ≤15 seconds or temperature <95°F: Boston=18.0%), leaving 93,225 Boston and 202,181 national temperatures for analysis.[2] High-influenza activity periods were defined as months that fully exceeded CDC ILINet baseline thresholds in region 1 (Boston analysis; outbreak-period *n*=6627) or nationally (national analysis; outbreak-period *n*=29,908).[5]

We accounted for the national study's multistage design to obtain nationally representative findings.[6] For the national study, time-of-day case mix differences in sex (male or female), age (years, analyzed with spline), urgency/immediacy of case (4 levels and unknown), pain (4 levels and unknown), race (black, white, or other), Hispanic or Latino ancestry (yes or no), hospital admission (yes or no), test ordering (yes, no, or unknown), procedure administration (yes, no, or unknown), medication ordering (yes, no, or unknown), ambulance arrival (yes, no, or unknown), and expected payment source (7 levels and unknown) were excluded as responsible factors for the time-of-day fever rate differences using multivariable logistic regression with a quasibinomial error distribution and average marginal predictions.[4,7] Anonymity requirements prevented similar analyses for Boston data.[2]

Our research extends a previous study that did not analyze outbreaks, but provides more details on methods, summarizes patient demographics, examines selection and other potential biases, demonstrates the robustness of findings to exclusion criteria changes (useful because many exclusions were made in Boston data), and shows that the large morning-evening changes in fever rates occurred on both weekdays and weekends (i.e., regardless of changes in workday schedules and availability of other care options).[2]

Results: Fever-range temperatures (≥100.4°F, ≥38.0°C) were rarest during mornings, and were about half as common during mornings as during evenings in periods of high influenza activity (ratio of 6 AM–noon vs. 6 PM–midnight: Boston=0.43, 95% CI=0.29-0.61; national=0.56, 95% CI=0.47-0.66; **Figure 1**). These periods included seasonal outbreaks and the 2009 H1N1 (swine flu) pandemic. Results did not change substantially after adjustment for time-of-day differences in the case mix of included patients (adjusted ratio of 6 AM–noon vs. 6 PM–midnight: national=0.59, 95% CI=0.50-0.70). The daily changes in fever rates were also similar when studying other common fever definitions used for COVID-19 (**Suppl. Figure 1**) and when analyzing time as a continuous variable instead of binning (**Suppl. Figure 2**).

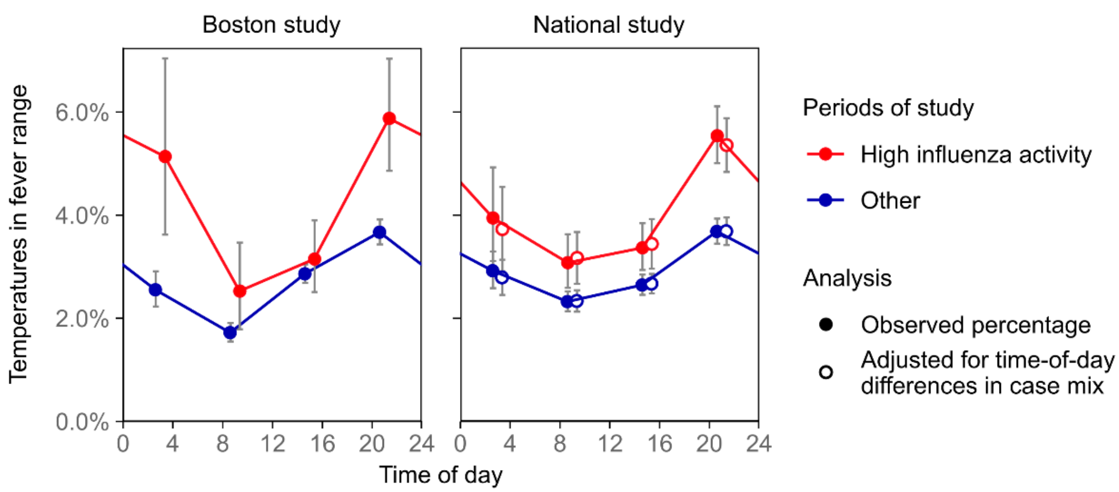

Figure 1. Time-of-day changes in the percentage of body temperatures that reach the fever range: Boston and US national studies. In both the Boston and US national studies, temperatures measured during mornings were less likely to reach the fever range (≥100.4°F, ≥38.0°C), especially during periods of high influenza activity (seasonal flu and the 2009 H1N1 pandemic). During these periods, fever-range temperatures were about half as common in the morning as in the evening. The results suggest that morning temperature measurements could miss many febrile disease cases, which raises concerns because workplace and school fever screens often occur during mornings, and because patients seen for potential COVID-19 may only have temperatures checked during mornings. A simple solution is twice-daily temperature measurement. National study results are nationally representative of adult visits to US emergency departments. Confidence intervals are 95%.

Discussion: Our results raise concerns that morning measurements could miss many (perhaps even half) of the individuals with fevers detectable during evenings, potentially allowing them to go to work, attend school, and travel. Physiologically, circadian rhythms usually reach temperature low points during mornings, and patients can lack fever signs or can present some signs without reaching cutoffs like ≥100.4°F (≥38.0°C).[1,2,8] Although there is a long history of studying circadian rhythms, their relevance to fever presentation remains little known, partly because the large datasets needed for detailed study have only become available recently, and partly because time-of-day variations in fever had lower importance[9] before COVID-19.

Temperature screenings are used for COVID-19 because measurements are simple, fever is thought to be the most common symptom,[10] and first symptoms often include fever.[11,12] The most evidence is available for hospitalized patients, who generally have high rates of fever (88.7%, including 43.8% on admission;[10] 94.3%, including 87.1% at illness onset;[13] 98.6% at onset;[14] 30.7% on triage or admission;[15] 83%, including 26% on admission;[16] 80.4% of severe and 82.4% of non-severe/common cases at onset;[17] and 85.0% with fever or chills on admission[18]) and fevers that present on many days (median fever days per patient: 9 in inpatients without ICU stays,[13] 31 in inpatients with ICU stays,[13] and 12 in surviving inpatients[19]), which allows multiple opportunities for screening detection. Less evidence is available for COVID-19 cases as a whole, though tracking of new cases also suggests fairly high rates of fever: 71% of contact-traced cases;[20] 75.0% of healthcare personnel, including 41.7% at first onset;[12] at onset, 53.3% of index cases and 56.3% of household members they infected;[21] and, at the time of positive COVID-19 tests, self-reported by 48.7% of healthcare workers and 43.7% of others.[22] Overall, reports to date show fever rates that are high during COVID-19's clinical course and intermediate at first onset. Our results suggest that some onset research could underestimate fever rates by using morning temperatures, but we cannot tell which studies would be affected because none report temperature measurement times.

Currently, fever screening is usually recommended once daily at morning arrival to workplaces and schools, yet our results suggest the morning may be the worst time. A simple solution is to measure temperature at both start and end of shift, and at least every 12 hours during extended shifts. The first measurement is retained to help detect cases before shifts, and the second is for cases previously missed. With this schedule, at least one measurement avoids the temperature low point, regardless of differences in shift or individual circadian timing. Similarly, evening temperature remeasurements could also be requested from patients seen during mornings for potential COVID-19, an approach that could be useful where SARS-CoV-2 testing is limited to febrile patients because of test shortages. Relatedly, departure and arrival screens could both be worthwhile for long flights.[23]

An alternative to twice-daily screening would be once-daily screening with a lower morning fever definition. However, this would not address interindividual circadian timing differences (common for night workers) and would require developing and validating the new definition. One morning-lowered fever definition has been proposed,[1] but appeared to perform poorly when tested.[2]

A limitation to fever and other symptom screenings is that they cannot detect asymptomatic or presymptomatic cases. However, screenings with partial detection abilities can confer benefits that grow multiplicatively in time. For example, suppose screening modestly improved case detection and isolation, reducing disease transmission 15%. Then, at the first, second, third, and fourth generations of transmission in a new outbreak, there would be roughly 85%, 72.3%, 61.4%, and 52.2% as many new cases as would otherwise occur (=85%^{n}). Though the growth of benefits eventually stops, it slows outbreaks, allowing more time to try case tracking and other limited countermeasures before closures and lockdowns become the only options for stopping spread. Similar reasoning has been used to explain how large benefits can accompany other imperfect, partial measures of blocking disease transmission, like face masks.[24] The growth of benefits is also why addressing screening failure points, like low morning fever rates, can be more beneficial than intuition may suggest.

We end with some cautions: First, our results are from clinicians using hospital-grade thermometers, and may not generalize to layperson measurements or lower-accuracy thermometer guns and thermal imagers. Second, fever screenings should balance false-negative risks with false-positive burdens, which could increase during evenings when healthy temperatures are higher.[1,2] Third, thermometer site, age, and other factors also affect measured temperature.[8,25] Screening practices may also benefit from adjustment for some of these factors, especially thermometer site. Fourth and most importantly, although most diseases include morning temperature lows, this has not yet been shown for COVID-19. We hope our research encourages study of this topic and of optimal screening strategies, especially to assist workplace and school reopenings where COVID-19 is regionally controlled, but control remains fragile.

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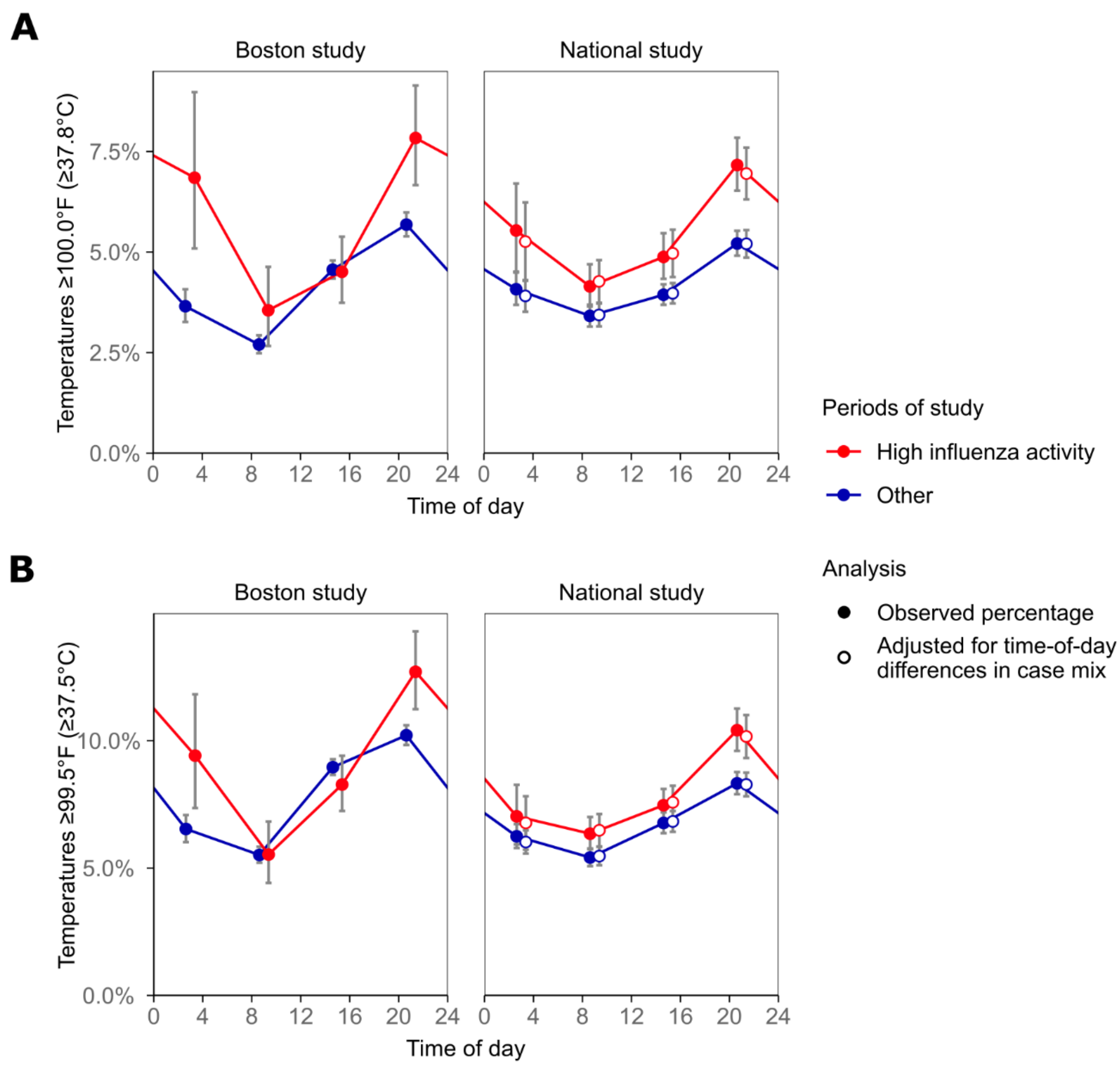
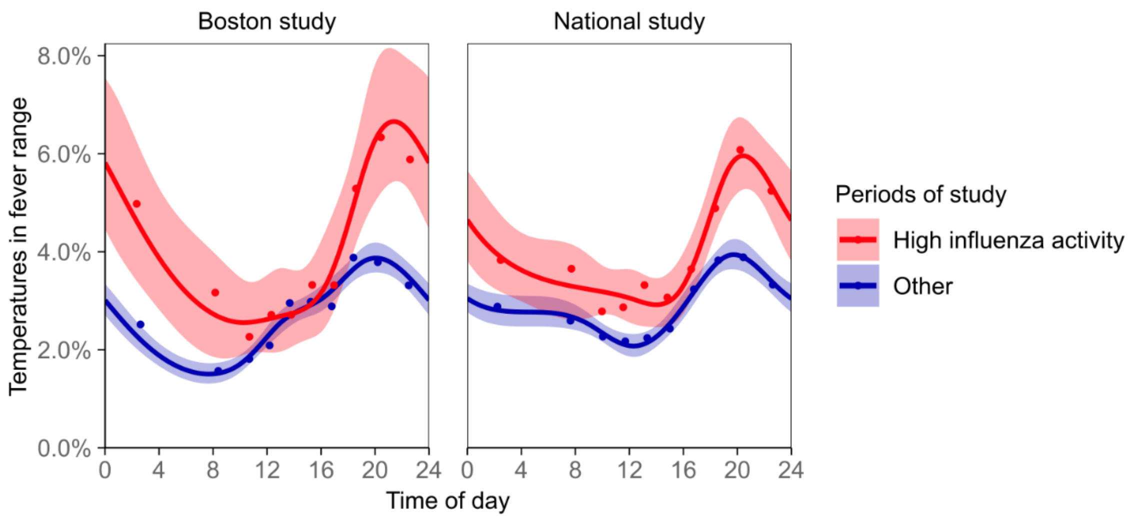


Suppl. Figure 1. Time-of-day changes in fever rates using other fever definitions that are commonly applied for COVID-19. (A) When the fever definition is lowered to ≥100.0°F (≥37.8°C), large time-of-day changes in fever rates are still observed, especially during periods of high influenza activity (ratio of fever rates at 6 AM–noon vs. 6 PM–midnight: Boston=0.45, 95% CI=0.32-0.60; national=0.58, 95% CI=0.50-0.67; national adjusted for case-mix changes=0.61, 95% CI=0.53-0.71). (B) When the fever definition is further lowered to ≥99.5°F (≥37.5°C), time-of-day changes in fever rates continue to be observed, including during high influenza activity (ratio of fever rates at 6 AM–noon vs. 6 PM–midnight: Boston=0.44, 95% CI=0.34-0.55; national=0.61, 95% CI=0.54-0.69; national adjusted for case-mix changes=0.64, 95% CI=0.56-0.72). However, more cases classified as having fever and fever rates during high influenza activity are no longer as distinguishable from fever rates during other periods. This may be because the lower threshold includes more individuals who do not physiologically have fever (false positives). If false positives are too common, they can be an obstacle to implementing screening. Confidence intervals are 95%. In the plot, points were shifted slightly on the x-axis to avoid overlapping each other.



Suppl. Figure 2. Time-of-day variation in the rate of fever (temperature ≥100.4°F, ≥38.0°C), with time analyzed as a continuous variable. Results are similar to the binned analysis in the main paper (Figure 1), but show the cycle of fever rates over the day with more detail. Curves are from logistic regressions using a quasibinomial error distribution and a cyclic cubic spline term for time of day, with knots placed at quintiles of the recorded times of day. To illustrate the correspondence between the data and the curves, points are also shown with the average time and fever rate for every 10% segment the recorded times of day. As in the previous figures, national study results are nationally representative of adult visits to US emergency departments. Confidence bands are 95% (pointwise).