Heat-related emergency hospitalizations for respiratory diseases in the Medicare population

<table>
<thead>
<tr>
<th>Journal:</th>
<th>American Journal of Respiratory and Critical Care Medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID:</td>
<td>Blue-201211-1969OC.R1</td>
</tr>
<tr>
<td>Manuscript Type:</td>
<td>OC - Original Contribution</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>06-Feb-2013</td>
</tr>
<tr>
<td>Complete List of Authors:</td>
<td>Anderson, G. Brooke; Johns Hopkins Bloomberg School of Public Health, Department of Biostatistics Dominici, Francesca; Harvard School of Public Health, Department of Biostatistics Wang, Yun; Harvard School of Public Health, Department of Biostatistics McCormack, Meredith; Johns Hopkins School of Public Health, Department of Environmental Health Sciences Bell, Michelle; Yale University, School of Forestry &amp; Environmental Studies Peng, Roger; Johns Hopkins Bloomberg School of Public Health, Department of Biostatistics</td>
</tr>
<tr>
<td>Keywords:</td>
<td>Chronic Obstructive Pulmonary Disease, Hospitalization, Hot temperature, Respiratory Tract Infections, Weather</td>
</tr>
</tbody>
</table>
Title: Heat-related emergency hospitalizations for respiratory diseases in the Medicare population

Authors: G. Brooke Anderson,1 Francesca Dominici,2 Yun Wang,2 Meredith C. McCormack,3,4 Michelle L. Bell,5 and Roger D. Peng1,*

Author affiliations:
1Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health
2Department of Biostatistics, Harvard School of Public Health
3Division of Pulmonary and Critical Care, Johns Hopkins School of Medicine
4Department of Environmental Health Sciences, Johns Hopkins School of Public Health
5School of Forestry & Environmental Studies, Yale University

*Corresponding author:
Roger D. Peng
Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health
615 N. Wolfe Street
Baltimore, MD 21205
Telephone: 410-955-2468
Fax: 410-955-0958
Email: rpeng@jhsph.edu
Author contributions:

Study concept and design: Anderson, Dominici, Bell, Peng

Acquisition of data: Dominici, Wang, Peng

Analysis or interpretation of data: Anderson, Dominici, McCormack, Bell, Peng

Drafting of manuscript: Anderson, Dominici, Wang, McCormack, Bell, Peng

Critical revision of the manuscript for important intellectual content: Anderson, Dominici, Wang, McCormack, Bell, Peng

Statistical analysis: Anderson, Dominici, Bell, Peng

Obtained funding: Dominici, Bell, Peng

Administrative, technical, or material support: Dominici, Peng

Study supervision: Dominici, Peng

Sources of support: Funding for Drs. Anderson, Dominici, Wang, Bell, and Peng was provided by grants R01ES019560 and R21ES020152 from the National Institute for Environmental Health Sciences. Funding for Drs. Dominici, Wang, and Bell was also provided by grant RD-83479801 from the US Environmental Protection Agency. Funding for Drs. Dominici and Wang was also provided by grant R01ES012054 from the National Institute for Environmental Health Sciences, grant R834894 from the US Environmental Protection Agency, and a grant from the Health Effects Institute. Funding for Dr. Bell was also provided by grants R01ES015028 and R21ES021427 from the National Institute for Environmental Health Sciences. Funding for Dr. McCormack was provided by grant K23ES016819 from the National Institutes of Health.

Although the research described in this article has been funded in part by the US Environmental
Protection Agency, it has not been subjected to the agency’s required peer and policy review and therefore does not necessarily reflect the views of the agency and no official endorsement should be inferred. The contents of this article do not necessarily reflect the views and policies of the Health Effects Institute.

**Running head:** Heat-related respiratory hospitalizations

**Descriptor number:** 6.04

**Total word count:** 2,847

**At a Glance Commentary:**

**Scientific Knowledge on the Subject.** Although outdoor heat is known to increase rates of respiratory mortality in the elderly, the relationship between heat and respiratory morbidity has been little studied in the United States at a national level.

**What this Study Adds to the Field.** We investigate the relationship between outdoor temperature and emergency respiratory hospitalizations in the largest population of elderly studied to date: approximately 12.5 million Medicare beneficiaries in 213 urban United States counties. We find a clear and consistent increase in respiratory hospitalizations with increasing outdoor temperature across the United States.

This article has an online data supplement, which is accessible from this issue’s table of content online at [www.atsjournals.org](http://www.atsjournals.org).
Abstract

Rationale: The heat-related risk of hospitalization for respiratory diseases among the elderly has not been quantified in the United States on a national scale. With climate change predictions of more frequent and more intense heat waves, it is of paramount importance to quantify the health risks related to heat, especially for the most vulnerable.

Objectives: To estimate the risk of hospitalization for respiratory diseases associated with outdoor heat in the US elderly.

Methods: An observational study of ~12.5 million Medicare beneficiaries in 213 United States counties, January 1, 1999—December 31, 2008. We estimate a national average relative risk of hospitalization for each 10°F (5.6°C) increase in daily outdoor temperature using Bayesian hierarchical models.

Measurements and Main Results: We obtained daily county-level rates of Medicare emergency respiratory hospitalizations (ICD-9 464–466, 480–487, 490–492) in 213 United States counties for 1999-2008. Overall, each 10°F increase in daily temperature was associated with a 4.3% increase in same-day emergency hospitalizations for respiratory diseases (95% posterior interval: 3.8, 4.8%). Counties’ relative risks were significantly higher in counties with cooler average summer temperatures.

Conclusions: We found strong evidence of an association between outdoor heat and respiratory hospitalizations in the largest population of elderly studied to date. Given projections of increasing temperatures from climate change and the increasing global prevalence of chronic pulmonary disease, the relationship between heat and respiratory morbidity is a growing concern.

Abstract word count: 231 words
Key words: Chronic Obstructive Pulmonary Disease, Hospitalization, Hot temperature, Respiratory Tract Infections, Weather
1 Introduction

Outdoor heat can cause spikes in respiratory deaths (1-2), but considerably less is known about heat’s impacts on respiratory morbidity. Given that: 1) climate change will increase exposure to extreme heat (3); 2) the prevalence of chronic respiratory diseases is increasing (4); and 3) the elderly will likely be most affected by heat-related problems (5), there is a pressing need to improve our understanding of respiratory heat effects among the elderly for both fatal and non-fatal outcomes.

There are two major limitations to current research on the relationship between heat and respiratory hospitalizations. First, this relationship has not been adequately studied worldwide to confidently identify a consistent link between respiratory hospitalizations and heat. The few studies that have investigated heat and respiratory hospitalizations have found somewhat conflicting results (6). For example, studies of Brisbane, Australia, (7-8) and Athens, Greece, (9) found hospitalizations rates decreased slightly during hot weather, while studies of California (10-11), New York (12-13), and 12 European cities (14) found respiratory hospitalizations increased with heat. While a meta-analysis of current research estimated a positive relationship between heat and respiratory hospitalizations across all studies, it lacked sufficient power to distinguish this effect from a null effect (6).

Second, outside of California and New York, little research has been done in the United States (US). US studies of heat and respiratory morbidity have been limited to single cities (12, 15) or single states (California (10-11, 16); New York (13)) or were retrospective studies of single heat waves (17-19). Worldwide, large heterogeneity exists between temperature-morbidity studies from different locations (6, 20). Therefore, although the relationship between heat and
respiratory hospitalizations has been well-studied in California and New York (10-11, 13),
temperature effect estimates based only on these states are unlikely to be representative of
national US effects.

In this study we estimate the risk of emergency hospital admissions for respiratory
diseases associated with outdoor heat exposure for approximately 12 million elderly individuals
in 213 US urban counties from 1999 to 2008. We investigate whether this association is
confounded by exposure to air pollution or modified by individual (age, gender) or county
(average summer temperature) characteristics. This is, to date, the largest elderly population
investigated to estimate acute heat-related risks of respiratory hospitalizations and the first
national study of these risks in the United States.

2 Methods

This study used a dataset created for environmental health research by aggregating
Medicare hospitalization rates by county and linking them with ambient air pollution and
temperature data (21). This dataset includes daily hospitalizations for 1999-2008 for 221 US
counties, based on Medicare inpatient claims for all fee-for-service Medicare beneficiaries ≥65
years. Hospitalization rates are aggregated by gender, age (65–74 years, 75–84 years, ≥85 years),
and medical condition (COPD: ICD-9-CM principal discharge diagnosis codes 490–492;
respiratory tract infections: 464–466, 480–487). The dataset includes measurements of weather
(temperature, dew point temperature) and air pollution (tropospheric ozone [O₃], particulate
matter with aerodynamic diameter ≤10µm [PM₁₀] and ≤2.5µm [PM₂.₅]). Analysis was limited to
the 213 study counties within the contiguous 48 states and, to ensure adequate information to
estimate model parameters and for convergence of model-fitting algorithms, with ≥5 years of weather data. Further data details are in an online data supplement.

We modeled the relationship between daily hospitalization rate and outdoor heat for May—September within each county using an overdispersed Poisson generalized linear model (1-2). Models controlled for day of week and dew point temperature (adjusted for temperature to limit collinearity). Models adjusted for long-term and seasonal trends in county hospitalization rates and temperature using smooth spline functions of time (1). Further details on model development are in the online data supplement.

For each county, we estimated the percentage increase in daily emergency respiratory hospitalizations associated with each 10°F (5.6°C) increase in daily average temperature (10-11). To estimate the national average association between heat and respiratory hospitalizations, we combined county-level estimates with a two-stage Bayesian hierarchical model, incorporating variation within and between county-level estimates (22). We estimated national average associations separately for COPD and respiratory tract infections and jointly for both causes (total respiratory hospitalizations). To investigate differences in susceptibility, we estimated heat-hospitalization associations after stratifying data by age (65–74 years, 75–84 years, ≥85 years) and gender. We estimated national average heat effects at single-day lags of 0, 1, and 2 days and cumulatively for lags 0–6. Finally, we investigated whether counties with cooler summers on average for the entire study period have statistically significant larger relative risks of heat-related hospital admissions than counties with warmer summers. We provide evidence toward this question using a two-level hierarchical Bayesian model (1, 22). Details are given in the online data supplement.
We assessed the sensitivity of model results to the degree of adjustment for seasonality and long-term trends as well as to the metric used for heat exposure (maximum temperature, minimum temperature, heat index). We also investigated sensitivity to air pollutant control (O$_3$, PM$_{10}$, and PM$_{2.5}$). Details on these sensitivity analyses are in the online data supplement.

### 3 Results

Our final dataset included 213 urban counties, covering ~12.5 million Medicare beneficiaries across the US (>30% of the US population ≥65 years (23)) (Table 1) and including locations with a variety of climates (Figure 1; Figure E1 in the online data supplement).

On average across the 213 counties, respiratory hospitalizations increased 4.3% (95% posterior interval [PI]: 3.8, 4.8%) for each 10°F increase in daily mean summer temperature (Figure 2). Results were similar for COPD (4.7%; PI: 3.9, 5.5%) and respiratory tract infections (4.1%; PI: 3.4, 4.7%) (Figure 2). Results were robust to changes in adjustment for seasonality (see Figure E2 in the online data supplement) and were similar using different temperature metrics (e.g., minimum and maximum temperature, heat index) (see Table E1 in the online data supplement).

Across counties, we found small to moderate correlations between temperature and air pollutants (median across counties: O$_3$: 0.39, PM$_{10}$: 0.42; PM$_{2.5}$: 0.45) (see Figure E3, and Table E2 in the online data supplement). However, both county-level and national average estimates were very similar for models with and without the adjustment for O$_3$, PM$_{10}$, and PM$_{2.5}$ (Figure 3; Table E3 in the online data supplement). Therefore we did not find evidence that the association
between outdoor temperature and respiratory admissions is attributable to exposure to air pollution.

Heat and respiratory hospitalizations were most strongly associated on the day of exposure (lag 0) (see Figure E4 in the online data supplement). One day following exposure (lag 1), the association was smaller but still positive and statistically significant (2.3%; PI: 1.8, 2.8%), while at lag 2, there was no evidence of an association (0.1%; PI: -0.3, 0.5%) (see Figure E4 in the online data supplement). When we modeled cumulative effects up to one week following exposure (lags 0–6), we found a cumulative effect of a 2.2% (PI: 1.3, 3.1%) increase in respiratory hospitalizations associated with a 10°F increase in the previous week’s daily mean temperature (see Figure E4 in the online data supplement).

The association between heat and respiratory hospitalizations was consistently positive and statistically significant in all subpopulations (i.e., age and gender) considered (Figure 2). Relative risk estimates were very similar for men and women (4.3%; PI: 3.6, 5.0% for men and 4.4%; PI: 3.7, 5.1% for women) (Figure 2) and for the different age groups (65–74 years: 4.8%; PI: 4.0, 5.6%; 75–84 years: 4.2%; PI: 3.5, 4.9%; 85 years and older: 4.2%; PI: 3.2, 5.2%) (Figure 2).

We investigated whether differences between county-specific risks of heat-related hospital admissions could be explained by differences between the counties’ average summer temperature, defined as average May–September temperature for 1999–2008 (Figure 1, Figure 4). For a county with average summer temperature 10°F cooler than the national average summer temperature, the county was estimated to have a 1.4% (PI: 0.4, 2.3%) higher relative risk of heat-related respiratory hospitalization than the national relative risk.
4 Discussion

We investigated the acute relationship between short-term exposure to outdoor heat and hospitalizations for respiratory diseases among the elderly in 213 US counties, geographically spread across the United States and with a variety of climates. Across these counties, daily rates of Medicare respiratory hospitalizations increased 4.3% (PI: 3.8, 4.8%) per 10°F increase in daily temperature. To translate this association to number of excess hospitalizations, each 10°F increase in daily temperature, for example, translates to approximately 30 excess respiratory Medicare hospitalizations per day across these 213 study counties, based on county-specific effect estimates and hospitalization rates for the most current year of this study (2008). Note that a larger increase in daily temperature would result in more excess hospitalizations and a lower increase in fewer hospitalizations (e.g., approximately 15 excess respiratory Medicare hospitalizations/day for a 5°F increase, approximately 45 for a 15°F increase). Across all study counties, the average within-county range between the hottest and coolest temperatures over the 10 study years for a specific date of the summer (e.g., June 1) was 15.1°F, while the average interquartile range was 5.8°F (see Supplemental Material for more details on this calculation).

We investigated this association for lags of a week or less and found the association was strongest at a same-day lag. The association was robust to control for air pollution, changes in control for long-term and seasonal trends, and changes in the metric used to estimate heat exposure. By jointly investigating this large set of locations, this study identified a consistent increase in respiratory hospitalizations associated with heat across a variety of US locations, and also identified heterogeneity between county-specific associations based on differences in local climate.
These acute heat effects are smaller than those found in several previous time series studies. Each 10°F increase in outdoor heat was found to increase respiratory hospitalization rates 12.3% in Mediterranean cities (14), 16.1% in New York, NY (12), and 19.3% in a meta-analysis of worldwide heat-morbidity studies (6). This difference cannot be explained by differences in exposure metrics, since our estimates changed little with alternate exposure metrics. The smaller effect size found in this study may result from differences in modifying factors, including population characteristics, housing structures, and air conditioning prevalence.

Our findings are more consistent with two California studies, which identified increases of 2.0% (11) and 2.6% (10) in respiratory hospitalizations per 10°F increase in daily outdoor heat. While the effect found in our study is higher, our study was restricted to a more susceptible population (people ≥65 years), while these California studies included all ages.

While epidemiological studies cannot definitively determine the pathway of heat’s effects on respiratory health, a large multi-community study can evaluate consistency between epidemiological health endpoints and potential pathways through close investigation of effect modification by age, gender, and local climate, as well as the role of air pollution. Our research helps clarify the link between outdoor heat and acute respiratory health outcomes by providing support for or against several plausible pathways for heat’s effects on respiratory health.

First, we extensively tested sensitivity of heat effect estimates to controlling for three pollutants linked to both outdoor heat and respiratory health (O₃, PM₁₀, and PM₂.₅) (21, 24). Our results provide evidence that increased respiratory risks during hot weather are not explained solely by increases in air pollution concentration—associations between heat and respiratory hospitalizations were almost unchanged with adjustment for pollutants. Pollen and mold concentrations have also been linked to both outdoor heat (25-26) and respiratory health (27-28).
Nationally representative data for these aeroallergens were not available to definitively address this question in the current study (29), but future research could investigate this pathway for heat effects at the community or regional level.

Our findings also provide evidence that increases in acute respiratory outcomes during heat are probably not caused by indoor crowding to avoid the heat. While indoor crowding may help spread respiratory infections (30), respiratory diseases take several days to progress from exposure to symptoms. We found, conversely, the strongest association between respiratory hospitalizations and heat was on the same day as exposure (lag 0). Several city- or state-level studies in the US (10-12), as well as international studies (6, 20), have similarly found same-day associations between respiratory hospitalizations and heat. These results suggest heat may aggravate existing respiratory infections rather than spread new infections through indoor crowding.

While epidemiologic evidence cannot definitively determine biological pathways, our results suggest that the pathway for acute respiratory heat effects may differ somewhat from the pathway for cardiovascular heat effects. Heat-related cardiovascular outcomes are likely caused by stress to the cardiovascular system from thermoregulatory responses to heat (31). Our results suggest that, while adverse systemic effects related to thermoregulation may play a role in respiratory heat effects, these effects are likely also caused by the direct effect of breathing hot air.

Thermoregulation helps humans maintain safe body temperatures in heat but is associated with systemic inflammation, increases in cardiac output, increases in skin blood flow, and increases in pulmonary ventilation (32-33). Additionally, while humans primarily lose body heat through surface sweating, hyperthermia can increase ventilation and cause thermal hyperpnea.
(second phase panting during which tidal volume and respiratory rate both increase) (32). These thermoregulatory responses could contribute to the observed increase in hospitalizations for respiratory infections and COPD exacerbations, especially since COPD is a disease characterized by ventilatory impairment, persistent pulmonary and systemic inflammation (33, 36) and coexisting cardiovascular disease (36-37).

However, if heat effects on respiratory health were mediated exclusively by a thermoregulatory pathway, risks would likely differ substantially by age, county climate and, possibly, gender. First, age and, to some degree, gender are linked to physiological differences in thermoregulation (38-40), and so we would expect differences in susceptibility by age and gender if respiratory heat effects were mediated exclusively by a thermoregulatory pathway. However, here we found little difference in respiratory susceptibility to heat by either age or gender. Second, if effects were mediated exclusively by a thermoregulatory pathway, heat effects would likely differ substantially based on a location’s climate since thermoregulatory response improves with repeated heat exposure (40). However, while respiratory heat effects were generally lower in counties with hotter average summer temperatures, heat-hospitalization associations remained positive across the range of county climates. Further, county climate modified respiratory heat effects much less than in similar research on heat and cardiorespiratory mortality (1).

Our findings are consistent with the hypothesis that acute respiratory heat effects are likely also caused by a direct effect of breathing hot air. We found limited effect modification of respiratory heat effects by climate, which could be explained if respiratory heat effects are triggered by very brief exposure to heat since even widespread use of air conditioning cannot eliminate brief (e.g., ≤10 minutes) outdoor heat exposure. While an hour or more of exposure is
required for some thermoregulatory responses to heat (41), a few minutes of heat exposure can trigger direct human airway responses to inhaling hot air. This rapid response has been demonstrated in studies of asthma (42-43), and it likely operates through the cholinergic reflex pathway (42, 44-45).

Studies of the association between heat and human mortality have found evidence of decreasing effects over decades (46-47) and smaller effects in hotter climates (1), suggesting protective adaptation to heat, possibly related to differences in housing stock or behavior during hot weather. Given this study’s timeframe, we were unable to explore temporal adaptation, but we did investigate evidence of differences in heat-hospitalization associations between hotter and milder counties. While our results are consistent with evidence of adaptation—smaller effects in counties where summers are typically very hot—this adaptation did not completely remove risk even in the hottest counties.

Any adaptations may take decades to realize or be impractical in certain communities. For example, architectural adaptations can only change slowly with changes in housing stock, and may be impractical in dense urban communities like New York City. Adaptation could also bring its own risks and impacts. Higher use of air conditioning will draw on already-stressed power grids, which could cause power outages during severe heat waves and so create new health threats (48). Additionally, the energy use associated with increased use of air conditioning will increase air pollution and accelerate climate change through release of greenhouse gases (49).

In the future, heat-related health hazards are likely to increase. Within this century, exposure to heat is expected to increase as the average global temperature rises at least 3°F (3), and heat waves are expected to become more frequent and severe (3). Also, a growing
percentage of the population will likely be particularly susceptible to heat-related respiratory morbidity, given projected increases in the global prevalence of chronic respiratory diseases (4) and aging of the US population (50).

In summary, in a 10-year study of Medicare respiratory hospitalizations and outdoor heat in 213 US counties, we found risk of respiratory hospitalization significantly increased with daily outdoor heat. This relationship persisted across age categories, genders, and county climates, and could not be explained by changing concentrations of air pollution. Heat-related respiratory hazards are likely to increase in the future with increasing prevalence of respiratory conditions (4) and rising temperatures from climate change (3).
References


**Figures Legends**

Figure 1: **213 US study counties and their average summer temperatures.** Colors correspond to the county’s daily mean temperatures, averaged from May to September (1999–2008).

Figure 2: **Percent increase in respiratory hospitalizations for each 10°F daily outdoor heat increase, 1999–2008 (lag 0).** Estimates are pooled across all 213 study counties; outdoor heat is measured as daily mean temperature, May—September. Horizontal lines show 95% posterior intervals. Abbreviations: COPD: chronic obstructive pulmonary disease; RTI: respiratory tract infections.

Figure 3: **Relative risk of heat-related respiratory hospitalization with and without adjustment for air pollution, 1999-2008 (lag 0).** Analysis for O\(_3\) (n=200), PM\(_{10}\) (n=165), and PM\(_{2.5}\) (n=196). Circles show community-level estimates. Larger circles indicate greater certainty. Black diamond shows estimate across all communities. Abbreviations: O\(_3\), ozone; PM\(_{10}\) and PM\(_{2.5}\), particulate matter with aerodynamic diameter ≤10µm and ≤2.5µm, respectively.

Figure 4: **Modification of county-level relative risk of heat-related respiratory hospitalization by a county’s average summer temperature (lag 0).** Average county summer temperature for May—September, 1999—2008. Circles show county-level estimates. Larger circles indicate greater certainty. Solid line shows the predicted pooled estimate by average summer temperature (shaded region shows 95% posterior interval). Abbreviation: T\(_{\text{mean}}\): mean daily temperature.
Table 1: Study population, total hospitalizations, and daily hospitalization counts and rates for 213 US counties, 1999–2008.

<table>
<thead>
<tr>
<th>Category</th>
<th>Number (range) of Medicare beneficiaries (in millions)*</th>
<th>Total hospitalizations, May—September, 1999—2008*</th>
<th>Hospitalization count/day (range) †</th>
<th>Daily hospitalization rate (range) per 100,000 beneficiaries †</th>
</tr>
</thead>
<tbody>
<tr>
<td>All respiratory</td>
<td>12.5 (11.5, 13.1)</td>
<td>1,141,458</td>
<td>2.3 (0.6, 31.9)</td>
<td>5.8 (3.4, 11.7)</td>
</tr>
<tr>
<td>By cause</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory tract infections</td>
<td>12.5 (11.5, 13.1)</td>
<td>756,395</td>
<td>1.6 (0.4, 21.6)</td>
<td>3.9 (2.5, 7.2)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>12.5 (11.5, 13.1)</td>
<td>385,063</td>
<td>0.8 (0.1, 10.3)</td>
<td>2.0 (0.4, 4.5)</td>
</tr>
<tr>
<td>By gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.2 (4.5, 5.4)</td>
<td>499,373</td>
<td>1.1 (0.3, 13.9)</td>
<td>6.3 (3.7, 12.6)</td>
</tr>
<tr>
<td>Female</td>
<td>7.3 (7.0, 7.7)</td>
<td>642,085</td>
<td>1.3 (0.3, 17.9)</td>
<td>5.5 (3.0, 11.0)</td>
</tr>
<tr>
<td>By age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 to 74 years</td>
<td>6.4 (6.0, 6.7)</td>
<td>358,830</td>
<td>0.8 (0.2, 10.1)</td>
<td>3.6 (1.8, 6.9)</td>
</tr>
<tr>
<td>75 to 84 years</td>
<td>4.4 (4.1, 4.7)</td>
<td>468,002</td>
<td>1.0 (0.2, 13.0)</td>
<td>6.7 (3.9, 12.9)</td>
</tr>
<tr>
<td>85 years and older</td>
<td>1.6 (1.4, 1.8)</td>
<td>314,626</td>
<td>0.6 (0.1, 9.6)</td>
<td>12.1 (7.5, 22.9)</td>
</tr>
</tbody>
</table>

*Total across all 213 study counties.
†Average values across all study days were computed for each county, and shown here are the median and range (in parentheses) of these county-specific values.
Online Data Supplement for “Heat-related emergency hospitalizations for respiratory diseases in the Medicare population”

G. Brooke Anderson, Francesca Dominici, Yun Wang, Meredith C. McCormack, Michelle L. Bell, and Roger D. Peng
Contents of Online Data Supplement:

1. Further Explanation of Methods
2. Tables
   • Table E1: Percent increase in hospitalizations per 10°F increase in daily outdoor heat using different metrics of heat exposure.
   • Table E2: Correlation between daily outdoor heat and air pollutants, May–September, for pollution lags of 0, 1, and 2 days.
   • Table E3: Associations between daily outdoor heat and respiratory hospitalizations estimated with and without control for air pollutants.

3. Figures
   • Figure E1: Distribution of daily mean temperature summary statistics across the 213 study counties.
   • Figure E2: Association between respiratory hospitalizations and a 10°F increase in daily outdoor heat using different degrees of freedom to control for long-term and seasonal changes in respiratory hospitalization rates.
   • Figure E3: County-level correlations between air pollutants and daily outdoor heat with lags of 0, 1, and 2 days for pollutants.
   • Figure E4: Percent increase in hospitalizations associated with a 10°F increase in outdoor heat at different lags.
Further Explanation of Methods

Further details on data

For the dataset used for this study, Medicare Part-A inpatient data were originally obtained through the National Claims History Files. Causes of hospitalization were determined by principal discharge diagnosis code: respiratory tract infections (ICD-9 464–466, 480–487) and chronic obstructive pulmonary disease (ICD-9 490–492). Transfers between hospitals were not counted as new hospitalizations. Medicare beneficiary enrollment data were used to calculate the potential pool of patients on any given day. Data were aggregated by day to create daily rates, and so Medicare data analyzed for this study lacked individual identifiers.

Air pollution data were obtained from the US Environmental Protection Agency’s Air Quality System for tropospheric ozone (O\textsubscript{3}) and particulate matter with aerodynamic diameter ≤10µm (PM\textsubscript{10}) and ≤2.5µm (PM\textsubscript{2.5}). Daily O\textsubscript{3} concentration was measured using a 24-hour average metric. For weather and pollution data, monitors were matched to counties by longitude and latitude. For counties without weather monitors, all weather stations within 35 kilometers were used to estimate the county’s weather. In counties with multiple weather or pollution monitors, values from different monitors were averaged after subtracting out a 365-day moving average; in counties with 2–9 monitors, maximum and minimum measurements were removed before averaging, while in counties with ≥10 monitors, a 10% trimmed mean was used.\[E1\]

Daily maximum, minimum, and dew point temperature were obtained from the National Climatic Data Center on the Earth-Info CD database. Daily mean temperature was calculated as the average of daily maximum and minimum temperature. To calculate daily heat index from daily mean temperature and dew point temperature, we created an R function based on JavaScript code from the National Weather Service’s online heat index calculator [E2]. There are several different equations and algorithms used to derive heat index from daily temperature and relative humidity; here we used the algorithm of the US National Weather Service to allow comparison between our results and weather conditions as reported by US meteorologists. The National Weather Service heat index algorithm is based on the heat index developed by Steadman [E3–E4] and includes adjustments for certain conditions (for example, if relative humidity is ≥85% and temperature is ≥80°F or if relative humidity is ≤13% and temperature is between 80°F and 112°F) [E2]. At temperatures below 40°F, heat index defaults to air temperature for this algorithm [E2].

In counties with limited data, model convergence problems can be common, especially for stratified analysis where total counts are small (e.g., hospitalizations stratified by age category). We therefore removed counties with <5 years of weather data, which excluded 6 counties from the original dataset of 221. We also excluded counties outside the contiguous 48 states, which removed two more counties. Our final dataset included 213 counties. As a test of whether our results were sensitive to this exclusion, we re-measured our main result (national relationship between temperature and respiratory hospitalizations) with these 8 counties included. Since this main analysis was performed on unstratified
data, we had adequate data to fit models to these 8 counties, and so this sensitivity analysis could be
performed to determine if exclusion of these counties might affect estimates for more detailed analysis (e.g.,
age-specific estimates performed with stratified data). We found the national estimate was identical with
and without these 8 counties included in analysis. Therefore, excluding these counties has very little effect
on national estimates but facilitates more detailed analysis, including age- and gender-specific analysis and
investigation of effect modification by long-term, county-specific characteristics (e.g., average summer
temperature in each county).

In many communities, particulate matter concentration is only measured once every three or six
days. Therefore, in our analysis of the sensitivity of main results to air pollution, we limited analysis to
counties with >150 days of joint data for weather and the air pollutant of interest. Similar exclusion criteria
have been used in previous research [E5-E7]. Following this exclusion, the following number of counties
remained to test sensitivity to air pollution: O$_3$, 200 counties; PM$_{10}$, 165 counties; PM$_{2.5}$, 196 counties. This
restriction did not affect the main results of our study, where we model the association between outdoor
temperature and respiratory hospitalizations in models that do not include air pollution measurements.

Further details on methods

The first-level model used to estimate the association between temperature and same-day
hospitalizations within each county (details on models for other lags are given later) can be described as:

\[
\log(\mu_t) = \alpha + \beta T_0 + \delta_i D_i + f(H_0) + f(L_t) + B_t \quad (1)
\]

where:

- $\mu_t$ Expected hospitalization count on day $t$
- $\alpha$ Model intercept
- $\beta$ Coefficient of temperature effect
- $T_0$ Mean same-day temperature ($^{0}\text{F}$)
- $\delta_i$ Vector of coefficients for day of week
- $D_i$ Day of week for day $t$
- $f(H_0)$ Function of mean dew point temperature on day $t$ (adjusted for daily mean temperature),
  modeled as a natural cubic spline, 2 degrees of freedom (df)
- $f(L_t)$ Function of time, modeled as a natural cubic spline with 7 df/year (used to model long-term and
  seasonal trends)
**Bt Offset term:** number of Medicare beneficiaries in study population who could be hospitalized on day \( t \) (i.e., population at risk)

Dew point temperature and air temperature are highly correlated: within our 213 study counties, the median of county-specific correlations between air temperature and dew point temperature for May—September is 0.78 (range of county-level correlations: -0.04, 0.89). Therefore, we adjusted dew point temperature for air temperature \( (H_0 \text{ in equation 1}) \) before including it in our model. After adjustment, the median correlation was -4.6e-17 (range: -4.3e-15, 4.1e-15).

Relative humidity is less strongly correlated with air temperature (for example, for our counties the median county-specific correlation is -0.07; range: -0.71, 0.20), and so some studies use relative humidity rather than dew point temperature to control for air moisture \([E8-E9]\). To ensure this modeling choice did not affect our results, we tested the sensitivity of our main result to using relative humidity to control for air moisture rather than dew point temperature. We found our main results were practically identical for the two models (model with dew point temperature control: 4.3%, PI: 3.8, 4.8; model with relative humidity control: 4.2%, PI: 3.7, 4.8%).

Models of temperature and health sometimes include control for holidays \([E9-E10]\). We tested controlling for all federal holidays between May and September (Independence Day, Labor Day, and Memorial Day). When we included holiday status in our main model as a binary factor, we estimated a national effect of 4.4% (PI: 3.8, 4.9%). By comparison, the national effect without holiday control was 4.3% (PI: 3.8, 4.8%). Since our main result was not sensitive to holiday control, we did not retain holiday as a factor in our final model.

For main results, we used daily average temperature as our metric of heat exposure. However, to allow comparison with previous research, we also separately modeled heat effects using metrics of daily minimum temperature, daily maximum temperature, and daily heat index (which incorporates temperature and relative humidity \([E2-E4]\)), by re-running our main model three times, once with each of these metrics in place of daily mean temperature.

Previous research has found evidence of non-linearity in the relationship between temperature and cardiorespiratory mortality within the summer (i.e., a different per-degree change in a health outcome at very hot temperatures versus mild temperatures during the summer) \([E11-E12]\). To ensure our model, which models the relationship between daily temperature \( (T_0) \) and the logarithm of daily hospitalizations \( (\log(\mu_t)) \) as a linear association, appropriately captures the association between summer temperature and respiratory hospitalizations, we tested the relationship fit with Model 1 for evidence of nonlinearity in the relationship between \( T_0 \) and \( \log(\mu_t) \). To do this, we fit a model similar to Model 1, but with the temperature term, \( T_0 \), replaced with a natural cubic spline of temperature with 2 degrees of freedom to model May–September temperatures. After fitting this nonlinear model, we compared deviance of the two
models (linear versus nonlinear) to determine evidence within that county of significant non-linearity (i.e., to determine if the non-linear model offered a significant improvement over the linear model). As a second test of sensitivity of results to use of a non-linear versus linear model, we compared the estimated percentage increase in hospitalizations per 10°F temperature increase as estimated by the linear model to the measurement from the county’s nonlinear model for a 10°F change in temperature centered at the county’s median value of May–September temperatures.

We found little evidence that a nonlinear model provided an improved fit to temperature-hospitalization data. In 193 of the 213 counties considered (91%), a natural cubic spline did not provide a significantly better fit to the data than a linear model as indicted by comparison of model deviance (significance level: 95%). Additionally, we found linear model estimates were similar to estimates from nonlinear models evaluated at a county’s median May–September temperature (estimate from linear model: 4.3%, PI: 3.8, 4.8%; estimate from nonlinear model evaluated at county’s median temperature: 3.8%, PI: 3.2, 4.4%). Because we found little evidence of significant non-linearity in the relationship between heat and respiratory Medicare hospitalizations, as well as limited sensitivity to using nonlinear versus linear models when effects are modeled at median May–September temperatures, we used linear models to model the association between temperature and hospitalizations in remaining analysis.

We fit model 1 for each county separately. From this model we estimated $\gamma^c$, the increase in $\log \mu$, per 10°F increase in daily temperature, as well as the variance of $\gamma^c$ ($\gamma^c$ is equal to $10\beta^c$ for the value of $\beta^c$ estimated in equation 1). For presentation, we translated this association into an estimate of percent increase in hospitalizations per 10°F through the conversion $100 \times (\exp(\gamma^c) - 1)$.

This metric—a percent change in health outcome per 10°F temperature increase—has been used in previous US studies of temperature and health [E13-E15]. Using this metric therefore aids comparability between our study and previous research. Additionally, this metric provides a good measure of the difference between hot and mild weather for a given day of the year (our model measures the percent increase in hospitalization risk for a 10°F higher temperature during the given time of the year, since we control for seasonality). In each of our 213 study counties, we measured how temperatures within each county vary for the same day of the year (e.g., June 1) across the 10 study years. For each county, we measured the difference between the hottest and coolest temperatures across the 10 study years for each day of the summer, and then took the median for the county of all these day-specific ranges. We performed a similar analysis for the interquartile range by day of year within each county. We found that, across all counties, the range between the hottest and coolest temperatures for a specific day of the year is, on average, 15.1°F (range of county-specific medians: 5.9°F, 22.4°F), while the average interquartile range is 5.8°F (range of county-specific medians: 2.1°F, 8.0°F). Therefore, when we measure risk for a 10°F increase in temperature, this metric is representative of the change in hospitalization risk between a day that has a hot temperature for that time of the year versus a day that is mild for the time of year.
To pool county-level estimates at the national and regional levels, we used a Bayesian hierarchical model that incorporated both within-county and between-county variance:

\[
\hat{\gamma}^c | \gamma^c, \hat{\upsilon}^c \sim N(\gamma^c, \hat{\upsilon}^c), c = 1, \ldots, 213 \tag{2}
\]

\[
\gamma^c | \phi, \tau^2 \sim N(\phi, \tau^2) \tag{3}
\]

where:

\(\hat{\gamma}^c\) Estimated increase in \(\log \mu_t\) per 10°F increase in temperature for county \(c\), from first-level county-specific model

\(\gamma^c\) True increase in \(\log \mu_t\) per 10°F increase in temperature for county \(c\)

\(\hat{\upsilon}^c\) Estimated variance of increase in \(\log \mu_t\) per 10°F increase in temperature for county \(c\), from first-level county-specific model

\(\phi\) True national increase in \(\log(\mu_t)\) per 10°F increase in temperature

\(\tau^2\) Variance between counties in true county-level increases in \(\log(\mu_t)\) per 10°F increase in temperature

We fit this second-stage model using the “tlnise” package in R [E16].

To test effects under different exposure metrics, we refit Model 1 within each county using minimum temperature, maximum temperature, or heat index instead of \(T_0\). We fit a separate model for each metric. To determine if results were sensitive to control for season, we refit Model 1 within each county using 5, 6, 8, or 9 df/year in \(f(L_t)\).

We investigated the sensitivity of results to control for air pollutants (\(O_3\), \(PM_{10}\), and \(PM_{2.5}\)) by fitting Poisson models with and without adjustment for these pollutants. Since health effects of pollutants can follow exposure by a day or two [E17-E19], we investigated pollution lags of 0, 1, and 2 days. To determine sensitivity of observed associations to pollutant control, for each pollutant analyzed, two models were fit for each community— one without control for the pollutant (equation 4) and one that included control for the pollutant (equation 5):

\[
\log(\mu_t) = \alpha + \beta T_0 + \delta_0 D_t + f(H_0) + f(L_t) + B_t \tag{4}
\]

\[
\log(\mu_t) = \alpha + \beta T_0 + \eta C_t + \delta_1 D_t + f(H_0) + f(L_t) + B_t \tag{5}
\]
with all coefficients as defined in equation 1, as well as:

$$\eta$$ Coefficient of pollutant effect

$$C_l$$ Concentration of given pollutant on lag \( l \) (\( l \) days before day \( t \))

Before fitting models for a specific county and pollutant, data within a county was reduced to only those days with joint data for both temperature and the pollutant being considered. This reduced dataset was used to calculate temperature-hospitalization associations both without (equation 4) and with (equation 5) control for the pollutant. We investigated pollutants at lags of 0 to 2 days, since pollutants can affect health at slightly delayed lags [E17-E19].

To investigate lags of temperature-hospitalization associations, we re-fit model 1, including temperature for the previous day (lag 1: \( T_1 \)) or two days earlier (lag 2: \( T_2 \)) in place of \( T_0 \). To estimate cumulative effects (lags 0–6), we used a distributed lag model and fit a crossbasis of temperature and lag-day, out to lag 6, using the R package “dlnm” [E20]. The lag function for this crossbasis was fit as a natural cubic spline with 3 degrees of freedom, with knots at equal log intervals to allow greater flexibility in the lag function at lags near exposure (e.g., lags 0, 1) and smoother changes with lag at further lags (e.g., lags 5, 6) [E9]. Other model specifications were as given in equation 1.

Finally, we investigated whether counties with cooler summers on average tend to have larger relative risks of hospital admissions as a result of a sudden increase in temperature from one day to the next. To analyze modifications by county climate in the relationship between temperature and respiratory hospitalization, we pooled county-level estimates in a Bayesian hierarchical model with average May–September climate as a potential modifier:

$$\gamma^c | \gamma^c, \hat{\theta}^c \sim N(\gamma^c, \hat{\theta}^c), c = 1, \ldots, 213$$  \hspace{1cm} (6)

$$\gamma^c | \theta_0, \theta_1, \tau^2 \sim N(\theta_0 + \theta_1(x_c - \bar{x}), \tau^2)$$  \hspace{1cm} (7)

with all coefficients as defined in equations 2 and 3, as well as:

$$x_c - \bar{x}$$ Difference between county \( c \)’s mean May–September temperature and the average of May–September temperature for all 213 counties

$$\theta_0$$ Overall estimate of increase in \( \log \mu \), per \( 10^0 \text{F} \) increase in temperature for a county with average summer temperature equal to \( \bar{x} \), the average of May–September temperature for all 213 counties

$$\theta_1$$ Estimate of effect modification by county average May–September temperature
All analysis was performed with R statistical software version 2.14.1.
Tables

- Table E1: Percent increase in hospitalizations per 10°F increase in daily outdoor heat using different metrics of heat exposure.
- Table E2: Correlation between daily outdoor heat and air pollutants, May–September, for pollution lags of 0, 1, and 2 days.
- Table E3: Associations between daily outdoor heat and respiratory hospitalizations estimated with and without control for air pollutants.
Table E1: Percent increase in hospitalizations per 10°F increase in daily outdoor heat using different metrics of heat exposure.

<table>
<thead>
<tr>
<th>Temperature metric</th>
<th>% increase in hospitalizations per 10°F increase in temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean temperature</td>
<td>4.3%(^a) (3.8, 4.8) (^b)</td>
</tr>
<tr>
<td>Maximum temperature</td>
<td>3.8% (3.4, 4.3)</td>
</tr>
<tr>
<td>Minimum temperature</td>
<td>3.4% (2.9, 3.9)</td>
</tr>
<tr>
<td>Heat index</td>
<td>3.4% (2.9, 3.8)</td>
</tr>
</tbody>
</table>

\(^a\)Pooled point estimate across 213 United States counties, 1999–2008.

\(^b\)95% posterior interval of pooled estimate across 213 United States counties, 1999–2008.

Table E2: Correlation between daily outdoor heat and air pollutants, May–September, for pollution lags of 0, 1, and 2 days.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>N (# of counties)</th>
<th>Pollutant at lag 0</th>
<th>Pollutant at lag 1</th>
<th>Pollutant at lag 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(_3)</td>
<td>200</td>
<td>0.39(^a) (-0.51, 0.62)(^b)</td>
<td>0.35 (-0.52, 0.59)</td>
<td>0.24 (-0.43, 0.49)</td>
</tr>
<tr>
<td>PM(_{10})</td>
<td>165</td>
<td>0.42 (-0.01, 0.68)</td>
<td>0.37 (-0.09, 0.65)</td>
<td>0.25 (-0.15, 0.47)</td>
</tr>
<tr>
<td>PM(_{2.5})</td>
<td>196</td>
<td>0.45 (-0.06, 0.62)</td>
<td>0.45 (-0.08, 0.61)</td>
<td>0.30 (-0.12, 0.42)</td>
</tr>
</tbody>
</table>

Abbreviations: O\(_3\), tropospheric ozone; PM\(_{10}\), particulate matter with aerodynamic diameter ≤10\(\mu\)m; PM\(_{2.5}\), particulate matter with aerodynamic diameter ≤2.5\(\mu\)m.

\(^a\)Median of all county-specific correlations.

\(^b\)Range of county-specific correlations.
Table E3: Associations between daily outdoor heat and respiratory hospitalizations estimated with and without control for air pollutants.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Lag 0 No control</th>
<th>Lag 0 Control</th>
<th>Lag 1 No control</th>
<th>Lag 1 Control</th>
<th>Lag 2 No control</th>
<th>Lag 2 Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>O₃</td>
<td>4.1% (3.6, 4.6)</td>
<td>4.2% (3.6, 4.8)</td>
<td>4.1% (3.6, 4.6)</td>
<td>4.0% (3.4, 4.7)</td>
<td>4.1% (3.6, 4.7)</td>
<td>4.1% (3.6, 4.7)</td>
</tr>
<tr>
<td>PM₁₀</td>
<td>3.4% (2.5, 4.3)</td>
<td>3.2% (2.3, 4.1)</td>
<td>3.5% (2.5, 4.4)</td>
<td>3.1% (2.0, 4.2)</td>
<td>4.1% (3.2, 5.0)</td>
<td>4.0% (3.0, 4.9)</td>
</tr>
<tr>
<td>PM₂.₅</td>
<td>3.7% (3.1, 4.4)</td>
<td>3.6% (2.8, 4.3)</td>
<td>4.2% (3.5, 4.8)</td>
<td>3.9% (3.2, 4.7)</td>
<td>4.4% (3.7, 5.1)</td>
<td>4.3% (3.6, 5.0)</td>
</tr>
</tbody>
</table>

Abbreviations: O₃, tropospheric ozone; PM₁₀, particulate matter with aerodynamic diameter ≤10µm; PM₂.₅, particulate matter with aerodynamic diameter ≤2.5µm.

*aPooled point estimate across 213 United States counties, 1999—2008. Estimates shown are the percent increase in daily respiratory hospitalizations associated with a 10°F increase in daily outdoor heat. The number of counties included in each analysis were: O₃: 200; PM₁₀: 165; PM₂.₅: 196.

*b95% pooled estimate across 213 United States counties, 1999—2008.
Figures

• Figure E1: Distributions of daily mean temperature summary statistics across the 213 study counties.
• Figure E2: Association between respiratory hospitalizations and a 10°F increase in daily outdoor heat using different degrees of freedom to control for long-term and seasonal changes in respiratory hospitalization rates.
• Figure E3: County-level correlations between air pollutants and daily outdoor heat at lags of 0, 1, and 2 days for pollutants.
• Figure E4: Percent increase in hospitalizations associated with a 10°F increase in outdoor heat at different lags.
Figure E1: Distributions of daily mean temperature summary statistics across the 213 study counties.
Each graph shows the distribution of county-level values of that metric (e.g., minimum, first quartile, etc.) of all daily mean temperature measurements in a county over the study period.
Figure E2: Association between respiratory hospitalizations and a 10°F increase in daily outdoor heat using different degrees of freedom to control for long-term and seasonal changes in respiratory hospitalization rates. Results are pooled over 213 US counties, 1999–2008. Outdoor heat is measured as daily mean temperature.
Figure E3: County-level correlations between air pollutants and daily outdoor heat at lags of 0, 1, and 2 days for pollutants.

Abbreviations: \( \text{O}_3 \), tropospheric ozone; \( \text{PM}_{10} \), particulate matter with aerodynamic diameter \( \leq 10 \mu \text{m} \); \( \text{PM}_{2.5} \), particulate matter with aerodynamic diameter \(< 2.5 \mu \text{m} \). Each histogram shows the distribution of county-level correlations between daily outdoor heat (measured as mean temperature) and the given air pollutant at the given lag (i.e., the graph for \( \text{O}_3 \) at lag 1 shows the distribution of county-level correlations between outdoor heat and previous day’s ozone concentration). Black vertical lines show median of the 213 county-level correlations for each pollutant and lag.
Figure E4: Percent increase in hospitalizations associated with a 10°F increase in outdoor heat at different lags. All estimates are pooled across all 213 study counties. Outdoor heat is measured as daily mean temperature.
References for Online Data Supplement


[E4] Rothfusz LP. The heat index equation (or, more than you ever wanted to know about heat index). Fort Worth, Texas: National Oceanic and Atmospheric Administration, National Weather Service, Office of Meteorology; 1990.


**Title:** Heat-related emergency hospitalizations for respiratory diseases in the Medicare population

**Authors:** G. Brooke Anderson,¹ Francesca Dominici,² Yun Wang,² Meredith C. McCormack,³,⁴ Michelle L. Bell,⁵ and Roger D. Peng¹,*

Author affiliations:

¹Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health

²Department of Biostatistics, Harvard School of Public Health

³Division of Pulmonary and Critical Care, Johns Hopkins School of Medicine

⁴Department of Environmental Health Sciences, Johns Hopkins School of Public Health

⁵School of Forestry & Environmental Studies, Yale University

*Corresponding author:

Roger D. Peng

Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health

615 N. Wolfe Street

Baltimore, MD 21205

Telephone: 410-955-2468

Fax: 410-955-0958

Email: rpeng@jhsph.edu
Author contributions:

Study concept and design: Anderson, Dominici, Bell, Peng

Acquisition of data: Dominici, Wang, Peng

Analysis or interpretation of data: Anderson, Dominici, McCormack, Bell, Peng

Drafting of manuscript: Anderson, Dominici, Wang, McCormack, Bell, Peng

Critical revision of the manuscript for important intellectual content: Anderson, Dominici, Wang, McCormack, Bell, Peng

Statistical analysis: Anderson, Dominici, Bell, Peng

Obtained funding: Dominici, Bell, Peng

Administrative, technical, or material support: Dominici, Peng

Study supervision: Dominici, Peng

Sources of support: Funding for Drs. Anderson, Dominici, Wang, Bell, and Peng was provided by grants R01ES019560 and R21ES020152 from the National Institute for Environmental Health Sciences. Funding for Drs. Dominici, Wang, and Bell was also provided by grant RD-83479801 from the US Environmental Protection Agency. Funding for Drs. Dominici and Wang was also provided by grant R01ES012054 from the National Institute for Environmental Health Sciences, grant R834894 from the US Environmental Protection Agency, and a grant from the Health Effects Institute. Funding for Dr. Bell was also provided by grants R01ES015028 and R21ES021427 from the National Institute for Environmental Health Sciences. Funding for Dr. McCormack was provided by grant K23ES016819 from the National Institutes of Health.

Although the research described in this article has been funded in part by the US Environmental
Protection Agency, it has not been subjected to the agency’s required peer and policy review and therefore does not necessarily reflect the views of the agency and no official endorsement should be inferred. The contents of this article do not necessarily reflect the views and policies of the Health Effects Institute.

Running head: Heat-related respiratory hospitalizations

Descriptor number: 6.04

Total word count: 2,607,847

At a Glance Commentary:

Scientific Knowledge on the Subject. Although outdoor heat is known to increase rates of respiratory mortality in the elderly, the relationship between heat and respiratory morbidity has been little studied in the United States outside of New York and California at a national level.

What this Study Adds to the Field. We investigate the relationship between outdoor temperature and emergency respiratory hospitalizations in the largest population of elderly studied to date: all fee-for-service, approximately 12.5 million Medicare beneficiaries in 213 urban United States counties. We find a clear and consistent increase in respiratory hospitalizations with increasing outdoor temperature across the United States.

This article has an online data supplement, which is accessible from this issue’s table of content online at www.atsjournals.org.
Abstract

Rationale: The heat-related risk of hospitalization for respiratory diseases among the elderly has not been quantified in the United States on a national scale. With climate change predictions of more frequent and more intense heat waves, it is of paramount importance to quantify the health risks related to heat, especially for the most vulnerable.

Objectives: To estimate the risk of hospitalization for respiratory diseases associated with outdoor heat in the US elderly.

Methods: An observational study of ~12.5 million Medicare beneficiaries in 213 United States counties, January 1, 1999—December 31, 2008. We estimate a national average relative risk of hospitalization for each 10°F (5.6°C) increase in daily outdoor temperature using Bayesian hierarchical models.

Measurements and Main Results: We obtained daily county-level rates of Medicare emergency respiratory hospitalizations (ICD-9 464–466, 480–487, 490–492) in 213 United States counties for 1999-2008. Overall, each 10°F increase in daily temperature was associated with a 4.3% increase in same-day emergency hospitalizations for respiratory diseases (95% posterior interval: 3.8, 4.8%). Counties’ relative risks were significantly higher in counties with cooler average summer temperatures.

Conclusions: We found strong evidence of an association between outdoor heat and respiratory hospitalizations in the largest population of elderly studied to date. Given projections of increasing temperatures from climate change and the increasing global prevalence of chronic pulmonary disease, the relationship between heat and respiratory morbidity is a growing concern.

Abstract word count: 231 words
**Key words:** Chronic Obstructive Pulmonary Disease, Hospitalization, Hot temperature, Respiratory Tract Infections, Weather
1 Introduction

Outdoor heat can cause spikes in respiratory deaths (1-2), but considerably less is known about heat’s impacts on respiratory morbidity. Given that: 1) climate change will increase exposure to extreme heat (3); 2) the prevalence of chronic respiratory diseases is increasing (4); and 3) the elderly will likely be most affected by heat-related problems (5), there is a pressing need to improve our understanding of respiratory heat effects among the elderly for both fatal and non-fatal outcomes.

There are two major limitations to current research on the relationship between heat and respiratory hospitalizations. First, this relationship has not been adequately studied worldwide to confidently identify a consistent link between respiratory hospitalizations and heat. The few studies that have investigated heat and respiratory hospitalizations have found somewhat conflicting results (6). For example, studies of Brisbane, Australia, (7-8) and Athens, Greece, (9) found hospitalizations rates decreased slightly during hot weather, while studies of California (10-11), New York (12-13), and 12 European cities (14) found respiratory hospitalizations increased with heat. While a meta-analysis of current research estimated a positive relationship between heat and respiratory hospitalizations across all studies, it lacked sufficient power to distinguish this effect from a null effect (6).

Second, outside of California and New York, little research has been done in the United States (US). US studies of heat and respiratory morbidity have been limited to single cities (12, 15) or single states (California (10-11, 16); New York (13)) or were retrospective studies of single heat waves (17-19). Worldwide, large heterogeneity exists between temperature-morbidity studies from different locations (6, 20). Therefore, although the relationship between heat and
respiratory hospitalizations has been well-studied in California and New York (10-11, 13),
temperature effect estimates based only on these states are unlikely to be representative of
national US effects.

In this study we estimate the risk of emergency hospital admissions for respiratory
diseases associated with outdoor heat exposure for approximately 12 million elderly individuals
in 213 US urban counties from 1999 to 2008. We investigate whether this association is
confounded by exposure to air pollution or modified by individual (age, gender) or county
(average summer temperature) characteristics. This is, to date, the largest elderly population
investigated to estimate acute heat-related risks of respiratory hospitalizations and the first
national study of these risks in the United States.

2 Methods

This study used a dataset created for environmental health research by aggregating
Medicare hospitalization rates by county and linking them with ambient air pollution and
temperature data (21–23). This dataset includes daily hospitalizations for 1999-2008 for 221 US
counties, based on Medicare inpatient claims for all fee-for-service Medicare beneficiaries ≥65
years. Hospitalization rates are aggregated by gender, age (65–74 years, 75–84 years, ≥85 years),
and medical condition (COPD: ICD-9-CM principal discharge diagnosis codes 490–492;
respiratory tract infections: 464–466, 480–487). The dataset includes measurements of weather
(temperature, dew point temperature) and air pollution (tropospheric ozone \[O_3\], particulate
matter with aerodynamic diameter \(\leq 10\mu m\) [PM\(_{10}\)] and \(\leq 2.5\mu m\) [PM\(_{2.5}\)])). Analysis was limited to
the 213 study counties within the contiguous 48 states and, to ensure adequate information to
estimate model parameters and for convergence of model-fitting algorithms, to counties with ≥5 years of weather data. Further data details are in an online data supplement.

We modeled the relationship between daily hospitalization rate and outdoor heat for May—September within each county using an overdispersed Poisson generalized linear model (1-2). Models controlled for day of week and dew point temperature (adjusted for temperature to limit collinearity). Models adjusted for long-term and seasonal trends in county hospitalization rates and temperature using smooth spline functions of time (1). Further details on model development are in the online data supplement.

For each county, we estimated the percentage increase in daily emergency respiratory hospitalizations associated with each 10°F (5.6°C) increase in daily average temperature (10-11). To estimate the national average association between heat and respiratory hospitalizations, we combined county-level estimates with a two-stage Bayesian hierarchical model, incorporating variation within and between county-level estimates (2422). We estimated national average associations separately for COPD and respiratory tract infections and jointly for both causes (total respiratory hospitalizations). To investigate differences in susceptibility, we estimated heat-hospitalization associations after stratifying data by age (65–74 years, 75–84 years, ≥85 years) and gender. We estimated national average heat effects at single-day lags of 0, 1, and 2 days and cumulatively for lags 0–6. Finally, we investigated whether counties with cooler summers on average tend to have statistically significant larger relative risks of heat-related hospital admissions than counties with warmer summers. We provide evidence toward this question using a two-level hierarchical Bayesian model (1, 2422). Details are given in the online data supplement.
We investigated the sensitivity of model results to the smoothness of adjustment for seasonality and long-term trends as well as to the metric used for heat exposure (maximum temperature, minimum temperature, heat index). We also investigated sensitivity to air pollutant control (O₃, PM₁₀, and PM₂.₅). Details on these sensitivity analyses are in the online data supplement.

### 3 Results

Our final dataset included 213 urban counties, covering ~12.5 million Medicare beneficiaries across the US (>30% of the US population ≥65 years (2523)) (Table 1) and including locations with a variety of climates (Figure 1; Figure E1 in the online data supplement).

On average across the 213 counties, respiratory hospitalizations increased 4.3% (95% posterior interval [PI]: 3.8, 4.8%) for each 10°F increase in daily mean summer temperature (Figure 2). Results were similar for COPD (4.7%; PI: 3.9, 5.5%) and respiratory tract infections (4.1%; PI: 3.4, 4.7%) (Figure 2). Results were robust to changes in adjustment for seasonality (see Figure E2 in the online data supplement) and were similar using different temperature metrics (e.g., minimum and maximum temperature, heat index) (see Table E1 in the online data supplement).

Across counties, we found small to moderate correlations between temperature and air pollutants (median across counties: O₃: 0.39, PM₁₀: 0.42; PM₂.₅: 0.45) (see Figure E3, and Table E2 in the online data supplement). However, both county-level and national average estimates were very similar for models with and without the adjustment for O₃, PM₁₀, and PM₂.₅ (Figure 3;
Table E3 in the online data supplement). Therefore we did not find evidence that the association between outdoor temperature and respiratory admissions is confounded by exposure to air pollution.

Heat and respiratory hospitalizations were most strongly associated on the day of exposure (lag 0) (see Figure E4 in the online data supplement). One day following exposure (lag 1), the association was smaller but still positive and statistically significant (2.3%; PI: 1.8, 2.8%), while at lag 2, there was no evidence of an association (0.1%; PI: -0.3, 0.5%) (see Figure E4 in the online data supplement). When we modeled cumulative effects up to one week following exposure (lags 0–6), we found a cumulative effect of a 2.2% (PI: 1.3, 3.1%) increase in respiratory hospitalizations associated with a 10°F increase in the previous week’s daily mean temperature (see Figure E4 in the online data supplement).

The association between heat and respiratory hospitalizations was consistently positive and statistically significant in all subpopulations (i.e., age and gender) considered (Figure 2). Relative risk estimates were very similar for men and women (4.3%; PI: 3.6, 5.0% for men and 4.4%; PI: 3.7, 5.1% for women) (Figure 2) and for the different age groups (65–74 years: 4.8%; PI: 4.0, 5.6%; 75–84 years: 4.2%; PI: 3.5, 4.9%; 85 years and older: 4.2%; PI: 3.2, 5.2%) (Figure 2).

We investigated whether differences between county-specific risks of heat-related hospital admissions could be explained by differences between the counties’ average summer temperature, defined as average May–September temperature for 1999–2008 (Figure 1, Figure 4). For a county with average summer temperature 10°F cooler than the national average summer temperature, the county was estimated to have a 1.4% (PI: 0.4, 2.3%) higher relative risk of heat-related respiratory hospitalization than the national relative risk.
4 Discussion

We investigated the acute relationship between short-term exposure to outdoor heat and hospitalizations for respiratory diseases among the elderly in 213 US counties, geographically spread across the United States and with a variety of climates. Across these counties, daily rates of Medicare respiratory hospitalizations increased 4.3% (PI: 3.8, 4.8%) per 10°F increase in daily temperature. To translate this association to number of excess hospitalizations, each 10°F increase in daily temperature, for example, translates to approximately 30 excess respiratory Medicare hospitalizations per day across these 213 study counties, based on county-specific effect estimates and hospitalization rates for the most current year of this study (2008). Note that a larger increase in daily temperature would result in more excess hospitalizations and a lower increase in fewer hospitalizations (e.g., approximately 15 excess respiratory Medicare hospitalizations/day for a 5°F increase, approximately 45 for a 15°F increase). Across all study counties, the average within-county range between the hottest and coolest temperatures over the 10 study years for a specific date of the summer (e.g., June 1) was 15.1°F, while the average interquartile range was 5.8°F (see Supplemental Material for more details on this calculation).

We investigated this association for lags of a week or less and found the association was strongest at a same-day lag and. The association was robust to control for air pollution, changes in control for long-term and seasonal trends, and changes in the metric used to estimate heat exposure. By jointly investigating this large set of locations, this study identified a consistent increase in respiratory hospitalizations associated with heat across a variety of US locations, and also identified heterogeneity between county-specific associations based on differences in local climate.
These acute heat effects are smaller than those found in several previous time series studies. Each 10°F increase in outdoor heat was found to increase respiratory hospitalization rates 28.0% in Mediterranean cities (14), 16.1% in New York, NY (12), and 19.3% in a meta-analysis of worldwide heat-morbidity studies (6). This difference cannot be explained by differences in exposure metrics, since our estimates changed little with alternate exposure metrics. The smaller effect size found in this study may result from differences in modifying factors, including population characteristics, housing structures, and air conditioning prevalence. Our findings are more consistent with two California studies, which identified increases of 2.0% (11) and 2.6% (10) in respiratory hospitalizations per 10°F increase in daily outdoor heat. While the effect found in our study is higher, our study was restricted to a more susceptible population (people ≥65 years), while these California studies included all ages.

While epidemiological studies cannot definitively determine the pathway of heat’s effects on respiratory health, a large multi-community study can evaluate consistency between epidemiological health endpoints and potential pathways through close investigation of effect modification by age, gender, and local climate, as well as the role of confounding by air pollution. Our research helps clarify the link between outdoor heat and acute respiratory health outcomes by providing support for or against several plausible pathways for heat’s effects on respiratory health.

First, we extensively tested sensitivity of heat effect estimates to confounding by controlling for three pollutants linked to both outdoor heat and respiratory health (O₃, PM₁₀, and PM₂.₅) (21-23, 24). Our results provide evidence that increased respiratory risks during hot weather are not explained solely by increases in air pollution concentration—associations between heat and respiratory hospitalizations were almost unchanged with adjustment for
pollutants. Pollen and mold concentrations have also been linked to both outdoor heat (27-2825-26) and respiratory health (29-3027-28). Nationally representative data for these aeroallergens were not available to definitively address this question in the current study (3129), but future research could investigate this pathway for heat effects at the community or regional level.

Our findings also provide evidence that increases in acute respiratory outcomes during heat are probably not caused by indoor crowding to avoid the heat. While indoor crowding may help spread respiratory infections (3230), respiratory diseases take several days to progress from exposure to symptoms. We found, conversely, the strongest association between respiratory hospitalizations and heat was on the same day as exposure (lag 0). Several city- or state-level studies in the US (12, 10-1112), as well as international studies (6, 20), have similarly found same-day associations between respiratory hospitalizations and heat. These results suggest heat may aggravate existing respiratory infections rather than spread new infections through indoor crowding.

While epidemiologic evidence cannot definitively determine biological pathways, our results suggest that the pathway for acute respiratory heat effects may differ somewhat from the pathway for cardiovascular heat effects. Heat-related cardiovascular outcomes are likely caused by stress to the cardiovascular system from thermoregulatory responses to heat (3331). Our results suggest that, while adverse systemic effects related to thermoregulation may play a role in respiratory heat effects, these effects are likely also mediated by an immediate effect of breathing hot air.

Thermoregulation helps humans maintain safe body temperatures in heat but is associated with systemic inflammation, increases in cardiac output, increases in skin blood flow, and increases in pulmonary ventilation (34-3532-33). Additionally, while humans primarily lose
body heat through surface sweating, hyperthermia can increase ventilation and cause thermal hyperpnea (second phase panting during which tidal volume and respiratory rate both increase) (3432). These thermoregulatory responses could contribute to the observed increase in hospitalizations for respiratory infections and COPD exacerbations, especially since COPD is a disease characterized by ventilatory impairment, persistent pulmonary and systemic inflammation (35,3833, 36) and coexisting cardiovascular disease (38-3936-37).

However, if heat effects on respiratory health were mediated exclusively by a thermoregulatory pathway, risks would likely differ substantially by age, county climate and, possibly, gender. First, age and, to some degree, gender are linked to physiological differences in thermoregulation (38-40-42), and so we would expect differences in susceptibility by age and gender if respiratory heat effects were mediated exclusively by a thermoregulatory pathway. However, here we found little difference in respiratory susceptibility to heat by either age or gender. Second, if effects were mediated exclusively by a thermoregulatory pathway, heat effects would likely differ substantially based on a location’s climate since thermoregulatory response improves with repeated heat exposure (4240). However, while respiratory heat effects were generally lower in counties with hotter average summer temperatures, heat-hospitalization associations remained positive across the range of county climates. Further, county climate modified respiratory heat effects much less than in similar research on heat and cardiorespiratory mortality (1).

Our findings are consistent with the hypothesis that acute respiratory heat effects are likely also mediated by an immediate direct effect of breathing hot air. We found limited effect modification of respiratory heat effects by climate, which could be explained if respiratory heat effects are triggered by very brief exposure to heat since even widespread use of air
conditioning cannot eliminate brief (e.g., ≤10 minutes) outdoor heat exposure. While an hour or more of exposure is required for some thermoregulatory responses to heat (4341), a few minutes of heat exposure can trigger direct human airway responses to inhaling hot air. This rapid response has been demonstrated in studies of asthma (44-45), and it is likely mediated through the cholinergic reflex pathway (42, 44, 46-47).

Studies of the association between heat and human mortality have found evidence of decreasing effects over decades (46-47) and smaller effects in hotter climates (1), suggesting protective adaptation to heat, possibly related to differences in housing stock or behavior during hot weather. Given this study’s timeframe, we were unable to explore temporal adaptation, but we did investigate evidence of differences in heat-hospitalization associations between hotter and milder counties. While our results are consistent with evidence of adaptation—smaller effects in counties where summers are typically very hot—this adaptation did not completely remove risk even in the hottest counties. Additionally,

Any adaptations may take decades to realize or be impractical in certain communities. For example, architectural adaptations can only change slowly with changes in housing stock, and may be impractical in dense urban communities like New York City. Adaptation could also bring its own risks and impacts. Higher use of air conditioning will draw on already-stressed power grids, which could cause power outages during severe heat waves and so create new health threats (48). Additionally, the energy use associated with increased use of air conditioning will increase air pollution and accelerate climate change through release of greenhouse gases (49).

In the future, the burden of heat-related respiratory morbidity as health hazards are likely to increase. Within this century, exposure to heat is expected to increase as the average global
temperature rises at least 3°F (3), and heat waves are expected to become more frequent and severe (3). Also, a growing percentage of the population will likely be particularly susceptible to heat-related respiratory morbidity, given projected increases in the global prevalence of chronic respiratory diseases (4) and aging of the US population (50).

In summary, in a 10-year study of Medicare respiratory hospitalizations and outdoor heat in 213 US counties, we found risk of respiratory hospitalization significantly increased with daily outdoor heat. This relationship persisted across age categories, genders, and county climates, and could not be explained by changing concentrations of air pollution. The health burdens from heat-related respiratory risks are likely to increase in the future with increasing prevalence of respiratory conditions (4) and rising temperatures from climate change (3).
References


Figures Legends

Figure 1: **213 US study counties and their average summer temperatures.** Colors correspond to the county’s daily mean temperatures, averaged from May to September (1999–2008).

Figure 2: **Percent increase in respiratory hospitalizations for each 10°F daily outdoor heat increase, 1999–2008 (lag 0).** Estimates are pooled across all 213 study counties; outdoor heat is measured as daily mean temperature, May—September. Horizontal lines show 95% posterior intervals. Abbreviations: COPD: chronic obstructive pulmonary disease; RTI: respiratory tract infections.

Figure 3: **Relative risk of heat-related respiratory hospitalization with and without adjustment for air pollution, 1999-2008 (lag 0).** Analysis for O₃ (n=200), PM₁₀ (n=165), and PM₂.₅ (n=196). Circles show community-level estimates. Larger circles indicate greater certainty. Black diamond shows estimate across all communities. Abbreviations: O₃, ozone; PM₁₀ and PM₂.₅, particulate matter with aerodynamic diameter ≤10µm and ≤2.5µm, respectively.

Figure 4: **Modification of county-level relative risk of heat-related respiratory hospitalization by a county’s average summer temperature (lag 0).** Average county summer temperature for May—September, 1999—2008. Circles show county-level estimates. Larger circles indicate greater certainty. Solid line shows the predicted pooled estimate by average summer temperature (shaded region shows 95% posterior interval). Abbreviation: Tₘₑ𝐚ₙ: mean daily temperature.
### Table 1: Study population, total hospitalizations, and daily hospitalization counts and rates for 213 US counties, 1999–2008.

<table>
<thead>
<tr>
<th>Category</th>
<th>Number (range) of Medicare beneficiaries (in millions)*</th>
<th>Total hospitalizations, May—September, 1999—2008*</th>
<th>Hospitalization count/day (range)†</th>
<th>Daily hospitalization rate (range) per 100,000 beneficiaries‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>All respiratory</td>
<td>12.5 (11.5, 13.1)</td>
<td>1,141,458</td>
<td>2.3 (0.6, 31.9)</td>
<td>5.8 (3.4, 11.7)</td>
</tr>
<tr>
<td>By cause</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory tract infections</td>
<td>12.5 (11.5, 13.1)</td>
<td>756,395</td>
<td>1.6 (0.4, 21.6)</td>
<td>3.9 (2.5, 7.2)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>12.5 (11.5, 13.1)</td>
<td>385,063</td>
<td>0.8 (0.1, 10.3)</td>
<td>2.0 (0.4, 4.5)</td>
</tr>
<tr>
<td>By gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.2 (4.5, 5.4)</td>
<td>499,373</td>
<td>1.1 (0.3, 13.9)</td>
<td>6.3 (3.7, 12.6)</td>
</tr>
<tr>
<td>Female</td>
<td>7.3 (7.0, 7.7)</td>
<td>642,085</td>
<td>1.3 (0.3, 17.9)</td>
<td>5.5 (3.0, 11.0)</td>
</tr>
<tr>
<td>By age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>65 to 74 years</td>
<td>6.4 (6.0, 6.7)</td>
<td>358,830</td>
<td>0.8 (0.2, 10.1)</td>
<td>3.6 (1.8, 6.9)</td>
</tr>
<tr>
<td>75 to 84 years</td>
<td>4.4 (4.1, 4.7)</td>
<td>468,002</td>
<td>1.0 (0.2, 13.0)</td>
<td>6.7 (3.9, 12.9)</td>
</tr>
<tr>
<td>85 years and older</td>
<td>1.6 (1.4, 1.8)</td>
<td>314,626</td>
<td>0.6 (0.1, 9.6)</td>
<td>12.1 (7.5, 22.9)</td>
</tr>
</tbody>
</table>

*Total across all 213 study counties.

†Average values across all study days were computed for each county, and shown here are the median and range (in parentheses) of these county-specific values.
Online Data Supplement for “Heat-related emergency hospitalizations for respiratory diseases in the Medicare population”

G. Brooke Anderson, Francesca Dominici, Yun Wang, Meredith C. McCormack, Michelle L. Bell, and Roger D. Peng
Contents of Online Data Supplement:

1. Further Explanation of Methods

2. Tables
   - Table E1: Percent increase in hospitalizations per 10°F increase in daily outdoor heat using different metrics of heat exposure.
   - Table E2: Correlation between daily outdoor heat and air pollutants, May–September, for pollution lags of 0, 1, and 2 days.
   - Table E3: Associations between daily outdoor heat and respiratory hospitalizations estimated with and without control for air pollutants.

3. Figures
   - Figure E1: Distribution of daily mean temperature summary statistics across the 213 study counties.
   - Figure E2: Association between respiratory hospitalizations and a 10°F increase in daily outdoor heat using different degrees of freedom to control for long-term and seasonal changes in respiratory hospitalization rates.
   - Figure E3: County-level correlations between air pollutants and daily outdoor heat with lags of 0, 1, and 2 days for pollutants.
   - Figure E4: Percent increase in hospitalizations associated with a 10°F increase in outdoor heat at different lags.
Further Explanation of Methods

Further details on data

For the dataset used for this study, Medicare Part-A inpatient data were originally obtained through the National Claims History Files. Causes of hospitalization were determined by principal discharge diagnosis code: respiratory tract infections (ICD-9 464–466, 480–487) and chronic obstructive pulmonary disease (ICD-9 490–492). Transfers between hospitals were not counted as new hospitalizations. Medicare beneficiary enrollment data were used to calculate the potential pool of patients on any given day. Data were aggregated by day to create daily rates, and so Medicare data analyzed for this study lacked individual identifiers.

Air pollution data were obtained from the US Environmental Protection Agency’s Air Quality System for tropospheric ozone (O\textsubscript{3}) and particulate matter with aerodynamic diameter ≤10µm (PM\textsubscript{10}) and ≤2.5µm (PM\textsubscript{2.5}). Daily O\textsubscript{3} concentration was measured using a 24-hour average metric. For weather and pollution data, monitors were matched to counties by longitude and latitude. For counties without weather monitors, all weather stations within 35 kilometers were used to estimate the county’s weather. In counties with multiple weather or pollution monitors, values from different monitors were averaged after subtracting out a 365-day moving average; in counties with 2–9 monitors, maximum and minimum measurements were removed before averaging, while in counties with ≥10 monitors, a 10% trimmed mean was used.\[E1\]

Daily maximum, minimum, and dew point temperature were obtained from the National Climatic Data Center on the Earth-Info CD database. Daily mean temperature was calculated as the average of daily maximum and minimum temperature. To calculate daily heat index from daily mean temperature and dew point temperature, we created an R function based on JavaScript code from the National Weather Service’s online heat index calculator [E1,E2]. There are several different equations and algorithms used to derive heat index from daily temperature and relative humidity; here we used the algorithm of the US National Weather Service to allow comparison between our results and weather conditions as reported by US meteorologists. The National Weather Service heat index algorithm is based on the heat index developed by Steadman [E2,E3,E4] and includes adjustments for certain conditions (for example, if relative humidity is ≥85% and temperature is ≥80°F or if relative humidity is ≤13% and temperature is between 80°F and 112°F) [E1,E2]. At temperatures below 40°F, heat index defaults to air temperature for this algorithm [E1,E2].

In counties with limited data, model convergence problems can be common, especially for stratified analysis where total counts are small (e.g., hospitalizations stratified by age category). We therefore removed counties with <5 years of weather data, which excluded 6 counties from the original dataset of 221. We also excluded counties outside the contiguous 48 states, which removed two more counties. Our final dataset included 213 counties. As a test of whether our results were sensitive to this exclusion, we re-measured our main result (national relationship between temperature and respiratory hospitalizations) with these 8 counties included. Since this main analysis was performed on unstratified
data, we had adequate data to fit models to these 8 counties, and so this sensitivity analysis could be performed to determine if exclusion of these counties might affect estimates for more detailed analysis (e.g., age-specific estimates performed with stratified data). We found the national estimate was identical with and without these 8 counties included in analysis. Therefore, excluding these counties has very little effect on national estimates but facilitates more detailed analysis, including age- and gender-specific analysis and investigation of effect modification by long-term, county-specific characteristics (e.g., average summer temperature in each county).

In many communities, particulate matter concentration is only measured once every three or six days. Therefore, in our analysis of the sensitivity of main results to air pollution, we limited analysis to counties with >150 days of joint data for weather and the air pollutant of interest. Similar exclusion criteria have been used in previous research [E4-E6E5-E7]. Following this exclusion, the following number of counties remained to test sensitivity to air pollution: O$_3$, 200 counties; PM$_{10}$, 165 counties; PM$_{2.5}$, 196 counties. This restriction did not affect the main results of our study, where we model the association between outdoor temperature and respiratory hospitalizations in models that do not include air pollution measurements.

Further details on methods

The first-level model used to estimate the association between temperature and same-day hospitalizations within each county (details on models for other lags are given later) can be described as:

$$\log(\mu_t) = \alpha + \beta T_0 + \delta_t D_t + f(H_0) + f(L_t) + B_t$$

where:

- $\mu_t$ Expected hospitalization count on day $t$
- $\alpha$ Model intercept
- $\beta$ Coefficient of temperature effect
- $T_0$ Mean same-day temperature (°F)
- $\delta_t$ Vector of coefficients for day of week
- $D_t$ Day of week for day $t$
- $f(H_0)$ Function of mean dew point temperature on day $t$ (adjusted for daily mean temperature), modeled as a natural cubic spline, 2 degrees of freedom (df)
- $f(L_t)$ Function of time, modeled as a natural cubic spline with 7 df/year (used to model long-term and seasonal trends)
Offset term: number of Medicare beneficiaries in study population who could be hospitalized on day \( t \) (i.e., population at risk)

Dew point temperature and air temperature are highly correlated: within our 213 study counties, the median of county-specific correlations between air temperature and dew point temperature for May—September is 0.78 (range of county-level correlations: -0.04, 0.89). Therefore, we adjusted dew point temperature for air temperature \( (H_0 \text{ in equation 1}) \) before including it in our model. After adjustment, the median correlation was -4.6e-17 (range: -4.3e-15, 4.1e-15).

Relative humidity is less strongly correlated with air temperature (for example, for our counties the median county-specific correlation is -0.07; range: -0.71, 0.20), and so some studies use relative humidity rather than dew point temperature to control for air moisture \([E7-E9]\). To ensure this modeling choice did not affect our results, we tested the sensitivity of our main result to using relative humidity to control for air moisture rather than dew point temperature. We found our main results were practically identical for the two models (model with dew point temperature control: 4.3%, PI: 3.8, 4.8; model with relative humidity control: 4.2%, PI: 3.7, 4.8%).

Models of temperature and health sometimes include control for holidays \([E8-E10]\). We tested controlling for all federal holidays between May and September (Independence Day, Labor Day, and Memorial Day). When we included holiday status in our main model as a binary factor, we estimated a national effect of 4.4% (PI: 3.8, 4.9%). By comparison, the national effect without holiday control was 4.3% (PI: 3.8, 4.8%). Since our main result was not sensitive to holiday control, we did not retain holiday as a factor in our final model.

For main results, we used daily average temperature as our metric of heat exposure. However, to allow comparison with previous research, we also separately modeled heat effects using metrics of daily minimum temperature, daily maximum temperature, and daily heat index (which incorporates temperature and relative humidity \([E1-E3,E2,E4]\)), by re-running our main model three times, once with each of these metrics in place of daily mean temperature.

Previous research has found evidence of non-linearity in the relationship between temperature and cardiorespiratory mortality within the summer (i.e., a different per-degree change in a health outcome at very hot temperatures versus mild temperatures during the summer) \([E10-E11]\). To ensure our model, which models the relationship between daily temperature \( (T_0) \) and the logarithm of daily hospitalizations \( (\log(\mu_t)) \) as a linear association, appropriately captures the association between summer temperature and respiratory hospitalizations, we tested the relationship fit with Model 1 for evidence of nonlinearity in the relationship between \( T_0 \) and \( \log(\mu_t) \). To do this, we fit a model similar to Model 1, but with the temperature term, \( T_0 \), replaced with a natural cubic spline of temperature with 2 degrees of freedom to model May–September temperatures. After fitting this nonlinear model, we compared deviance of the two
models (linear versus nonlinear) to determine evidence within that county of significant non-linearity (i.e.,
to determine if the non-linear model offered a significant improvement over the linear model). As a second
test of sensitivity of results to use of a non-linear versus linear model, we compared the estimated
percentage increase in hospitalizations per \(10^\circ F\) temperature increase as estimated by the linear model to
the measurement from the county’s nonlinear model for a \(10^\circ F\) change in temperature centered at the
county’s median value of May–September temperatures.

We found little evidence that a nonlinear model provided an improved fit to temperature-
hospitalization data. In 193 of the 213 counties considered (91%), a natural cubic spline did not provide a
significantly better fit to the data than a linear model as indicted by comparison of model deviance
(significance level: 95%). Additionally, we found linear model estimates were similar to estimates from
nonlinear models evaluated at a county’s median May–September temperature (estimate from linear model:
4.3%, PI: 3.8, 4.8%; estimate from nonlinear model evaluated at county’s median temperature: 3.8%, PI:
3.2, 4.4%). Because we found little evidence of significant non-linearity in the relationship between heat
and respiratory Medicare hospitalizations, as well as limited sensitivity to using nonlinear versus linear
models when effects are modeled at median May–September temperatures, we used linear models to model
the association between temperature and hospitalizations in remaining analysis.

We fit model 1 for each county separately. From this model we estimated \(\gamma\), the increase in
\(\log \mu\), per \(10^\circ F\) increase in daily temperature, as well as the variance of \(\gamma\) (\(\gamma\) is equal to \(10 \beta\) for the
value of \(\beta\) estimated in equation 1). For presentation, we translated this association into an estimate of
percent increase in hospitalizations per \(10^\circ F\) through the conversion \(100 \times (\exp(\gamma) - 1)\).

This metric—a percent change in health outcome per \(10^\circ F\) temperature increase—has been used in
previous US studies of temperature and health \[^{E12-E14}\|^{'E13-E15}\. Using this metric therefore aids
comparability between our study and previous research.

Additionally, this metric provides a good measure of the difference between hot and mild weather
for a given day of the year (our model measures the percent increase in hospitalization risk for a \(10^\circ F\) higher
temperature during the given time of the year, since we control for seasonality). In each of our 213 study
counties, we measured how temperatures within each county vary for the same day of the year (e.g., June 1)
across the 10 study years. For each county, we measured the difference between the hottest and coolest
temperatures across the 10 study years for each day of the summer, and then took the median for the county
of all these day-specific ranges. We performed a similar analysis for the interquartile range by day of year
within each county. We found that, across all counties, the range between the hottest and coolest
temperatures for a specific day of the year is, on average, 15.1\(^\circ F\) (range of county-specific medians: 5.9\(^\circ F\),
22.4\(^\circ F\)), while the average interquartile range is 5.8\(^\circ F\) (range of county-specific medians: 2.1\(^\circ F\), 8.0\(^\circ F\)).
Therefore, when we measure risk for a \(10^\circ F\) increase in temperature, this metric is representative of the
change in hospitalization risk between a day that has a hot temperature for that time of the year versus a day that is mild for the time of year.

To pool county-level estimates at the national and regional levels, we used a Bayesian hierarchical model that incorporated both within-county and between-county variance:

\[ \hat{\gamma}^c | \gamma^c, \hat{\upsilon}^c \sim N(\gamma^c, \hat{\upsilon}^c), c = 1, \ldots, 213 \]  
\[ \gamma^c | \phi, \tau^2 \sim N(\phi, \tau^2) \]

where:

- \( \hat{\gamma}^c \): Estimated increase in \( \log \mu_t \) per 10°F increase in temperature for county \( c \), from first-level county-specific model
- \( \gamma^c \): True increase in \( \log \mu_t \) per 10°F increase in temperature for county \( c \)
- \( \hat{\upsilon}^c \): Estimated variance of increase in \( \log \mu_t \) per 10°F increase in temperature for county \( c \), from first-level county-specific model
- \( \phi \): True national increase in \( \log(\mu_t) \) per 10°F increase in temperature
- \( \tau^2 \): Variance between counties in true county-level increases in \( \log(\mu_t) \) per 10°F increase in temperature

We fit this second-stage model using the “tlnise” package in R [E15E16].

To test effects under different exposure metrics, we refit Model 1 within each county using minimum temperature, maximum temperature, or heat index instead of \( T_0 \). We fit a separate model for each metric. To determine if results were sensitive to control for season, we refit Model 1 within each county using 5, 6, 8, or 9 df/year in \( f(L_t) \).

We investigated the sensitivity of results to control for air pollutants (O\(_3\), PM\(_{10}\), and PM\(_{2.5}\)) by fitting Poisson models with and without adjustment for these pollutants. Since health effects of pollutants can follow exposure by a day or two [E16-E18E17-E19], we investigated pollution lags of 0, 1, and 2 days. To determine sensitivity of observed associations to pollutant control, for each pollutant analyzed, two models were fit for each community—one without control for the pollutant (equation 4) and one that included control for the pollutant (equation 5):

\[ \log(\mu_t) = \alpha + \beta T_0 + \delta_i D_i + f(H_0) + f(L_i) + B_i \]  

(4)
\[ \log(\mu_i) = \alpha + \beta T_0 + \eta C_l + \delta_i D_i + f(H_0) + f(L_i) + B_i \]  

(5)

with all coefficients as defined in equation 1, as well as:

\[ \eta \] Coefficient of pollutant effect

\[ C_l \] Concentration of given pollutant on lag \( l \) (\( l \) days before day \( t \))

Before fitting models for a specific county and pollutant, data within a county was reduced to only those days with joint data for both temperature and the pollutant being considered. This reduced dataset was used to calculate temperature-hospitalization associations both without (equation 4) and with (equation 5) control for the pollutant. We investigated pollutants at lags of 0 to 2 days, since pollutants can affect health at slightly delayed lags [E16–E18E17–E19].

To investigate lags of temperature-hospitalization associations, we re-fit model 1, including temperature for the previous day (lag 1: \( T_1 \)) or two days earlier (lag 2: \( T_2 \)) in place of \( T_0 \). To estimate cumulative effects (lags 0–6), we used a distributed lag model and fit a crossbasis of temperature and lag-day, out to lag 6, using the R package “dlm” [E19E20]. The lag function for this crossbasis was fit as a natural cubic spline with 3 degrees of freedom, with knots at equal log intervals to allow greater flexibility in the lag function at lags near exposure (e.g., lags 0, 1) and smoother changes with lag at further lags (e.g., lags 5, 6) [E8E9]. Other model specifications were as given in equation 1.

Finally, we investigated whether counties with cooler summers on average tend to have larger relative risks of hospital admissions as a result of a sudden increase in temperature from one day to the next. To analyze modifications by county climate in the relationship between temperature and respiratory hospitalization, we pooled county-level estimates in a Bayesian hierarchical model with average May–September climate as a potential modifier:

\[ \gamma_c | \gamma^c_0, \nu_c \sim N(\gamma^c_0, \nu_c^2), c = 1, \ldots, 213 \]  

(6)

\[ \gamma^c | \theta_0, \theta_1, \tau^2 \sim N(\theta_0 + \theta_1(x_c - \bar{x}), \tau^2) \]  

(7)

with all coefficients as defined in equations 2 and 3, as well as:

\[ x_c - \bar{x} \] Difference between county \( c \)’s mean May–September temperature and the average of May–September temperature for all 213 counties
Overall estimate of increase in $\log \mu_i$ per 10°F increase in temperature for a county with average summer temperature equal to $\bar{x}$, the average of May–September temperature for all 213 counties

$\theta_1$ Estimate of effect modification by county average May–September temperature

All analysis was performed with R statistical software version 2.14.1.
Tables

- Table E1: Percent increase in hospitalizations per 10°F increase in daily outdoor heat using different metrics of heat exposure.
- Table E2: Correlation between daily outdoor heat and air pollutants, May–September, for pollution lags of 0, 1, and 2 days.
- Table E3: Associations between daily outdoor heat and respiratory hospitalizations estimated with and without control for air pollutants.
Table E1: Percent increase in hospitalizations per 10°F increase in daily outdoor heat using different metrics of heat exposure.

<table>
<thead>
<tr>
<th>Temperature metric</th>
<th>% increase in hospitalizations per 10°F increase in temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean temperature</td>
<td>4.3%(^a) (3.8, 4.8) (^b)</td>
</tr>
<tr>
<td>Maximum temperature</td>
<td>3.8% (3.4, 4.3)</td>
</tr>
<tr>
<td>Minimum temperature</td>
<td>3.4% (2.9, 3.9)</td>
</tr>
<tr>
<td>Heat index</td>
<td>3.4% (2.9, 3.8)</td>
</tr>
</tbody>
</table>

\(^a\)Pooled point estimate across 213 United States counties, 1999–2008.
\(^b\)95% posterior interval of pooled estimate across 213 United States counties, 1999–2008.

Table E2: Correlation between daily outdoor heat and air pollutants, May–September, for pollution lags of 0, 1, and 2 days.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>N (# of counties)</th>
<th>Pollutant at lag 0</th>
<th>Pollutant at lag 1</th>
<th>Pollutant at lag 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(_3)</td>
<td>200</td>
<td>0.39(^a) (-0.51, 0.62)(^b)</td>
<td>0.35 (-0.52, 0.59)</td>
<td>0.24 (-0.43, 0.49)</td>
</tr>
<tr>
<td>PM(_{10})</td>
<td>165</td>
<td>0.42 (-0.01, 0.68)</td>
<td>0.37 (-0.09, 0.65)</td>
<td>0.25 (-0.15, 0.47)</td>
</tr>
<tr>
<td>PM(_{2.5})</td>
<td>196</td>
<td>0.45 (-0.06, 0.62)</td>
<td>0.45 (-0.08, 0.61)</td>
<td>0.30 (-0.12, 0.42)</td>
</tr>
</tbody>
</table>

Abbreviations: O\(_3\), tropospheric ozone; PM\(_{10}\), particulate matter with aerodynamic diameter ≤10µm;
PM\(_{2.5}\), particulate matter with aerodynamic diameter ≤2.5µm.

\(^a\)Median of all county-specific correlations.
\(^b\)Range of county-specific correlations.
Table E3: Associations between daily outdoor heat and respiratory hospitalizations estimated with and without control for air pollutants.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Lag 0 No control for pollutant</th>
<th>Lag 0 Control for pollutant</th>
<th>Lag 1 No control for pollutant</th>
<th>Lag 1 Control for pollutant</th>
<th>Lag 2 No control for pollutant</th>
<th>Lag 2 Control for pollutant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O₃</td>
<td>4.1% a (3.6, 4.6) b</td>
<td>4.2% (3.6, 4.8)</td>
<td>4.1% (3.6, 4.6)</td>
<td>4.0% (3.4, 4.7)</td>
<td>4.1% (3.6, 4.7)</td>
<td>4.1% (3.6, 4.7)</td>
</tr>
<tr>
<td>PM₁₀</td>
<td>3.4% (2.5, 4.3)</td>
<td>3.2% (2.3, 4.1)</td>
<td>3.5% (2.5, 4.4)</td>
<td>3.1% (2.0, 4.2)</td>
<td>4.1% (3.2, 5.0)</td>
<td>4.0% (3.0, 4.9)</td>
</tr>
<tr>
<td>PM₂.₅</td>
<td>3.7% (3.1, 4.4)</td>
<td>3.6% (2.8, 4.3)</td>
<td>4.2% (3.5, 4.8)</td>
<td>3.9% (3.2, 4.7)</td>
<td>4.4% (3.7, 5.1)</td>
<td>4.3% (3.6, 5.0)</td>
</tr>
</tbody>
</table>

Abbreviations: O₃, tropospheric ozone; PM₁₀, particulate matter with aerodynamic diameter ≤10µm; PM₂.₅, particulate matter with aerodynamic diameter ≤2.5µm.

aPooled point estimate across 213 United States counties, 1999—2008. Estimates shown are the percent increase in daily respiratory hospitalizations associated with a 10°F increase in daily outdoor heat. The number of counties included in each analysis were: O₃: 200; PM₁₀: 165; PM₂.₅: 196.

b95% pooled estimate across 213 United States counties, 1999—2008.
Figures

- Figure E1: Distributions of daily mean temperature summary statistics across the 213 study counties.
- Figure E2: Association between respiratory hospitalizations and a 10°F increase in daily outdoor heat using different degrees of freedom to control for long-term and seasonal changes in respiratory hospitalization rates.
- Figure E3: County-level correlations between air pollutants and daily outdoor heat at lags of 0, 1, and 2 days for pollutants.
- Figure E4: Percent increase in hospitalizations associated with a 10°F increase in outdoor heat at different lags.
Figure E1: Distributions of daily mean temperature summary statistics across the 213 study counties.
Each graph shows the distribution of county-level values of that metric (e.g., minimum, first quartile, etc.) of all daily mean temperature measurements in a county over the study period.
Figure E2: Association between respiratory hospitalizations and a 10°F increase in daily outdoor heat using different degrees of freedom to control for long-term and seasonal changes in respiratory hospitalization rates. Results are pooled over 213 US counties, 1999–2008. Outdoor heat is measured as daily mean temperature.
Figure E3: County-level correlations between air pollutants and daily outdoor heat at lags of 0, 1, and 2 days for pollutants.

Abbreviations: O$_3$, tropospheric ozone; PM$_{10}$, particulate matter with aerodynamic diameter $\leq$10µm; PM$_{2.5}$, particulate matter with aerodynamic diameter $\leq$2.5µm. Each histogram shows the distribution of county-level correlations between daily outdoor heat (measured as mean temperature) and the given air pollutant at the given lag (i.e., the graph for O$_3$ at lag 1 shows the distribution of county-level correlations between outdoor heat and previous day’s ozone concentration). Black vertical lines show median of the 213 county-level correlations for each pollutant and lag.
Figure E4: Percent increase in hospitalizations associated with a 10°F increase in outdoor heat at different lags.

All estimates are pooled across all 213 study counties. Outdoor heat is measured as daily mean temperature.
References for Online Data Supplement


[E4] Rothfusz LP. The heat index equation (or, more than you ever wanted to know about heat index). Fort Worth, Texas: National Oceanic and Atmospheric Administration, National Weather Service, Office of Meteorology; 1990.


