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Citation	Gronlund, Carina J., Antonella Zanobetti, Joel D. Schwartz, Gregory A. Wellenius, and Marie S. O'Neill. 2014. "Heat, Heat Waves, and Hospital Admissions among the Elderly in the United States, 1992–2006." Environmental Health Perspectives 122 (11): 1187-1192. doi:10.1289/ehp.1206132. http://dx.doi.org/10.1289/ehp.1206132.
Published Version	doi:10.1289/ehp.1206132
Accessed	March 1, 2017 3:38:41 PM EST
Citable Link	http://nrs.harvard.edu/urn-3:HUL.InstRepos:13454663
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Heat, Heat Waves, and Hospital Admissions among the Elderly in the United States, 1992–2006

Carina J. Gronlund, Antonella Zanobetti, Joel D. Schwartz, Gregory A. Wellenius, and Marie S. O'Neill 1,4,5

¹Department of Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, Michigan, USA; ²Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA; ³Department of Epidemiology, Brown University, Providence, Rhode Island, USA; ⁴Department of Epidemiology, and ⁵Risk Science Center, University of Michigan School of Public Health, Ann Arbor, Michigan, USA

BACKGROUND: Heat-wave frequency, intensity, and duration are increasing with global climate change. The association between heat and mortality in the elderly is well documented, but less is known regarding associations with hospital admissions.

OBJECTIVES: Our goal was to determine associations between moderate and extreme heat, heat waves, and hospital admissions for nonaccidental causes among Medicare beneficiaries ≥ 65 years of age in 114 cities across five U.S. climate zones.

METHODS: We used Medicare inpatient billing records and city-specific data on temperature, humidity, and ozone from 1992 through 2006 in a time-stratified case-crossover design to estimate the association between hospitalization and moderate [90th percentile of apparent temperature (AT)] and extreme (99th percentile of AT) heat and heat waves (AT above the 95th percentile over 2–8 days). In sensitivity analyses, we additionally considered confounding by ozone and holidays, different temperature metrics, and alternate models of the exposure–response relationship.

RESULTS: Associations between moderate heat and hospital admissions were minimal, but extreme heat was associated with a 3% (95% CI: 2%, 4%) increase in all-cause hospital admissions over the subsequent 8 days. In cause-specific analyses, extreme heat was associated with increased hospitalizations for renal (15%; 95% CI: 9%, 21%) and respiratory (4%; 95% CI: 2%, 7%) diseases, but not for cardiovascular diseases. An added heat-wave effect was observed for renal and respiratory admissions.

CONCLUSION: Extreme heat is associated with increased hospital admissions, particularly for renal causes, among the elderly in the United States.

CITATION: Gronlund CJ, Zanobetti A, Schwartz JD, Wellenius GA, O'Neill MS. 2014. Heat, heat waves, and hospital admissions among the elderly in the United States, 1992–2006. Environ Health Perspect 122:1187–1192; http://dx.doi.org/10.1289/ehp.1206132

Introduction

Heat waves, or extreme heat events, are predicted to increase in frequency, intensity, and duration with climate change (Intergovernmental Panel on Climate Change 2007). The elderly are more vulnerable to heat-related mortality, so the changing population structure (Vincent and Velkoff 2010) may also lead to an increased health burden from heat. The associations between temperature and mortality are well studied (Gosling et al. 2009; Hajat and Kosatsky 2010). In the United States, associations between heat and daily mortality are stronger in cities with milder summers and lower air conditioning prevalence (Anderson and Bell 2009, 2011; Curriero et al. 2002; Medina-Ramón and Schwartz 2007; O'Neill and Ebi 2009). Although extreme heat events in the United States are associated with increased deaths (Ostro et al. 2009; Semenza et al. 1996), the role of heat-wave duration versus intensity as a health determinant remains unclear (Anderson and Bell 2011; Gasparrini and Armstrong 2011).

Studies examining associations between heat and hospital admissions have had mixed results (Turner et al. 2012; Ye et al. 2012). For example, in London, England, a 1995 heat wave was not associated with

total hospital admissions but was associated with hospitalizations for respiratory and renal diseases and increased mortality (Kovats et al. 2004). On the other hand, heat waves in Adelaide, Australia, have been associated with increased hospitalizations but not increased mortality (Nitschke et al. 2007). In 12 European cities, respiratory admissions increased with temperature in Mediterranean and North-Continental cities, but associations between temperature and cardiovascular admissions tended to be negative and nonsignificant (Michelozzi et al. 2009). A recent analysis of 213 U.S. counties found a 4% increase in respiratory admissions for each 10°F increase in same-day temperature (Anderson et al. 2013).

Understanding associations between heat waves and hospital admissions in the United States is important to predict how climate change may increase the future burden of heat-related morbidity; to identify vulnerable subpopulations for potential interventions; and to refine activation thresholds for heathealth warning systems.

We analyzed Medicare inpatient billing records from 114 cities in the United States from 1992 through 2006 to evaluate *a*) the associations between moderate and extreme heat measured as daily mean apparent

temperature (AT) and all-cause and cause-specific hospital admissions among elderly Medicare beneficiaries residing in five U.S. climate zones, *b*) the added effect of extreme heat durations of 2–8 days, *c*) whether observed associations are confounded by ambient ozone levels and holidays, and *d*) the sensitivity of our findings to the choice of temperature metric and the modeling of the exposure–response relationship.

Methods

Study cities and climate zones. The 200 counties with the highest number of cardiovascular hospital admissions in 2004-2006 were assigned to their respective Metropolitan Statistical Areas to form the study cities, which were then assigned to the U.S. Department of Energy, Energy Information Administration's (EIA) five climate zones (EIA 2010), as previously described (Zanobetti et al. 2012; see also Supplemental Material, "Study Cities and Climate Zones Methods"). These climate zones were based on numbers of cooling-degree days (annual sum of daily mean temperatures > 18.3°C) and heatingdegree days (annual sum of daily mean temperatures < 18.3°C).

Address correspondence to C.J. Gronlund, University of Michigan School of Public Health, Department of Epidemiology, 2669 SPH Tower, 1415 Washington Heights, Ann Arbor, MI 48109-2029 USA. Telephone: (734) 615-9215. E-mail: gronlund@umich.edu

Supplemental Material is available online (http://dx.doi.org/10.1289/ehp.1206132).

This research was supported by the U.S. Environmental Protection Agency Science to Achieve Results Program (grant R832752010); a National Occupational Research Agenda Pre-Doctoral Scholarship from the University of Michigan Center for Occupational Health and Safety Engineering a National Institute for Occupational Safety and Health-funded Education and Research Center grant 2T42OH008455); the National Institute on Aging Interdisciplinary Research Training in Health and Aging (grant T32AG027708); the U.S. Centers for Disease Control and Prevention (grant EH000348); the National Institute of Environmental Health Sciences (grants ES015774 and R21-ES020695); and a University of Michigan Dow Sustainability Fellowship

The authors declare they have no actual or potential competing financial interests.

Received: 12 October 2012; Accepted: 4 June 2014; Advance Publication: 6 June 2014; Final Publication: 1 November 2014.

Health outcomes. We obtained emergency hospital admissions for individuals ≥ 65 years of age from 1992 through 2006 from the U.S. Centers for Medicare and Medicaid Services MedPAR billing records (CMMS 2006). Ninety-seven percent of Americans ≥ 65 years of age receive Medicare insurance coverage. We categorized admissions according to the primary admission International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; Centers for Disease Control and Prevention 2013) codes as allcause (all ICD-9-CM codes < 800), cardiovascular (CVD; 390-429), heat (992 and E900.0), renal (580-589), and respiratory (Resp; 480–487, 490–492, and 494–496). The "heat" category also included secondary causes of admission related to heat. The research was approved by the institutional review boards at Harvard University and University of Michigan, and waivers of the informed consent requirement were granted.

Environmental variables. We obtained daily temperature and dew point data for each city from the National Climatic Data Center Cooperative Summary of the Day station files [National Climatic Data Center (NCDC) 2010b]. Data from a single monitor for each city were used except in 6 cities where multiple observations were missing from all the nearby monitors, in which case hourly data from the National Climatic Data Center's Integrated Surface Database Lite (NCDC 2010a) were converted to daily values. For 25 stations missing dew point data, dew point data were obtained from the nearest station with dew point data. We calculated AT using daily mean temperature (MT) and dew point $[AT(^{\circ}C) = -2.653]$ $+ (0.994 \times MT) + 0.0153 \times (\text{dew point}^2)$ (Kalkstein and Valimont 1986). We excluded from our analysis 20 cities that were missing AT measurements on at least 15% of the study days.

We chose AT as our main heat exposure metric to jointly account for effects of temperature and humidity, but we also addressed the sensitivity of our results to the alternative metric choices of MT, daily minimum temperature (MI), daily maximum temperature (MA), and diurnal temperature range (DTR; the difference between MA and MI).

Because ambient ozone levels rise during hot weather and are associated with increased rates of hospital admissions, ozone can potentially confound associations between heat and hospital admissions (Medina-Ramón et al. 2006). We obtained ozone data from the U.S. Environmental Protection Agency's Air Quality System (U.S. EPA 2014), and daily 8-hr averages were calculated and standardized as described previously (Medina-Ramón et al. 2006). For ozone analyses, we excluded an additional 10 cities that were missing

ozone measurements on at least 15% of the study days.

Main statistical analysis. We used a time-stratified case-crossover design to evaluate the association between heat and hospital admissions in each city using data on hospital admissions occurring between May and September. Control days were chosen such that cases and controls were matched on calendar month and day of week. We applied Poisson regression and accounted for over-dispersion using a quasi-Poisson model in the glm package in R (R Development Core Team, Vienna, Austria) (Guo et al. 2011).

We modeled temperature effects as natural cubic splines (NCSs) of AT with 3 degrees of freedom (df). We expected greater changes in the effect estimates at the extremes of temperature, so we placed the internal knots at the 10th and 90th cityspecific percentiles of warm-season AT. We centered the splines at the 75th percentiles of warm-season AT, which served as the reference temperatures. A priori, moderate heat was defined as the 90th percentile of warmseason AT, and extreme heat was defined as the 99th percentile of warm-season AT. To reduce collinearity between temperature lags in our models, we modeled AT exposure as 2-day sums of lags from lags 0-7, instead of individual lags, or as four 2-day lag strata. This is a constrained distributed lag model where lags 0 and 1 are constrained to have the same effect, lags 2 and 3 are constrained to have the same effect, and so on (Armstrong 2006; Schwartz et al. 2004). We used the dlnm package in R to generate the temperature-lag crossbases (Gasparrini et al. 2010).

To distinguish between effects of heat intensity and duration, we included a term for heat waves, or extreme heat duration, in additional models. This term was an indicator variable for 2-day mean AT above the 95th percentile of city-specific warm-season AT for at least 2, 4, 6, or 8 days in duration. For example, the city-specific model of the effect on hospital admissions of being in a heat wave for at least 8 days is as follows:

ln(hospital admissions) =

$$\alpha_1 \mathit{YMW}_1 + \ldots + \alpha_{525} \mathit{YMW}_{525}$$

- + $NCS(AT, 3 df)_{01}$
- + NCS(AT, 3 df)₂₃
- + NCS(AT, 3 df)₄₅
- $+ NCS(AT, 3 df)_{67} + HW,$ [1]

where YMW_1-YMW_{525} were the indicator variables for each year/month/day-of-week combination (how seasonal and long-term effects in a case-crossover design using Poisson regression are controlled for); NCS_{01} , NCS_{23} , NCS_{45} , and NCS_{67} were the four natural cubic splines of AT (one for each of four lag strata: days 0–1, 2–3, 4–5, and 6–7) each with 3 df;

and *HW* was the single heat wave indicator variable for an 8-day heat wave. The cumulative effects over 8 days following a day of moderate or extreme heat and the effects of 2–8 day-long heat waves were calculated as the sums of the lag-specific effects (and heat-wave effect for the heat wave models) within each city.

For each city, we estimated a single moderate or extreme heat effect at lag day 0 or over lag days 0-7 separately. We then pooled city-specific results in each of the five climate zones and overall in a random-effects meta-analysis using inverse variance weighting (DerSimonian and Laird 1986) using the meta package in R, and calculated Q statistics for heterogeneity within and between climate zones. To pool the cumulative effects of extreme heat plus the added heat-wave effect across cities in models with a heat-wave term, we first estimated the main extreme heat effect and the added heat-wave effect for each city, or 2 effects per city, and their corresponding covariances. Then we performed a restricted maximum likelihood multivariate meta-analysis of these effects using the mvmeta package in R (Gasparrini et al. 2012). All analyses were performed in R version 2.15 or 3.0.

Sensitivity analyses. We evaluated confounding by ozone and the holidays Memorial Day, Independence Day, and Labor Day (which all occur in the first or last week of the month) by comparing the risk ratios (percent increase/100 + 1) for AT from models with and without inclusion of the confounders (ozone or holidays). We examined the sensitivity of our results to temperature metric by modeling different metrics for temperature (MT, MI, MA, or DTR) in place of AT.

In a time-stratified case-crossover design, each case's controls are selected from the same time stratum as the case, and seasonal effects and long-term time trends are assumed to vary inconsequentially within each time stratum. In our main models, this time stratum was a month, for a total of five time strata per year, each 30 or 31 days long. To examine the sensitivity of our results to the length of the time stratum, we used either six time strata (each 25 or 26 days long) or four time strata (each 38 or 39 days long) per year in separate models.

We assumed a functional form of the association between daily temperature and hospital admission to be no more complex than that modeled by a natural cubic spline with 3 df (2 internal knots). However, we examined the sensitivity of our results to the modeling of the functional form in the largest city in each of the five climate zones by varying knot locations in natural cubic splines as well as in piecewise linear splines (which are more easily interpreted). We also examined the sensitivity of our results to lag structure by using a natural cubic spline lag structure with 3 internal

knots as opposed to four discrete lag strata. We also compared the case-crossover results using Poisson regression with a quasi-Poisson distribution to those of a case-crossover design using Cox proportional hazards regression with robust standard errors. Finally, we attempted to identify heat and cold thresholds, or knot locations, using the SiZer method, which identifies significant increases or decreases in locally weighted polynomial smoothers for different spans of the smoother (see Supplemental Material, "Alternative Threshold Identification Using SiZer").

Results

We examined the association between heat and rates of hospitalization in 114 cities broadly distributed across the contiguous United States (see Supplemental Material, Figure S1).

Cardiovascular, respiratory, and renal admissions accounted for approximately 24%, 8%, and 1% of all-cause admissions in each climate zone from May through September (Table 1). Heat-related admissions were uncommon, accounting for only 0.1% of all-cause admissions. In hotter climates (climate zones 4 and 5), the differences between the 99th and 75th percentiles of warm-season AT were smaller than in cooler climates (climate zones 1–3), though the number of days meeting the definitions for 2-, 4-, 6-, and 8-day long heat waves were similar between climates. Mean daily ozone levels were slightly higher in climate zone 4.

The functional form of the association between AT and hospital admissions in the largest city in each climate zone (Minneapolis, MN; Chicago, IL; New York City, NY;

Los Angeles, CA; and Houston, TX) varied widely by city, admissions cause, and lag day (Figure 1). For all-cause, renal, and respiratory diseases, the association between AT at lag 0 and hospital admission was approximately linear (Figure 1A,C,D). However, at subsequent lags, the association was U-shaped for these three causes of admission, and for the cumulative effects of AT over 8 days, the form of the association was U-shaped (Figure 1E,G,H). This difference in functional form by lag persisted regardless of whether the form was modeled as a piecewise linear spline versus a natural cubic spline and regardless of knot placement (see Supplemental Material, Figure S2, for all-cause admissions in New York City). Focusing only on the range of AT above the 75th percentile, there was a positive association between hospital admissions

Table 1. Means^a (ranges) of hospital admissions among elderly Medicare beneficiaries, apparent temperature (AT), heat waves, and ozone, by climate zone, May–September. 1992–2006.

iviay-september, 1992-2000.						
Variable	Zone 1 (13 cities)	Zone 2 (34 cities)	Zone 3 (22 cities)	Zone 4 (24 cities)	Zone 5 (21 cities)	All zones (114 cities)
Hospital admissions (mean daily count) ^b						
All natural causes	53 (19-97)	241 (16-571)	266 (21-570)	142 (16-336)	98 (18-201)	186 (16-571)
Cardiovascular	13 (5-24)	59 (4-133)	65 (5-135)	33 (4-77)	24 (4-53)	45 (4-135)
Heat-related	0.0 (0.0-0.1)	0.2 (0.0-0.7)	0.3 (0.0-0.6)	0.1 (0.0-0.2)	0.1 (0.0-0.2)	0.2 (0.0-0.7)
Renal	0.6 (0.2-1.2)	2.8 (0.1-6.0)	3.0 (0.2-6.2)	1.8 (0.1-4.1)	1.2 (0.2-2.0)	2.2 (0.1-6.2)
Respiratory	5 (2-8)	21 (2-47)	22 (2-49)	13 (1-31)	8 (2-16)	16 (1-49)
75th–90th–95th–99th percentiles of AT (°C)	23.4–26.7–28.4–31.4	25.5–28.9–30.5–33.4	27.2–30.1–31.6–34.1	24.8–26.8–28.1–30.3	33.9–35.2–35.8–37.0	27.4–29.9–31.2–33.5
Annual no. of days in a heat wave (consecutive 2-day means each above 95th percentile of AT) by heat-wave duration						
2-day	7.6 (7.3–7.9)	7.7 (7.1–8.1)	7.7 (7.1–7.8)	7.7 (7.4–8)	7.7 (7.4–7.9)	7.7 (7.1-8.1)
4-day	2.6 (1.8-3.4)	2.8 (2.3-3.7)	2.9 (2.3-4.7)	3.4 (2.2-4.3)	3.1 (2.4-4.0)	3.0 (1.8-4.7)
6-day	0.8 (0.2-1.2)	1.0 (0.3-2.3)	1.0 (0.3-3.1)	1.7 (0.5-2.6)	1.4 (0.5-2.7)	1.2 (0.2-3.1)
8-day	0.2 (0.0-0.6)	0.4 (0.0-1.4)	0.4 (0.0-2.1)	0.9 (0.0-1.7)	0.6 (0.1-2.2)	0.5 (0.0-2.2)
Mean daily ozone (ppb) ^c	45 (37-49)	45 (36-54)	46 (33-56)	50 (27-71)	44 (29-57)	46 (27-71)

^aPopulation-weighted means of the city-specific means. ^bICD-9-CM codes: all natural causes (all ICD-9-CM codes < 800), cardiovascular (390–429), heat [including 992 (effects of heat and light) and E900.0 (excessive heat due to weather conditions)], renal (580–589), and respiratory (480–497, 490–492, and 494–496). The "heat" category also includes admissions with any secondary causes related to heat. ^eNumber of cities contributing to ozone calculations: 11, 32, 22, 20, and 19 for zones 1–5, respectively.

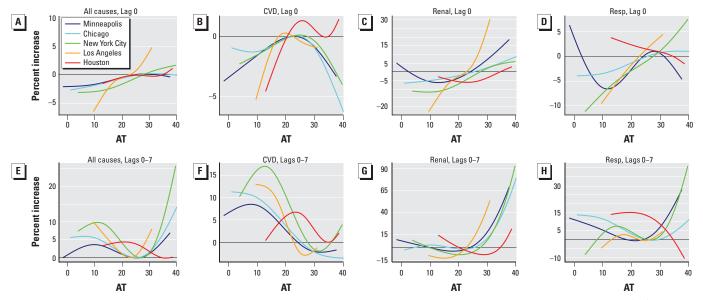


Figure 1. Percent increases for the largest city in each of five climate zones in hospital admissions among U.S. elderly for apparent temperature (AT) versus the 75th percentile of AT, May–September, 1992–2006, at lag 0 (A–D) and over lags 0–7 (E–H) for all causes (A,E), cardiovascular (CVD) diseases (B,F), renal diseases (C,G), and respiratory (Resp) diseases (D,H).

and AT in most instances at lag 0 and over lags 0–7. In contrast to the other causes of admission, for cardiovascular admissions, the association at lag 0 was an inverse U-shape; and above the 75th percentile of AT, there was a weak inverse association between hospital admission and AT in Minneapolis, Chicago, New York City, and Los Angeles. Although this inverse U-shape became a U-shape in subsequent lags, the cumulative effect over 8 days for AT above the 75th percentile and hospital admission was still weakly protective.

In meta-analyses, the magnitude of the associations between moderate heat and hospital admissions for all causes, cardiovascular diseases, and respiratory diseases were small, with increases in admissions at the 90th versus the 75th percentile of AT of –0.4% to 1.3% over lags 0–1 or lags 0–7 (Table 2). The associations between moderate heat over lags 0–1 and lags 0–7 and admissions for renal diseases were

stronger, with increases in admissions of 3.9% (95% CI: 2.9%, 4.9%) and 4.3% (95% CI: 3.0%, 5.6%), respectively. The associations between extreme heat (99th vs. 75th percentile of AT) and hospital admissions were stronger than for moderate heat over lags 0-1 and lags 0-7. Specifically, the "main" (as opposed to heat-wave) extreme heat-associated increases in respiratory admissions over these time periods were 3.3% (95% CI: 1.3%, 5.4%) and 4.3% (95% CI: 1.8%, 6.9%), respectively; and extreme heat-associated increases in renal admissions were even higher at 9.3% (95% CI: 4.3%, 14.5%) and 14.2% (95% CI: 8.5%, 20.1%), respectively. We failed to observe a decline in the effects of extreme heat in the 7 days following the day of extreme heat, with the cumulative lag 0-7 effects similar to or higher than the lag 0-1 effects.

For renal and respiratory causes of admission, we observed a significant "added

Table 2. Pooled percent increases (95% CIs) in hospital admissions for different causes for moderate heat, a extreme heat, and consecutive days of extreme heat (heat waves).

Variable	All causes	Cardiovascular	Renal	Respiratory		
Sum of the main effects of moderate heat						
Lag days 0-1	0.7 (0.5, 0.8)	-0.4 (-0.6, -0.2)	3.9 (2.9, 4.9)	1.3 (0.8, 1.8)		
Lag days 0–7	0.5 (0.3, 0.7)	-1.3(-1.6, -1.0)	4.3 (3.0, 5.6)	0.0 (-0.6, 0.7)		
Sum of the main effects of extreme heat						
Lag days 0-1	1.4 (0.8, 2.0)	-1.6 (-2.7 , -0.6)	9.3 (4.3, 14.5)	3.3 (1.3, 5.4)		
Lag days 0–3	2.1 (1.5, 2.8)	-2.0 (-2.9 , -1.0)	12.6 (8.2, 17.3)	4.8 (2.6, 6.9)		
Lag days 0–5	2.9 (2.2, 3.6)	-2.0 (-3.0, -1.0)	11.3 (6.0, 16.8)	5.5 (3.2, 7.8)		
Lag days 0–7	3.2 (2.4, 4.0)	-1.8 (-2.7, -0.8)	14.2 (8.5, 20.1)	4.3 (1.8, 6.9)		
Added heat-wave effect for 4 heat-wave durations						
2-day	0.2 (-0.3, 0.7)	-0.4 (-1.3, 0.5)	2.6 (-1.0, 6.4)	0.4 (-1.3, 2.2)		
4-day	1.5 (0.9, 2.2)	0.6 (-0.6, 1.8)	4.6 (-0.5, 9.9)	2.1 (0.1, 4.3)		
6-day	0.9 (-0.1, 1.9)	-0.6 (-2.4, 1.2)	10.7 (3.1, 18.8)	2.8 (-0.1, 5.9)		
8-day ^d	-0.8 (-2.3, 0.6)	-0.9 (-3.5, 1.8)	12.8 (1.8, 25.0)	1.1 (-3.6, 5.9)		
Sum of the main effects of extreme heat and the						
added heat-wave effect for 4 heat-	wave durations					
2-day	1.6 (1.1, 2.1)	-2.0 (-2.8, -1.2)	12.1 (8.4, 15.9)	3.7 (1.8, 5.7)		
4-day	3.7 (2.9, 4.4)	-1.4 (-2.4, -0.3)	17.8 (12.8, 23.0)	7.0 (4.3, 9.8)		
6-day	3.8 (2.7, 4.9)	-2.6 (-4.3, -1.0)	23.2 (14.2, 32.8)	8.5 (4.8, 12.2)		
8-day	2.3 (0.8, 3.9)	-2.7 (- 5.2, - 0.1)	28.9 (16.1, 43.0)	5.4 (0.0, 11.1)		

^a90th vs. 75th percentile of apparent temperature (AT). ^b99th vs. 75th percentile of AT. ^cTwo-day mean AT above the 95th percentile of city-specific warm-season AT for at least 2, 4, 6, or 8 days. ^dEight-day heat waves were too infrequent and daily admissions counts too small in 22 cities to model the added 8-day heat-wave effects.

Table 3. Pooled percent increases (95% CIs) in hospital admissions for different causes for extreme heat on lag day 0 and the cumulative extreme heat effects over lag days 0–7.

Climate zone	All causes	Cardiovascular	Renal	Respiratory
Extreme heat on lag day 0				
1	0.9 (0.2, 1.7)	0.1 (-1.3, 1.6)	10.7 (3.8, 18.0)	2.7 (-0.1, 5.5)
2	0.6 (0.2, 1.0)	-1.9 (-2.6 , -1.3)	3.9 (0.6, 7.4) ^a	2.8 (1.3, 4.3) ^a
3	0.3 (-0.2, 0.7)	-1.5 (-2.3 , -0.6)	5.0 (1.2, 8.9)	$-0.2(-2.0, 1.6)^a$
4	1.5 (0.7, 2.3) ^a	-0.9 (-1.9, 0.2)	7.3 (2.4, 12.5) ^a	3.1 (0.8, 5.3) ^a
5	0.7 (0.3, 1.2)	0.3 (-0.4, 1.1)	3.6 (0.0, 7.3)	0.7 (-0.9, 2.4)
All	0.7 (0.5, 1.0) ^a	−1.0 (−1.4, −0.6) ^b	5.3 (3.4, 7.3) ^a	1.7 (0.9, 2.6) ^a
Extreme heat over lag days 0-7				
1	3.8 (1.6, 6.1)	0.0 (-5.5, 5.8)	-2.8 (-26.8, 29.2) ^a	11.8 (2.3, 22.2)
2	3.7 (2.1, 5.3) ^a	-3.7 (-5.4 , -2.0)	21.6 (10.1, 34.3) ^a	8.1 (3.4, 13.0) ^a
3	3.4 (1.4, 5.4) ^a	-1.4 (-3.8, 1.0)	14.2 (3.3, 26.4)	$0.7 (-5.0, 6.7)^a$
4	3.3 (1.5, 5.2) ^a	-1.9 (-4.3, 0.6)	21.2 (7.9, 36.3) ^a	5.3 (-1.5, 12.6) ^a
5	1.6 (0.5, 2.7)	0.0 (-1.9, 2.1)	9.0 (0.3, 18.4)	-0.5 (-4.0, 3.1)
All	3.2 (2.4, 4.0) ^a	-1.8 (-2.8, -0.7)	14.7 (8.8, 20.9) ^a	4.3 (1.7, 6.9) ^{a,b}

Extreme heat, 99th vs. 75th percentile of apparent temperature. City-specific results are available upon request. a Significant heterogeneity within climate zone category (p < 0.05 in Q-test for heterogeneity). b Significant heterogeneity between climate zones 1–5 (p < 0.05 in Q-test for heterogeneity).

heat-wave effect" for heat waves defined as at least 6 days of AT above the 95th percentile of AT, with increases in admissions of 10.7% and 2.8%, respectively. In pooling the city-specific cumulative main effects of extreme heat over 6 days and the added heat-wave effect, we estimated increases in admissions for renal and respiratory diseases for a 6-day heat wave to be 23.2% (95% CI: 14.2%, 32.8%) and 8.5% (95% CI: 4.8%, 12.2%), respectively.

When comparing the effects of extreme heat by climate zone, we found significant heterogeneity between climate zones in the cumulative 8-day effect estimates for admissions for respiratory diseases, with pooled increases of 11.8% (95% CI: 2.3%, 22.2%) in climate zone 1 and –0.5% (95% CI: –4.0%, 3.1%) in climate zone 5 (Table 3). For admissions for both respiratory and renal diseases, we found significant heterogeneity in effect estimates within climate zones 1, 2, 3, and/or 4.

Results of sensitivity analyses. Confounding by ozone of the association between AT and hospital admissions was minimal. Both moderate heat and extreme heat risk ratios at lag 0 and over lags 0–7 from the models with ozone differed from those in the models without ozone by < 10% in all cities (results not shown). Confounding by holidays was also minimal. In models with terms for holidays versus models without holiday terms, the risk ratios for moderate and extreme heat at lag 0 and over lags 0–7 also did not differ by > 10% in any city.

When we varied the length of the time stratum, the extreme heat effect estimates were similar, but associations over lag days 0-7 between moderate heat and hospital admissions were slightly stronger [e.g., for respiratory diseases, 1.0% (95% CI: 0.3%, 1.6%) vs. 0.2% (95% CI: -0.5%, 0.8%)] when seasonal effects were controlled for with a smaller number of time strata (4 vs. 5 time strata per warm season). Nevertheless, the corresponding risk ratios differed by < 10%, for moderate and extreme heat at lag 0 as well as over lags 0-7 (see Supplemental Material, Figure S3). Different temperature metrics had similar associations between hospital admission for all natural causes and moderate and extreme heat at lag 0 and over lags 0-7, though the associations between moderate DTR and hospital admissions over lags 0-7 were slightly higher than for moderate AT (0.9% vs. 0.6%) (see Supplemental Material, Figure S4).

In sensitivity analyses of the functional form of the association between AT and hospital admissions, the piecewise linear spline models produced qualitatively different results for moderate heat over lags 0–7 for Chicago and New York City, predicting a null or inverse association where the more flexible natural cubic spline models predicted a positive

association (see Supplemental Material, Figures S2 and S5). Otherwise, the results were not sensitive to spline type, knot location, lag form, or the use of Poisson regression versus Cox proportional hazards regression with robust standard errors. The SiZer method failed to identify distinct heat and cold thresholds (see Supplemental Material, "Alternative Threshold Identification Using SiZer").

Discussion

This large, multicity study of heat, heat waves, and hospital admissions among elderly Medicare beneficiaries suggests that morbidity related to hot weather presents an important health burden. With the frequency and intensity of hot weather predicted to increase over time and with an aging population, these results have important implications for enhancing public health preparedness.

Extreme heat on the day of or the day before admission was strongly associated with hospitalizations for renal diseases. For extreme heat, we found a 15% (95% CI: 9%, 21%) increase in hospital admissions for renal disease over the 8 days following a day of extreme heat. Additionally, excess admissions for renal diseases occurred even with increases in moderate heat. Positive associations between temperature, heat events, and admissions for renal diseases have been reported in several other studies in the United States and elsewhere (Fletcher et al. 2012; Green et al. 2010; Hansen et al. 2008; Knowlton et al. 2009; Kovats et al. 2004; Mastrangelo et al. 2006, 2007; Nitschke et al. 2007, 2011; Semenza 1999; Wang et al. 2012). Renal admissions increased 8% (95% CI: 5%, 12%) among individuals 65-84 years of age in New York State for a 2.8°C increase in mean temperature (Fletcher et al. 2012). Among individuals ≥ 65 years of age, admissions for acute renal failure increased 11% (95% CI: 6%, 15%) for a 5.6°C increase in AT in California (Green et al. 2010). During the 2006 heat wave in California, renal admissions increased 4% (95% CI: 1%, 7%) (Knowlton et al. 2009). During the 1995 heat wave in Chicago, renal admissions increased by 109% (95% CI: 84%, 140%) (Semenza 1999). This body of evidence suggests a need to target patients with renal conditions for additional protective measures during hot weather in cities across the United States, although individuals with previously identified renal conditions may not account for the entire increase in renal admissions associated with heat.

We found a slight decrease in hospital admissions for cardiovascular diseases with moderate heat or extreme heat (1–2%) and an increase in admissions for respiratory diseases of 4% in the 8 days following extreme heat. Other studies of associations between cardiovascular and respiratory admissions and

heat and heat waves in the United States have found increased risks of cardiovascular and respiratory diseases on lag days 0-1 (Ye et al. 2012). Studies using time series of admissions and temperature data from earlier time periods (e.g., Schwartz et al. 2004) tended to find stronger associations between cardiovascular admissions and heat than our study. These differences in results by time period may be related to the implementation of heat-health warning systems in several U.S. cities and increased awareness of the dangers of heat to the elderly after the 1995 Chicago heat wave (Bassil and Cole 2010). More similar to our findings, a study in California from 1999-2005 (Green et al. 2010) and a study in New York State from 1991-2004 (Lin et al. 2009) did not find increases in cardiovascular hospital admissions with heat on lag days 0 or 1. In a meta-analysis of the associations between heat and admissions for cardiovascular and respiratory diseases from studies worldwide, Turner et al. (2012) also did not find significant associations for cardiovascular admissions, though their results were suggestive of an association between respiratory admissions and heat (for a 1°C increase in temperature, risk ratio = 1.020; 95% CI: 0.986, 1.055).

Using a data set very similar to ours, Anderson et al. (2013) found an association between respiratory hospital admissions and a 10°F increase in temperature of 4.3% (95% posterior interval: 3.8%, 4.8%). This effect is similar though slightly higher than our effect estimate of 1.7% (95% CI: 0.9%, 2.6%) (Table 3) for extreme heat (99th vs. 75th percentile of AT), which corresponds to an average of 11°F across cities. Additionally, they found a cumulative association between a 10°F increase in the previous week's temperature and respiratory admissions of 2.2% (95% posterior interval: 1.3%, 3.1%) which was similar to our estimate of 4% for extreme heat over the subsequent 8 days, though they modeled the association between temperature and hospital admissions as linear at all lags. In contrast, we found a linear association at early lags (0-1) and a U-shaped association at later lags for respiratory admissions.

The associations between temperature and hospital admissions for all natural causes were robust to knot placement and time strata length and were similar between metrics, though moderate DTR effects were slightly higher. Differences in hypothesized underlying biological mechanisms, such as an inability to cool off through sweating versus adjust to sudden large changes in temperature, may account for small differences observed between DTR and the other metrics.

The associations between cardiovascular and respiratory hospital admissions and heat were weaker than between cardiovascular and respiratory mortality and heat found

in previous U.S. studies. Anderson and Bell (2009) found a 5% increase in cardiovascular mortality and 6% increase in respiratory mortality among individuals ≥ 75 years of age for an increase in mean daily temperature from the 90th to 99th percentile on lag days 0-1. In the United States, deaths associated with extreme heat were higher among individuals dying out of hospital as well as individuals with preexisting atrial fibrillation (Medina-Ramón et al. 2006; Zanobetti et al. 2013). Therefore, heat may have a strong, deleterious association with cardiovascular mortality and a protective association with hospital admissions, because heat-related deaths may tend to be more sudden and individuals who might have been hospitalized for cardiovascular diseases die instead as a result of extreme heat.

Consistent with studies of the added heatwave effect in the association between heat and mortality in the United States (Anderson and Bell 2011; Gasparrini and Armstrong 2011), we did not see a substantial added heat-wave effect for cardiovascular and respiratory admissions. In a multicity U.S. study modeling temperature as a spline and heat wave as an indicator variable, Gasparrini and Armstrong (2011) and Barnett et al. (2012) found added heat-wave effects of 0-7% in the United States. with the greatest added heat-wave effect when the temperature spline had the fewest df, as did Rocklov et al. (2012) in Sweden. This finding can be explained by the fact that intensity and duration of extreme heat are correlated, so estimates of heat-wave effects diminish as the independent effects of extreme heat are allowed to be more intense in the model. In our model, with a temperature spline with only 3 df (and main effect results that were insensitive to knot location), we still found only a small added heat-wave effect of 1-3% for respiratory diseases. In contrast to admissions for cardiovascular and respiratory diseases, we found a more significant added heat-wave effect in the association between heat and hospital admissions for renal diseases (for heat waves at least 6 days long, 10.7%; 95% CI: 3.1%, 18.8%).

Even after accounting for displacement, or the harvesting effect, whereby the exposure advances a health outcome by only a few days because the affected individuals are already very frail (Schwartz et al. 2004), a day of extreme heat was still associated with a significant increase in admissions for renal and respiratory diseases in many cities over the subsequent 7 days. In contrast, for cardiovascular admissions, the cumulative effects of extreme or moderate AT over the subsequent 7 days were slightly protective. Mortality displacement patterns have varied widely in studies of heat-associated cardiovascular and respiratory mortality in the United States and Europe, with some studies finding the sum of effects over multiple lags to be deleterious

(e.g., Braga et al. 2001; Hajat et al. 2005 for London respiratory diseases), not significantly different from the null (e.g., Baccini et al. 2008) or protective (e.g., Hajat et al. 2005 for London cardiovascular diseases). Further studies specifically designed to understand the potentially competing risks (Andersen et al. 2012) between hospital admissions and mortality are warranted. Such research will enhance our knowledge on what conditions should activate heat-health warning systems.

Although associations between extreme heat and admissions for respiratory diseases varied significantly by climate zone, the EIA climate zones did not fully explain cityspecific variation in the association between heat and admissions for renal or respiratory diseases. Factors other than prevailing weather conditions, including vegetation, housing stock, access to air conditioning, and social factors, may play important roles in determining the extent to which extreme heat puts the health of older people at risk in any given community; and using information on neighborhood of residence as well as city of residence, we are actively investigating characteristics of vulnerability to heat-associated hospital admissions.

Conclusion

The associations between extreme heat and hospital admissions for all causes over lag days 0–1 as well as 0–7 were statistically significant and of public health significance in the United States in all climate zones. Elderly individuals with respiratory and especially renal conditions, and providers of services to such people, may benefit from taking additional precautions when heat warnings are issued.

REFERENCES

- Andersen PK, Geskus RB, de Witte T, Putter H. 2012. Competing risks in epidemiology: possibilities and pitfalls. Int J Epidemiol 41:861–870.
- Anderson GB, Bell ML. 2009. Weather-related mortality: a study of how heat, cold, and heat waves affect mortality in the United States. Epidemiology 20:205–213.
- Anderson GB, Bell ML. 2011. Heatwaves in the United States:
 Mortality risk during heatwaves and effect modification by
 heatwave characteristics in 43 U.S. communities. Environ
 Health Perspect 119:210–218; doi:10.1289/ehp.1002313.
- Anderson GB, Dominici F, Wang Y, McCormack MC, Bell ML, Peng RD. 2013. Heat-related emergency hospitalizations for respiratory diseases in the Medicare population. Am J Respir Crit Care Med 187:1098–1103.
- Armstrong B. 2006. Models for the relationship between ambient temperature and daily mortality. Epidemiology 17:624-631.
- Baccini M, Biggeri A, Accetta G, Kosatsky T, Katsouyanni K, Analitis A, et al. 2008. Heat effects on mortality in 15 European cities. Epidemiology 19:711–719.
- Barnett AG, Hajat S, Gasparrini A, Rocklov J. 2012. Cold and heat waves in the United States. Environ Res 112:218–224.
- Bassil KL, Cole DC. 2010. Effectiveness of public health interventions in reducing morbidity and mortality during heat episodes: a structured review. Int J Environ Res Public Health 7:991–1001.

- Braga AL, Zanobetti A, Schwartz J. 2001. The time course of weather-related deaths. Epidemiology 12:662–667.
- Centers for Disease Control and Prevention. 2013. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Available: http://www.cdc.gov/nchs/icd/icd9cm.htm [accessed 19 May 2014].
- CMMS (Centers for Medicare and Medicaid Services). 2006. Medicare Provider Analysis and Review (MedPAR) Expanded Modified Record. Baltimore, MD:Centers for Medicare and Medicaid Services, Department of Health and Human Services.
- Curriero FC, Zeger SL, Strug L, Heiner KS, Samet JM, Patz JA. 2002. Temperature and mortality in 11 cities of the Eastern United States. Am J Epidemiol 155:80–87.
- DerSimonian R, Laird N. 1986. Meta-analysis in clinical trials. Control Clin Trials 7:177–188.
- EIA (Energy Information Administration). 2010. U.S. Climate Zones for 2003 CBECS. Commercial Buildings Energy Consumption Survey (CBECS). Available: http://www. eia.doe.gov/emeu/cbecs/climate_zones.html [accessed 18 May 2010].
- Fletcher BA, Lin S, Fitzgerald EF, Hwang SA. 2012. Association of summer temperatures with hospital admissions for renal diseases in New York State: a case-crossover study. Am J Epidemiol 175:907–916.
- Gasparrini A, Armstrong B. 2011. The impact of heat waves on mortality. Epidemiology 22:68–73.
- Gasparrini A, Armstrong B, Kenward MG. 2010. Distributed lag non-linear models. Stat Med 29:2224–2234.
- Gasparrini A, Armstrong B, Kenward MG. 2012. Multivariate meta-analysis for non-linear and other multi-parameter associations. Stat Med 31:3821–3839.
- Gosling S, Lowe J, McGregor G, Pelling M, Malamud B. 2009.
 Associations between elevated atmospheric temperature and human mortality: a critical review of the literature.
 Clim Change 92:299–341.
- Green R, Basu R, Malig B, Broadwin R, Kim J, Ostro B. 2010.
 The effect of temperature on hospital admissions in nine
 California counties. Int J Pub Health 55:113–121.
- Guo Y, Barnett AG, Pan X, Yu W, Tong S. 2011. The impact of temperature on mortality in Tianjin, China: a casecrossover design with a distributed lag non-linear model. Environ Health Perspect 119:1719–1725; doi:10.1289/ abn.1103508
- Hajat S, Armstrong BG, Gouvia N, Wilkinson P. 2005. Mortality displacement of heat-related deaths: a comparison of Delhi, São Paulo, and London. Epidemiology 16:613–620.
- Hajat S, Kosatsky T. 2010. Heat-related mortality: a review and exploration of heterogeneity. J Epidemiol Community Health 64:753–760.
- Hansen A, Bi P, Nitschke M, Ryan P, Pisaniello D, Tucker G. 2008. The effect of heat waves on hospital admissions for renal disease in a temperate city of Australia. Int J Epidemiol 37:1359–1365.
- Intergovernmental Panel on Climate Change. 2007. Climate Change 2007. The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change (Solomon S, Qin D, Manning M, Chen Z, Marquis M, Averyt KB, et al., eds). Cambridge, UK:Cambridge University Press.
- Kalkstein LS, Valimont, KM. 1986. An evaluation of summer discomfort in the United States using a relative climatological index. Bull Am Meteorol Soc 7:842-848.
- Knowlton K, Rotkin-Ellman M, King G, Margolis HG, Smith D, Solomon G, et al. 2009. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ Health Perspect 117:61–67; doi:10.1289/ ehn 11594
- Kovats RS, Hajat S, Wilkinson P. 2004. Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. Occup Environ Med 61:893–898.
- Lin S, Luo M, Walker RJ, Liu X, Hwang SA, Chinery R. 2009. Extreme high temperatures and hospital admissions for respiratory and cardiovascular diseases. Epidemiology 20:728-746
- Mastrangelo G, Buja A, Fedeli U, Hajat S, Fadda E, Spolaore P. 2006. Contrasting patterns of hospital admissions and mortality during heat waves: are deaths from circulatory disease a real excess or an artifact? Med Hypotheses 66:1075-1078

- Mastrangelo G, Fedeli U, Visentin C, Milan G, Fadda E, Spolaore P. 2007. Pattern and determinants of hospitalization during heat waves: an ecologic study. BMC Public Health 7:200; doi:10.1186/1471-2458-7-200.
- Medina-Ramón M, Schwartz J. 2007. Temperature, temperature extremes, and mortality: a study of acclimatization and effect modification in 50 United States cities. Occup Environ Med 64:827–833.
- Medina-Ramón M, Zanobetti A, Schwartz J. 2006. The effect of ozone and PM_{10} on hospital admissions for pneumonia and chronic obstructive pulmonary disease: a national multicity study. Am J Epidemiol 163:579–588.
- Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, et al. 2009. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med 179:383–389.
- NCDC (National Climatic Data Center). 2010a. Integrated Surface Database Lite. Available: http://www.ncdc.noaa.gov/oa/climate/isd/index.php [accessed 1 September 2010].
- NCDC (National Climatic Data Center). 2010b. 3200
 Meteorological Dataset: Surface Land Daily Cooperative
 Summary of the Day. Available: http://www.ncdc.noaa.
 gov/oa/climate/stationlocator.html [accessed 1 September
 2010]
- Nitschke M, Tucker GR, Bi P. 2007. Morbidity and mortality during heatwaves in Metropolitan Adelaide. Med J Australia 187:662–665.
- Nitschke M, Tucker GR, Hansen AL, Williams S, Zhang Y, Bi P. 2011. Impact of two recent extreme heat episodes on morbidity and mortality in Adelaide, South Australia: a case-series analysis. Environ Health 10:42; doi:10.1186/1476-069X-10-42.
- O'Neill MS, Ebi KL. 2009. Temperature extremes and health: Impacts of climate variability and change in the United States. J Occup Environ Med 51:13–25.
- Ostro BD, Roth LA, Green RS, Basu R. 2009. Estimating the mortality effect of the July 2006 California heat wave. Environ Res 109:614–619.
- Rocklov J, Barnett AG, Woodward A. 2012. On the estimation of heat-intensity and heat-duration effects in time series models of temperature-related mortality in Stockholm, Sweden. Environ Health 11:23; doi:10.1186/1476-069X-11-23.
- Schwartz J, Samet JM, Patz JA. 2004. Hospital admissions for heart disease: The effects of temperature and humidity. Epidemiology 15:755–761.
- Semenza JC. 1999. Acute renal failure during heat waves. Am J Prev Med 17:97.
- Semenza JC, Rubin CH, Falter KH, Selanikio JD, Flanders WD, Howe HL, et al. 1996. Heat-related deaths during the July 1995 heat wave in Chicago. N Engl J Med 335:84–90.
- Turner LR, Barnett AG, Connell D, Tong S. 2012. Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. Epidemiology 4:594–606.
- U.S. EPA (U.S. Environmental Protection Agency). 2014. AirData. Daily Summary Data. Available: http://aqsdr1.epa. gov/aqsweb/aqstmp/airdata/download_files.html#Daily [accessed 27 May 2014].
- Vincent GK, Velkoff VA. 2010. The next four decades: The older population in the United States: 2010 to 2050. (Current Population Reports). Washington, DC:U.S. Census Bureau. Available: http://www.census.gov/prod/2010pubs/p25-1138.pdf [accessed 1 October 2014].
- Wang XY, Barnett AG, Yu W, Fitzgerald G, Tippett V, Aitken P, et al. 2012. The impact of heatwaves on mortality and emergency hospital admissions from non-external causes in Brisbane, Australia. Occup Environ Med 69:163–169.
- Ye X, Wolff R, Yu W, Vaneckova P, Pan X, Tong S. 2012. Ambient temperature and morbidity: a review of epide-miological evidence. Environ Health Perspect 120:19–28; doi:10.1289/ehp.1003198.
- Zanobetti A, O'Neill MS, Gronlund CJ, Schwartz JD. 2012. Summer temperature variability and long-term survival among elderly people with chronic disease. Proc Natl Acad Sci USA 109:6608-6613.
- Zanobetti A, O'Neill MS, Gronlund CJ, Schwartz JD. 2013. Susceptibility to mortality in weather extremes: assessing effect modification by ZIP code area level characteristics, personal characteristics and specific cause of admission in a multi-city case-only analysis. Epidemiology 24:809–819.