Original Investigation

Cause-Specific Risk of Hospital Admission Related to Extreme Heat in Older Adults

Jennifer F. Bobb, PhD; Ziad Obermeyer, MD; Yun Wang, PhD; Francesca Dominici, PhD

IMPORTANCE Heat exposure is known to have a complex set of physiological effects on multiple organ systems, but current understanding of the health effects is mostly based on studies investigating a small number of prespecified health outcomes such as cardiovascular and respiratory diseases.

OBJECTIVES To identify possible causes of hospital admissions during extreme heat events and to estimate their risks using historical data.

DESIGN, SETTING, AND POPULATION Matched analysis of time series data describing daily hospital admissions of Medicare enrollees (23.7 million fee-for-service beneficiaries [aged ≥65 years] per year; 85% of all Medicare enrollees) for the period 1999 to 2010 in 1943 counties in the United States with at least 5 summers of near-complete (>95%) daily temperature data.

EXPOSURES Heat wave periods, defined as 2 or more consecutive days with temperatures exceeding the 99th percentile of county-specific daily temperatures, matched to non–heat wave periods by county and week.

MAIN OUTCOMES AND MEASURES Daily cause-specific hospitalization rates by principal discharge diagnosis codes, grouped into 283 disease categories using a validated approach.

RESULTS Risks of hospitalization for fluid and electrolyte disorders, renal failure, urinary tract infection, septicemia, and heat stroke were statistically significantly higher on heat wave days relative to matched non–heat wave days, but risk of hospitalization for congestive heart failure was lower ($P < .05$). Relative risks for these disease groups were 1.18 (95% CI, 1.12-1.25) for fluid and electrolyte disorders, 1.14 (95% CI, 1.06-1.23) for renal failure, 1.10 (95% CI, 1.04-1.16) for urinary tract infections, 1.06 (95% CI, 1.00-1.11) for septicemia, and 2.54 (95% CI, 2.14-3.01) for heat stroke. Absolute risk differences were 0.34 (95% CI, 0.22-0.46) excess admissions per 100 000 individuals at risk for fluid and electrolyte disorders, 0.25 (95% CI, 0.12-0.39) for renal failure, 0.24 (95% CI, 0.09-0.39) for urinary tract infections, 0.21 (95% CI, 0.01-0.41) for septicemia, and 0.16 (95% CI, 0.10-0.22) for heat stroke. For fluid and electrolyte disorders and heat stroke, the risk of hospitalization increased during more intense and longer-lasting heat wave periods ($P < .05$). Risks were generally highest on the heat wave day but remained elevated for up to 5 subsequent days.

CONCLUSIONS AND RELEVANCE Among older adults, periods of extreme heat were associated with increased risk of hospitalization for fluid and electrolyte disorders, renal failure, urinary tract infection, septicemia, and heat stroke. However, the absolute risk increase was small and of uncertain clinical importance.

Supplemental content and Interactive at jama.com

Author Affiliations: Department of Biostatistics, Harvard School of Public Health, Boston, Massachusetts (Bobb, Wang, Dominici); Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts (Obermeyer).

Corresponding Author: Francesca Dominici, PhD, Department of Biostatistics, 655 Huntington Ave, Bldg II, Room 441, Boston, MA 02115 (fdominic@hsph.harvard.edu).

JAMA. 2014;312(24):2659-2667. doi:10.1001/jama.2014.15715

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Extreme heat is the most common cause of severe weather fatalities in the United States,[1] and these weather-related outcomes are expected to escalate[2] as heat waves become more frequent, more intense, and longer lasting with climate change.[3] Exposure to extreme heat can lead to a complex cascade of dysfunction in multiple organ systems resulting from the direct effects of heat and the body's inflammatory response, causing altered mental status, renal failure, coagulopathy, and cardiovascular collapse.[4,5] Older adults are particularly vulnerable to heat-related complications because of the declining ability of the body to thermoregulate with age, as well as because of social/behavioral factors, such as increased likelihood of living alone, being homebound, or taking medications that interfere with fluid balance.[4,6,7]

Although extreme heat is known to adversely affect multiple physiological processes, previous studies of the health effects have examined only a few major categories of health outcomes, such as cardiovascular and respiratory diseases or well-known heat-related diseases, such as heat stroke or dehydration.[8-10] Many studies, including multicity studies from the United States and Europe, have demonstrated that heat contributes to elevated mortality.[11-15] However, the complete spectrum of health effects of extreme heat on multiple organ systems has not been characterized.

We used the totality of Medicare inpatient claims data to systematically examine possible ways in which exposure to heat waves might be associated with serious illness requiring hospitalization in older adults. Our objectives were to (1) estimate the relative and absolute risks of hospitalization for all plausible heat-related diseases; (2) investigate whether these risks increase when heat waves are more extreme and longer lasting; and (3) characterize the time course of hospitalization for heat-related illnesses in the days immediately following exposure.

Methods

Study Population

We obtained billing claims from Medicare inpatient claims data (MEDPAR and denominator files; eAppendix in the Supplement) and assembled data from 27.9 million Medicare beneficiaries per year, aged 65 years or older, enrolled in the fee-for-service program for at least 1 month from January 1, 1999, to December 31, 2010, and residing in the United States. For each enrollee, we extracted age, sex, race, and county of residence from the denominator file and the date and principal *International Classification of Diseases, Ninth Revision* (*ICD-9*) code for each hospitalization from the MEDPAR file.

We grouped the 15 072 possible *ICD-9* codes into 283 mutually exclusive, clinically meaningful disease categories using the validated Clinical Classifications Software (CCS) algorithm[16] developed by the Agency for Healthcare Research and Quality. We excluded 69 disease groups that occur rarely in older adults (mostly pregnancy- or fertility-related); this left 214 disease groups, accounting for more than 99.9% of hospitalizations.

Climate Data

The National Climatic Data Center[17] provides daily average temperature data for more than 4000 temperature monitors in the United States (**Figure 1**A). We assigned to each county the average daily temperature across monitors that belong to each county or that were within 35 km from each county's geometric center. Counties without a monitor within 35 km from their geometric center or with fewer than 5 summers (June-August) with at least 95% of days with daily temperature data were excluded.

We considered 6 definitions of heat waves to capture the effects of increasing levels of duration and intensity. For our main analysis, we defined a heat wave as a period of at least 2 consecutive days with average daily temperatures exceeding the 99th percentile of the distribution of daily temperatures for that county. To assess whether the risk of hospital admission increases under a more severe and longer-lasting heat wave, we extended this definition to include periods of at least 2 or at least 4 consecutive days with average daily temperatures exceeding the 97th, 98th, or 99th percentile. We defined a heat wave day to be the second or later day (≥2-day definitions) or the fourth or later day (≥4-day definitions) of the heat wave period.

We matched each heat wave day to a non-heat wave day by county and week. A single non-heat wave day was randomly selected from a set of candidate non-heat wave days, defined as all days within 3 days of the heat wave day in other years, and which were not themselves within 3 days of a different heat wave event. For example, heat wave days on July 14-15, 2005, would have as candidate non-heat wave days any day in that same county during the period July 11-18 and during the years 1999-2004 and 2006-2010, provided those days were not within 3 days of a different heat wave event.

Statistical Analysis

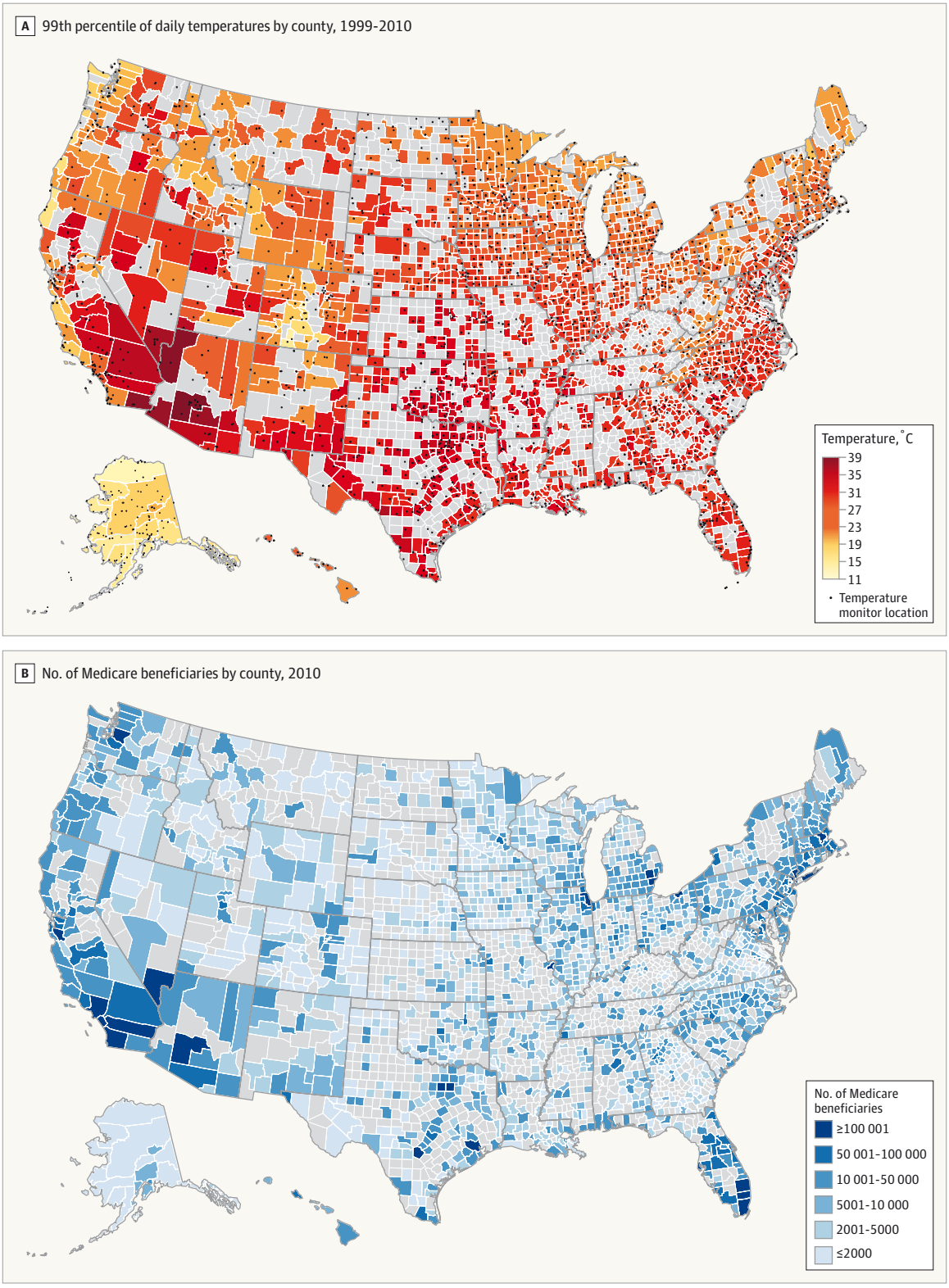
For each county and each day, we calculated (1) the number of individuals at risk of hospitalization by summing the number of individuals enrolled in the fee-for-service program and (2) the number of hospital admissions in each disease group by summing the number of admissions for each of the *ICD-9* codes listed as the primary diagnosis and by summing these counts across the *ICD-9* codes of each disease group.

We applied log-linear mixed-effects regression models to the multisite time series data of hospital admissions, separately for each disease group. Only days that were either a heat wave day or a matched non-heat wave day were included in the analysis. An indicator variable for calendar year was included in the model to account for secular changes in the hospitalization rates. We estimated the national average (across all 1943 counties included in the study) absolute risk difference and relative risk (RR) of hospital admissions on a heat wave day compared with a matched non-heat wave day for each disease group (eAppendix in the Supplement). We applied the Bonferroni-Holm method to adjust the *P* values for multiple comparisons.[18] Risk estimates with adjusted $P<.05$ were considered statistically significant. The 95% confidence intervals were corrected by using $\alpha=.05/D$, where D is the number of disease groups.[19]

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Figure 1. Maps of the 99th Percentile of Daily Temperatures Over the Study Period, 1999-2010, and No. of Medicare Beneficiaries, 2010



Counties in gray represent those with insufficient temperature data, which were excluded from this study.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Table. Characteristics of Heat Waves During the Study Period, 1999-2010[a]

Heat Wave Definition		Counties With ≥1 Heat Wave Event, No. (%)	Frequency of Heat Waves, Mean No. per Year (IQR)	Duration of Heat Waves, Mean (IQR), d	Temperature, Mean (IQR), °C	
No. of Days	Temperature Percentile				During Heat Wave Days	During Non–Heat Wave Days
≥2	>97	1943 (100)	2.6 (2.4-2.8)	3.3 (3.0-3.6)	28.3 (26.9-30.1)	23.1 (21.0-25.5)
≥2	>98	1943 (100)	1.8 (1.6-1.9)	3.1 (2.8-3.3)	28.8 (27.4-30.5)	23.1 (21.1-25.5)
≥2	>99	1943 (100)	0.9 (0.8-1.0)	2.8 (2.5-3.0)	29.5 (28.1-31.1)	23.1 (21.2-25.5)
≥4	>97	1942 (99.9)	0.8 (0.7-0.9)	5.5 (4.8-6.0)	28.5 (27.0-30.4)	23.2 (21.2-25.6)
≥4	>98	1935 (99.6)	0.5 (0.3-0.6)	5.1 (4.5-5.6)	29.0 (27.5-30.8)	23.2 (21.3-25.5)
≥4	>99	1723 (88.7)	0.2 (0.1-0.2)	4.2 (4.0-5.0)	29.6 (28.1-31.4)	23.2 (21.1-25.8)

Abbreviation: IQR, interquartile range.

[a] Heat waves are defined as at least 2 or at least 4 consecutive days with temperatures exceeding the 97th, 98th, or 99th percentile of a county's daily temperatures, 1999-2010. The heat wave definition used in the main analysis was at least 2 days' duration with temperatures exceeding the 99th percentile of the county's daily temperatures. Non–heat wave days are not in the heat wave period but are matched by county and week.

We hypothesized that the heat wave–related RR would increase when the heat wave was more extreme and longer lasting. We tested whether the RR under the most severe definition of a heat wave (≥4 days, >99th percentile) was statistically significantly higher than the RR under the least severe definition (≥2 days, >97th percentile). To characterize the time course of heat-related hospitalizations, we estimated the RR on days 1 to 7 after the heat wave day (eAppendix in the Supplement). Statistical analyses were conducted using R software, version 3.0.2 (http://www.r-project.org).

Results

Our final study population consisted of 23.7 million Medicare enrollees per year residing in 1943 counties (Figure 1B), of which 224 were rural. This population comprises 85% of all Medicare enrollees (eTable 1 in the Supplement). The 1270 counties that were excluded from our analysis included 416 rural counties and comprised 4.2 million Medicare enrollees. Average daily temperature values for pairs of monitors within a 35-km radius were highly correlated (eTable 2 in the Supplement), with 97% of counties having all pairwise correlations of monitors assigned to the county exceeding 0.95. The **Table** reports summary statistics on the occurrence and duration of heat wave periods.

Risk of Hospitalization on Heat Wave Days vs Non–Heat Wave Days

Figure 2 shows the heat wave–related absolute risk difference and RR estimates for the 30 disease groups with the largest baseline hospitalization rates on non–heat wave days and for heat stroke and other external causes (estimates for all 214 disease groups are shown in **interactive** Table 1 at jama.com). Of the 214 disease groups, 5 diseases (fluid and electrolyte disorders, renal failure, urinary tract infections, septicemia, and heat stroke) had statistically significantly elevated risk differences and RRs of hospitalization during heat wave days. Relative risks for these disease groups were 1.18 (95% CI, 1.12-1.25) for fluid and electrolyte disorders, 1.14 (95% CI, 1.06-1.23) for renal failure, 1.10 (95% CI, 1.04-1.16) for urinary tract infections, 1.06 (95% CI, 1.00-1.11) for septicemia, and 2.54 (95% CI, 2.14-3.01) for heat stroke. Absolute risk differences were 0.34 (95% CI, 0.22-0.46) excess daily admissions per 100 000 individuals at risk for fluid and electrolyte disorders, 0.25 (95% CI, 0.12-0.39) for renal failure, 0.24 (95% CI, 0.09-0.39) for urinary tract infections, 0.21 (95% CI, 0.01-0.41) for septicemia, and 0.16 (95% CI, 0.10-0.22) for heat stroke. For congestive heart failure, the hospitalization rate was reduced on heat wave days, with 0.30 (95% CI, 0.11-0.49) fewer daily admissions per 100 000 individuals at risk relative to matched non–heat wave days.

Figure 3 shows heat wave–related RR estimates under several heat wave definitions, from the least severe (≥2 days, >97th percentile) to the most severe (≥4 days, >99th percentile), for disease groups with statistically significant RRs under the ≥2-day, >99th-percentile definition (estimates for all 214 disease groups are shown in **interactive** Table 2 at jama.com). The RR of hospitalization under the most severe definition was significantly higher than the RR under the least severe definition for fluid and electrolyte disorders and heat stroke.

Figure 4 shows heat wave–related RR estimates for admissions occurring up to 7 days after the heat wave day for disease groups identified as statistically significant under the ≥2-day, >99th-percentile definition of a heat wave event. The risks were generally highest on the heat wave day (lag 0) and remained elevated for 1 to 5 subsequent days. None of the risks remained statistically significant at lags longer than 5 days after the heat wave day.

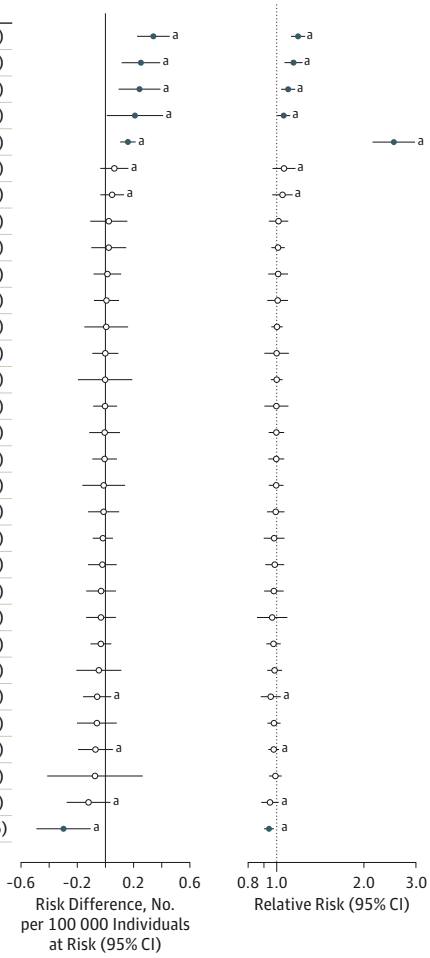
To characterize the physiological outcomes associated with fluid and electrolyte disorder hospitalizations, we examined the *ICD-9* discharge codes for this disease group and found that 47.5% and 24.3% of the admissions were discharged for dehydration and hyposmolality and/or hyponatremia, respectively (eTable 3 in the Supplement). To investigate whether sepsis might have been related to hospitalization rather than to heat exposure, we tabulated the admission diagnoses from all patients with a discharge diagnosis of sepsis and found that approximately 70% of patients discharged for sepsis were admitted with infections or symptoms compatible with early sepsis (eTable 4 in the Supplement). Finally, to compare our results with prior studies,[20,21] we reestimated the risks for the 200 most popu-

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Figure 2. Heat Wave–Related Risk Difference and Relative Risk of Disease Groups, on Average Across All Counties

CCS Code	Disease Group	Total No. of Admissions: Matched Non-Heat Wave Days	Total No. of Admissions: Heat Wave Days	Daily Admission Rate, No. per 100 000 Individuals at Risk (95% CI): Matched Non-Heat Wave Days	Daily Admission Rate, No. per 100 000 Individuals at Risk (95% CI): Heat Wave Days
55	Fluid and electrolyte disorders	9354	11 382	1.85 (1.63-2.09)	2.19 (1.95-2.45)
157	Renal failure (acute/unspecified)	5826	6850	1.77 (1.54-2.04)	2.02 (1.78-2.30)
159	Urinary tract infections	9810	10 855	2.55 (2.27-2.86)	2.79 (2.51-3.10)
2	Septicemia (except in labor)	11 066	12 289	3.71 (3.34-4.11)	3.92 (3.56-4.31)
244	Heat stroke and other external causes	793	2167	0.10 (0.07-0.15)	0.26 (0.19-0.36)
114	Peripheral vascular disease	3681	4089	1.07 (0.89-1.28)	1.13 (0.96-1.34)
50	Diabetes mellitus with complications	4836	5077	1.02 (0.85-1.21)	1.06 (0.91-1.25)
197	Skin infections	5375	5566	1.70 (1.46-1.97)	1.72 (1.50-1.97)
100	Acute myocardial infarction	11 343	11 453	2.31 (2.05-2.60)	2.33 (2.09-2.60)
146	Diverticulosis and diverticulitis	5146	5207	1.24 (1.05-1.46)	1.25 (1.08-1.45)
131	Respiratory failure	4664	4818	1.07 (0.90-1.27)	1.08 (0.92-1.26)
122	Pneumonia	15 576	15 632	3.42 (3.09-3.79)	3.43 (3.12-3.76)
231	Other fractures	3337	3374	0.93 (0.76-1.12)	0.92 (0.77-1.10)
106	Cardiac dysrhythmias	14 818	14 841	4.13 (3.75-4.54)	4.13 (3.78-4.50)
110	Cerebrovascular insufficiency	3498	3658	0.89 (0.72-1.09)	0.89 (0.73-1.07)
226	Hip fracture	8378	8374	1.77 (1.56-2.02)	1.77 (1.57-2.00)
102	Nonspecific chest pain	8146	8114	1.38 (1.20-1.60)	1.38 (1.20-1.58)
127	Chronic obstructive pulmonary disease	9460	9508	2.59 (2.29-2.93)	2.58 (2.31-2.89)
153	Gastrointestinal hemorrhage	6621	6565	1.58 (1.37-1.83)	1.57 (1.38-1.79)
245	Syncope	4972	4826	0.88 (0.73-1.05)	0.86 (0.73-1.01)
238	Complications (surgical/medical)	5583	5605	1.36 (1.17-1.58)	1.34 (1.16-1.54)
145	Bowel obstruction	5256	5223	1.36 (1.16-1.59)	1.33 (1.15-1.53)
95	Other nervous system disorders	2275	2211	0.88 (0.71-1.10)	0.85 (0.70-1.03)
254	Rehabilitation care	10 125	9788	1.26 (1.08-1.47)	1.23 (1.06-1.42)
237	Complications (device/implant/graft)	9144	9323	2.73 (2.42-3.06)	2.68 (2.41-2.98)
149	Biliary tract disease	5114	4955	1.25 (1.06-1.47)	1.19 (1.02-1.38)
109	Stroke	11 716	11 583	2.72 (2.44-3.04)	2.66 (2.41-2.94)
101	Coronary atherosclerosis	18 154	17 880	2.92 (2.63-3.25)	2.85 (2.58-3.15)
203	Osteoarthritis	12 476	13 003	6.75 (6.14-7.41)	6.67 (6.13-7.26)
205	Back problems	6835	6717	2.29 (1.99-2.62)	2.16 (1.91-2.45)
108	Congestive heart failure	21 949	20 558	4.96 (4.54-5.41)	4.66 (4.29- 5.06)



Heat waves were defined as at least 2 consecutive days with average daily temperatures exceeding the 99th percentile of a county's daily temperatures, 1999-2010. Non–heat wave days are matched to heat wave days by county and week. The number of matched non–heat wave days is equal to the number of heat wave days, with an average of 1.4 heat wave days per county per year. The risk difference is the additional number of daily hospital admissions (per 100 000 individuals at risk) on a heat wave day compared with a non–heat wave day. Risk difference estimates are ordered from largest to smallest for the 30 disease groups with the largest baseline risks plus the heat stroke group. Solid circles indicate multiple comparison–adjusted statistically significant results. CCS indicates Clinical Classifications Software.

[a] Statistically significant estimates, unadjusted for multiple comparisons (results for all disease groups are shown in **interactive** Table 1 at jama.com).

lated counties, but we did not find significant associations between heat exposure and respiratory illnesses as previously reported (eAppendix and eTable 5 in the Supplement).

Sensitivity Analyses

We assessed the sensitivity of our results to adjustment for long-term trends and for day of the week (eAppendix in the Supplement), and the results remained unchanged (eFigure, A, in the Supplement). Also, RRs remained statistically significant for all diseases except septicemia under a resampling approach that accounted for serial autocorrelation in the time series data (eFigure, B, in the Supplement).

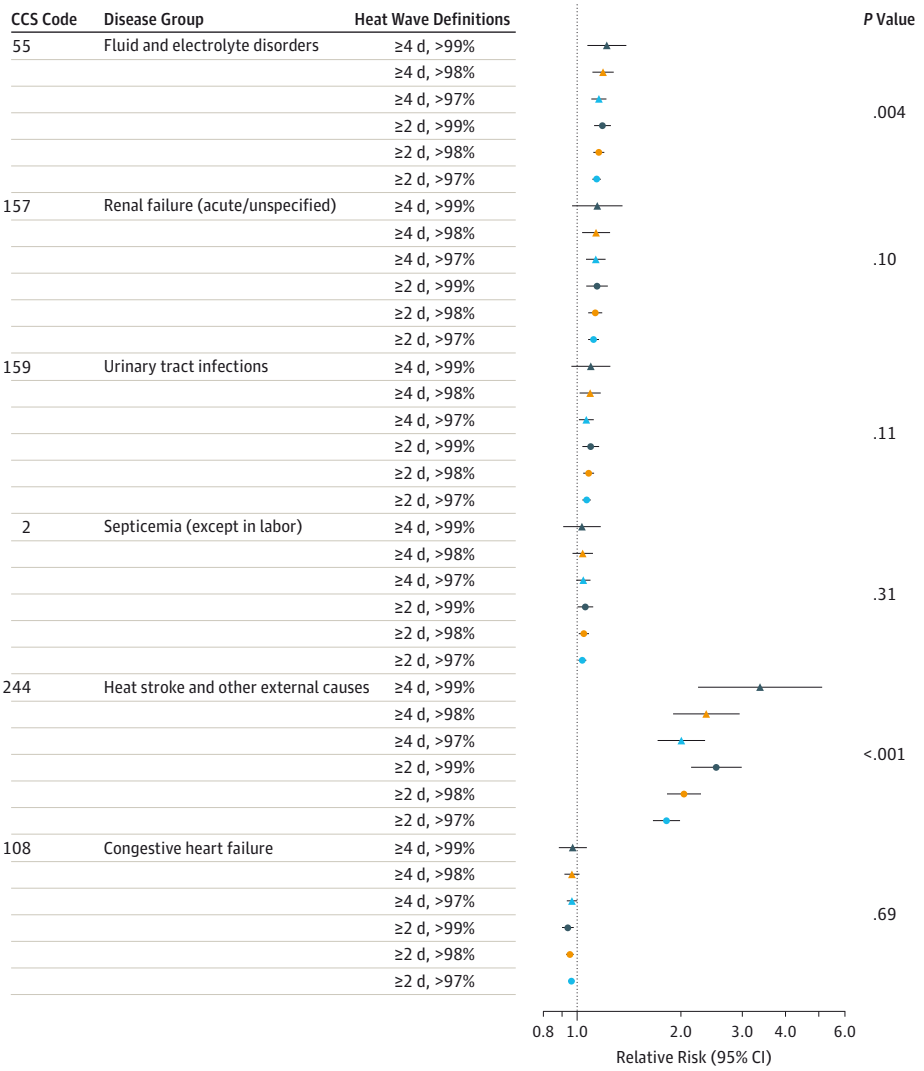
Discussion

We found evidence of an association between heat exposure and elevated hospital admissions for fluid and electrolyte disorders, heat stroke, septicemia, urinary tract infection, and renal failure in a large population of older adults in the United States. Relative risks ranged from 1.06 (95% CI, 1.00-1.11) for septicemia to 2.54 (95% CI, 2.14-3.01) for heat stroke. These risks were larger when the heat wave periods were longer and more extreme and were largest on the heat wave day but remained elevated and statistically significant for 1 to 5 subsequent days.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Figure 3. Heat Wave–Related Relative Risk of Disease Groups, on Average Across All Counties, for 6 Heat Wave Definitions Capturing Different Degrees of Duration and Severity



Results are shown for the disease groups with a statistically significant relative risk under the ≥2-day, >99th percentile definition (results for all disease groups are shown in **interactive** Table 2 at jama.com). *P* values are for test of whether the RR under the most severe (≥4 days, >99%) heat wave definition differed from the RR under the least severe (≥2 days, >97%) heat wave definition. 95% CIs are adjusted for multiple comparisons using the Bonferroni correction method. CCS indicates Clinical Classifications Software.

To our knowledge, this is the largest and most comprehensive study of heat-related morbidity to date, testing 214 diseases classified from 15 072 *ICD-9* codes in a population of 23.7 million older adults per year for 12 years from 1943 urban and rural counties.

The estimated absolute risks of cause-specific hospitalizations were small and of uncertain clinical significance; however, these estimates likely underestimate the overall health burden. The primary goal of our approach—which relied on accurate diagnostic coding and a conservative adjustment for multiple hypothesis testing—was to characterize the cascade of physiological events caused by exposure to extreme heat. Our absolute risk estimates do not capture the lagged associations, in which elevated hospitalization rates persisted in the days following a heat wave. Moreover, the same physiological processes that led to these excess hospitalizations may also contribute to other adverse outcomes, including loss of functional capacity, missed work, physician visits not resulting in hospitalization, and, importantly, mortality. In addition, if climate change leads to more frequent and extreme heat waves,[3] these excess heat-related hospitalizations might be expected to increase.

Our results are consistent with the current understanding of pathophysiological processes associated with exposure to heat in older adults.[4,6,22] Fluid and electrolyte disturbances, for example, had an RR of 1.18 (95% CI, 1.12-1.25) on heat wave days. This was likely the result of volume depletion, with dehydration (code 276.51) the most common *ICD-9* code in this category. Other sequelae of volume depletion and decreased arterial pressure were manifested in the next most frequent *ICD-9* codes, hyponatremia (code 276.1) and hyperkalemia (code 276.7), predictable consequences of antidiuretic hormone secretion and prerenal acute kidney injury, respectively (eTable 5 in the Supplement).

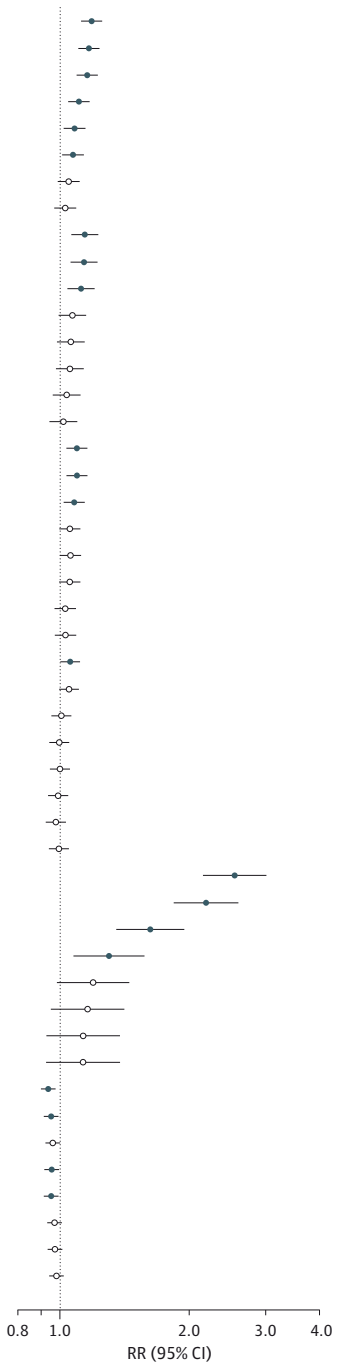
By considering all causes of hospitalization rather than prespecifying a small number of individual diseases, our study pro-

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Figure 4. Heat Wave–Related Relative Risk of Disease Groups, on Average Across All Counties

CCS Code	Disease Group	Lag, d
55	Fluid and electrolyte disorders	0
		1
		2
		3
		4
		5
		6
		7
157	Renal failure (acute/unspecified)	0
		1
		2
		3
		4
		5
		6
		7
159	Urinary tract infections	0
		1
		2
		3
		4
		5
		6
		7
2	Septicemia (except in labor)	0
		1
		2
		3
		4
		5
		6
		7
244	Heat stroke and other external causes	0
		1
		2
		3
		4
		5
		6
		7
108	Congestive heart failure	0
		1
		2
		3
		4
		5
		6
		7



Heat waves are defined as at least 2 consecutive days with average daily temperatures exceeding the 99th percentile of a county's daily temperatures, 1999-2010. Relative risk estimates are calculated for different lags between exposure to a heat wave day and hospital admissions on subsequent days. Lag 0 indicates same day as the heat wave day, lag 1 indicates relative risk at 1 day after the heat wave day, etc. Solid circles indicate multiple comparison–adjusted statistically significant results. Results are shown for the disease groups with a statistically significant relative risk at lag 0. 95% CIs are adjusted for multiple comparisons. CCS indicates Clinical Classifications Software.

vides new insights into previously unsuspected possible outcomes associated with heat exposure. We found a higher risk of hospitalization for sepsis, which to our knowledge has not been considered before. Some of these excess admissions may be due to the constellation of vital sign abnormalities that characterize both the systemic inflammatory response syndrome as well as volume depletion and heat-related illness. Given the magnitude of the association, it seems unlikely that only these factors are at play; it is possible that volume depletion facilitates progression of localized infections to sepsis and shock. Although it also is possible that the many frail, elderly participants in this study acquired nosocomial infections after hospitalization for other causes and were subsequently discharged with a diagnosis of sepsis, this is unlikely, as approximately 70% of patients discharged with a diagnosis of sepsis were initially admitted with infections or signs and symptoms compatible with early sepsis (eTable 4 in the Supplement). Clinicians are aware of the increased risk of heat stroke

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

on hot days, but to our knowledge there is no increased level of vigilance for sepsis. More generally, this finding highlights a strength of our methods, which allowed us to consider a broad range of possible outcomes without an a priori hypothesis.

Another unexpected finding was the lower hospital admission rate for congestive heart failure on heat wave days compared with non-heat wave days. Because it was unexpected, this finding may represent chance. However, it is possible that insensible fluid losses make volume overload less likely. Studies of acute heat-related mortality have found evidence of increased risks of mortality due to cardiovascular diseases, including ischemic heart disease, congestive heart failure, and myocardial infarction.[11,13] Some studies of heat-related hospitalizations have reported elevated admissions for cardiovascular diseases,[8,11,21,23,24] but a recent meta-analysis did not find a statistically significant association.[25] The association we observed may have been obscured in prior studies[21,25] because they grouped together all cardiovascular diseases—including coronary syndromes, valvular disease, congestive heart failure, and others—by *ICD-9* code hierarchies rather than more clinically salient categories. Also different from prior studies,[20,21,26] we did not find an association between heat and respiratory diseases (eTable 5 in the Supplement).

Our approach incorporated several features and internal checks to try to maximize the likelihood of the validity of our results. First, we grouped the 15 072 *ICD-9* codes into clinically meaningful disease categories using a validated algorithm designed for clinical and quality research.[16] Second, we corrected for multiple comparisons to reduce the possibility of identifying spurious associations. Third, we controlled for confounding by county-level factors and temporal trends by matching heat wave days to non-heat wave days by county and week and by adjusting for day of the week and study year as covariates in the regression model. Fourth, we investigated whether heat wave risks were higher under more extreme and longer-lasting heat wave periods and whether the risks were higher on the same day of exposure compared with subsequent days. Fifth, by defining a heat wave day based on separate temperature percentiles for each county, our results account for the possibility of acclimatization to warmer weather.[27] Sixth, by considering all diseases simultaneously, our approach automatically provides negative controls. For example, we did not find significant associations for acute (eg, gastrointestinal bleeding) or chronic (eg, secondary malignancies) conditions with no plausible relation to temperature.

Our study has several limitations. First, while the primary *ICD-9* code typically captures the major acute reason for hospitalization, important diagnoses are sometimes reported as associated diagnostic codes, which we did not include in our analysis. Also, there is increased scrutiny of admissions for dehydration, which are considered to be avoidable hospitalizations,[28] and this may have created incentives for clinicians and coders to select alternative diagnoses for admissions, such as renal failure (a consequence of dehydration) or urinary tract infection (because asymptomatic bacteriuria is a relatively common finding in elderly persons).[29] Second, some of the disease groups defined by the CCS algorithm are more heterogeneous than others. For example, the heat stroke group (group 244) includes heat stroke, heat exhaustion, and other heat-related illnesses, which were the primary diagnoses driving our risk estimates for this group, but it also includes other related diagnoses. Third, as in any observational study, our results may be subject to confounding bias. However, our matched time series analysis allowed for a more rigorous adjustment for confounding than traditional regression approaches.[30] Fourth, by looking at a wide range of outcomes, this study is hypothesis generating and, therefore, the results should be interpreted cautiously. We used the Bonferroni correction to reduce the likelihood of false-positive results and reported the results both with and without this correction.

One potential complication is that some individuals hospitalized on heat wave days might have been hospitalized a few days later even without exposure to heat; that is, heat exposure led to a sooner, but not an extra, hospitalization. If that were the case, we would expect a lower hospitalization rate in the days following a heat wave. However, our analysis showed that hospitalization rates in the days after heat waves were not below baseline. This issue has been investigated in mortality studies,[31-34] but the evidence is mixed and may depend on population characteristics and other factors.[13]

Our analysis of hospitalization rates on days after a heat wave provides 2 additional insights. For some diseases, risk of hospitalization remained elevated for up to 5 days following a heat wave day. This suggests that prevention and treatment of heat-related illnesses is critical not only during the heat wave itself but also on subsequent days. Additionally, quantifying the extra number of hospital admissions attributable to heat waves without consideration of a delayed effect may underestimate the health care burden of heat.

Conclusions

Among older adults, periods of extreme heat were associated with increased risk of hospitalization for fluid and electrolyte disorders, renal failure, urinary tract infections, septicemia, and heat stroke. However, the absolute risk increase was small and of uncertain clinical importance.

ARTICLE INFORMATION

Author Contributions: Drs Bobb and Wang had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Bobb, Dominici.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Bobb, Obermeyer, Dominici.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Bobb, Obermeyer, Dominici.
Obtained funding: Bobb, Dominici.
Administrative, technical, or material support: Wang.
Study supervision: Dominici.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017

Funding/Support: This study was supported by National Institute of Environmental Health Sciences grants R21ES022585 (to Drs Bobb and Dominici), P30ES000002 (to Drs Bobb and Wang), 2001196559 (to Drs Wang and Dominici), and R01ES019560, R21ES020152, 2001382807, and 5R21ES021427-02 (to Dr Dominici); Environmental Protection Agency grants RD-83479801, 4909-RFA11-1/12-3, and 83489401-0 (to Dr Dominici); National Institutes of Health Office of the Director grant DP5 OD012161 (to Dr Obermeyer); National Cancer Institute grant 2P01CA134294-06 (to Drs Wang and Dominici); and Agency for Healthcare Research and Quality grant 1K18HS021991-01A1 (to Drs Wang and Dominici).

Role of the Funders/Sponsors: The funding agencies/sponsors listed above had no involvement in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Disclaimer: The research described in this article was funded wholly or in part by the US Environmental Protection Agency through a grant to Harvard School of Public Health but it has not been subjected to the Environmental Protection Agency's required peer and policy review and therefore does not necessarily reflect the views of the Environmental Protection Agency and no official endorsement should be inferred.

Additional Contributions: We thank Stacey C. Tobin, PhD, ELS, the Tobin Touch, who was compensated to provide editorial assistance.

REFERENCES

1. National Weather Service. National weather service 73-year list of severe weather fatalities. 2013. http://www.nws.noaa.gov/om/hazstats/resources/weather_fatalities.pdf. Accessed May 24, 2013.

2. McMichael AJ, Woodruff RE, Hales S. Climate change and human health: present and future risks. *Lancet*. 2006;367(9513):859-869.

3. Patz JA, Frumkin H, Holloway T, Vimont DJ, Haines A. Climate change: challenges and opportunities for global health. *JAMA*. 2014;312(15):1565-1580.

4. Bouchama A, Knochel JP. Heat stroke. *N Engl J Med*. 2002;346(25):1978-1988.

5. Leon LR, Helwig BG. Heat stroke: role of the systemic inflammatory response. *J Appl Physiol (1985)*. 2010;109(6):1980-1988.

6. Semenza JC, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR. Excess hospital admissions during the July 1995 heat wave in Chicago. *Am J Prev Med*. 1999;16(4):269-277.

7. Semenza JC, Rubin CH, Falter KH, et al. Heat-related deaths during the July 1995 heat wave in Chicago. *N Engl J Med*. 1996;335(2):84-90.

8. Michelozzi P, Accetta G, De Sario M, et al; PHEWE Collaborative Group. High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. *Am J Respir Crit Care Med*. 2009;179(5):383-389.

9. Schwartz J, Samet JM, Patz JA. Hospital admissions for heart disease: the effects of temperature and humidity. *Epidemiology*. 2004;15(6):755-761.

10. Ye X, Wolff R, Yu W, Vaneckova P, Pan X, Tong S. Ambient temperature and morbidity: a review of epidemiological evidence. *Environ Health Perspect*. 2012;120(1):19-28.

11. Anderson BG, Bell ML. Weather-related mortality: how heat, cold, and heat waves affect mortality in the United States. *Epidemiology*. 2009;20(2):205-213.

12. Baccini M, Biggeri A, Accetta G, et al. Heat effects on mortality in 15 European cities. *Epidemiology*. 2008;19(5):711-719.

13. Basu R. High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. *Environ Health*. 2009;8:40.

14. Bobb JF, Dominici F, Peng RD. A Bayesian model averaging approach for estimating the relative risk of mortality associated with heat waves in 105 US cities. *Biometrics*. 2011;67(4):1605-1616.

15. D'Ippoliti D, Michelozzi P, Marino C, et al. The impact of heat waves on mortality in 9 European cities: results from the EuroHEAT project. *Environ Health*. 2010;9:37.

16. Elixhauser A, Steiner C, Palmer L. Clinical Classifications Software for *ICD-9-CM*. Rockville, MD: Agency for Healthcare Research and Quality; 2014. http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp. Accessed June 18, 2014.

17. National Climatic Data Center. Global summary of the day. 2013. http://www7.ncdc.noaa.gov/CDO/cdoselect.cmd?datasetabbv=GSOD&countryabbv=US&georegionabbv=&resolution=40. Accessed March 23, 2014.

18. Holm S. A simple sequentially rejective multiple test procedure. *Scand J Stat*. 1979;6(2):65-70.

19. Dunn OJ. Multiple comparisons among means. *J Am Stat Assoc*. 1961;56(293):52-64.

20. Anderson GB, Dominici F, Wang Y, McCormack MC, Bell ML, Peng RD. Heat-related emergency hospitalizations for respiratory diseases in the Medicare population. *Am J Respir Crit Care Med*. 2013;187(10):1098-1103.

21. Gronlund CJ, Zanobetti A, Schwartz JD, Wellenius GA, O'Neill MS. Heat, heat waves, and hospital admissions among the elderly in the United States, 1992-2006. *Environ Health Perspect*. 2014;122(11):1187-1192.

22. Hansen AL, Bi P, Ryan P, Nitschke M, Pisaniello D, Tucker G. The effect of heat waves on hospital admissions for renal disease in a temperate city of Australia. *Int J Epidemiol*. 2008;37(6):1359-1365.

23. Gasparrini A, Armstrong B, Kovats S, Wilkinson P. The effect of high temperatures on cause-specific mortality in England and Wales. *Occup Environ Med*. 2012;69(1):56-61.

24. Lin S, Luo M, Walker RJ, Liu X, Hwang SA, Chinery R. Extreme high temperatures and hospital admissions for respiratory and cardiovascular diseases. *Epidemiology*. 2009;20(5):738-746.

25. Turner LR, Barnett AG, Connell D, Tong S. Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. *Epidemiology*. 2012;23(4):594-606.

26. Green RS, Basu R, Malig B, Broadwin R, Kim JJ, Ostro B. The effect of temperature on hospital admissions in 9 California counties. *Int J Public Health*. 2010;55(2):113-121.

27. Medina-Ramón M, Schwartz J. Temperature, temperature extremes, and mortality: a study of acclimatisation and effect modification in 50 US cities. *Occup Environ Med*. 2007;64(12):827-833.

28. Agency for Healthcare Research and Quality. AHRQ QI: prevention quality indicators No. 10: technical specifications: dehydration admission rate [version 4.4]. Rockville, MD: Agency for Healthcare Research and Quality; 2012. http://www.qualitymeasures.ahrq.gov/content.aspx?id=38564. Accessed June 18, 2014.

29. Nicolle LE, Bradley S, Colgan R, Rice JC, Schaeffer A, Hooton TM; Infectious Diseases Society of America; American Society of Nephrology; American Geriatric Society. Infectious Diseases Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis*. 2005;40(5):643-654.

30. Stuart EA. Matching methods for causal inference: a review and a look forward. *Stat Sci*. 2010;25(1):1-21.

31. Braga AL, Zanobetti A, Schwartz J. The effect of weather on respiratory and cardiovascular deaths in 12 US cities. *Environ Health Perspect*. 2002;110(9):859-863.

32. Armstrong B, Gasparrini A, Hajat S. Estimating mortality displacement during and after heat waves. *Am J Epidemiol*. 2014;179(12):1405-1406.

33. Braga AL, Zanobetti A, Schwartz J. The time course of weather-related deaths. *Epidemiology*. 2001;12(6):662-667.

34. Saha MV, Davis RE, Hondula DM. Mortality displacement as a function of heat event strength in 7 US cities. *Am J Epidemiol*. 2014;179(4):467-474.

Copyright 2014 American Medical Association. All rights reserved.

Downloaded From: http://jamanetwork.com/pdfaccess.ashx?url=/data/journals/jama/931868/ by a University of Hawaii at Manoa User on 05/27/2017