Supplementary Online Content

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eAppendix. Supplemental Methods

eMethods 1. Details on the Medicare data, statistical model, and risk estimation

Details on the Medicare data files
We used the Medicare Provider Analysis and Review (MEDPAR) data from the Centers for Medicare & Medicaid Services (CMS) to identify Medicare fee-for-service beneficiaries who were aged ≥65 years and had 1 or more hospitalizations in an acute-care US hospital for a medical condition classified in 1 of 283 Clinical Classifications Software (CCS) disease groups during the period January 1, 1999 to December 31, 2010. The MEDPAR data includes hospitalization information (eg, dates of admission and discharge, admission and discharge diagnosis codes, residential county) for each Medicare fee-for-service beneficiary who was hospitalized in the US. We then constructed daily hospitalization data for each county (Y_t^c), denoting the number of hospitalizations for each disease group on day t in county c.

We used the Medicare beneficiary denominator file from CMS to identify all Medicare beneficiaries aged ≥65 years who were enrolled in the fee-for-service plan between January 1999 and December 2010. The denominator file includes demographic and death information for each individual Medicare beneficiary (eg, date of birth and death, age, gender, race, place of residence at ZIP code or county level). From the denominator file, we calculated for each county the daily number of Medicare fee-for-service beneficiaries who were at risk (n_t^c) for hospitalizations. Because the Medicare fee-for-service enrollment occurs on monthly basis, we first calculated person-years for each beneficiary to account for new enrollment, disenrollment, or death during an index year at the month level. We then linked the monthly-based data with the daily-based hospitalization data to obtain the daily numbers of all-cause admissions and discharges to adjust the monthly-based person-years information.

The final linked study sample, a time series dataset, included the number of Medicare fee-for-service beneficiaries who were at risk, the number of admissions that occurred for each targeted day, each targeted county, and each of the 283 CCS groups.

Statistical model
Separately for each disease group, we fit the model

$$\log E(Y_t^c) = \log(n_t^c) + \alpha + a^c + \beta hw_t^c + \sum_{j=1}^{6} \gamma_j dow_{jt} + \sum_{k=1}^{11} \delta_k year_{kt},$$

where Y_t^c is the number of hospitalizations for a disease group on day t in county c, assumed to follow a Poisson distribution, n_t^c is the number of individuals at risk, $a^c \sim N(0, \sigma^2)$ is a county-specific random intercept to account for within-county correlation of the observations, hw_t^c is an indicator for whether the day is a heat wave versus non-heat wave day. In the regression model, we also adjusted for day of the week and for study year, both as categorial variables. Specifically, dow_{jt} ($j = 1, \ldots, 6$) were indicator variables for day of the week (where Monday is the reference day), and $Year_{kt}$ ($k = 1, \ldots, 11$) were indicator variables for study year (where 2010 is the reference year). We fit this model to the data separately for each disease group.

Estimation of heat wave-related risks
The relative risk (RR) is given by the coefficient $\exp(\beta)$. The expected number of admissions (per 100,000 individuals at risk) on a non-heat wave day is given by $100{,}000 \times exp(\alpha)$ and the expected number of admissions on a heat wave day is given by $100{,}000 \times exp(\alpha + \beta)$. The heat wave-related absolute risk difference (RD), defined as the additional number of hospital

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admissions (per 100,000 individuals at risk) on a heat wave day as compared to a non-heat wave day, is given by $100{,}000 \times \{exp(\alpha + \beta) - exp(\alpha)\}$. Standard errors for α and β were obtained directly from the model fit, and standard errors for the RD were calculated by using the delta method.

Testing for higher risk when heat waves are longer and more extreme

We evaluated whether the log RR for the most severe heat wave period (4-day, 99th percentile, $d = 6$) was larger than the log RR for the least severe heat wave period (2-day, 97th percentile, $d = 1$) definitions. Under the dth definition of heat wave ($d = 1$ and $d = 6$), let $ctrl_d$ be an indicator for whether a day is a non-heat wave day and let hw_d be an indicator for whether a day is a heat wave day. We then expanded the above model above as

$$\log E(Y_t^c) = \log(n_t^c) + \alpha + a^c + \alpha_6 ctrl_{6}{}_t^c + \beta_1 hw_{1}{}_t^c + \beta_6 hw_{6}{}_t^c + \sum_{j=1}^{6} \gamma_j dow_{jt} + \sum_{k=1}^{11} \delta_k year_{kt}.$$

Only days that were either a heat wave day or a matched non-heat wave day under either of these 2 heat wave definitions were included in the analysis. Note that every day that was a heat wave day under the 4-day, 99th percentile definition was, by definition, also a heat wave day under the 2-day, 97th percentile definition. This implies that if $hw_6 = 1$ then $hw_1 = 1$. Thus, the log RR of admissions comparing a day that was a heat wave day only under the 2-day, 97th percentile definition to a matched non-heat wave day is given by β_1, and the log RR of admissions comparing a heat wave day under the 4-day, 99th percentile definition to a matched non-heat wave day is given by $\beta_1 + \beta_6 - \alpha_6$. Therefore, to test whether the log RR for the 4-day, 99th percentile definition differred from the log RR for the 2-day, 97th percentile definition, we tested whether $\beta_6 - \alpha_6$ differed from zero.

Lagged analysis

To investigate possible delayed effects of heat waves on hospitalizations, we conducted a lagged analysis, where we considered hospitalizations at lags of 1 through 7 days following a heat wave day. For each lag l ($l = 1, \ldots, 7$), we compared the number of hospital admissions on day l following a heat wave day to the number of hospital admissions on the matched non-heat wave day. For example, if July 14, 2005 was a heat wave day and July 16, 2002 was a matched non-heat wave day, then for a lag of $l = 7$, we would compare the number of admissions on July 21, 2005 (7 days after the heat wave day) to the number of admissions on July 16, 2002 (the matched non-heat wave day). Specifically, for each lag l we replaced the outcome Y_t^c in the statistical model (described above) with a new lagged outcome variable $Ylag_{t+l}^c$, which takes the value Y_{t+l}^c if day t was a heat wave day and takes the value Y_t^c if day t was a non-heat wave day.

eMethods 2. Statistical methods for the sensitivity analyses

Adjustment for temporal trends in hospitalizations

We investigated the sensitivity of the heat wave-related risk estimates to adjustment for the temporal covariates in the statistical model described in **eMethods 1**. We considered an unadjusted model that did not include day of the week or study year, a model that adjusted for year as a continuous variable without including day of the week, and a model that adjusted for year as a categorical variable without including day of the week. Results are summarized in **eFigure 1A**.

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Bootstrap-based standard error estimates
We compared our model-based standard error estimates for the heat wave-related risks (described in **eMethods 1**) to those obtained using re-sampling methods. We used a block bootstrap approach[1] to account for serial autocorrelation in the daily hospitalization data as follows. First, we sampled 146 blocks of days with replacement, where each block consisted of 30 consecutive days from January 1, 1999 to December 31, 2010, to obtain a new daily time series consisting of 4380 days. Second, for each day under the resampled time series, we identified whether that day was a heat wave day (separately for each county), and we matched it to a non-heat wave day from that county using our original matching algorithm. Third, for each resampled dataset, we fit the statistical model described in **eMethods 1** to obtain the heat wave-related risk estimates. We also fit each of the models with different degrees of adjustment for temporal trends in hospitalizations, as described in the preceding subsection. We repeated the above steps 300 times and took the average and standard deviation of the risk estimates over the 300 repetitions. Results are summarized in **eFigure 1B**.

Heat wave-related risks for aggregate categories of hospital admissions
To provide a basis for comparison with previous studies that considered broad categories of respiratory, cardiovascular, and all-cause hospitalizations, we conducted a sensivity analysis in which we estimated heat wave-related risks for aggregate disease groups. Specifically, for each county and each day, we summed the number of hospitalizations over all groupings classified as “diseases of the respiratory system” under the CCS multi-level clustering algorithm (CCS groups 122–134) to obtain the total number of respiratory admissions. Similarly, we summed the number of hospitalizations over all groupings classified as “diseases of the circulatory system” (CCS groups 96–121) to obtain the total number of cardiovascular admissions. Finally, we summed the number of hospitalizations over all of the disease groupings to obtain all-cause hospitalizations. In addition, because previous studies estimated health risks in populations from large, urban areas, we conducted this sensitivity analysis both in our entire study population of 1943 urban and rural counties, as well as in the subset of our population residing in the 200 most populous counties. Results are summarized in **eTable 7.**

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eTable 1. Counties, Fee-for-Service Medicare Enrollees Aged ≥65 Years in 2010, and Hospital Admissions in 2010

Sample	**Counties** No. (%)	**Enrollees** No. in millions (%)	**Admissions** No. in millions (%)
Entire US	3213 (100)	27.9 (100)	9.0 (100)
US excluding Puerto Rico	3135 (98)	27.7 (99)	9.0 (100)
Counties with at least 1 temperature monitor within 35 km	2257 (70)	25.4 (91)	8.2 (91)
Final sample: counties with at least 5 years of sufficient summer temperature data	1943 (60)	23.7 (85)	7.7 (85)

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eTable 2. Summary Statistics of Pairwise Correlations of Weather Monitors Within a 35 km Radius by Geographical Region and Over All Counties

	Counties			**Summary statistics of pairwise correlations**					
Region	No. in region[b]	No. (%) with all pairwise correlations of monitors greater than 0.80	No. (%) with all pairwise correlations of monitors greater than 0.95	Min.	25%	Median	Mean	75%	Max.
East North Central	284	284 (100)	284 (100)	0.98	1.00	1.00	1.00	1.00	1.00
East South Central	100	100 (100)	100 (100)	0.96	0.99	0.99	0.99	0.99	1.00
Middle Atlantic	72	72 (100)	72 (100)	0.98	0.99	1.00	0.99	1.00	1.00
Mountain	113	113 (100)	106 (94)	0.86	0.99	0.99	0.99	1.00	1.00
New England	48	48 (100)	47 (98)	0.91	0.99	0.99	0.99	1.00	1.00
Pacific	90	82 (91)	60 (67)	0.15	0.95	0.96	0.95	0.97	1.00
South Atlantic	347	346 (100)	344 (99)	0.10	0.99	0.99	0.99	0.99	1.00
West North Central	269	269 (100)	269 (100)	0.95	1.00	1.00	1.00	1.00	1.00
West South Central	205	203 (99)	200 (98)	0.77	0.99	1.00	0.99	1.00	1.00
All counties	1528	1517 (99)	1482 (97)	0.10	0.99	0.99	0.99	1.00	1.00

[a] Regions are defined by the US Census.
[b] Counties without any weather monitors within 35 km of a different monitor were excluded from this analysis.

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eTable 3. Rate of Discharge for Each ICD-9 Diagnostic Code Belonging to the Fluids and Electrolyte Disorders Disease Group (CCS Group 55)

The numerator is the number of patients discharged for each of the listed ICD-9 codes (third column). The denominator is the total number of patients discharged for fluid and electrolyte disorders in the combined 2009 and 2010 Medicare fee-for-service inpatient claims data (N=344,718).

ICD-9 code within CCS group 55[a] (fluid and electrolyte disorders)	**Description**	**Discharge by ICD-9 code** (No.)	**Rate of discharge for each ICD-9 code among hospitalizations for fluid and electrolyte disorders** (%)
27651	Dehydration	163,662	47.5
2761	Hyposmolality and/or hyponatremia	83,718	24.3
2767	Hyperpotassemia	28,270	8.2
2768	Hypopotassemia	17,154	5.0
2760	Hyperosmolality and/or hypernatremia	15,180	4.4
2766	Fluid overload	10,387	3.0
9951	Angioneurotic edema not elsewhere classified	8,950	2.6
27650	Volume depletion, unspecified	7,643	2.2
27652	Hypovolemia	4,172	1.2
2762	Acidosis	2,164	0.6
27669	Other fluid overload	1,681	0.5
2769	Electrolyte and fluid disorders not elsewhere classified	1,181	0.3
2763	Alkalosis	321	0.1
2764	Mixed acid-base balance disorder	235	0.1

CCS= Clinical Classifications Software[a]; ICD-9= International Classification of Diseases, Ninth Revision.

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eTable 4. Admission Diagnosis, Grouped by CCS Category, for All Patients Discharged With a Diagnosis of Sepsis (CCS Group 2)

The numerator is the number of patients admitted with a diagnosis in each CCS group (third column). The denominator is the total number of patients with a discharge diagnosis of sepsis in the combined 2009 and 2010 Medicare fee-for-service inpatient claims data (N=756,514).

ICD-9 code within CCS group 2[a] (sepsis)	**Description**	**Admission by ICD-9 code** (No.)	**Rate of admission for each ICD-9 code among patients discharged for sepsis** (%)
2	Septicemia (except in labor)	232,196	30.69
246	Fever of unknown origin	64,185	8.48
159	Urinary tract infections	56,313	7.44
122	Pneumonia	55,900	7.39
259	Residual codes; unclassified	52,623	6.96
133	Other lower respiratory disease	45,159	5.97
252	Malaise and fatigue	25,266	3.34
131	Respiratory failure; insufficiency; arrest (adult)	23,207	3.07
251	Abdominal pain	17,921	2.37
117	Other circulatory disease	16,638	2.20
85	Coma; stupor; and brain damage	11,427	1.51
55	Fluid and electrolyte disorders	11,365	1.50
157	Acute and unspecified renal failure	10,410	1.38
250	Nausea and vomiting	9,399	1.24
197	Skin and subcutaneous tissue infections	8,895	1.18

CCS= Clinical Classifications Software.[a] Restricted to CCS groups with admission rate >1%.

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eTable 5. Point Estimates and 95% Confidence Intervals (CI) of the Heat Wave-Related Relative Risk (RR) of All-Cause, Respiratory, and Cardiovascular Aggregate Disease Groups in the Entire Study Population and in the 200 Most Populous Counties

Heat waves (HW) are defined as at least 2 consecutive days with average daily temperatures exceeding the 99th percentile of a county's daily temperatures, 1999–2010.

	Total no. of admissions		**Daily admissions rate: no. per 100,000 individuals at risk (95% CI)**		
	Matched non-HW days	**HW days**	**Matched non-HW days**	**HW days**	**RR (95% CI)**
Entire study population					
All-cause	393,269	400,514	98.06 (96.62, 99.53)	98.34 (96.95, 99.76)	1.003 (0.998, 1.008)
Respiratory	40,424	40,807	9.61 (9.29, 9.95)	9.69 (9.38, 10.00)	1.008 (0.992, 1.023)
Cardiovascular	119,158	117,720	26.71 (26.13, 27.31)	26.14 (25.60, 26.70)	0.979 (0.970, 0.987)
Most populous counties					
All-cause	228,342	232,305	100.80 (98.24, 103.43)	100.67 (98.16, 103.24)	0.999 (0.992, 1.005)
Respiratory	23,039	23,588	9.49 (9.04, 9.97)	9.65 (9.21, 10.10)	1.016 (0.996, 1.036)
Cardiovascular	68,011	66,857	26.18 (25.25, 27.14)	25.51 (24.63, 26.41)	0.974 (0.963, 0.986)

[a] The RR is the ratio of hospital admission rates comparing a heat wave day to a non-heat wave day.
[b] Disease groups are defined by the Clinical Classifications Software (CCS) multi-level clustering algorithm (see eMethods 2 for details).

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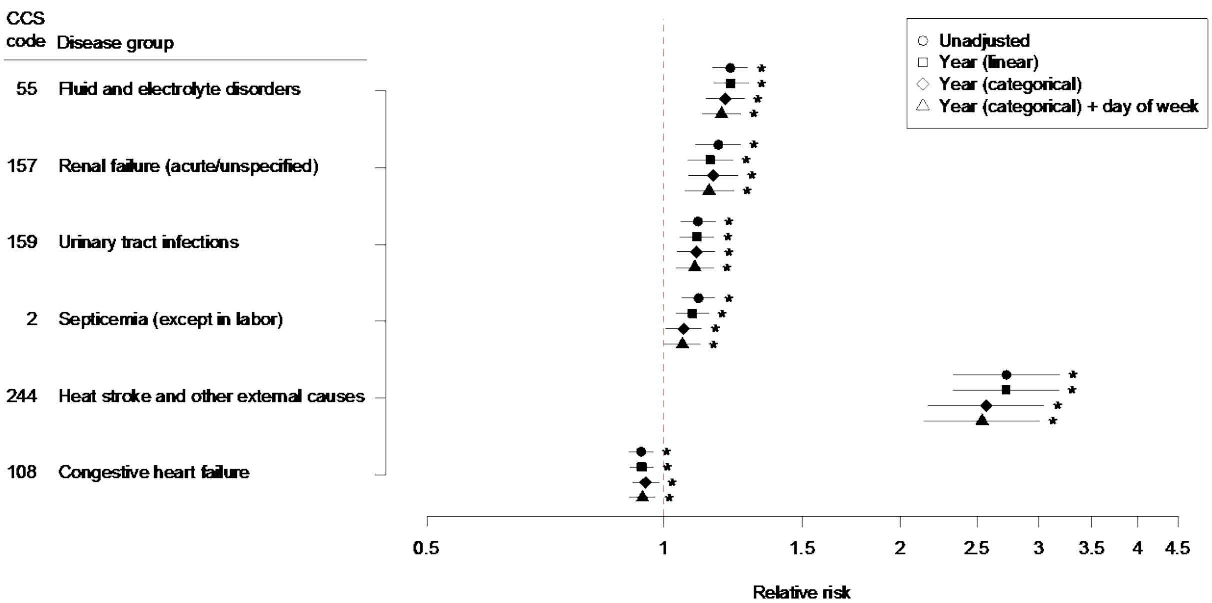
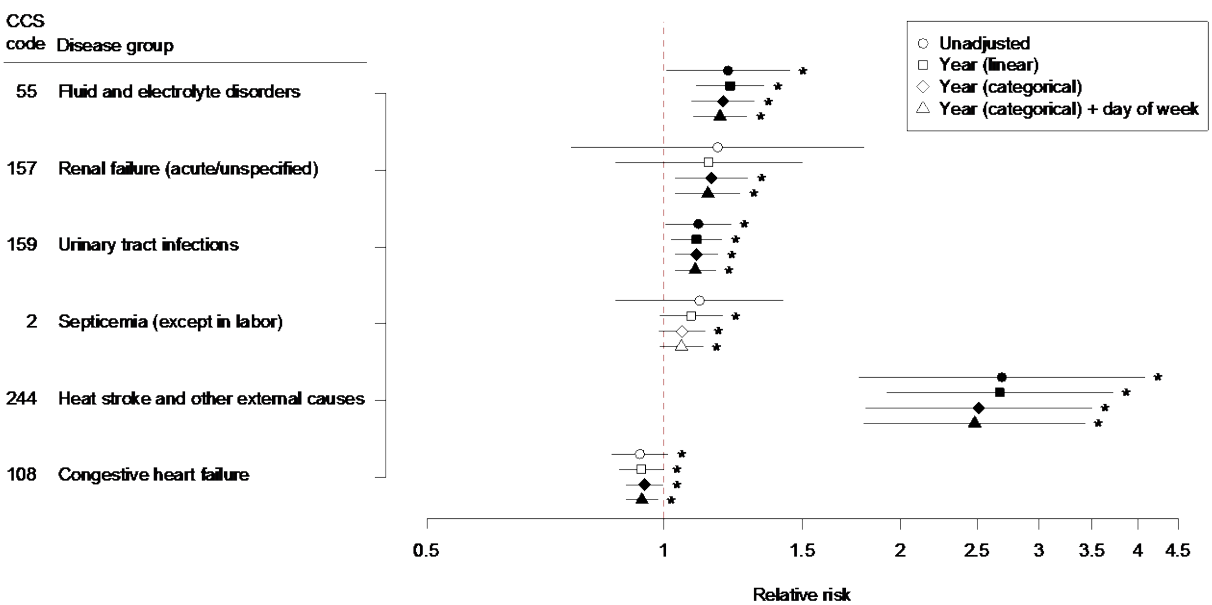
eFigure. Sensitivity of the Heat Wave-Related Relative Risk (RR) Estimates and 95% Confidence Intervals (CI) to (A) Adjustment for Temporal Trends and (B) the Model-Based Standard Error Estimates

A.



B.



Black points denote statistically significant estimates adjusted for multiple comparisons and asterisks next to the estimates denote statistical significance before multiple comparison adjustment. Models shown are the unadjusted model, the model that adjusts for study year as a continuous variable, the model that adjusts for study year as a categorical variable, and the model that adjusts for study year as a categorical variable plus day of the week (analysis presented in the main manuscript text). Disease groups are defined by the Clinical Classifications Software (CCS) algorithm. 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. CI are adjusted by multiple comparisons using the Bonferroni correction method. Estimates and standard errors in panel (**B**) were obtained as described in **eMethods 2.**

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Supplemental material references

1. Künsch HR. The jackknife and the bootstrap for general stationary observations. *Ann Stat.* 1989;17(3):1217-1241.

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