

The effect of temperature on hospital admissions in nine California counties

Rochelle S. Green · Rupa Basu · Brian Malig · Rachel Broadwin · Janice J. Kim · Bart Ostro

Received: 1 December 2008 / Revised: 12 June 2009 / Accepted: 17 July 2009 / Published online: 22 September 2009
© Birkhäuser Verlag, Basel/Switzerland 2009

Abstract

Objectives This study examined the association between mean daily apparent temperature and hospital admissions for several diseases in nine California counties from May to September, 1999 to 2005.

Methods We conducted a time-stratified case-crossover study limited to cases with residential zip codes located within 10 km of a temperature monitor. County-specific estimates were combined, using a random effects meta-analysis. The analyses also considered the effects of ozone and particulate matter (PM_{2.5}).

Results We found that a 10°F increase in mean apparent temperature was associated with a 3.5% [95% confidence interval (CI) 1.5–5.6] increase in ischemic stroke and increases in several other disease-specific outcomes including all respiratory diseases (2.0%, 95% CI 0.7–3.2), pneumonia (3.7%, 95% CI 1.7–3.7), dehydration (10.8%, 95% CI 8.3–13.6), diabetes (3.1%, 95% CI 0.4–5.9), and acute renal failure (7.4%, 95% CI 4.0–10.9). There was little evidence that the temperature effects we found were due to confounding by either PM_{2.5} or ozone.

Conclusion Our results indicate that increases in ambient temperature have important public health impacts on morbidity.

Keywords Temperature · Heat · Hospital admissions · Case-crossover · Age · California

Introduction

Several studies around the world have documented a relationship between increased ambient temperature and mortality (Basu et al. 2005, 2008; Basu and Ostro 2008; Garssen et al. 2005; Kovats et al. 2006; Le Tertre et al. 2006; Stafoggia et al. 2006). Fewer investigators, however, have examined the association between ambient temperature and morbidity, especially during non-heat wave periods. Several studies have reported temperature effects on hospital admissions during heat waves. For example, during the Chicago heat wave of 1995 there were increases in hospital visits for cardiovascular disease and other medical conditions including respiratory diseases, diabetes, emphysema, nervous system disorders and acute renal failure (Semenza 1999; Semenza et al. 1999). A recent study in Australia also found an increase in hospitalization for acute renal failure during heat wave periods (Hansen et al. 2008b). During non-heat wave periods, temperature was associated with hospital admissions for heart disease in general and myocardial infarction in particular in persons age 65 and older in 12 US cities (Schwartz et al. 2004). However, none of these studies controlled for the effects of ambient air pollution, including ozone and particulate matter, both of which have been associated with hospital admissions in dozens of studies (US Environmental Protection Agency 2006, October 2004). In addition, most

This paper belongs to the special issue “Climate changes health”.

The opinions expressed in this article are solely those of the authors and do not represent the policy or position of the State of California or the California Environmental Protection Agency.

R. S. Green (✉) · R. Basu · B. Malig · R. Broadwin · B. Ostro
Office of Environmental Health Hazard Assessment,
California Environmental Protection Agency, 1515 Clay Street,
16th Floor, Oakland, CA 94612, USA
e-mail: sgreen@oehha.ca.gov

J. J. Kim
Infectious Disease Branch,
California Department of Public Health,
Richmond, CA, USA

studies have based exposures to temperature on city- or county-wide averages, which could result in exposure misclassification.

Our current study examines hospital admissions for a large number of potential heat-related outcomes in nine California counties, which comprise about 65% of the state's population. We attempted to address several issues by: (1) examining hospital admissions during the entire warm season to see if effects are observed in periods other than during temperature extremes; (2) controlling for air pollution when examining cardiovascular and respiratory outcomes; and (3) using Geographic Information Systems (GIS) methods to improve exposure assessment by assigning temperature to individuals at a smaller spatial scale.

Methods

Daily hospital admissions data were obtained for nine California counties from the Office of Statewide Health Planning and Development (OSHPD), Healthcare Quality and Analysis Division, from 1 May 1999, through 31 September 2005 [OSHPD Patient Discharge Data (PDD), 1999–2005. Sacramento, California]. The nine California counties included Contra Costa, Fresno, Kern, Los Angeles, Orange, Riverside, Sacramento, San Diego, and Santa Clara, which were the same nine counties used in an earlier investigation of temperature and mortality (Basu et al. 2008). We retrieved information on date of admission, primary diagnosis of admission, county and zip code of residence, age, gender, and ethnicity. We examined hospital admissions for all cardiovascular diseases [International Classification of Diseases, 9th Revision (ICD-9) codes 390–459], ischemic heart disease (ICD-9 codes 410–414), acute myocardial infarction (ICD-9 code 410), heart failure (ICD-9 code 428), hemorrhagic stroke (ICD-9 codes 430–432), ischemic stroke (ICD-9 codes 433–436), all respiratory diseases (ICD-9 codes 460–519), pneumonia (ICD-9 codes 480–486), asthma (ICD-9 code 493), chronic bronchitis or emphysema (COPD) (ICD-9 codes 491–493), diabetes (ICD-9 code 250), dehydration (ICD-9 code 276.5), heat stroke (ICD-9 code 992), intestinal infectious diseases (ICD-9 codes 001–009), and acute renal failure (ICD-9 code 584).

Weather data were obtained from monitors operated by the California Irrigation Management Information System (CIMIS) and the US Environmental Protection Agency (US EPA) for the study period. During the study period there were a few heat waves lasting 2 or 3 days, but none with the duration or intensity of the 2006 California heat wave, which lasted about 10 days. Using ArcGIS Version 9.2 (Environmental Systems Research Institute 1995–2008) we created circular buffers with a 10-km radius around each monitor in the nine counties and selected hospitalized

subjects for whom the geographic centroid of their residential zip code fell within the buffer of a monitor. If the zip code centroid was located within 10 km of more than one monitor, the closest monitor was chosen. Mean daily apparent temperature in degrees Fahrenheit (°F) was calculated to account for temperature and relative humidity using a method that has been described previously (Basu et al. 2008). Our analysis was limited to the warm months (May through September).

Study design and data analysis

We used the time-stratified case-crossover approach (Levy et al. 2001) for data analysis and selected referent periods every third day of the same month and the same year as the case period. The case-crossover design can be viewed as a matched case-control study design which involves cases only, and each individual serves as his/her own control. Thus, temperatures on the day of hospitalization (case period) are compared with temperatures on several days when hospitalization did not occur (referent periods). This method effectively controls for individual-level confounding, and we have controlled for season by limiting our analysis to the warmer months. In addition to a linear term for apparent temperature, day of the week was added to the model as an indicator variable. We examined several lag times: a single day effect of same day temperature exposure (lag 0), single day effects of the previous days of exposure (lag 1, lag 2, lag 3), and moving averages over the same day and previous days of exposure (lag 01, lag 03, lag 06). Lag 03 is the cumulative average of same day temperature and all 3 days prior; lag 06 is the cumulative average of same day temperature and all 6 days prior. We also examined various cause-specific hospital admissions stratified by age (less than 5 years, 5–18 years, 19–64 years and 65 years or older), ethnicity (White, Black, Hispanic, Asian) and gender.

We examined possible confounding by air pollution of either PM_{2.5} (particulate matter less than 2.5 µm in aerodynamic diameter) or ozone for selected outcomes by adding PM_{2.5} (24-h average) to the model described above or by restricting the analysis to cases and control periods matched on ozone level (maximum 1-h) within 4 parts per billion (ppb) (Schwartz 2005). Since PM_{2.5} data were collected only on an every third or sixth day basis, we did not use the matching approach for this pollutant. For comparison purposes, we also ran the models for the same outcomes without PM_{2.5}, but only including days when PM_{2.5} data was available. We also examined effect modification by these two pollutants individually by putting an interaction term in the model for temperature and PM_{2.5} and for temperature and ozone.

Finally, we tested for non-linearity of the heat effect. For selected outcomes we separately added each of the

Table 1 Environmental variables and number of hospital admissions in the study population in the nine California counties, May–September, 1999–2005

Environmental variables	Contra Costa	Fresno	Kern	Los Angeles	Orange	Riverside	Sacramento	San Diego	Santa Clara
Apparent temperature on “case-days” (°F)									
Mean	64.9	75.6	77.1	69.9	71.0	77.5	71.5	68.7	64.6
25th percentile	60.3	70.3	71.8	65.6	66.7	70.0	66.1	64.5	61.3
75th percentile	69.3	81.4	83.1	74.1	75.0	85.1	76.9	72.8	68.3
Difference of apparent temperature between “case-day” and “control-days” (°F)									
Mean	0.1	0.2	0.1	0.1	0.0	0.0	0.1	0.0	0.1
25th percentile	−4.7	−6.2	−5.9	−3.6	−3.3	−5.4	−6.3	−3.4	−4.3
75th percentile	4.9	6.5	6.2	3.8	3.4	5.4	6.4	3.5	4.5
Ozone (max 1 h) on “case-days” (ppb)									
Mean	51.8	82.9	81.6	63.9	56.4	84.5	64.1	54.7	44.2
25th percentile	41.9	69.6	71.0	52.7	48.3	72.3	53.3	48.4	35.6
75th percentile	59.7	95.8	92.7	73.2	62.8	97.0	73.8	60.5	49.7
Difference of ozone (max 1 h) between “case-day” and “control-days” (ppb)									
Mean	−0.2	0.2	0.0	−1.0	−0.6	−0.5	−0.1	−0.3	−0.3
25th percentile	−12.3	−15.2	−12.6	−14.7	−11.0	−16.6	−13.1	−8.2	−10.3
75th percentile	12.0	15.5	12.6	12.8	9.8	15.6	13.0	7.7	9.6
PM _{2.5} on “case-days” (µg/m ³)									
Mean	6.9	10.9	13.2	19.0	14.6	25.6	9.1	12.8	10.7
25th percentile	4.6	7.7	10.3	14.3	11.0	16.5	6.0	9.9	7.0
75th percentile	8.4	13.0	15.2	22.1	17.4	32.0	10.9	15.1	12.9
Difference of PM _{2.5} between “case-day” and “control-days” (µg/m ³)									
Mean	0.1	0.1	0.0	0.0	−0.2	0.0	0.0	0.1	0.1
25th percentile	−2.7	−3.0	−3.4	−5.6	−4.6	−9.2	−2.8	−3.3	−4.1
75th percentile	2.8	3.5	3.5	5.6	4.3	9.1	2.9	3.4	4.1
Pearson correlation between apparent temperature and ozone (max 1 h)									
	0.55	0.67	0.75	0.45	0.25	0.48	0.65	0.09	0.50
Pearson correlation between apparent temperature and PM _{2.5}									
	0.18	0.44	0.39	0.15	0.17	0.04	0.28	0.18	0.41
Population under study									
Number of hospital admissions	27,880	43,417	34,610	426,805	68,681	54,260	63,463	105,167	28,813

following terms to the base model, without pollutants: (1) a square term for mean apparent temperature, (2) an indicator variable and interaction term for temperatures above 75°F [23.9°C], and (3) an indicator variable and interaction term for temperatures falling in the top 5th percentile for a monitor.

All case-crossover analyses were conducted with SAS statistical software (SAS Institute Inc. 2003) using the PHREG procedure for conditional logistic regression. We first obtained county-specific effect estimates and then combined all nine county-specific estimates using a meta-analysis with a random effects model (Anderson et al. 2005; DerSimonian and Laird 1986). The meta-analyses were conducted using R statistical software (R Development Core Team R). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated per 10°F

increases in mean daily apparent temperature. The results are presented as the percent excess risk in hospital admission per 10°F (5.6°C) using the following calculation: $(OR - 1) \times 100\%$.

Results

Our study population consisted of 853,096 individuals who were admitted to a hospital with the above listed diagnoses and criteria. The mean apparent temperature on “case-days” for the study period ranged from 64.6°F (18.1°C) in Santa Clara County to 77.5°F (25.3°C) in Riverside County, while the mean difference in temperature between the “case-day” and “control-days” was highest in Fresno County (0.2°F) (Table 1). The number of total hospital

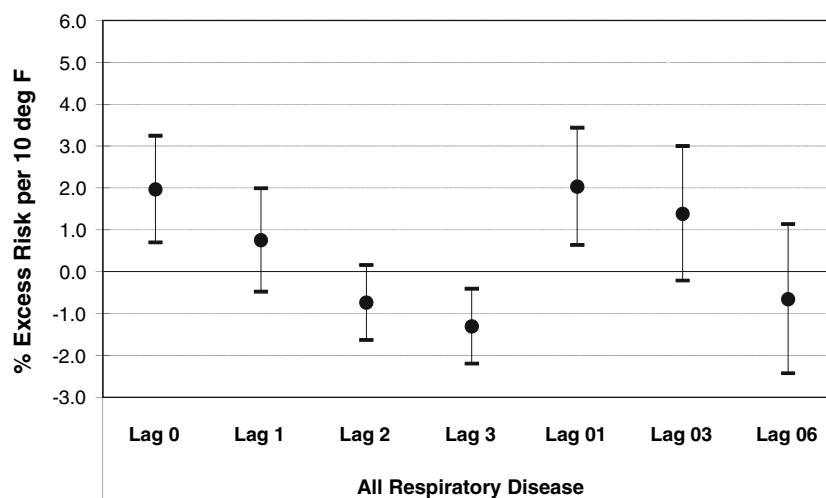


Fig. 1 Meta-analysis results for various lag periods for mean daily apparent temperature [per 10°F (5.6°C)] and percent excess risk for hospital admission for respiratory disease in nine California counties. *Lag 0* same day temperature, *Lag 1* temperature the previous day, *Lag 2* temperature 2 days previously, *Lag 3* temperature 3 days

previously, *Lag 01* cumulative average of same day temperature and previous day, *Lag 03* cumulative average of same day temperature and all 3 days prior, *Lag 06* cumulative average of same day temperature and all 6 days prior

admissions ranged from 27,880 in Contra Costa County to 426,805 in Los Angeles County (Table 1).

In general, we found the strongest associations for the same day apparent temperature (lag 0). For example, Fig. 1 shows the results of the meta-analysis for all lags for the broad categories of respiratory disease admissions (ICD-9 codes 460–519). The effect estimates diminished as the lag time increased. At lag 0 the excess risk of respiratory disease per 10°F (5.6°C) was 2.0% (95% CI 0.7–3.2%), while the excess risk at lag 1 was 0.8% (CI –0.5 to 2.0%).

A similar pattern of decreasing effects with increasing lag periods was observed for other disease categories, such as dehydration and diabetes (data not shown). Therefore, all subsequent results are shown for lag 0. We did not find an association between temperature and all cardiovascular (ICD-9 codes 390–459) disease admissions in general or for ischemic heart disease or heart failure admissions in particular (Table 2). However, we did observe a strong negative association between temperature and hemorrhagic stroke. For the sub-categories of respiratory disease that we examined, only pneumonia was significantly related to apparent temperature (excess risk, 3.7%; CI 1.7–5.7%). Neither asthma nor chronic obstructive pulmonary disease (chronic bronchitis or emphysema) was associated with apparent temperature (Table 2).

Table 2 also summarizes the results for the other disease categories that were examined. Diabetes, dehydration, acute renal failure, and heat stroke were all positively associated with increased temperature in our analysis. For example, the excess risk associated with a 10°F increase in apparent temperature was 7.4% (CI 4.0–10.9%) for acute renal failure. Heat stroke was strongly associated with

apparent temperature, although there were only 477 cases of heat stroke in the nine counties (404%, CI 309–521%).

Although we did not find differences in effect estimates by gender or ethnicity, the effect of apparent temperature did differ by age for several of the outcomes we studied. Figure 2 shows the results for pneumonia and ischemic stroke by subgroups of age. The number of cases in each age group is listed in Figs. 2, 3, and 4. For pneumonia, the effects of temperature are highest for those under 5 years (excess risk, 5.9%; CI –1.7 to 14.1%) and those aged 19–64 years (excess risk, 4.1%; CI 1.3–7.0%). Results were similar for those 65 years or older. An effect of high temperature was observed for ischemic stroke in individuals 65 years or older (excess risk, 3.5%; CI 1.5–5.6%), but not in the 19–64 years of age group. Hospital admission for dehydration was significantly associated with apparent temperature in all age groups except those under age 5 years (Fig. 3), with the highest effect estimate seen in those age 5–18 years (excess risk, 19.7%; CI 6.4–34.7%). This same subgroup (age 5–18 years) was the only for which we observed an association between intestinal infectious disease admissions and apparent temperature (excess risk, 21.3%; CI 5.2–39.8%) (Fig. 3).

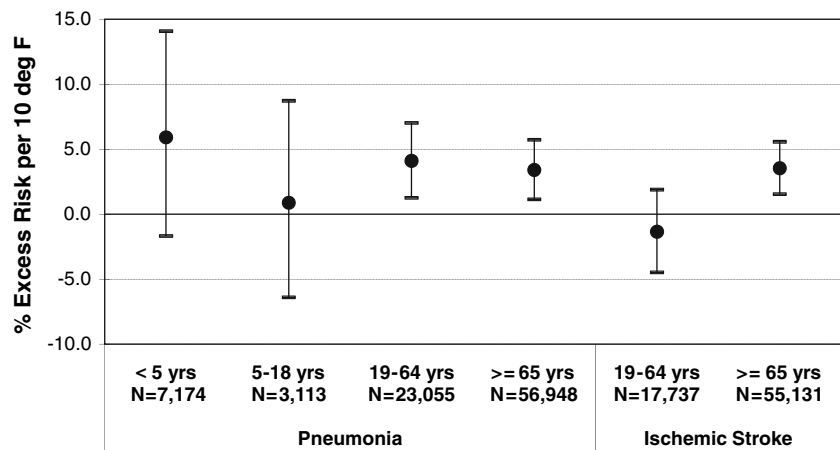
Figure 4 shows the results of the meta-analysis for diabetes and acute renal failure by age. The effect of temperature on diabetes admissions was significant in both the 19–64 year age group and in those ages 65 or greater, with the largest effect in the latter group. Acute renal failure showed a strong positive association with temperature only in the 65 or over age group (excess risk, 10.7%; CI 6.5–15.2%). Our results by race/ethnicity and by gender

Table 2 Meta-analysis results for apparent temperature (lag 0) and hospital admissions, for nine California counties, 1999–2005

Diagnosis	ICD-9 code	Number of cases	Percent excess risk per 10°F (95% CI) ^a
Respiratory diseases			
All respiratory disease	460–519	238,754	2.0 (0.7, 3.2)
All pneumonia	480–486	90,290	3.7 (1.7, 5.7)
Asthma	493	28,944	−1.1 (−4.0, 1.9)
Chronic Bronchitis or Emphysema	491–492	36,588	0.5 (−2.7, 3.8)
Cardiovascular and cerebrovascular diseases			
All cardiovascular disease	390–459	503,585	−0.2 (−1.2, 1.0)
Ischemic heart disease	410–414	158,222	0.9 (−0.3, 2.3)
Acute myocardial infarction	410	57,231	−0.4 (−3.6, 2.9)
Heart failure	428	82,034	−2.0 (−4.7, 0.7)
All cerebrovascular disease	430–438	91,806	−0.3 (−2.3, 1.7)
Hemorrhagic stroke	430–432	13,563	−10.4 (−13.7, −7.0)
Ischemic stroke	433–436	72,954	1.5 (−0.8, 3.8)
Other diseases			
Diabetes	250	50,282	3.1 (0.4, 5.9)
Intestinal infectious disease	001–009	10,985	2.7 (−1.3, 7.0)
Dehydration	276.5	31,235	10.8 (8.0, 13.6)
Acute renal failure	584	17,778	7.4 (4.0, 10.9)
Heat stroke	992	477	404.0 (309.2, 520.8)

^a Percent excess risk (95% CI) per 10°F (5.6°C) using case-crossover approach. Results refer to the baseline model, which includes mean daily apparent temperature and day of week

Fig. 2 Meta-analysis for lag 0 (same day) mean daily apparent temperature [per 10°F (5.6°C)] and percent excess risk for hospital admission for all pneumonia and ischemic stroke, by age, in nine California counties. *N* is the number of cases in each age category



did not uncover any significant effect modification for any outcome considered, and therefore are not shown.

Figure 5 shows the results of the analyses controlling for PM_{2.5} and matching on ozone, for selected outcomes. The unadjusted analyses presented in Fig. 5 include only days with PM_{2.5} data in order to facilitate the comparisons with the data adjusted for PM_{2.5}. The effect estimates for these models with fewer days of observation were slightly lower than the models with all days included for all respiratory disease, pneumonia and diabetes. Adding PM_{2.5} to the base model reduced the effect estimates for all respiratory disease admissions to 0.8% (−0.3 to 1.9%) and for all pneumonia admissions to 2.7%, but the latter remained significant (95% CI 0.6–4.9). With PM_{2.5} in the model, the

effect estimates for ischemic stroke in those 65 years or older and for diabetes increased slightly.

Matching on ozone within 4 ppb had a similar effect on the estimates for all respiratory disease and all pneumonia, but the 95% confidence interval for the pneumonia estimate widened and included zero (Fig. 5). The sample sizes were smaller for the analyses matched on ozone than for the ones where only days with PM_{2.5} data were included. For example, there were 769,126 observations (case- and control-days) on days with PM_{2.5} data and only 214,492 when matched on ozone. There was heterogeneity in the pneumonia results when matched on ozone, with San Diego County and Santa Clara County each showing significant effect estimates of over 12% per 10°F increases in

Fig. 3 Meta-analysis for lag 0 (same day) mean daily apparent temperature [per 10°F (5.6°C)] and percent excess risk for hospital admission for dehydration and for infectious intestinal disease (gastroenteritis), by age, in nine California counties. *N* is the number of cases in each age category

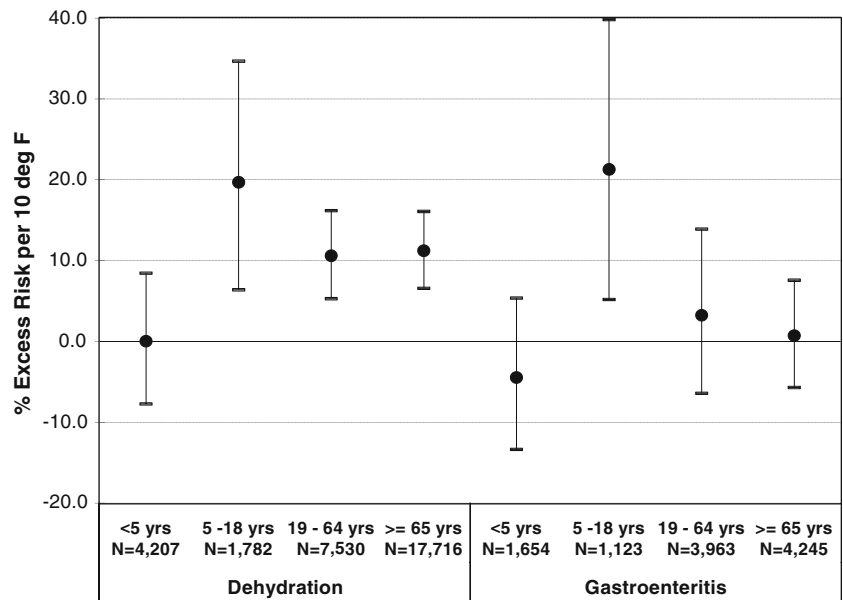
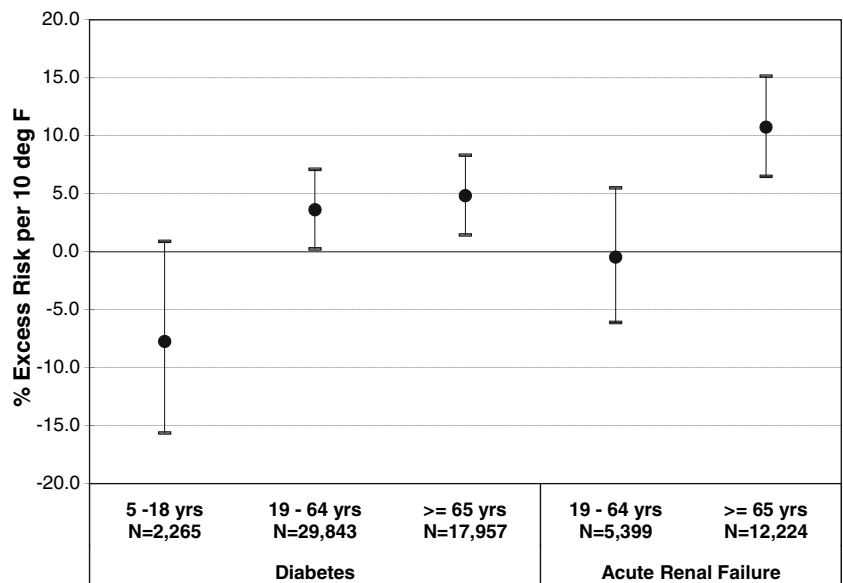


Fig. 4 Meta-analysis for lag 0 (same day) mean daily apparent temperature [per 10°F (5.6°C)] and percent excess risk for hospital admission for diabetes and acute renal failure, by age, in nine California counties. *N* is the number of cases in each age category



temperature. When the model was matched on ozone, the effect estimate for ischemic stroke in those ages 65 and older increased moderately, while the estimate for diabetes increased slightly.

There was little evidence for effect modification by either PM_{2.5} or ozone in this data set. Very few counties showed significant interactions, and the directions of the interaction terms were not consistent. With respect to temperature, there was little evidence of non-linearity of the effect. Neither the square term for temperature nor the interaction variables for temperature above 75°F or temperature in the top 5% were significant for the vast majority of outcomes and counties we examined. For the few counties where we observed significant interactions, the direction of those interactions was not consistent,

Discussion

In our study of nine California counties during the warm season, we observed associations between high apparent temperature and hospital admissions for all respiratory disease, pneumonia, ischemic stroke, diabetes, dehydration, acute renal failure and heat stroke. Most of these associations, but not all, continued to be observed after controlling for ozone and particulate matter, both of which have been shown to be associated with hospital admissions for cardiopulmonary disease. There was little evidence of effect modification by either particulate matter or ozone. In addition, we identified several age subgroups that appear to be particularly susceptible to the effects of high apparent temperatures. While a few previous studies have examined

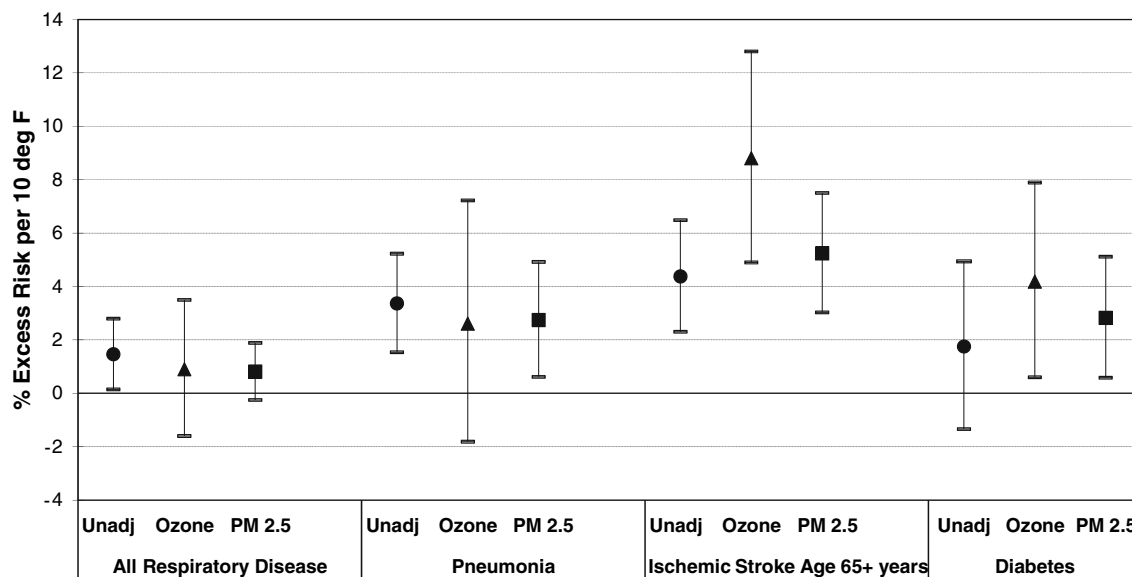


Fig. 5 Meta-analysis for lag 0 (same day) mean daily apparent temperature [per 10°F (5.6°C)] and percent excess risk for hospital admissions unadjusted for pollutants, matched on 1-h maximum ozone [lag 0] (cumulative average of same day ozone and previous

day)] within 4 parts per billion, and adjusted for daily PM_{2.5} (lag 0), by outcome, in nine California counties. Unadjusted analyses include only days with PM_{2.5} data

morbidity during heat waves (Hansen et al. 2008a, b; Knowlton et al. 2009; Semenza 1999; Semenza et al. 1999) we found associations between high ambient temperature and hospital admissions for several causes in periods without identified heat waves. Furthermore, we did not find evidence on non-linearity in the temperature effect.

Our finding of a higher effect estimate in the younger and older age groups for some causes is consistent with our previous study of the effect of temperature on mortality in nine California counties (Basu and Ostro 2008). In the current analysis of hospital admissions, we found that the school-aged children (5–18 years old) group was most susceptible to the effects of temperature on dehydration and intestinal infectious disease. Other studies have found higher effects of air pollution in children who play sports (McConnell et al. 2002), and the effect of high temperature may have been more pronounced in this age group because they are more likely than adults to engage in outdoor activities during the warm months of the year. Our finding of a greater effect of temperature on dehydration and intestinal infectious disease in the 5- to 18-year-old age category is consistent with outbreaks of food-borne illness such as *Salmonella enteritidis* occurring more frequently in the summer in schools and residential institutions (Gillespie et al. 2005). Furthermore, a time-series analysis of salmonellosis in ten European countries found a linear relationship between temperature and the number of reported cases above a threshold of 6°C (Kovats et al. 2004). *Salmonella enteritidis* was the serotype that was most sensitive to the effects of temperature in this analysis.

In this study of hospital admissions we did not find effect modification by race/ethnicity or gender. Our previous study of temperature and mortality in the same nine California counties also did not find differences by gender (Basu and Ostro 2008), but it did find a higher effect of temperature on all-cause mortality in Blacks compared with Whites and Hispanics. Hospital admissions may not be a completely accurate measure of temperature-related morbidity in all racial/ethnic groups because of possible differences in health care utilization. Further studies of temperature using emergency room visits as the measure of morbidity may find differences by race/ethnicity because Blacks are less likely to have regular medical care provision and more likely to seek care in emergency departments (Schappert and Burt 2006).

Our findings of an excess risk of pneumonia are consistent with those seen in a study of the Chicago heat wave in July 1995 (Semenza et al. 1999). In that study, the pneumonia excess was found when combined primary and secondary, but not primary alone, diagnoses were analyzed, while our study examined the primary diagnosis. Reporting differences may have led to our positive finding for pneumonia, as it is up to the admitting physician to determine primary versus secondary diagnosis. Consistent with our findings, a recent time-series study of hospital admissions in 12 European cities found a positive association for high temperature and all respiratory causes (ICD-9 codes 460–519) (Michelozzi et al. 2009).

In this study we did not find an effect of high temperature on hospital admissions for all cardiovascular diseases,

which is consistent with the findings of the recent European study (Michelozzi et al. 2009). However, studies of hospital admissions in other parts of the United States have found some associations. A study of the California heat wave of 2006 (Knowlton et al. 2009) found a slight increase in all cardiovascular diseases for both hospital admissions and emergency department visits. However, that study included both primary and secondary diagnoses, which may have accounted for the difference in their findings compared with ours. Morabito et al. (2005) found that myocardial infarction was associated with 9 h per day of severe discomfort caused by hot climatic conditions. A study of hospital admissions in elderly people in Denver (Koken et al. 2003) found that higher temperatures increased the risk of hospital admission for acute myocardial infarction and congestive heart failure, while decreasing the risk of admission for coronary atherosclerosis and pulmonary heart disease. Schwartz et al. (2004) found an effect of high temperature on hospital admissions for cardiovascular disease in 12 US cities. The effect was smaller for admissions for myocardial infarction specifically. That study also found that there was a suggestion of harvesting at very high temperatures. None of these studies, however, controlled for air pollution effects. Thus, differences from our own null findings may be due to: (1) real differences in population sensitivity; (2) higher apparent temperatures observed in the other studies; or (3) unmeasured effects from highly correlated air pollution exposures.

Among the cardiovascular subgroups, however, we did observe a temperature effect for ischemic stroke in those 65 years and older. This effect was still observed after controlling for both ozone and PM_{2.5}. A study of hospital admissions for acute stroke in Scotland found that ischemic stroke was associated with increase in mean temperature during the preceding 24 h (Dawson et al. 2008), while hemorrhagic stroke was not associated with increase in temperature. This is consistent with our findings of an effect for ischemic, but not hemorrhagic stroke. Since heat has been shown to increase blood viscosity and clotting, it is plausible that the incidence of hemorrhagic stroke may actually be decreased on hot days (Keatinge et al. 1986).

Our finding of an effect of ambient apparent temperature on hospitalization for acute renal failure is consistent with two previous studies conducted during heat waves. An analysis of the Chicago hospitalization data during the summer of 1995 found that a primary diagnosis of acute renal failure was significantly elevated over baseline during the heat wave period (Semenza 1999). A more recent study conducted in Adelaide, a temperate city in South Australia with hot dry summers and mild winters, found that hospital admissions for acute renal failure were increased during heat waves compared with non-heat wave periods, with an

incidence rate ratio of 1.255 (95% CI 1.037–1.519) (Hansen et al. 2008b). A study conducted in California also found an increase in both emergency department visits and hospitalizations for acute renal failure during the heat wave period in 2006 (Knowlton et al. 2009). This association is biologically plausible because heat exposure causes blood to be redistributed away from splanchnic and renal vascular beds, putting additional stress on the renal system (Semenza et al. 1999).

This current study has several strengths. First, very few studies of ambient temperature and morbidity have been conducted during non-heat wave events, and this is the first study to focus on California, where the climate is mild and air pollution levels are high. Most previous studies did not consider multiple outcomes in the same geographic location, such as cardiovascular, respiratory, diabetes, renal failure and heat stroke. To our knowledge, this was the first study to examine the effect of ambient temperature in intestinal infectious diseases, an outcome which may increase in the future due to effects of global warming on food-borne and waterborne diseases (Rose et al. 2001). Second, misclassification of exposure was less likely than in previous studies that used county averages of temperature, since our study was limited to subjects whose residential zip codes were located within 10 km of a temperature monitor. Many counties in California are fairly large, and using a county-level monitor may not accurately capture exposure. Third, we were able to examine many outcomes and population subgroups using a case-crossover analysis. This methodology accounts for individual-level known and unknown confounders since each person acts as his/her own control. Finally, we were able to examine both confounding and effect modification by air pollution for the positive associations between temperature and morbidity that we observed. In our study, controlling for ozone and particulate matter reduced the effect of temperature on respiratory disease in the combined meta-analysis but did not alter the effect estimates for other outcomes which were significantly elevated in the unadjusted analyses. We did not find consistent evidence of effect modification by either pollutant.

There were also some potential limitations to this study. Use of hospital admission data limits the amount of individual-level data. For example, there was no information on air conditioning use in the hospital records. We did not know where people spent most of their time, and work and leisure patterns affect actual exposure to high temperatures. Finally, there may be variation among hospitals and physicians in terms of who gets admitted to hospitals, which diseases are assigned to primary and secondary diagnoses, and in the classification of diseases.

Even without extremes in apparent temperature, we observed an association between temperature and hospital

admissions in California. Reducing heat exposure and mitigating the effects of heat through adequate hydration during hot weather are important steps in reducing heat-related morbidity. In addition, our analysis supports policies aimed at reducing future increases in temperature.

Acknowledgments This work was supported by the California Energy Commission's Public Interest Energy Research (PIER) Program [grant number 500-99-013].

References

- Anderson HR, Atkinson RW, Peacock JL, Sweeting MJ, Marston L (2005) Ambient particulate matter and health effects: publication bias in studies of short-term associations. *Epidemiology* 16:155–163
- Basu R, Ostro BD (2008) A multicounty analysis identifying the populations vulnerable to mortality associated with high ambient temperature in California. *Am J Epidemiol* 168:632–637
- Basu R, Dominici F, Samet JM (2005) Temperature and mortality among the elderly in the United States: a comparison of epidemiologic methods. *Epidemiology* 16:58–66
- Basu R, Feng WY, Ostro BD (2008) Characterizing temperature and mortality in nine California counties. *Epidemiology* 19:138–145
- Dawson J, Weir C, Wright F, Bryden C, Aslanyan S, Lees K, Bird W, Walters M (2008) Associations between meteorological variables and acute stroke hospital admissions in the west of Scotland. *Acta Neurol Scand* 117:85–89
- DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. *Control Clin Trials* 7:177–188
- Environmental Systems Research Institute (1995–2008) Arc GIS Version 9.2. Redlands, California
- Garssen J, Harmsen C, de Beer J (2005) The effect of the summer 2003 heat wave on mortality in the Netherlands. *Eur Surveill* 10:165–168
- Gillespie IA, O'Brien SJ, Adak GK, Ward LR, Smith HR (2005) Foodborne general outbreaks of *Salmonella enteritidis* phage type 4 infection, England and Wales, 1992–2002: where are the risks? *Epidemiol Infect* 133:795–801
- Hansen A, Bi P, Nitschke M, Ryan P, Pisaniello D, Tucker G (2008a) The effect of heat waves on mental health in a temperate Australian city. *Environ Health Perspect* 116:1369–1375
- Hansen AL, Bi P, Ryan P, Nitschke M, Pisaniello D, Tucker G (2008b) The effect of heat waves on hospital admissions for renal disease in a temperate city of Australia. *Int J Epidemiol* 37:1359–1365
- Keatinge WR, Coleshaw SR, Easton JC, Cotter F, Mattock MB, Chelliah R (1986) Increased platelet and red cell counts, blood viscosity, and plasma cholesterol levels during heat stress, and mortality from coronary and cerebral thrombosis. *Am J Med* 81:795–800
- Knowlton K, Rotkin-Ellman M, King G, Margolis HG, Smith D, Solomon G, Trent R, English P (2009) The 2006 California heat wave: impacts on hospitalizations and emergency department visits. *Environ Health Perspect* 117:61–67
- Koken PJ, Piver WT, Ye F, Elixhauser A, Olsen LM, Portier CJ (2003) Temperature, air pollution, and hospitalization for cardiovascular diseases among elderly people in Denver. *Environ Health Perspect* 111:1312–1317
- Kovats RS, Edwards SJ, Hajat S, Armstrong BG, Ebi KL, Menne B (2004) The effect of temperature on food poisoning: a time-series analysis of salmonellosis in ten European countries. *Epidemiol Infect* 132:443–453
- Kovats RS, Johnson H, Griffith C (2006) Mortality in southern England during the 2003 heat wave by place of death. *Health Stat Q* 29:6–8
- Le Tertre A, Lefranc A, Eilstein D, Declercq C, Medina S, Blanchard M, Chardon B, Fabre P, Filleul L, Jusot J, Pascal L, Prouvost H, Cassadou S, Ledrans M (2006) Impact of the 2003 heat wave on all-cause mortality in 9 French cities. *Epidemiology* 17:75–79
- Levy D, Lumley T, Sheppard L, Kaufman J, Checkoway H (2001) Referent selection in case-crossover analyses of acute health effects of air pollution. *Epidemiology* 12:186–192
- McConnell R, Berhane K, Gilliland F, London SJ, Islam T, Gauderman WJ, Avol E, Margolis HG, Peters JM (2002) Asthma in exercising children exposed to ozone: a cohort study. *Lancet* 359:386–391
- Michelozzi P, Accetta G, De Sario M, D'Ippoliti D, Marino C, Baccini M, Biggeri A, Anderson HR, Katsouyanni K, Ballester F, Bisanti L, Cadum E, Forsberg B, Forastiere F, Goodman PG, Hojs A, Kirchmayer U, Medina S, Paldy A, Schindler C, Sunyer J, Perucci CA (2009) High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. *Am J Respir Crit Care Med* 179:383–389
- Morabito M, Modesti PA, Cecchi L, Crisci A, Orlandini S, Maracchi G, Gensini GF (2005) Relationships between weather and myocardial infarction: a biometeorological approach. *Int J Cardiol* 105:288–293
- R Development Core Team R: A language and environment for statistical computing, version 2.5.0. R Foundation for Statistical Computing, Vienna, Austria. Available via <http://www.r-project.org/>. Accessed 23 April 2007
- Rose JB, Epstein PR, Lipp EK, Sherman BH, Bernard SM, Patz JA (2001) Climate variability and change in the United States: potential impacts on water- and food-borne diseases caused by microbiologic agents. *Environ Health Perspect* 109(Suppl 2):211–221
- SAS Institute Inc. (2003) SAS Statistical Software, version 9.1. Cary, NC
- Schappert SM, Burt CW (2006) Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 2001–02. *Vital Health Stat* 13:1–66
- Schwartz J (2005) How sensitive is the association between ozone and daily deaths to control for temperature? *Am J Respir Crit Care Med* 171:627–631
- 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, McCullough JE, Flanders WD, McGeehin MA, Lumpkin JR (1999) Excess hospital admissions during the July 1995 heat wave in Chicago. *Am J Prev Med* 16:269–277
- Stafoggia M, Forastiere F, Agostini D, Biggeri A, Bisanti L, Cadum E, Caranci N, de' Donato F, De Lisio S, De Maria M, Michelozzi P, Miglio R, Pandolfi P, Picciotto S, Rognoni M, Russo A, Scarnato C, Perucci CA (2006) Vulnerability to heat-related mortality: a multicity, population-based, case-crossover analysis. *Epidemiology* 17:315–323
- US Environmental Protection Agency (2006) Air quality criteria for ozone and related photochemical oxidants (final) EPA/600/R-05/004aF-cF, US EPA, Washington, DC
- US Environmental Protection Agency (October 2004) Air quality criteria for particulate matter. EPA 600/P-99/002aF-bF, US EPA, Washington, DC