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Associations between ambient temperature and hepatobiliary and renal hospitalizations in California, 1999 to 2009

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ABSTRACT

Background: High ambient temperature has been linked to a number of types of morbidity, such as cardiovascular disease and dehydration. Fewer studies have explored specifically the relationship between ambient temperature and liver, kidney, and urinary system morbidity despite known biological impacts of extreme high temperatures on those systems.
Objective: We assessed the relationship between temperature and hospitalizations related to selected renal system (urinary stones, urinary tract infections, septicemia, chronic kidney disease, and a composite of selected kidney diseases) and hepatobiliary (biliary tract disease, other liver diseases [e.g. cirrhosis], non-diabetic pancreatic disorders) ailments.
Methods: We compiled data on daily hospitalization counts for hepatobiliary and renal system diseases in California for 1999 through 2009, and matched it with meteorological data. Relationships between temperature and admissions during the warm season (May–October) were assessed at the climate zone-level cumulative over 14 days following exposure using distributed lag non-linear models, with adjustment for time trends and relative humidity, then combined using random-effects meta-regression to create statewide estimates.
Results: Higher mean temperatures in the warm season were associated with significant increases in renal admissions for urinary tract infection [% change per 10 °F: 7.3, 95% CI: 5.6, 9.1], septicemia [% increase: 2.9; 95% CI: 1.5, 4.3], urinary stones [% increase: 15.2; 95% CI: 10.3, 20.4], and composite kidney disease. Additionally, increased temperatures were linked to increased admissions for biliary tract disease, but lower risk of other liver diseases. Some differences in association by race/ethnicity and regional meteorology were observed.
Conclusions: Exposure to higher temperatures was associated with increased risk of multiple renal system hospitalization types, with additional links to specific hepatobiliary morbidities observed.

1. Introduction

Exposure to extreme levels of heat can outpace a person's ability to thermoregulate, resulting in heat stroke, with acute liver and kidney failure being common complications (Davis et al., 2017; Leon and Helwig, 2010). However, not as much is known regarding manifestations of lesser heat exposures on the hepatobiliary and urinary systems. Given the anticipated rise in temperatures related to greenhouse gas emissions (Ipcc, 2014), greater knowledge of the relationship between heat and health is needed to anticipate the resulting changes in illness and better understand consequences from decisions affecting climate-forcing emissions.

Few studies have examined effects of ambient heat exposure on the hepatobiliary system. Seasonal trends have previously been noted for pancreatitis (Gallerani et al., 2004; Räty et al., 2009), though there has been a lack of consistency regarding the timing. Season and temperature have also been implicated in gallstone morbidity (Liu et al., 2014; Reda et al., 2015; Zangbar et al., 2016) and cirrhosis (McNally et al., 2011).

Previous studies have observed seasonal patterns to the occurrence of specific renal morbidities over the year. For example, urinary tract infections and kidney stones had greater incidences observed during the warm season in a number of areas (Geraghty et al., 2017; Rossignol et al., 2013; Simmering et al., 2018). Geographic differences in urolithiasis have also been observed, and appear to coincide with temperature gradients (Fakheri and Goldfarb, 2011). In reference to specifically acute effects, relationships between extreme heat exposure and genitourinary disease have been seen (Bobb et al., 2014; Gasparrini

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et al., 2011; Vaneckova and Bambrick, 2013). Similarly, other categorizations of kidney-related morbidity have been linked with short-term exposures to high temperatures in a number of studies (Borg et al., 2017; Guirguis et al., 2014; Knowlton et al., 2009; Li et al., 2011; Sherbakov et al., 2017).

In this study, we examined possible impacts of temperatures on hospitalizations for renal, hepatic, and pancreatic ailments across California, a state with a large and diverse population and varied climate zones that include coastal regions, inland valleys, mountains, and deserts. We examined geographic differences in health effects as well as how age and race/ethnicity modifies these relationships to identify possible vulnerable populations. Greater knowledge of these relationships between temperature and these outcomes enhances our ability to estimate the current burden of disease related to temperature, develop research into the biological mechanisms relating to temperature health effects, inform intervention strategies to improve heat-related health outcomes in vulnerable populations, and better predict future morbidity and healthcare usage related to climate change.

2. Materials and methods

2.1. Meteorological data

Daily minimum and maximum temperature data for the state of California was obtained from Maurer et al. (2002). This dataset is an observationally-based product comprised of daily station data interpolated to a 12×12 km^2 grid. The source station data are from the National Centers for Environmental Information (NCEI) first-order Automated Surface Observing System and Cooperative Observer (COOP) Summary of the Day (National Climatic Data Center, 2009). For this study, daily mean temperatures were calculated as the average of the observed daily minimum and maximum value. Daily relative humidity data are from the National Centers for Environmental Prediction (NCEP) North American Regional Reanalysis (Messinger et al., 2006). This is an observationally-based reanalysis product that assimilates historical observations into the NCEP Eta dynamical model of the atmosphere via the Regional Climate Data Assimilation System to produce gridded dynamically consistent daily data at a 32×32 km^2 spatial resolution. Reanalyzed humidity data are needed because of the paucity of direct humidity observations over California. With these two datasets, a complete set of temperatures and relative humidity were available for all dates in the study period.

Climate zones (Supplement Fig. 1), subdivisions of California based on factors such as temperature, weather and energy use, were sourced from the California Energy Commission. To each, we assigned zip code tabulation areas (ZCTAs) by estimating their location based on their population-weighted centroid. Based on these locations, each ZCTA is assigned temperature and relative humidity values. Daily exposure means are then calculated, weighted by ZCTA population, to create climate zone-level series of daily exposures.

2.2. Health outcome data

Counts of hospitalizations in California were tabulated from the Office of Statewide Health Planning and Development Patient Discharge Data. Data were limited to unscheduled admissions to acute care facilities. ICD-9-CM diagnoses were grouped into categories of interest based on the Clinical Classification Software (CCS) (HCUP CCS 2017). The outcomes emphasized were biliary tract disease (BTD; e.g. cholelithiasis and cholecystitis) (CCS: 149), other liver disease (151) which includes non-biliary tract, non-cancer, and non-hepatitis liver ailments like cirrhosis, non-diabetes pancreatic disorders (152), chronic kidney disease (CKD) (158), urinary stones (160), urinary tract infection (159), and septicemia (2). Also, to provide an approximate comparison with other studies, we created a kidney disease category combining hospitalizations for nephritis, nephrosis, and renal sclerosis (156), chronic kidney disease (158), and acute and unspecified renal failure (157). Patient locations were estimated using their reported residential zip code, which were matched to ZCTA centroids and their corresponding climate zones. Total counts were compiled by climate zone based on date of admission and diagnosis category. Age (0–18, 19–64, 65+ years) and race/ethnicity-specific counts (White non-Hispanic, Hispanic) were also tabulated, when the sample size permitted, to assess specific associations in larger demographic groups. The research protocol was approved by the California Committee for the Protection of Human Subjects, and a waiver of informed consent was obtained for use of this data collected previously for administrative purposes.

2.3. Statistical analysis

Associations between mean daily temperature and daily counts of hospitalizations were explored using distributed lag non-linear models with R 3.4.3 and the dlnm package (Gasparrini, 2011; R Core Team, 2017). Data were subset specifically to the warm season (May–October) because of our primary interest in warm season relationships. For temperature, a cross-basis matrix was generated by combining functions relating temperature and lag. To explore the acute exposure-response relationship, we tested two dose-response characterizations: 1) a linear function and 2) a natural spline function with 3 degrees of freedom with knot placement at the 50th and 75th percentiles of warm season temperatures to better detect any non-linearity at higher temperatures. For the exposure-lag structure for acute effects, we tested associations over a 14 day period, with internal knots placed between 0 and 1, 2 and 3, and 5 and 6. A version using stratified lag periods with breaks at 1, 3, and 7 was also assessed.

Core covariates of the statistical models included categorical predictors for day of week, a spline of relative humidity (3 degrees of freedom placed evenly over the humidity range) and a spline of time in days over the study period (2 degrees of freedom per calendar year * 11 study years) to model seasonal and long-term time trends. In the second stage, curves were combined via random effects metaregression using the mvmeta package in R. Model fit over statewide models were evaluated using the sum of overdispersion-modified quasi-AICs (qAICs) over the 16 climate zones, with preference given to those with lower sums.

Maximum or minimum temperature were substituted for mean temperature in sensitivity analyses to assess whether those better predicted the relationship. Additionally, mean temperatures were converted to warm season percentile values to test associations with relative temperature values. To investigate the degree of influence temperatures at high extremes exerted, another analysis excluding the top 5th percentile of values was conducted.

For a limited number of outcomes, analyses stratified by age and race/ethnicity were assessed to see whether associations differed by demographic using a test of differences between estimates (Altman and Bland, 2003). Also, climate zone-level variables were evaluated as possible effect modifiers using univariate meta-regression. Those variables included zone-level temperature averages, zone-level standard deviation to represent temperature variability within a region, and an indicator distinguishing coastal and non-coastal climate zones.

3. Results

Mean warm season temperatures for climate zones typically ranged between 65 and 75 °F (Table 1), though the northern coastal climate zone (Zone 1) was notably cooler and the southern desert climate zone (Zone 15) was markedly warmer. Differences between coastal and inland temperatures were evident. For example, the 95th percentile of max temperature for coastal zones did not exceed 90 °F, but all inland zones did and some were in excess of 100 °F for that metric. There was also less variation in temperature within coastal climate zones compared to inland zones, related to higher humidity near the coast.

Table 1
Means (5th and 95th percentile) of meteorologic variables for each California climate zone, May–October 1999–2009.

Climate Zone	Coastal/ Inland	Mean Daily Average Temperature, °F[a] (5th, 95th Percentile)	Standard Deviation of Daily Average Temperature, °F	Mean Daily Minimum Temperature, °F (5th, 95th Percentile)	Mean Daily Maximum Temperature, °F (5th, 95th Percentile)	Mean Daily % Relative Humidity (5th, 95th Percentile)
1	Coastal	57.4 (51.1, 62.9)	3.7	48.8 (41.3, 54.5)	66.0 (58.6, 73.1)	84.7 (74.6, 91.8)
2	Inland	64.6 (55.6, 74.2)	5.5	49.6 (42.5, 55.9)	79.6 (65.5, 93.9)	72.4 (59.1, 84.1)
3	Coastal	62.4 (56.1, 70.2)	4.1	52.9 (47.7, 57.6)	71.9 (63.5, 84.1)	68.5 (52.0, 81.0)
4	Inland	66.9 (57.6, 76.2)	5.6	54.6 (46.5, 61.5)	79.2 (67.0, 92.5)	61.6 (40.3, 78.5)
5	Coastal	62.2 (55.8, 68.5)	4.0	50.9 (44.5, 56.1)	73.4 (65.0, 83.8)	68.5 (53.2, 79.4)
6	Coastal	67.3 (60.5, 74.4)	4.2	58.4 (51.8, 64.3)	76.1 (67.5, 86.7)	72.2 (61.4, 81.2)
7	Coastal	68.8 (61.5, 76.3)	4.5	60.3 (53.1, 66.8)	77.2 (67.6, 87.4)	69.4 (54.4, 78.7)
8	Inland	69.6 (62.0, 77.3)	4.6	60.3 (53.6, 66.3)	78.9 (68.8, 90.1)	63.7 (49.7, 76.9)
9	Inland	70.7 (61.1, 79.4)	5.5	59.0 (51.5, 66.1)	82.3 (69.5, 94.1)	72.4 (61.6, 81.1)
10	Inland	71.9 (60.7, 81.5)	6.4	57.3 (48.7, 65.9)	86.6 (70.5, 98.6)	49.9 (31.0, 69.5)
11	Inland	73.0 (58.6, 84.6)	8.0	58.0 (47.0, 68.4)	88.0 (68.7, 101.4)	42.7 (21.0, 72.5)
12	Inland	71.1 (59.4, 81.9)	6.8	56.0 (47.1, 64.9)	86.2 (70.2, 99.8)	47.7 (27.7, 70.5)
13	Inland	75.5 (60.9, 87.0)	8.1	60.3 (48.3, 71.5)	90.7 (73.0, 103.3)	31.7 (16.2, 57.1)
14	Inland	73.9 (58.0, 85.5)	8.6	57.7 (43.7, 70.1)	90.1 (71.4, 102.3)	30.3 (16.9, 51.1)
15	Inland	83.8 (68.6, 94.8)	8.1	68.1 (54.7, 80.5)	99.5 (82.1, 110.7)	26.1 (12.5, 44.7)
16	Inland	62.0 (47.3, 72.9)	8.0	45.5 (34.1, 55.8)	78.4 (60.1, 90.8)	44.1 (28.9, 66.3)
Overall	–	68.8 (55.8, 84.7)	8.8	56.1 (44.1, 68.7)	81.5 (64.9, 101.2)	56.6 (21.3, 83.8)

Abbreviations.
[a] °F = (9/5) * °C + 32.

Table 2
Mean daily counts of hospitalization by climate zone for the outcomes studied, 1999–2009.

Climate Zone	Estimated population	Kidney Disease	CKD	Septicemia	UTI	Urinary Stones	Biliary Tract Disease	Other Liver Disease	Pancreatic Disorders
1	177,820	0.3	0.0	0.9	0.5	0.1	0.5	0.2	0.4
2	919,141	1.6	0.1	3.9	2.7	0.6	2.5	0.8	1.7
3	3,829,327	7.3	0.3	15.2	12.1	2.2	10.1	3.2	6.8
4	1,909,081	2.4	0.1	5.8	5.1	1.1	4.6	1.4	2.9
5	378,221	0.4	0.0	1.3	1.2	0.2	0.9	0.3	0.7
6	2,812,446	4.5	0.2	11.1	10.3	2.1	7.5	2.2	5.4
7	2,090,070	3.1	0.2	6.6	6.4	1.0	5.1	1.6	3.7
8	4,547,879	7.7	0.4	19.1	19.4	3.6	14.6	4.3	10.2
9	5,938,357	10.8	0.5	29.0	24.8	5.3	18.9	6.3	12.0
10	3,714,599	6.0	0.3	14.0	12.8	2.7	10.4	3.5	7.6
11	986,357	2.1	0.1	4.7	4.1	1.0	3.4	0.9	2.4
12	4,554,803	8.2	0.3	17.3	14.4	3.4	12.2	3.8	9.1
13	2,204,797	4.4	0.2	8.3	8.3	1.7	6.7	2.6	5.4
14	894,505	1.8	0.1	3.5	3.2	0.9	2.9	0.9	2.2
15	595,642	1.2	0.1	1.9	2.4	0.5	2.2	0.8	1.4
16	436,777	0.6	0.0	1.2	1.3	0.4	1.2	0.4	1.0
All	35,989,818	62.5	2.9	143.6	128.8	26.6	103.6	33.2	72.9

Among the outcomes we examined, the most common were infection-related, specifically UTI and septicemia, averaging more than eight daily visits across the state, while CKD was most rare (Table 2). For most of these outcomes, the majority belonged to persons between 19 and 64 years of age, though the majority of UTI and septicemia belonged to those 65 years and older. Juvenile cases (0–18 years old) comprised less than 10% of cases for all outcomes except UTI (12%). White non-Hispanic was the largest race/ethnicity represented, ranging from 41% (CKD) to 63% (urinary stones) of cases, depending on the outcome. Hispanic was the second largest group, representing between 20 and 37% of outcome-specific cases. For most categories, incidences were typically higher in inland climate zones.

Models using a linear exposure-response and stratified lag formulations were the best fit for all outcomes except for composite kidney disease, and results from those models are our focus going forward. Among specific renal morbidity categorizations, we observed statistically significant increases in septicemia (% change with 10 °F increase: 2.9; 95% CI: 1.5, 4.3), urinary tract infections (% increase: 7.3; 95% CI: 5.6, 9.1), and urinary stones (% increase: 15.2; 95% CI: 10.3, 20.4) (Table 3over 14 days following increased temperatures. Risk of CKD hospitalizations also trended higher, but with a greater degree of uncertainty around that estimate. The composite kidney category was also significantly higher at the high temperature point. When specifying a spline for describing the exposure-response, which was reported as the better fit using qAIC, the risk was greater (% increase from median to 95th percentile: 16.3%; 95% CI: 11.0, 21.7) compared to a 11.1% increase (7.5, 14.9) from our default model using a linear relationship. Increased temperatures were related to increases in biliary tract disease (% increase: 3.6%; 95% CI: 1.9, 5.3) but decreases in "other liver outcomes" (% increase: -5.3%; 95% CI: -8.0, −2.5). Pancreatic disorders were not strongly related to temperature.

Table 3
Cumulative effect estimates over a 14-day period associated with a 10 °F increase in mean temperature during the warm season.

Outcome	% change per 10 °F increase	P-value
Biliary Tract Disease	3.6 (1.9, 5.3)	< .001
Other Liver Diseases	−5.3 (−8.0, −2.5)	< .001
Kidney Disease	12.9 (8.7, 17.3)	< .001
CKD	8.0 (−2.5, 19.6)	0.14
Urinary Stones	15.2 (10.3, 20.4)	< .001
UTI	7.3 (5.6, 9.1)	< .001
Septicemia	2.9 (1.5, 4.3)	< .001
Pancreatic Disorders	1.3 (−0.8, 3.3)	0.23

When examining the exposure-response over the lag period, a

Table 4
Cumulative effect estimates associated with a 10 °F increase in warm season temperature, stratified by race/ethnicity and age, for the most common outcomes.

Outcome	Demographic Category	Stratum	N	% change for 10 °F increase	p(difference)
Biliary Tract Disease	Race/Ethnicity	White NH	96,976	2.3 (−0.2, 4.8)	0.21
		Hispanic	78,599	4.6 (1.9, 7.4)	
	Age	19-64	138,216	3.5 (0.7, 6.4)	0.76
		65+	65,891	4.1 (1.1, 7.3)	
UTI	Race/Ethnicity	White NH	141,851	5.2 (2.6, 7.9)	0.02
		Hispanic	71,499	10.1 (7.0, 13.3)	
	Age	0-18	32,439	6.1 (−0.1, 12.8)	0.64
		19-64	82,062	7.9 (5.0, 10.8)	(ref)
		65+	146,205	7.1 (4.6, 9.7)	0.71
Septicemia	Race/Ethnicity	White NH	165,316	2.4 (0.6, 4.2)	0.02
		Hispanic	61,999	6.4 (3.5, 9.5)	
	Age	19-64	93,845	3.2 (0.9, 5.7)	0.62
		65+	184,551	2.5 (0.5, 4.4)	

number of the outcomes (i.e. kidney disease, urinary tract infections, septicemia) showed the strongest relationship with temperature on the same day) (Supplement Fig. 2). Surprisingly, this includes “other liver diseases”, which showed significantly higher same-day hospitalizations, but also significantly lower hospitalizations in the days following, ending in a cumulatively negative association. Associations with other outcomes had a greater delay, specifically urinary stones which peaked 1–3 days subsequently, and biliary tract disease which was elevated both then and 7–14 days after.

Converting mean temperature to climate zone-specific percentile values did not appear to enhance model fits. Similarly, use of minimum and maximum temperature values resulted in similar model preferences and associations. In our sensitivity analyses testing how high temperature extremes impacted this association, we found that associations persisted even after eliminating days in the top 5th percentile for each zone.

For the more common outcomes (i.e. biliary tract disease, UTI, and septicemia), analyses stratified by race/ethnicity and age group showed that most associations were still observable in each stratum (Table 4). While associations were still strong in both strata, we observed higher associations among Hispanics compared to non-Hispanic white, with increases of 10.1% (95% CI: 7.0%, 13.3%), 6.4 (95% CI: 3.5%, 9.5%), and 4.6% (95% CI: 1.9%, 7.4%) in UTI, septicemia and biliary tract disease, respectively, per 10 °F increase in temperature (Table 4). Differences in effect by age were less pronounced, with UTI and septicemia morbidity increased relatively more for the 19–64 age group than the 65+ group, while biliary tract disease increased relatively more in the 65+ group.

In meta-regression analyses, we observed evidence that climate zones with higher variation, as represented by standard deviation in mean temperature, had weaker associations between temperature and both urinary stones ($p = 0.02$) and urinary tract infections ($p = 0.08$). Temperature impacts on biliary outcomes seemed to be stronger in coastal regions ($p = 0.04$). Climate zones with lower mean temperatures tended to report larger negative temperature associations with other liver diseases.

4. Discussion

Our results point to a link between higher ambient temperatures and increases in hospital admissions for a number of renal illnesses, and biliary tract disease, though other liver diseases were negatively associated. For infection-related outcomes, admissions for Hispanics appeared more sensitive to temperature increases. Regional climate also appeared to alter some of the temperature-hospitalization relationships we observed.

Bobb et al. (2014) observed links between heat waves and hospital admissions for urinary tract infections and septicemia hospitalizations, albeit specifically in older adults, in parallel with what we observed for higher temperatures. However, septicemia is caused by multiple pathogens, entering via a number of possible routes, which may behave differently under influences of temperature. For example, one study estimated more than a third of severe sepsis to originate from a respiratory site, while around 15% started in the genitourinary system (Mayr et al., 2010). A study examining more pathogen-specific diagnoses did not find strong links to specific pathogens (Hopp et al., 2018). Daily temperatures were also linked to urinary tract infection admissions, and more specifically lower urinary tract infection admissions in Australia (Borg et al., 2017). They hypothesized that this was possibly a result of increased urinary bacterial load, decreased flushing of bacteria via urination, and changes to urinary pH that may be more hospitable for certain bacteria.

Among the findings we report, the relationship to urolithiasis is the one best corroborated by other studies. Fletcher et al. (2012) linked high daily temperatures in the summer with hospital admissions in New York State, and Ross et al. (2018) observed strong relationships between wet bulb temperature and kidney stone hospital visits in South Carolina. Tasian et al. (2014) observed higher mean temperatures with kidney stone presentation in 5 U.S. cities as identified through a commercial claims database that also covers outpatient visits. Borg et al. (2017) linked daily temperature to both urinary stone emergency visits and inpatient admissions in Australia; Condemi et al. (2015), Ordon et al. (2016), and Chi et al. (2017) see daily relationships for kidney stones and renal colic in cities in Italy, Canada, and Korea, respectively. Possible reasons include the fact that dehydration may be linked to increased urine calcium and super-saturation of calcium oxalate and calcium phosphate from the body’s choice to conserve electrolytes during heat stress, promoting solid aggregation (Borg et al., 2017; Eisner et al., 2012; Masterson et al., 2013).

Our findings linking higher temperatures and kidney impacts join a number of previous studies. Fletcher et al. (2012) found links between temperature and broader renal disease. Winquist et al. (2016) similarly observed increases in overall renal disease emergency visits, and more specifically, nephritis/nephrosis visits, as have extreme heat/heat wave studies previously conducted (Chen et al., 2017; Isaksen et al., 2015; Knowlton et al., 2009). These categorizations are likely dominated by acute kidney injury, which has also been studied and strongly linked to temperature in California (Sherbakov et al., 2017). The broader categorization we used for closer comparison, combining related kidney CCS groups, yielded similarly strong associations. One possible pathway may involve volume depletion from excessive sweating (Rahman et al., 2012). Blood pressure is also typically reduced in hotter weather (Halonen et al., 2011a). With this combination, less blood is filtered and the glomerular filtration rate decreases, which may lead to acute kidney injury (Hsu and Hsu, 2011). Kidney stones and urinary tract infections, mentioned in previous paragraphs, are also linked to nephritis and acute renal failure (Hsiao et al., 2015; Rahman et al., 2012). While our study observed that CKD hospitalizations trended higher with higher temperatures, that finding was not significant though our ability to detect that relationship was weaker due to its rarity. A stronger link was observed in a study in South Australia (Borg et al., 2017), while a New York study reported weak evidence of that relationship (Fletcher et al., 2012). In investigations of CKD mechanisms, biomarkers of kidney injury have been observed with occupational exposures to high temperature in places such as Central and South America, India, and Sri Lanka (Garcia-Trabanino et al., 2015; Glaser et al., 2016; Laws et al., 2016; Wesseling et al., 2016), and specifically in California (Moyce et al., 2017) despite differing climates. These occupational studies imply that excessive exposure to high temperatures, at least when paired with high levels of physical exertion, can have dramatic impacts on renal system health. Proposed pathways for this include increased vasopressin in response to volume depletion and tubular injury via repeated stimulation of the aldose reductase pathway, and increased urea causing tubular damage (Roncal-Jimenez et al., 2015).

Biliary tract disease hospitalizations, which we linked to temperature, are typically dominated by cholelithiasis and cholecystitis, which is often related to cholelithiasis. Connections between temperature and gallstones are less developed. Gallstones may be a sign of alterations in cholesterol synthesis, and previous studies have observed a link between ambient temperature and serum cholesterol levels (Basu et al., 2016; Halonen et al., 2011b; Sartini et al., 2017).

Similarly, few studies have explored relationships between liver disease and temperature. Contrary to our observations, Bobb et al. (2014) did not specifically observe links between biliary tract disease and heat wave days. Our study might be more sensitive to such a relationship because our analysis focuses on continuous temperature and incorporates lagged effects. Among our category of "other liver diseases", cirrhosis and hepatic encephalopathy were the dominant diagnoses. Chan and colleagues did not observe a link between temperature and cirrhosis hospitalizations or mortality in Hong Kong (Chan et al. 2012, 2013). However, a study of the alcohol-attributable fraction of cirrhosis was inversely correlated with temperature regionally, possibly due to a similar correlation between temperature and proportion of heavy episodic drinking and total drinkers (Ventura-Cots et al., 2018).

Our analysis identified increased vulnerability of Hispanic subgroup to morbidity from UTI, septicemia, and biliary tract disease associated with heat. Similarly, Fletcher et al. (2012) also reported increased hospitalization for acute renal failure for Hispanics, in addition to Blacks and those in the lowest income category. However, such differences for that outcome have been less evident in California (Green et al., 2010; Knowlton et al., 2009). Increased vulnerability to temperature in these groups may be attributed to factors including poorer baseline health status, greater linguistic isolation, and less air conditioner use among these subgroups (Gronlund, 2014).

In regards to effect modification by age, some previous studies have reported indications of greater increases in ER or hospitalization rates of renal diseases associated with heat in younger populations (Borg et al., 2017; Fletcher et al., 2012; Isaksen et al., 2015; Knowlton et al., 2009). This could be due to a number of reasons. Younger populations may be more subject to occupational heat exposure or engage in intense exercise, which leads to acute dehydration-predisposing outcomes, while the elderly were less likely exposed to such exposure and their symptoms tend to be more gradual (Borg et al., 2017; Davis et al., 2017). Furthermore, increased heat-related circulatory and cardiovascular mortality and morbidity have been observed among older adults (Isaksen et al., 2015), which may act as competing risks with kidney issues during periods of increased temperature. In contrast, heat stress results in severe hepatic oxidative damage in older animals, which has been documented in toxicological studies (Hall et al., 2000; Zhang et al., 2003). We observed significant positive associations of UTI, septicemia, and biliary tract disease, with heat in both 19–64 and 65+ age groups, but only marginally higher associations for UTI and septicemia in younger group and slightly higher association for BTD in older group.

In our meta-regressions, we observed some limited evidence that areas with less temperature variation showed stronger associations between high temperatures and UTI and urinary stones. Other papers have observed similar evidence (Medina-Ramon and Schwartz, 2007; O'Neill and Ebi, 2009). In California, the coastal regions exhibit lower temperature variance overall due to modulation by the Pacific Ocean. However, coastal heat waves have been shown to be more intense relative to the mean summer climate (Guirguis et al. 2018a,b) due to the episodic retreat of coastal clouds during an onset of a southwestern heat wave (Clemesha et al., 2018), or when heat waves occur due to Santa Ana winds, mainly outside of the warm season. Thus the association we observed could represent a combination of factors including differing timing/clustering of high temperature days, a lack of biological acclimatization in these regions, and decreased availability or usage of mitigation measures, such as residential air conditioning, which has been shown to affect health outcomes during heat events in southern California (Guirguis et al., 2018).

Our study design induces a number of shortcomings that should be mentioned. Exposures are estimated at the climate-zone level and related to temperature counts at that level, and we made efforts to population-weight daily temperatures to better describe them. However, individual experiences of ambient temperature within a climate zone are obviously not uniform, so some exposure misclassification is expected. In addition to differing residential locations within a climate zone, an individual's time indoors, mitigative efforts during hot weather, and movement away from the residence can alter the degree of relevance for these temperature estimates. Also, average temperature was estimated by using a day's minimum and maximum temperature, and may not be a truly accurate measure of mean temperature. However, minimum and maximum temperature which were more accurately assessed did not appear to improve the model. Additionally, our analysis did not differentiate between early and late season temperatures, and timing has been related to sensitivity to temperature effects in other studies (Anderson and Bell, 2011). Our database did not permit the ability to differentiate repeat visits by the same person, so some individuals are represented more than one time.

5. Conclusions

We observed evidence of a relationship between warm season ambient temperatures and urinary, biliary tract, and kidney disease hospitalizations. This and other studies examining temperature associations with morbidity outcomes should foster a greater understanding of how environmental conditions, and the factors that change them, may impact health. Additionally, a sensitivity analyses showed that temperature relationships persisted even after eliminating the hottest 5% of days from each region, providing further evidence that these effects should be considered even during periods of moderately high temperatures. Also, we provide some evidence that demographic and regional factors may influence those relationships, and those factors merit consideration when evaluating impacts.

Declarations of interest

None.

Disclaimer

The views expressed here are those of the authors and do not necessarily represent those of the Office of Environmental Health Hazard Assessment, the California Environmental Protection Agency, or the State of California.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2019.108566.

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