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Susceptibility to heat-related fluid and electrolyte imbalance

emergency department visits in Atlanta, GA

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Abstract

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Background

Increases in morbidity and mortality from increasing temperatures are some of the most likely primary health impacts of climate change. It is critical to identify potentially susceptible populations to heat morbidity for targeted prevention and more accurate risk assessment. Fluid and electrolyte imbalance (FEI) may provide an especially sensitive and objectively measurable indicator of heat morbidity.

Objective

To examine heterogeneity of heat-morbidity associations by determinants of heat vulnerability (sex, race, comorbid congestive heart failure, kidney disease, and diabetes, and neighborhood socioeconomic conditions defined by poverty and education levels), focusing on FEI emergency department (ED) visits, and to explore associations of temperature and FEI ED visits considering a variety of temperature metrics.

Methods

Associations of warm-season (May-September) same-day temperatures and FEI ED visits were estimated using Poisson generalized linear models allowing for overdispersion; data were from a 20-year daily time series spanning 1993-2012 in Atlanta, GA. Analyses explored associations between all FEI ED visits and different temperature metrics (maximum, minimum, average, and diurnal change in ambient temperature, apparent temperature, and heat index), modeled using linear, quadratic, and cubic terms to allow for non-linear associations. Analyses by strata of determinants of heat vulnerability examined potential heterogeneity of effects for both maximum temperature (TMax) and maximum apparent temperature (ATMax).

Results

Ambient temperature was significantly associated with FEI ED visits regardless of the metric used to define temperature; for example, we found an RR of 1.125 (95% CI: 1.102, 1.150) per interquartile range increase in maximum temperature from the 25^{th} to 75^{th} percentile. Modifier-stratified analyses suggested that risks are great for all populations, but perhaps particularly for males and possibly for nonwhite groups (e.g., Hispanics) and those living in undereducated areas. We found some unanticipated patterns of effect modification in that for the comorbidities, there was a tendency for the 'absent' strata to have stronger associations than 'present' strata, with significant differences observed for comorbid renal disease.

Conclusion

This work highlights the utility of FEI as an indicator of heat morbidity that affects all populations, the health threat posed by warm season temperatures, and considerations regarding assessment of vulnerable populations in heat-health research.

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Introduction

Climate change and the health burden of extreme heat

Climate change is predicted to increase the intensity, frequency, and duration of extreme heat events (Meehl and Tebaldi 2004), as well as increase global temperatures. Increases in morbidity and mortality from these heat events are some of the most likely primary health impacts of climate change (Johnson and Wilson 2009; Knowlton et al. 2009).

By characterizing heat-health associations, we can identify factors conferring susceptibility and vulnerability to heat, which can provide critical information to risk assessment and targeted prevention efforts. Because the physiological mechanism of dehydration plays an important role in health-related illnesses, and makes them largely preventable, fluid and electrolyte imbalance (FEI) emergency department (ED) visits may be a sensitive indicator of population morbidity due to heat.

Heat-related Mortality

The most deadly weather event in the United States is heat, even more so than tornadoes, heavy rains/floods, hurricanes, hail, wind storms, lightning, winter storms, and cold (Chagnon et al. 1996; Hattis et al. 2012; Luber and McGeehin 2008). Between 1979 and 1999, heat exposure lead to 8,015 deaths, according to the Centers for Disease Control and Prevention (Hattis et al. 2012). Certain groups are at higher risk than others for heat mortality. Basu found that epidemiological studies of high ambient temperature published between 2001-2008 reported elevated risk for mortality for cardiovascular disease, respiratory disease, cerebrovascular disease, diabetes, and pre-existing psychiatric disorders (Basu 2009). Studies of heat mortality provide evidence that those of black or non-white racial groups are at increased risk (Basu 2009; Medina-Ramón et al. 2006). There is mixed evidence with respect for sex and heat mortality: two reviews found evidence that females are at greater risk than males (Basu 2009), but another study found no difference in the effect of temperature between females and males (O'Neill 2003). A study of temperature and mortality in 11 US cities found indicators for education and poverty to be important effect modifiers (Curriero et al. 2002), and stronger associations for extreme temperature-related mortality have been observed for the less educated (high school education or less) at an individual level as well as at a neighborhood level compared to those with more education (O'Neill 2003).

A challenge to identifying the true health impact of heat on mortality is related to pre-existing medical conditions, which are more likely to be listed on death certificates than heat as the cause of death, but which make individuals more susceptible to heat. The variability in definitions of heat-related illness is another challenge (Chagnon et al. 1996). For example, estimates of heat mortality are likely underestimates, since death certificates may not list "heat stress" even if the heat was the underlying cause (Kinney et al. 2008). Moreover, heat exposure may not only initiate a process that results in death, but may be a cause of significant non-deadly morbidity that should be considered as part of estimating heat health impacts. Studies focusing on heat morbidity may provide a broader picture of the health effects attributable to heat than heat mortality. Furthermore, since heat-related deaths and illnesses are preventable, it is worthwhile to target a health outcome closer to the level of prevention.

Heat-related Morbidity

Studies of emergency department (ED) visits and hospital admissions have demonstrated the burden of heat morbidity (Basu et al. 2012; Green et al. 2010; Knowlton et al. 2009; Pudpong and Hajat 2011; Schwartz et al. 2004; Semenza et al. 1999; Turner et al. 2012; Ye et al. 2012). A study from the National Electronic Injury Surveillance System-All Injury Program demonstrated that of the 26,527 annual ED visits between 2001-2004 for environmental/weather-related exposures (defined as: heat, environmental cold, fires/storms/flood, and lightning), heat accounts 78% (20,775) annually (Sanchez et al. 2010). Of these heat-related illness ED visits, the most common types were heat exhaustion (73.1%) dehydration (7.6%), and heatstroke (3.6%) (Sanchez et al. 2010). Health care utilization data also capture exacerbations of existing underlying disease or symptoms. ED visits and hospitalizations for conditions exacerbated by heat exposure and associated with increased temperatures and heat waves include heart disease, diabetes, and renal disease (Basu et al. 2012; Green et al. 2010; Hansen et al. 2008; Knowlton et al. 2009; Li et al. 2015; Pillai et al. 2014; Schwartz et al. 2004; Semenza et al. 1999).

Heat may aggravate these conditions through the physiological mechanism of dehydration, which inhibits circulation necessary for the body to cool itself in hot conditions (McGeehin and Mirabelli 2001). FEI morbidity has shown strong associations with warm season temperatures in previous analyses in Atlanta (Winquist et al. 2016) and other locations (Basu et al. 2012; Green et al. 2010; Knowlton et al. 2009). A diagnosis of FEI suggests general dehydration (El-Sharkawy et al. 2015), but the full group of ICD-9 codes for FEI (276) include: hyperosmolality and/or hypernatremia, hyposmolality and/or hyponatremia, acidosis, alkalosis, mixed acid-base balance disorder, volume depletion (includes dehydration), fluid overload, hyperpotassemia, hypopotassemia, and electrolyte and fluid disorders not elsewhere classified (includes electrolyte imbalance, hyperchloremia, hypochloremia) (ICD-9-CM Tabular List of Diseases, FY07). These disorders of FEI can be quickly and objectively established by measuring a patient's electrolytes and acid–base status, taken in combination with their history and clinical presentation (Weiss-Guillet et al. 2003). FEI may serve as a sensitive indicator of population morbidity due to heat, especially considering that dehydration is part of the diagnosis for heat exhaustion, and may lead to heat stroke (Jardine 2007). However, it is not clearly supported that FEI *alone* causes heat illnesses (defined as heat cramps, heat exhaustion, or heat stroke) (Noakes 1998); FEI may be part of a more complex relationship between heat and other health outcomes. Some populations are especially prone to FEI, such as patients with diabetes mellitus (Ito et al. 1989), renal failure (Allison and Lobo 2004), congestive heart failure (Dei Cas et al. 1995;

Milionis et al. 2002), and myocardial infarctions (Goldberg et al. 2006; Goldberg et al. 2004), and may thus present a pathway for increased susceptibility to heat for these patients.

Susceptible populations

While there is evidence for morbidity related to heat, there is limited information on potentially sensitive subpopulations for FEI specifically. Assessing patterns of association for certain population characteristics may assist with identifying sensitive subpopulations, which may ultimately aid in targeted prevention efforts and provide information for more accurate risk assessment. There is evidence that susceptibility to heat differs for a number of individual-level factors, such as age (Basu 2009; Choudhary and Vaidyanathan 2014; Hess et al. 2014; Medina-Ramón et al. 2006; Mo et al. 2014), sex (Bai et al. 2014; Basu 2009; Choudhary and Vaidyanathan 2014; Hess et al. 2014), race (Kaiser et al. 2007; Medina-Ramón et al. 2006; O'Neill 2003; O'Neill et al. 2008; O'Neill et al. 2005), as well as community-level factors, such as socioeconomic status (Hess et al. 2014; Kinney et al. 2008). While FEI represents an important heat-related outcome that can affect all populations, previous studies assessing susceptibility to heat have generally not considered FEI morbidity.

Furthermore, susceptibility to heat may also differ by presence of co-morbid/pre-existing conditions. For example, some populations who experience FEI have underlying health conditions, such as congestive heart failure (Dei Cas et al. 1995; Milionis et al. 2002), kidney disease (Claure 2012; Mahaldar 2012), or diabetes (Sotirakopoulos et al. 2012), that that have also shown associations with heat (Basu et al. 2012; Green et al. 2010; Medina-Ramón et al. 2006; Schwartz 2005; Semenza et al. 1999; Winquist et al. 2016). It is possible that underlying diseases such as these exacerbate patients' risk of dehydration with high temperatures. To our knowledge, no previous studies have examined this question.

Objectives

Heterogeneity of Heat-Morbidity Associations

Previous work in Atlanta found strong associations of warm season temperature and FEI emergency department visits, with strongest effects observed among patients in the 19-64 year old age group (Winquist et al. 2016). The present study expands on this analysis to examine heterogeneity of heat-morbidity associations by determinants of heat vulnerability (sex, race, comorbid congestive heart failure, kidney disease, and diabetes diagnoses, and neighborhood socioeconomic conditions as defined by poverty and education levels), with a specific focus on FEI. In order to test the hypothesis that populations with determinants of heat vulnerability are at greater risk of an ED visit for FEI than those without determinants of heat vulnerability, the present study explores and compares the heat morbidity relationship for each stratum of the determinants of heat vulnerability.

Exposure Metrics

Studies have used a variety of different temperature metrics to define heat exposure for different reasons. Evidence suggests that apparent temperature is the best temperature indicator for mortality during extreme heat events (Green et al. 2010; Ho et al. 2016; Mastrangelo et al. 2007; Michelozzi et al. 2009). Other popular heat exposure metrics are the daily or two-day averaged minimum or maximum air temperatures (Hajat et al. 2010; Ho et al. 2016; Kosatsky et al. 2012; Linares and Diaz 2008; Martiello and Giacchi 2010; Smargiassi et al. 2009). Heat-trapping urban environments intensify heat stress by preventing overnight cooling, which is indicated by minimum air temperature (Khalaj et al. 2010; Martiello and Giacchi 2010). Average temperature most likely represents the experience of the entire day and night (Hajat et al. 2002; Kovats et al. 2004). ED visits for cardiovascular and respiratory diseases have been shown to be positively associated with diurnal temperature range when it was above a certain range (Liang et al. 2008; Liang et al. 2009). Because each measure of temperature may be suited for certain scenarios, a secondary objective of the present study is to explore the heat-morbidity relationship for FEI for different exposure metrics.

Methods

Emergency department visit data for 20-county Atlanta spanning the period 1/1/1993-12/31/2012 were previously collected for the Studies of Particles and Health in Atlanta (Darrow et al. 2012; Metzger et al. 2004; Peel et al. 2005; Sarnat et al. 2010; Strickland et al. 2010; Tolbert et al. 2000; Winquist et al. 2016). Briefly, data on ED visits to hospitals in the Atlanta metropolitan area were obtained from individual hospitals (for the period 1993-2004) and from Georgia Hospital Association (for the period 2005-2012). Data elements of specific interest to this analysis were admission date, primary and secondary International Classification of Diseases 9th Revision (ICD-9) diagnosis codes, patient age, sex, race, and ZIP code of residence. Data were restricted to patients whose ZIP code was at least partially within one of the 20 counties in the Atlanta metropolitan area. Use of the emergency department data was in accordance with agreements with the hospitals and the Georgia Hospital Association, and this study was approved prior to its conduct by the Emory University Institutional Review Board.

ED visits for FEI were identified as visits with a primary ICD-9 diagnosis code of 276. These data were aggregated to daily counts of ED visits for FEI overall, and for strata of potential heat vulnerability determinants: patient sex (female/male), patient race [non-white (black/Hispanic/other)/white], the presence (yes/no) of underlying congestive heart failure (ICD-9 code 428), kidney disease (ICD-9 codes 580-593), and/or diabetes (ICD-9 code 250 or 249 on or after 10/1/2008), identified via the presence of ICD-9 codes for these conditions in secondary diagnosis variables. Daily FEI ED visit counts were also stratified by area-level socioeconomic indicators of poverty and education using ZIP code tabulation area (ZCTA; Census Bureau boundaries created from census blocks to approximate ZIP codes) information from the 1990 and

2000 US Census long form and the American Community Survey (ACS) 5-year (2007-2011) summary file, all normalized to 2010 ZCTA borders ("The Time-Series Research Package," GeoLytics, Inc., East Brunswick, NJ, 2013). Data from different time points were used to account for possible changes in area-level SES over the 1993-2012 study period. We assumed that any changes occurred gradually, and thus assigned values of each SES variable to each ZCTA by year, weighted by proximity in time to the data source (e.g., in 2002, ZCTAs were assigned SES indicator values averaged as $^5/_7$ Census 2000 data and $^2/_7$ ACS data; in 2007 and later years, ZCTAs were assigned values with full weight given to ACS data). These data were merged with ZIP code level ED data by year. To do so, each ZIP code in the ED visit dataset was assigned to one of 191 ZCTAs. Assignments were accomplished by matching ZIP-to-ZCTA ID numbers and verifying locations of ZIP code centroids via ZCTA map shape files in ArcGIS. Ultimately, for the current analysis, daily counts of ED visits for FEI were aggregated by 'poverty area' defined as ZCTAs with ≥ 20% of the population living below the federal poverty line (yes/no), and 'undereducated area' defined as ZCTAs with ≥ 25% of the adult population without a high school graduation (yes/no).

The analyses for the current study were restricted to the warm season, as defined by the period from May to September. Meteorological data, including daily metrics (maximum, minimum, average, and diurnal change) for ambient temperature and dew point temperature, were collected from the National Climatic Data Center station at Atlanta Hartsfield International airport. Apparent temperature, a measure that combines temperature and humidity, was calculated using these data (Steadman 1984). We also considered the heat index as calculated using the National Weather Service approach (Anderson et al. 2013).

Associations of warm-season temperatures and FEI ED visits were estimated using Poisson generalized linear models allowing for overdispersion. We assessed and compared associations of different temperature metrics, including: maximum, minimum, and average ambient air temperature; maximum, minimum, and average apparent temperature; maximum and minimum heat index; and diurnal change in ambient temperature and apparent temperature; Analyses were also conducted for each strata of interest to examine the heterogeneity of effects by determinants of heat vulnerability with daily maximum temperature (TMax) and daily maximum apparent temperature (ATMax). In all analyses, temperature metrics were modeled using linear, quadratic and cubic terms to allow for possible nonlinear relationships with FEI (Winquist et al. 2016). All analyses also considered same day (lag 0) temperatures, as this lag showed strongest associations with FEI in our previous work. Covariates in the model were consistent with those used by Winquist et al. (2016) and included control for time using a cubic spline with monthly knots within the warm season for each year, indicator variables for year, and terms for the interaction between the linear term for day of the warm season and each year indicator variable, day of week, federal holidays, and periods of hospital participation, and same day average dew point temperature modeled using cubic terms (except for models of apparent temperature and heat index metrics as these include dew point information). Sensitivity analyses were conducted to examine the influence of changes to covariate control on model results; these analyses considered: omitting all time variables, omitting time splines only, substituting monthly or biweekly control variables for time splines, omitting hospital participation variables, omitting dew point temperature, omitting holiday variables, omitting day of week, and omitting cubic temperature variables. All analyses were also conducted with data restricted to the time period 1998-2012, as low mean daily ED visit numbers in earlier years led to model convergence issues for some strata of interest.

We used the approximate interquartile range (IQR; 75^{th}-25^{th} percentile) of the temperature metric of interest to represent a meaningful increment in exposure for expressing rate ratios (RR). For TMax, for example, the exact 25^{th} percentile was 27.2 °C and the 75^{th} percentile was 32.0 °C; we rounded the IQR of 4.8 °C to a 5 °C change between 27 °C and 32 °C for estimating RRs; the

25th percentile (e.g. 27 °C for TMax) was used as a reference temperature in estimating RRs for other temperature increments. We calculated these estimates by applying the parameter estimate values from the linear, squared and cubic terms for maximum temperature to the temperature contrast being considered (Winquist et al. 2016).

Associations across subgroups (e.g., of sex, or of race) were compared as an assessment of heterogeneity of the overall heat-morbidity relationship. Significant differences in the rate ratio for the interquartile range for each strata of each heat vulnerability determinant were tested using a Wald test for heterogeneity (Kaufman and MacLehose 2013).

Results

Temperature Metrics

Table 1 shows descriptive statistics of the different temperature metrics in Atlanta during the warm seasons for 1993-2012. Table 2 shows that the maximum, minimum, and average temperature, apparent temperature, and heat index metrics were moderately to highly correlated with one another (Spearman correlation coefficients > 0.70). The diurnal change in temperature (TDC) and apparent temperature (ATDC) metrics were highly correlated with each other (Spearman correlation coefficient = 0.96), but not with the other temperature metrics, which showed correlations ranging from 0.43 to -0.30.

The estimated rate ratios for all FEI ED visits for a 1 IQR change in temperatures during 1993-2012 were positive and statistically significant for all temperature metrics (Table 3). The strongest RR was for average apparent temperature (ATAvg) with an RR of 1.137 (95% CI: 1.113, 1.162) per IQR. The weakest RRs were for minimum apparent temperature (ATmin), minimum heat index (HIMin), and the two diurnal change metrics (RRs ≤ 1.096 per IQR); 95% confidence intervals were generally non-overlapping with those for the other metrics suggesting significantly weaker estimated effects. The RRs for maximum and average temperature and apparent temperature metrics were very similar, likely due to their high correlation (Table 2). Observed associations of TMax [RR of 1.125 (95% CI: 1.102, 1.150) per IQR] and ATMax [RR of 1.125 (95% CI: 1.103, 1.149)] were consistent with results presented in Winquist et al. (2016).

Figure 1 shows estimated RRs across different temperature increments for each temperature metric, using the 25th percentile of each metric as the reference. For most metrics, we observed increasing RRs with increasing temperature compared to the 25th percentile reference temperature. TDC and ATDC metrics that had the weakest RRs per IQR, also showed the widest 95% CIs and most curvilinear trends, with RRs decreasing at the upper ranges.

Heterogeneity of Heat Morbidity Associations

Table 4 shows descriptive statistics of FEI ED visits stratified by modifiers of interest in Atlanta during the warm seasons for 1993-2012. Some strata, such as presence of comorbid CHF had extremely low mean daily counts of FEI ED visits (mean of 1.2 visits/day). Modifier information was missing for some ED visits, particularly for race where 33% of visits (21,985) were missing race information. The missingness in the race data was in part due to 3 years (2007-2009) for which race was completely missing.

Analyses by determinants of heat vulnerability focused on TMax and ATMax metrics. Table 5 presents estimated rate ratios for FEI ED visits in relation to TMax and ATMax overall and by strata of each heat vulnerability determinant, for the full (1993-2012) and reduced (1998-2012) time periods. Among stratified analyses, most strata showed significant positive associations regardless of temperature metric; results were also consistent across the two time periods (although models did not converge for some strata when assessing the full time period due to low daily counts in early years). Factors with statistically heterogeneous estimated effects were sex, with RRs for males [e.g., RR of 1.176 (95% CI: 1.138, 1.216) per IQR TMax during 1993-2012] significantly stronger than for females [e.g., RR of 1.088 (95% CI: 1.060, 1.118) per IQR TMax], and renal disease comorbidity, with RRs among patients without comorbid renal disease diagnosis [e.g., RR of 1.137 (95% CI: 1.112, 1.164) per IQR TMax during 1993-2012] significantly stronger than RRs among patients with comorbid renal disease diagnosis [e.g., RR of 1.048 95% CI: (0.995, 1.104) per IQR TMax]. Some suggested differences in effects were found for race, with RRs among Hispanics considerably stronger than those for other groups, and undereducated area, with stronger RRs among patients residing in an undereducated area than those residing in other areas; however, these differences were not significant at the 0.05 level. Sensitivity analyses for associations with TMax and ATMax, in which covariate control was modified compared to main analyses, are shown in Table 6. For each reduced model, the RR of interest was less than 2% different from main model results.

Figure 2 shows stratum-specific RR estimates expressed for a range of TMax increments, using 27˚C (25^{th} percentile) as a reference, for the reduced time period (1998-2012). These plots show that the RR per IQR (75^{th}-25^{th} percentiles) estimates presented in Table 5 adequately represent effect modification for each factor, and that the differences in RRs observed for sex and renal disease persisted at the upper temperature increments and were not unique to the RR per IQR. For the strata for which significant differences were seen (sex and renal disease), the differences between strata persisted for the temperature windows above the IQR but not below it, and there was a widening disparity at the upper temperature windows. While most strata showed trends that were somewhat linear, curvilinear trends appeared for nonwhite strata of Hispanic and Other.

Discussion

Overview

Using a 20-year time series of ED visits and temperature in Atlanta, GA, this study evaluated heat-morbidity associations for FEI by determinants of heat vulnerability (sex, race, comorbid congestive heart failure, kidney disease, and diabetes diagnoses, and neighborhood socioeconomic conditions as defined by poverty and education levels), and explored the effects of defining exposure differently with a variety of temperature metrics. Through these additional temperature metric analyses and exploring effect modification by the determinants of interest, this work expanded upon that presented by Winquist et al. (2016). The present findings indicate that temperature is associated with FEI, regardless of the metric used to define temperature, and suggest that risks are great for all populations, but perhaps particularly for males and possibly for nonwhite groups (e.g., Hispanics) and those living in undereducated areas. We found some unanticipated patterns of effect modification in that for the comorbidities, there was a tendency for the 'absent' strata to have stronger associations than 'present' strata, with significant differences observed for comorbid renal disease. Below we explore the implications of our observed results.

Sex

Previous studies have shown mixed evidence for modification of heat-health associations by sex. A number of studies have shown stronger heat morbidity for females (Astrom et al. 2011; Borrell et al. 2006; Fouillet et al. 2006; Hajat et al. 2007; Ishigami et al. 2008; Kysely 2004; Martiello and Giacchi 2010; Michelozzi et al. 2004; Rainham and Smoyer-Tomic 2003; Rey et al. 2007; Rooney et al. 1998; Stafoggia et al. 2006), but other studies have found stronger effects for males (Bai et al. 2014; Beggs and Vaneckova 2008; Choudhary and Vaidyanathan 2014; Schmeltz et al. 2015) as was found in our study. The finding of males having a significantly stronger RR than females is supported by studies of ED visits (Sanchez et al. 2010) and hospital admissions (Beggs and Vaneckova 2008) that have shown that men are more likely than women to seek care for heat-related diagnoses (Pillai et al. 2014). Males may be more likely to be exposed than females, based on occupational or recreational activities (Beggs and Vaneckova 2008; Sanchez et al. 2010). It is possible that differing physiological and metabolic processes between males and females also play a role, especially given that males have a higher metabolic rate, which has been shown to be related to higher muscle mass and lower subcutaneous adipose tissue compare to females (Acharya et al. 2013). Although men comprised a significant majority of US ED visits for environmental-exposure-related injuries during the period 2001-2004 (Sanchez et al. 2010), in our study, females presented 11,139 more ED visits for FEI than males (Table 4). A study of heat-related Georgia hospitalizations from ED visits found significant interaction between age and sex (Pillai et al. 2014). Some of the differences in observed associations between males and females here may thus be due to differential age distribution between sexes. Future studies that further characterize both heat exposure and health outcomes by sex are needed to fully investigate the reasons for these findings.

Race

We observed significant positive associations for all race categories (except ‘other’). Nonwhite patients generally had stronger associations than white patients, although these differences were small (i.e., for TMax during 1993-2012, RR among nonwhite patients was ~1% different from white patients); Hispanic patients appeared to drive the elevated RR for nonwhite patients (i.e., for TMax during 1993-2012, RR among Hispanic patients was ~20% different from white) patients. While Hispanic patients appeared to have considerably stronger risks than other racial categories, this may be a chance finding; there were considerably fewer cases in this category (1,938 ED visits; 3% of visits for race strata) compared to other race strata. However, the results are suggestive and could be followed up by study with greater power. Hispanic ethnicity has been shown to be associated with heat-related health impacts (Schwartz 2005; Uejio et al. 2011). It is also important to consider, however, that race may function as a distal measure of vulnerability (Gronlund 2014) and that it may be more relevant to study race in conjunction with other measures of vulnerability which have been shown to be associated with being a racial/ethinic minority, such as income, health status, built environment characteristics related to heat exposure, air conditioning use, and occupational heat exposure (Harlan et al. 2006; Harlan et al. 2013; O'Neill et al. 2005; Stoecklin-Marois M 2013).

Comorbidities

For the comorbidities of interest, there was a tendency for the ‘absent’ strata to have stronger associations than ‘present’ strata. This may be explained by a number of reasons. First, this could have been a result of low counts and thus low power in the ‘present’ strata (see Table 2); for example, the ‘present’ strata had only 3,566 ED visits (~5% of total ED visits) with comorbid CHF, 9,477 ED visits (~14% of total ED visits) with comorbid renal disease, and 9,737 ED visits (~15% of total ED visits) with comorbid diabetes.

Second, it is important to consider the definition of comorbidity used. The present study’s definition of comorbidity aimed to capture individuals who presented as a new case of FEI, but who had an underlying condition represented in the secondary diagnosis code variables at the same visit as FEI coded as primary. This definition intended to capture patients with an underlying disease, but before the disease had progressed to a more severe condition, in which case it is more likely that the primary reason for the ED visit would have been coded as the underlying condition. Other studies of heat morbidity using ED visits have found significant associations for the comorbidities of interest (renal disease/failure, diabetes, cardiovascular diseases/outcomes other than CHF) (Basu et al. 2012; Fuhrmann et al. 2015; Winquist et al. 2016). It is possible that patients in these studies also experienced FEI, but that FEI was not coded as the primary diagnosis. Thus, similar to the proposed explanation that cardiovascular morbidity cases are missed because they progress too quickly to mortality (Kovats et al. 2004; Linares and Diaz 2008; Winquist et al. 2016), it is possible that FEI cases progress quickly to a more severe manifestation of disease, and are therefore not coded as primary FEI. Future studies of modification of heat-FEI associations by comorbidities might define “presence” as any visits for FEI (in any ICD-9 diagnosis code positions) and for the comorbidity of interest (in any ICD-9 diagnosis code positions). This method has been used by Pillai et al. (2014) and Knowlton et al.

(2009), in that they identified comorbid conditions among ED visit cases as ICD-9 codes from any of the first 10 diagnosis code positions. However, studies that explore diagnoses beyond the primary diagnosis have found support for the phenomenon of inconsistent coding of ED visits (Kilbourne 1999; Semenza et al. 1999; Winquist et al. 2016).

Third, it is also important to consider that the effect modification observed for comorbidities was the result of additive, rather than multiplicative, interaction, and that there may be more complex and competing risk factors at play in these relationships. For populations with multiple risk factors for the outcome, which may be the case with patients with underlying chronic diseases, the risk due to temperature may be small relative to the other risk factors; thus in multiplicative models, it is possible for the population with greater risk factors to have smaller RRs than that for the population with fewer risk factors, which is the pattern observed in the current study.

Finally, the reciprocal relationship between fluid and electrolyte imbalance and kidney function makes it challenging to disentangle the source of exacerbation due to heat. Fluid and electrolyte imbalance affects renal function, and renal function affects how well fluids and electrolytes are balanced in the body. For example, as renal function declines, the kidneys cannot maintain homeostasis, leading to potential hyponatremia and hypernatremia, which are types of FEI (Mahaldar 2012). Furthermore, dialysis modalities have been shown to prompt issues of FEI (Claure 2012). Added stress from heat further disrupts renal processes. High environmental temperatures can induce excessive sweating, which can lead to fluid and electrolyte imbalance in the body. If other factors, such as underlying disease or the effects of certain medications compromise renal function, the body may not be able to effectively mitigate FEI. The selected comorbidities for the current study are all linked to renal function. Diabetes can lead to chronic renal failure/impairment (Collins et al. 2009), and CHF patients often take medications that can decrease renal function (Dei Cas et al. 1995). Thus, temporality and directionality further complicate heat-morbidity relationships for FEI and the comorbidities of interest. Elevated ambient temperature can affect the cardiovascular and renal systems, which means that CHF and kidney disease may have increased risk through heat-related mechanisms other than FEI.

Socioeconomic Status

While no differences in RRs were found by poverty compared to non-poverty areas, there was an indication, albeit not statistically significant, of stronger associations for patients living in undereducated compared to educated areas as anticipated. However, there is mixed evidence with regards to education and heat mortality and morbidity. Among mortality studies, some studies have found stronger associations among populations with low education levels compared to higher education levels (Michelozzi et al. 2005; O'Neill 2003) and others have found no differences in associations by education level (Basu and Ostro 2008; Medina-Ramón et al. 2006). Similarly, for morbidity during heat waves, while higher education levels have been shown to be associated with lower heat-morbidity associations (Gronlund 2014; Larrieu et al. 2008), low education levels have also been shown to be protective (Kaiser et al. 2007). It is important to consider that education levels may represent other facets of socioeconomic conditions in neighborhoods, including income level, occupation and awareness of health risk (Gronlund 2014) that complicate direct interpretation of results. For example, neighborhood- and community-level measures of poverty and low-income have been shown to be associated with heat-related mortality (Anderson and Bell 2009) as well as heat-related morbidity (Fletcher et al. 2012). Potential challenges for low-income populations include lack of private health insurance (Zhang et al. 2013), lack of access to transportation to cooling shelters and/or lack of access to or resources to utilize air conditioning (Hansen et al. 2011; Sampson et al. 2013) that make them more vulnerable to fluid and electrolyte imbalance outcomes.

One limitation of the current analysis was that the socioeconomic status data were for the ZCTA-level, yet other spatial scales for neighborhood socioeconomic conditions may also be relevant. For example, socioeconomic vulnerability has been shown to be predictive of heat-related death at the level of the census block group (Harlan et al. 2013).

Previous Work on FEI

Heat morbidity studies that do include FEI may only consider 'dehydration,' identified by the specific ICD-9 code 276.5 (Basu et al. 2012; Green et al. 2010), and there are few studies including the full group of FEI ICD-9 codes (276) or ICD-10 codes (Khalaj et al. 2010; Knowlton et al. 2009; Mastrangelo et al. 2007; Semenza et al. 1999). Our overall results are consistent with these studies, which showed positive associations with dehydration for same-day apparent temperature (Basu et al. 2012) and for mean apparent temperature (Green et al. 2010), as well as positive associations with FEI on days of extreme heat (Khalaj et al. 2010), during a heat wave period (Knowlton et al. 2009). Hospital admissions for FEI during a heat wave were significantly elevated (Semenza et al. 1999), as was the association between heat wave duration for heat-related diseases which include FEI (Mastrangelo et al. 2007)

Temperature Metrics

While all temperature metrics showed significant, positive associations with FEI ED visits, TMax and ATMax served as our primary metrics because they yielded similar results, showed strong effects with FEI, and can be compared to other studies, as these metrics are commonly used in the literature.

All of the temperature metrics considered in the present study yielded statistically significant positive RRs for all FEI ED visits (between 1.055 and 1.137). Measures of apparent temperature and heat index, both of which include dew point in their calculation, were similar, and measures of apparent temperature seemed similar to corresponding measures of air temperature (TMax and ATMax, TMin and ATMin, TAvg and ATAvg). Measures of diurnal temperature change (TDC, ATDC) appeared lower than the other metrics, indicating that this may not be the most sensitive measure for FEI. All of these temperature metrics were highly correlated with one another, except with TDC and ATDC. Our results suggest that air temperature, apparent temperature, and heat index may be regarded as equivalent measures, which is relevant to public health practice because the National Weather Service uses heat index for surveillance and for issuing heat warnings.

Of the six epidemiological studies including FEI as an outcome, two use the same exposure metric: mean apparent daily temperature using calculations described by Basu, Feng, and Ostro (2008) (Basu et al. 2008), which include temperature and relative humidity (Basu et al. 2012; Green et al. 2010). Semenza et al. (1999) also used apparent temperature, in the context of highest hourly heat index (Semenza et al. 1999). Knowlton et al. did not use a temperature metric as the exposure, but rather compared a heat wave period to a non-heat wave period (Knowlton et al. 2009). An Italian study of hospital admissions during heat waves included FEI along with acute renal failure and heat stroke within the category of heat-related diseases and explored heat wave duration and intensity as exposures (Mastrangelo et al. 2007). The most recent of these studies, Khalaj et al. 2010, compared the influence of four different temperature metrics on all hospital admissions (including dehydration and FEI): daily maximum temperature, daily minimum temperature, and apparent temperature (a combination of heat, low wind speed and high humidity) at two time points: 9 am and 3 pm (Khalaj et al. 2010). Daily maximum temperature was found to predict the strongest associations, and the best predictor was the 3-day moving average of the maximum temperature, which represents sustained high temperatures (Khalaj et al. 2010). The literature supports the present study's selection of TMax and ATMax as primary metrics, but also reveals that there has not been much work done comparing temperature metrics for ED visits for a specific outcome. The present study addressed this gap and showed that while TMax and ATMax may be the most relevant exposure metrics for FEI, a variety of metrics yield similar results.

Risks Posed by Warm Season Temperature

While extreme heat events have been well-studied, with hospital admissions providing much of the evidence (Fuhrmann et al. 2015; Knowlton et al. 2009; Mastrangelo et al. 2007; Michelozzi et al. 2009; Ostro et al. 2010; Pudpong and Hajat 2011; Semenza et al. 1999; Wichmann et al. 2011), there have been fewer time-series studies of ED visits and temperature (Alessandrini et al. 2011; Basu et al. 2012; Hess et al. 2014; Knowlton et al. 2009; Pillai et al. 2014; Pudpong and Hajat 2011; Wichmann et al. 2011; Winquist et al. 2016). The present study shows that temperatures during the warm season are associated with FEI ED visits for all populations. While heat warning systems and heat response plans focus on the anticipation of extreme heat events (Bernard and McGeehin 2004) perhaps prevention efforts should also target the risks posed by elevated temperatures throughout warm months.

Conclusion

In evaluating associations between warm season temperature and morbidity in Atlanta, this time-series study focused on a single outcome: ED visits for fluid and electrolyte imbalance. We explored these associations for heterogeneity by determinants of heat vulnerability (sex, race, comorbid conditions, and measures of socioeconomic status) as well as for the effects of using different temperature metrics.

We found that warm season temperature was associated with FEI for each metric we used, and that risks were great for all populations, but the heterogeneity in the association for sex indicated that males experience differential susceptibility. Because all groups showed positive associations, some groups (i.e., comparing among comorbid strata) we did not expect to show vulnerability resulted in unanticipated results. This work highlights the utility of FEI as an indicator of heat morbidity that affects all populations, highlights the health threat posed by warm season temperatures, and raises considerations regarding assessment of vulnerable populations in heat-health research.

References

Acharya S, Gurung DB, Saxena VP (2013) Effect of Metabolic Reactions on Thermoregulation in Human Males and Females Body Applied Mathematics 4:39-48

Alessandrini E, Zauli Sajani S, Scotto F, Miglio R, Marchesi S, Lauriola P (2011) Emergency ambulance dispatches and apparent temperature: a time series analysis in Emilia-Romagna, Italy. Environ Res 111(8):1192-200 doi:10.1016/j.envres.2011.07.005

Allison SP, Lobo DN (2004) Fluid and electrolytes in the elderly. Current Opinion in Clinical Nutrition and Metabolic Care 7:23-33 doi:10.1097/01.mco.0000109603.04238.d4

Anderson BG, Bell ML (2009) Weather-Related Mortality How Heat, Cold, and Heat Waves Affect Mortality in the United States. Epidemiology 20(2):205-213 doi:10.1097/EDE.0b013e318190ee08

Anderson GB, Bell ML, Peng RD (2013) Methods to calculate the heat index as an exposure metric in environmental health research. Environ Health Perspect 121(10):1111-9 doi:10.1289/ehp.1206273

Astrom DO, Forsberg B, Rocklov J (2011) Heat wave impact on morbidity and mortality in the elderly population: a review of recent studies. Maturitas 69(2):99-105 doi:10.1016/j.maturitas.2011.03.008

Bai L, et al. (2014) The effects of summer temperature and heat waves on heat-related illness in a coastal city of China, 2011-2013. Environ Res 132:212-9 doi:10.1016/j.envres.2014.04.002

Basu R (2009) High ambient temperature and mortality: a review of epidemiologic studies from 2001 to 2008. Environ Health 8:40 doi:10.1186/1476-069X-8-40

Basu R, Feng WY, Ostro BD (2008) Characterizing temperature and mortality in nine California counties. Epidemiology 19(1):138-45 doi:10.1097/EDE.0b013e31815c1da7

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(6):632-7 doi:10.1093/aje/kwn170

Basu R, Pearson D, Malig B, Broadwin R, Green R (2012) The effect of high ambient temperature on emergency room visits. Epidemiology 23(6):813-20 doi:10.1097/EDE.0b013e31826b7f97

Beggs PJ, Vaneckova P (2008) Admission to hospital for effects of heat and light: NSW, 1993-94 to 2003-04. N S W Public Health Bull 19(7-8):132-7

Bernard SM, McGeehin MA (2004) Municipal Heat Wave Response Plans. American Journal of Public Health 94(9):1520-1522 doi:10.2105/AJPH.94.9.1520

Borrell C, et al. (2006) Socioeconomic position and excess mortality during the heat wave of 2003 in Barcelona. Eur J Epidemiol 21(9):633-640 doi:10.1007/s10654-006-9047-4

Chagnon SA, Kunkel KE, Reinke BC (1996) Impacts and Responses to the 1995 Heat Wave: A Call to Action. Bulletin of the American Meteorological Society 77(7):1497-1506

Choudhary E, Vaidyanathan A (2014) Heat stress illness hospitalizations--environmental public health tracking program, 20 States, 2001-2010. MMWR Surveill Summ 63(13):1-10

Claure RaBJ (2012) Acid-base and electrolyte abnormalities during renal support for acute kidney injury: Recognition and management. vol 34, p 186--193

Collins KJ, Clinical S, Pancras S (2009) Fluid balance of elderly people in hot environments. GM 39

Curriero FC, Heiner KS, Samet JM, Zeger SL, Strug L, Patz JA (2002) Temperature and mortality in 11 cities of the eastern United States. Am J Epidemiol 155(1):80-7

Darrow LA, Hess J, Rogers CA, Tolbert PE, Klein M, Sarnat SE (2012) Ambient pollen concentrations and emergency department visits for asthma and wheeze. Journal of Allergy and Clinical Immunology 130(3):630-638 doi:10.1016/j.jaci.2012.06.020
Dei Cas L, Metra M, Leier CV (1995) Electrolyte disturbances in chronic heart failure: metabolic and clinical aspects. Clin Cardiol 18(7):370-6
El-Sharkawy AM, Sahota O, Lobo DN (2015) Acute and chronic effects of hydration status on health. Nutr Rev 73 Suppl 2:97-109 doi:10.1093/nutrit/nuv038
Fletcher BA, Lin S, Fitzgerald EF, Hwang SA (2012) Association of summer temperatures with hospital admissions for renal diseases in New York State: a case-crossover study. Am J Epidemiol 175(9):907-16 doi:10.1093/aje/kwr417
Fouillet A, et al. (2006) Excess mortality related to the August 2003 heat wave in France. Int Arch Occup Environ Health 80(1):16-24 doi:10.1007/s00420-006-0089-4
Fuhrmann CM, Sugg MM, Konrad CE, 2nd, Waller A (2015) Impact of Extreme Heat Events on Emergency Department Visits in North Carolina (2007-2011). J Community Health doi:10.1007/s10900-015-0080-7
Goldberg A, et al. (2006) Hyponatremia and long-term mortality in survivors of acute ST-elevation myocardial infarction. Arch Intern Med 166(7):781-6 doi:10.1001/archinte.166.7.781
Goldberg A, et al. (2004) Prognostic importance of hyponatremia in acute ST-elevation myocardial infarction. Am J Med 117(4):242-8 doi:10.1016/j.amjmed.2004.03.022
Green RS, Basu R, Malig B, Broadwin R, Kim JJ, Ostro B (2010) The effect of temperature on hospital admissions in nine California counties. Int J Public Health 55(2):113-21 doi:10.1007/s00038-009-0076-0
Gronlund CJ (2014) Racial and Socioeconomic Disparities in Heat-Related Health Effects and Their Mechanisms: a Review. Current Epidemiology Reports 1(3):165-173
Hajat S, Kovats RS, Atkinson RW, Haines A (2002) Impact of hot temperatures on death in London: a time series approach. J Epidemiol Community Health 56(5):367-72
Hajat S, Kovats RS, Lachowycz K (2007) Heat-related and cold-related deaths in England and Wales: who is at risk? Occupational and Environmental Medicine 64(2):93-100 doi:10.1136/oem.2006.029017
Hajat S, et al. (2010) Heat–Health Warning Systems: A Comparison of the Predictive Capacity of Different Approaches to Identifying Dangerously Hot Days. American Journal of Public Health 100(6):1137-1144 doi:10.2105/AJPH.2009.169748
Hansen A, Bi P, Nitschke M, Pisaniello D, Newbury J, Kitson A (2011) Perceptions of heat-susceptibility in older persons: barriers to adaptation. Int J Environ Res Public Health 8(12):4714-28 doi:10.3390/ijerph8124714
Hansen AL, Bi P, Ryan P, Nitschke M, Pisaniello D, Tucker G (2008) The effect of heat waves on hospital admissions for renal disease in a temperate city of Australia. Int J Epidemiol 37(6):1359-1365 doi:10.1093/ije/dyn165
Harlan SL, Brazel AJ, Prashad L, Stefanov WL, Larsen L (2006) Neighborhood microclimates and vulnerability to heat stress. Soc Sci Med 63(11):2847-63 doi:10.1016/j.socscimed.2006.07.030
Harlan SL, Declet-Barreto JH, Stefanov WL, Petitti DB (2013) Neighborhood effects on heat deaths: social and environmental predictors of vulnerability in Maricopa County, Arizona. Environ Health Perspect 121(2):197-204 doi:10.1289/ehp.1104625
Hattis D, Ogneva-Himmelberger Y, Ratick S (2012) The spatial variability of heat-related mortality in Massachusetts. Applied Geography 33:45-52 doi:10.1016/j.apgeog.2011.07.008
Hess JJ, Saha S, Luber G (2014) Summertime acute heat illness in U.S. emergency departments from 2006 through 2010: analysis of a nationally representative sample. Environ Health Perspect 122(11):1209-15 doi:10.1289/ehp.1306796

Ho HC, Knudby A, Xu Y, Hodul M, Aminipouri M (2016) A comparison of urban heat islands mapped using skin temperature, air temperature, and apparent temperature (Humidex), for the greater Vancouver area. Sci Total Environ 544:929-38 doi:10.1016/j.scitotenv.2015.12.021
Ishigami A, et al. (2008) An ecological time-series study of heat-related mortality in three European cities. Environmental Health 7 doi:Artn 5
10.1186/1476-069x-7-5
Ito H, Fujimaki H, Inoue J, Shiraki M (1989) [Disorders of fluid and electrolyte metabolism in elderly diabetics]. Nihon Ronen Igakkai Zasshi 26(3):233-9
Jardine DS (2007) Heat illness and heat stroke. Pediatr Rev 28(7):249-58
Johnson DP, Wilson JS (2009) The socio-spatial dynamics of extreme urban heat events: The case of heat-related deaths in Philadelphia. Applied Geography 29(3):419-434 doi:10.1016/j.apgeog.2008.11.004
Kaiser R, Le Tertre A, Schwartz J, Gotway CA, Daley WR, Rubin CH (2007) The effect of the 1995 heat wave in Chicago on all-cause and cause-specific mortality. Am J Public Health 97 Suppl 1:S158-62 doi:10.2105/AJPH.2006.100081
Kaufman JS, MacLehose RF (2013) Which of these things is not like the others? Cancer 119(24):4216-22 doi:10.1002/cncr.28359
Khalaj B, Lloyd G, Sheppeard V, Dear K (2010) The health impacts of heat waves in five regions of New South Wales, Australia: a case-only analysis. Int Arch Occup Environ Health 83(7):833-42 doi:10.1007/s00420-010-0534-2
Kilbourne EM (1999) The spectrum of illness during heat waves. Am J Prev Med 16(4):359-60
Kinney PL, O'Neill MS, Bell ML, Schwartz J (2008) Approaches for estimating effects of climate change on heat-related deaths: challenges and opportunities. Environmental Science & Policy 11(1):87-96 doi:10.1016/j.envsci.2007.08.001
Knowlton K, et al. (2009) The 2006 California heat wave: impacts on hospitalizations and emergency department visits. Environ Health Perspect 117(1):61-7 doi:10.1289/ehp.11594
Kosatsky T, Henderson SB, Pollock SL (2012) Shifts in Mortality During a Hot Weather Event in Vancouver, British Columbia: Rapid Assessment With Case-Only Analysis. American Journal of Public Health 102(12):2367-2371 doi:10.2105/AJPH.2012.300670
Kovats RS, Hajat S, Wilkinson P (2004) Contrasting patterns of mortality and hospital admissions during hot weather and heat waves in Greater London, UK. Occup Environ Med 61(11):893-8 doi:10.1136/oem.2003.012047
Kysely J (2004) Mortality and displaced mortality during heat waves in the Czech Republic. Int J Biometeorol 49(2):91-7 doi:10.1007/s00484-004-0218-2
Larrieu S, et al. (2008) Factors associated with morbidity during the 2003 heat wave in two population-based cohorts of elderly subjects: PAQUID and Three City. Eur J Epidemiol 23(4):295-302 doi:10.1007/s10654-008-9229-3
Li M, Gu S, Bi P, Yang J, Liu Q (2015) Heat waves and morbidity: current knowledge and further direction-a comprehensive literature review. Int J Environ Res Public Health 12(5):5256-83 doi:10.3390/ijerph120505256
Liang WM, Liu WP, Chou SY, Kuo HW (2008) Ambient temperature and emergency room admissions for acute coronary syndrome in Taiwan. Int J Biometeorol 52(3):223-229 doi:10.1007/s00484-007-0116-5
Liang WM, Liu WP, Kuo HW (2009) Diurnal temperature range and emergency room admissions for chronic obstructive pulmonary disease in Taiwan. Int J Biometeorol 53(1):17-23 doi:10.1007/s00484-008-0187-y
Linares C, Diaz J (2008) Impact of high temperatures on hospital admissions: comparative analysis with previous studies about mortality (Madrid). Eur J Public Health 18(3):317-22 doi:10.1093/eurpub/ckm108

Luber G, McGeehin M (2008) Climate change and extreme heat events. Am J Prev Med 35(5):429-35 doi:10.1016/j.amepre.2008.08.021

Mahaldar AR (2012) Acid base and fluid electrolyte disturbances in Chronic Kidney Disease.

Martiello MA, Giacchi MV (2010) High temperatures and health outcomes: a review of the literature. Scand J Public Health 38(8):826-37 doi:10.1177/1403494810377685

Mastrangelo G, Fedeli U, Visentin C, Milan G, Fadda E, Spolaore P (2007) Pattern and determinants of hospitalization during heat waves: an ecologic study. BMC Public Health 7:200 doi:10.1186/1471-2458-7-200

McGeehin MA, Mirabelli M (2001) The potential impacts of climate variability and change on temperature-related morbidity and mortality in the United States. Environmental Health Perspectives 109:185-189 doi:Doi 10.2307/3435008

Medina-Ramón M, Zanobetti A, Cavanagh DP, Schwartz J (2006) Extreme Temperatures and Mortality: Assessing Effect Modification by Personal Characteristics and Specific Cause of Death in a Multi-City Case-Only Analysis. Environmental Health Perspectives 114(9):1331-1336 doi:10.1289/ehp.9074

Meehl GA, Tebaldi C (2004) More intense, more frequent, and longer lasting heat waves in the 21st century. Science 305(5686):994-7 doi:10.1126/science.1098704

Metzger KB, et al. (2004) Ambient air pollution and cardiovascular emergency department visits. Epidemiology 15(1):46-56

Michelozzi P, et al. (2009) High temperature and hospitalizations for cardiovascular and respiratory causes in 12 European cities. Am J Respir Crit Care Med 179(5):383-9 doi:10.1164/rccm.200802-217OC

Michelozzi P, et al. (2004) Impact of heat waves on mortality - Rome, Italy, June-August 2003 (Reprinted from MMWR, vol 53, pg 369-371, 2004). Jama-J Am Med Assoc 291(21):2537-2538

Michelozzi P, et al. (2005) The impact of the summer 2003 heat waves on mortality in four Italian cities. Euro Surveill 10(7):161-5

Milionis HJ, Alexandrides GE, Liberopoulos EN, Bairaktari ET, Goudevenos J, Elisaf MS (2002) Hypomagnesemia and concurrent acid-base and electrolyte abnormalities in patients with congestive heart failure. European Journal of Heart Failure 4(2):167-173

Mo WC, et al. (2014) Heat-related illness in Jinshan District of Shanghai: A retrospective analysis of 70 patients. World J Emerg Med 5(4):286-90 doi:10.5847/wjem.j.issn.1920-8642.2014.04.008

Noakes T (1998) Fluid and electrolyte disturbances in heat illness. International Journal of Sports Medicine 19 Suppl 2:S146-S149 doi:10.1055/s-2007-971982

O'Neill MS (2003) Modifiers of the Temperature and Mortality Association in Seven US Cities. American Journal of Epidemiology 157(12):1074-1082 doi:10.1093/aje/kwg096

O'Neill MS, Kinney PL, Cohen AJ (2008) Environmental equity in air quality management: local and international implications for human health and climate change. J Toxicol Environ Health A 71(9-10):570-7 doi:10.1080/15287390801997625

O'Neill MS, Zanobetti A, Schwartz J (2005) Disparities by race in heat-related mortality in four US cities: the role of air conditioning prevalence. J Urban Health 82(2):191-7 doi:10.1093/jurban/jti043

Ostro B, Rauch S, Green R, Malig B, Basu R (2010) The Effects of Temperature and Use of Air Conditioning on Hospitalizations. American Journal of Epidemiology 172(9):1053-1061 doi:10.1093/aje/kwq231

Peel JL, et al. (2005) Ambient air pollution and respiratory emergency department visits. Epidemiology 16(2):164-174

Pillai SK, et al. (2014) Heat Illness: Predictors of Hospital Admissions Among Emergency Department Visits-Georgia, 2002-2008. J Commun Health 39(1):90-98 doi:10.1007/s10900-013-9743-4

Pudpong N, Hajat S (2011) High temperature effects on out-patient visits and hospital admissions in Chiang Mai, Thailand. Sci Total Environ 409(24):5260-7 doi:10.1016/j.scitotenv.2011.09.005
Rainham DGC, Smoyer-Tomic KE (2003) The role of air pollution in the relationship between a heat stress index and human mortality in Toronto. Environmental Research 93(1):9-19 doi:10.1016/S0013-9351(03)00060-4
Rey G, et al. (2007) The impact of major heat waves on all-cause and cause-specific mortality in France from 1971 to 2003. Int Arch Occ Env Hea 80(7):615-626 doi:10.1007/s00420-007-0173-4
Rooney C, McMichael AJ, Kovats RS, Coleman MP (1998) Excess mortality in England and Wales, and in Greater London, during the 1995 heatwave. Journal of Epidemiology and Community Health 52(8):482-486
Sampson N, et al. (2013) Staying cool in a changing climate: Reaching vulnerable populations during heat events. Global Environ Change 23:475–84.
Sanchez CA, Thomas KE, Malilay J, Annest JL (2010) Nonfatal natural and environmental injuries treated in emergency departments, United States, 2001-2004. Fam Community Health 33(1):3-10 doi:10.1097/FCH.0b013e3181c4e2fa
Sarnat SE, et al. (2010) An examination of exposure measurement error from air pollutant spatial variability in time-series studies. Journal of Exposure Science and Environmental Epidemiology 20:135-146
Schmeltz MT, Sembajwe G, Marcotullio PJ, Grassman JA, Himmelstein DU, Woolhandler S (2015) Identifying individual risk factors and documenting the pattern of heat-related illness through analyses of hospitalization and patterns of household cooling. PLoS One 10(3):e0118958 doi:10.1371/journal.pone.0118958
Schwartz J (2005) Who is sensitive to extremes of temperature?: A case-only analysis. Epidemiology 16(1):67-72
Schwartz J, Samet JM, Patz JA (2004) Hospital admissions for heart disease: the effects of temperature and humidity. Epidemiology 15(6):755-61
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(4):269-77
Smargiassi A, Goldberg MS, Plante C, Fournier M, Baudouin Y, Kosatsky T (2009) Variation of daily warm season mortality as a function of micro-urban heat islands. Journal of Epidemiology and Community Health 63(8):659-664 doi:10.1136/jech.2008.078147
Sotirakopoulos N, Kalogiannidou I, Tersi M, Armentzioiou K, Sivridis D, Mavromatidis K (2012) Acid-base and electrolyte disorders in patients with diabetes mellitus. Saudi J Kidney Dis Transpl 23(1):58-62
Stafoggia M, et al. (2006) Vulnerability to heat-related mortality - A multicity, population-based, case-crossover analysis. Epidemiology 17(3):315-323 doi:10.1097/01.ede.0000208477.36665.34
Steadman R (1984) A universal scale of apparent temperature. J Clim Appl Meteorol 23:1674–1687
Stoecklin-Marois M H-BT, Mitchell D, Schenker M (2013) Heat-related illness knowledge and practices among California hired farm workers in The MICASA Study. Ind Health 51(1):47–55
Strickland MJ, et al. (2010) Short-term associations between ambient air pollutants and pediatric asthma emergency department visits. Am J Respir Crit Care Med 182(3):307-16 doi:200908-1201OC [pii]
10.1164/rccm.200908-1201OC
Tolbert PE, et al. (2000) Interim results of the study of particulates and health in Atlanta (SOPHIA). J Expo Anal Environ Epidemiol 10(5):446-60

Turner LR, Barnett AG, Connell D, Tong S (2012) Ambient temperature and cardiorespiratory morbidity: a systematic review and meta-analysis. Epidemiology 23(4):594-606 doi:10.1097/EDE.0b013e3182572795

Uejio C, Wilhelmi O, Golden J, Mills D, Gulino S, Samenow J (2011) Intra-urban societal vulnerability to extreme heat: The role of heat exposure and the built environment, socioeconomics, and neighborhood stability. Health Place 17(2):498–507

Weiss-Guillet EM, Takala J, Jakob SM (2003) Diagnosis and management of electrolyte emergencies. Best Pract Res Clin Endocrinol Metab 17(4):623-51

Wichmann J, Andersen Z, Ketzel M, Ellermann T, Loft S (2011) Apparent Temperature and Cause-Specific Emergency Hospital Admissions in Greater Copenhagen, Denmark. Plos One 6(7) doi:ARTN e22904

10.1371/journal.pone.0022904

Winquist A, Grundstein A, Chang HH, Hess J, Sarnat SE (2016) Warm season temperatures and emergency department visits in Atlanta, Georgia. Environmental Research 147:314–323

Ye X, Wolff R, Yu W, Vaneckova P, Pan X, Tong S (2012) Ambient temperature and morbidity: a review of epidemiological evidence. Environ Health Perspect 120(1):19-28 doi:10.1289/ehp.1003198

Zhang Y, Nitschke M, Bi P (2013) Risk factors for direct heat-related hospitalization during the 2009 Adelaide heatwave: a case crossover study. Sci Total Environ 442:1-5 doi:10.1016/j.scitotenv.2012.10.042

Appendix

Table 1. Descriptive statistics of different temperature metrics in Atlanta during the warm seasons (May-September) for 1993-2012 (n=3060 days, in units of °C)

Temperature Metric	Abbreviation	Mean	Std Dev	Minimum	25th Pctl	50th Pctl	75th Pctl	Maximum
Maximum ambient air temperature	TMax	29.4	3.7	13.3	27.2	30.0	32.0	40.6
Minimum ambient air temperature	TMin	19.9	3.4	5.0	18.3	20.6	22.2	28.3
Average ambient air temperature	TAvg	24.7	3.4	11.7	22.8	25.3	27.0	33.9
Maximum apparent temperature	ATMax	30.3	3.9	14.2	28.0	30.8	33.0	40.2
Minimum apparent temperature	ATMin	21.4	4.1	5.1	19.3	22.6	24.4	30.4
Average apparent temperature	ATAvg	25.9	3.8	11.3	23.8	26.7	28.6	34.9
Maximum heat index	HIMax	30.6	4.6	13.2	27.8	30.8	33.8	43.4
Minimum heat index	HIMin	20.2	3.8	4.0	18.2	21.2	22.9	30.8
Diurnal change in air temperature	TDC	9.5	2.5	1.1	7.8	9.5	11.1	17.2
Diurnal change in apparent temperature	ATDC	8.8	2.2	1.4	7.5	8.8	10.3	17.2

Table 2. Spearman correlations between different temperature metrics in Atlanta during the warm seasons (May-September) for 1993-2012 (n=3060 days)

Temperature Metric (Celsius)	Abbreviation	TMax	TMin	TAvg	ATMax	ATMin	ATAvg	HIMax	HIMin	TDC	ATDC
Maximum ambient air temperature	**TMax**	1.00									
Minimum ambient air temperature	**TMin**	0.75*	1.00								
Average ambient air temperature	**TAvg**	0.95*	0.91*	1.00							
Maximum apparent temperature	**ATMax**	0.96*	0.84*	0.97*	1.00						
Minimum apparent temperature	**ATMin**	0.71*	0.99*	0.89*	0.82*	1.00					
Average apparent temperature	**ATAvg**	0.88*	0.95*	0.98*	0.96*	0.95*	1.00				
Maximum heat index	**HIMax**	0.94*	0.84*	0.96*	0.99*	0.83*	0.96*	1.00			
Minimum heat index	**HIMin**	0.73*	1.00*	0.90*	0.83*	1.0*	0.95*	0.84*	1.00		
Diurnal change in air temperature	**TDC**	0.43*	-0.19*	0.15*	0.26*	-0.23*	0.03	0.23*	-0.21*	1.00	
Diurnal change in apparent temperature	**ATDC**	0.34*	-0.27*	0.07*	0.22*	-0.30*	-0.04	0.20*	-0.29*	0.96*	1.00

*=p<0.05

Table 3. Estimated rate ratios for all fluid and electrolyte imbalance ED visits in relation to a change of approximately 1 IQR (from the 25th to 75th percentile) for different temperature metrics in Atlanta during the warm seasons (May-September) for 1993-2012 (n=3060 days)

Temperature Metric	Abbreviation	IQR (25th-75th percentile, in °C)	RR (95% CI)	p-value
Max ambient air temperature	TMax	5 (27-32)	1.125 (1.102, 1.150)	<.0001
Min ambient air temperature	TMin	4 (18-22)	1.105 (1.077, 1.133)	<.0001
Average ambient air temperature	TAvg	4 (23-27)	1.134 (1.109, 1.159)	<.0001
Max apparent temperature	ATMax	5 (28-33)	1.125 (1.103, 1.149)	<.0001
Min apparent temperature	ATMin	5 (19-24)	1.080 (1.058, 1.102)	<.0001
Average apparent temperature	ATAvg	5 (24-29)	1.137 (1.113, 1.162)	<.0001
Max heat index	HIMax	6 (28-34)	1.122 (1.098, 1.146)	<.0001
Min heat index	HIMin	5 (18-23)	1.096 (1.072, 1.120)	<.0001
Diurnal change in air temperature	TDC	3 (8-11)	1.077 (1.058, 1.096)	<.0001
Diurnal change in apparent temperature	ATDC	3 (7-10)	1.055 (1.1036, 1.073)	<.0001

Figure 1. Plots of estimated rate ratios for fluid and electrolyte imbalance ED visits in relation to different temperature increments from the 25th percentile reference for different temperature metrics, in Atlanta during warm seasons (May-September) for 1993-2012. * RRs marked by asterisk are equivalent to those reported in Table 3 and represent the RR per IQR from the 25th to 75th percentile.

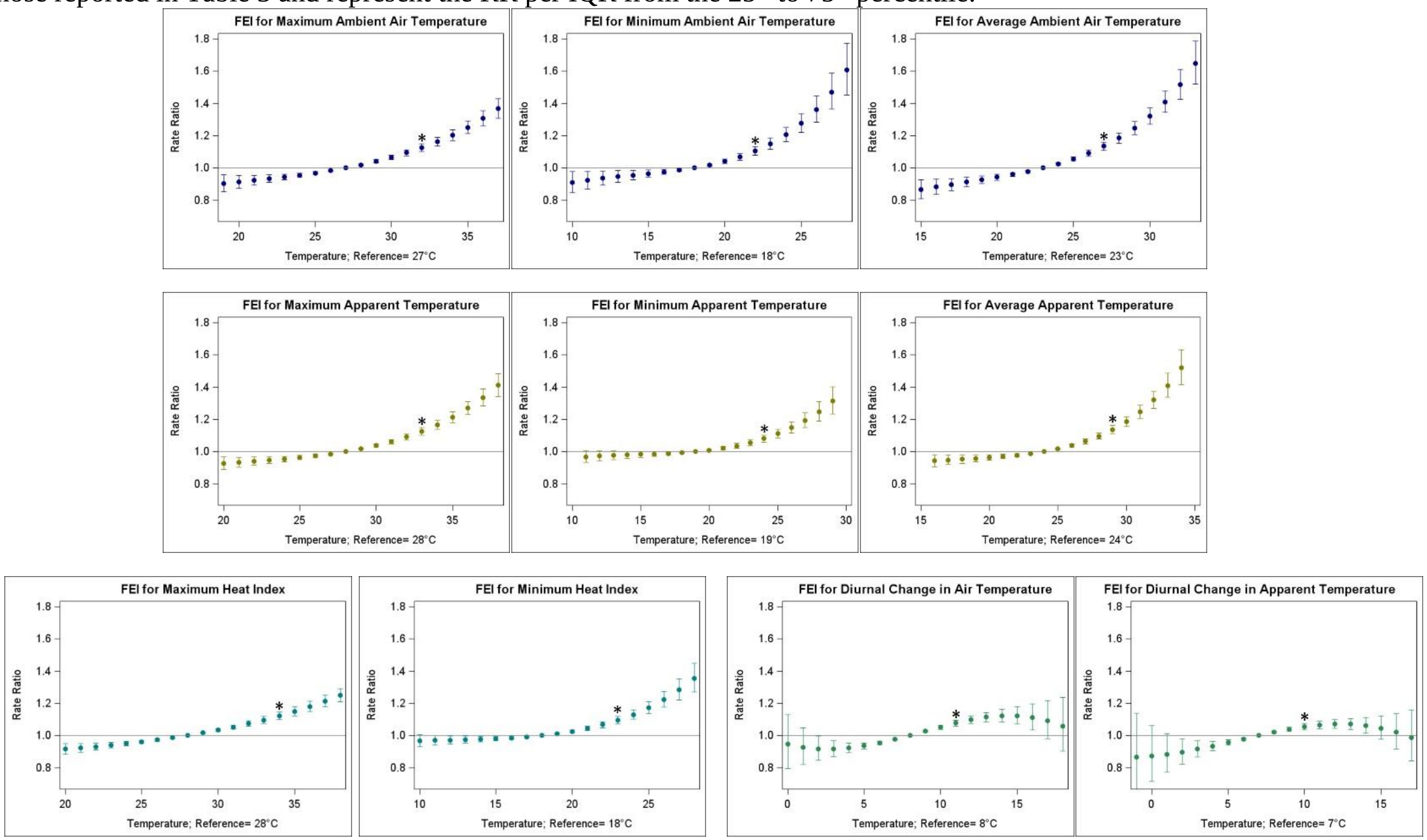

Table 4. Descriptive statistics of fluid and electrolyte imbalance ED visits stratified by modifiers of interest in Atlanta during warm seasons (May-September) for 1993-2012

					Daily Counts of Fluid and Electrolyte Imbalance ED Visits						
	Strata	Total number of ED visits	Sum of total ED visits for complementary strata[1]	# of Days	Mean	Standard Deviation	Minimum	25th Percentile	50th Percentile	75th Percentile	Maximum
All FEI Daily count of ED visits for Fluid and electrolyte imbalance [276]	---	66,369	---	3060	21.7	12.8	0	12	21	31	75
Sex	Female	38,426	65,713	3060	12.6	7.6	0	7	12	18	45
	Male	27,287		3060	8.9	6.1	0	4	8	13	36
Race[2]	Black	14,972	44,384	2601	5.8	5.3	0	2	4	9	27
	Hispanic	1,938		2601	0.7	1.2	0	0	0	1	8
	Other	1,646		2601	0.6	0.9	0	0	0	1	6
	White	25,828		2601	9.9	6.6	0	5	10	14	36
Comorbid Congestive Heart Failure	Present	3,566	66,369	3060	1.2	1.4	0	0	1	2	8
	Absent	62,803		3060	20.5	12.0	0	12	20	29	69
Comorbid Renal Disease	Present	9,477	66,369	3060	3.1	3.6	0	0	2	5	21
	Absent	56,892		3060	18.6	10.1	0	11	19	26	54
Comorbid Diabetes	Present	9,737	66,369	3060	3.2	3.1	0	1	2	5	21
	Absent	56,632		3060	18.5	10.4	0	11	19	26	61
Poverty Area ZCTA WITH ge 20% under poverty level	Poverty Area	11,623	66,343	3060	3.8	3.5	0	1	3	6	19
	Non Poverty Area	54,720		3060	17.9	10.2	0	11	18	25	56
Undereducated Area ZCTA WITH ge 25% without high school education	Undereducated Area	9,005	66,343	3060	2.9	2.0	0	1	3	4	12
	Non Undereducated Area	57,338		3060	18.7	12.0	0	9	18	28	67

[1] There were 656 visits missing sex data, 21,985 visits missing race data, 26 visits missing poverty area data, and 26 visits missing undereducated area data.
[2]The number of days with race data available was lower than 3060 as race information was not available/ was not acquired for the 2007-2009 period.

Table 5. Estimated rate ratios for fluid and electrolyte imbalance ED visits in relation to a change of approximately 1 IQR (from the 25th to 75th percentile) for TMax (27 °C to 32 °C) and ATMax (28 °C to 33 °C) in Atlanta during the warm seasons (May-September) for 1993-2012 (n=3060 days) and for 1998-2012 (n=2295 days).

Heat Vulnerability Factor	**Strata**	**TMax RR (95% CI) All years included (1993-2012)**	1-sided p-value[1]	**TMax RR (95% CI) Reduced time period (1998-2012)**	1-sided p-value[1]	**ATMax RR (95% CI) All years included (1993-2012)**	1-sided p-value[1]	**ATMax RR (95% CI) Reduced time period (1998-2012)**	1-sided p-value[1]
Overall Result		1.125 (1.102, 1.150)**	--	1.121 (1.096 1.1460)**	--	1.125 (1.103, 1.149)**	--	1.123 (1.099, 1.147)**	--
Sex	Female	1.088 (1.060, 1.118)**	**0.000**	1.085 (1.054, 1.117)**	**0.001**	1.085 (1.057, 1.114)**	**0.000**	1.085 (1.055, 1.116)**	0.000
	Male	1.176 (1.138, 1.216)**		1.169 (1.128, 1.210)**		1.181 (1.143, 1.219)**		1.174 (1.135, 1.214)**	
Race[2]	White	1.141 (1.102, 1.180)**	0.599	1.128 (1.087, 1.170)**	0.594	1.127 (1.090, 1.164)**	0.266	1.116 (1.077, 1.156)**	0.274
	Nonwhite	1.157 (1.113, 1.202)**		1.145 (1.099, 1.193)**		1.159 (1.116, 1.204)**		1.150 (1.105, 1.197)**	
	Black	1.143 (1.095, 1.193)**	--	1.132 (1.081, 1.185)**	--	1.143 (1.097, 1.192)**	--	1.135 (1.086, 1.187)**	--
	Hispanic	1.366 (1.211, 1.541)**	--	1.368 (1.209, 1.549)**	--	1.304 (1.159, 1.466)**	--	1.304 (1.155, 1.471)**	--
	Other	--	--	1.028 (0.902, 1.171)	--	--	--	1.072 (0.962, 1.195)	--
Comorbid Congestive Heart Failure	Present	--	--	1.048 (0.959, 1.145)	0.128	--	--	1.069 (0.981, 1.166)	0.254
	Absent	1.130 (1.106, 1.155)**		1.125 (1.099, 1.151)**		1.129 (1.105, 1.153)**		1.126 (1.101, 1.151)**	
Comorbid Renal Disease	Present	1.048 (0.995, 1.104)	**0.005**	1.049 (0.993, 1.108)	**0.012**	1.069 (1.016, 1.125)	**0.037**	1.071 (1.014, 1.130)*	0.063
	Absent	1.137 (1.112, 1.164)**		1.137 (1.112, 1.164)**		1.134 (1.110, 1.159)**		1.132 (1.106, 1.159)**	
Comorbid Diabetes	Present	1.096 (1.040, 1.156)*	0.298	1.100 (1.040, 1.163)*	0.471	1.102 (1.047, 1.160)*	0.391	1.106 (1.047, 1.167)*	0.541
	Absent	1.130 (1.105, 1.156)**		1.124 (1.098, 1.152)**		1.129 (1.105, 1.154)**		1.126 (1.100, 1.152)**	
Poverty Area	Poverty Area	1.132 (1.079, 1.187)**	0.815	1.130 (1.075, 1.188)**	0.730	1.131 (1.080, 1.185)**	0.819	1.128 (1.074, 1.183)**	0.859
	Non Poverty Area	1.125 (1.099, 1.151)**		1.119 (1.092, 1.147)**		1.125 (1.100, 1.150)**		1.122 (1.096, 1.149)**	
Undereducated Area	Undereducated Area	1.175 (1.114, 1.239)**	0.094	1.172 (1.104, 1.244)**	0.123	1.183 (1.124, 1.245)**	0.069	1.179 (1.113, 1.248)**	0.077
	Non Undereducated Area	1.118 (1.093, 1.144)**		1.114 (1.087, 1.141)**		1.116 (1.092, 1.141)**		1.115 (1.089, 1.141)**	

= $p<0.0001$;** *= $p<0.05$

[1]p-values are for test for heterogeneity

[2]The number of days with race data available was lower than 3060 as race information was not available/ was not acquired for the 2007-2009 period.

Table 6. Summary table comparing results of sensitivity analyses for associations of fluid and electrolyte imbalance ED visits and TMax and ATMax in Atlanta during the warm seasons (May-September) during 1993-2012

	Maximum Temperature (Change from 27^{o}C to 32^{o}C)			**Maximum Apparent Temperature (Change from 28^{o}C to 33^{o}C)**		
Model	**RR (95% CI)**	**p-value**	**% difference from original**	**RR (95% CI)**	**p-value**	**% difference from original**
Original: All FEI, all covariates	1.125 (1.102, 1.150)	<0.0001	---	1.125 (1.103, 1.149)	<.0001	---
Omitted time variables: year, year-specific cubic splines with monthly knots, year-day interaction variables	1.109 (1.089, 1.131)	<0.0001	-1.43%	1.095 (1.077, 1.113)	<.0001	2.70%
Omitted time splines: year-specific cubic splines with monthly knots	1.122 (1.101, 1.144)	<0.0001	-0.29%	1.103 (1.085, 1.121)	<.0001	-2.02%
Omitted time splines, added month as a class variable	1.132 (1.109, 1.155)	<0.0001	0.57%	1.130 (1.108, 1.152)	<.0001	0.37%
Omitted splines, added biweek as a class variable	1.135 (1.112,1.159)	<0.0001	0.86%	1.133 (1.111, 1.156)	<.0001	0.68%
Omitted hospital participation	1.131 (1.108, 1.155)	<0.0001	0.53%	1.132 (1.109, 1.155)	<.0001	0.55%
Omitted cubic terms for dew point temperature	1.124 (1.101, 1.148)	<0.0001	-0.09%	---	---	---
Omitted holiday variables	1.125 (1.102, 1.149)	<0.0001	-0.03%	1.126 (1.103, 1.149)	<.0001	0.03%
Omitted day of week	1.130 (1.106, 1.54)	<0.0001	0.36%	1.129 (1.106, 1.153)	<.0001	0.35%
Omitted cubic temp	1.125 (1.106, 1.144)	<0.0001	-0.04%	---	---	---

Figure 2. Plots of estimated rate ratios for fluid and electrolyte imbalance ED visits in relation to different temperature increments from the 25th percentile reference for TMax by modifiers of interest in Atlanta during warm seasons (May-September) for 1998-2012. * RRs marked by asterisk are equivalent to those reported in Table 5 and represent the RR per IQR from the 25th to 75th percentile