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Heat Exposure and Emergency Department Visits for Sepsis in Phoenix, Arizona

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B.A.
Augustana College
2017

Thesis Committee Chair: Stefanie Ebelt, Sc.D.

An abstract of
a thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

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Abstract

Purpose: As climate change and global warming continues, the frequency and severity of extreme heat events are likely to increase. High heat can lead to death and severe illnesses requiring emergency care. Sepsis is initially diagnosed and treated in emergency departments (EDs). Little is known about the potential impact of outdoor temperatures on risk of sepsis. To address this gap, we assessed the association between heat exposure and emergency department (ED) visits for sepsis patients in Phoenix, Arizona during 2016-2019.

Methods: We examined daily counts of ED visits for patients with a diagnosis of sepsis present on arrival at the ED and assessed focus of infection (FOI) sites for sepsis-related visits, using diagnosis code information. We estimated associations of these outcomes with daily population-weighted average (PWA) temperature exposure data from Daymet using Poisson time-series analysis. We controlled for long term time trends, vapor pressure as a proxy of dewpoint temperature, day of week, and federal holidays. We estimated rate ratios (RRs) and 95% confidence intervals (CI) for the primary model determining the association between sepsis-related ED visits and PWA maximum temperature. In secondary models, we assessed associations of sepsis-related ED visits for each focus of infection site and PWA maximum temperature, and estimated season-specific associations.

Results: In overall year-round models, we observed a positive association between same-day PWA maximum temperature and sepsis-related ED visits (RR of 1.014 95% CI (1.000 – 1.028) for a 5 degree increase in temperature from 24 – 29 degrees C). When stratifying by FOI-specific ED visits, associations of same-day maximum temperature and ED visits for sepsis infections at urogenital sites were positive. Associations were strongest for warm seasons, including Spring, Summer, and Autumn.

***Conclusions**:* Results of this study suggest that outdoor heat exposure may be an important risk factor for sepsis, during the warm season and for urogenital-based infections. Exposure mitigation measures during times of high heat may reduce emergency care needs. Increases in emergency department preparedness during times of high heat may be needed to ensure positive outcomes for patients.

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1. Introduction

With climate change resulting in increases and severity of extreme weather events, the threat to human health is elevated (Sarofim et al., 2016). Oftentimes underestimated, a small change in temperature can lead to an increase in deaths and severe illnesses. Heat is the leading cause of weather-related deaths in the U.S. (Gubernot, 2013). According to U.S. national injury surveillance, heat-related illnesses (HRI) are the most common form of injury due to environmental exposures examined and accounted for 20,775 emergency department (ED) visits between 2001 and 2004 (Pillai et al, 2013). As temperatures rise due to climate change, heat-related ED visits may continue to rise as well.

Research has shown that risk of heat-related ED visits is associated with age, sex and diagnosed medical conditions, such as heart disease, diabetes, renal disease, and electrolyte disturbances (Pillai et al, 2013). For example, as air temperature increases and the body tries to regulate its temperature, the associated cardiovascular strain may increase and exacerbate underlying medical conditions (Gubernot, 2013). In addition to being at higher risk of HRI, patients who have underlying medical conditions (heart disease, diabetes, renal disease, and electrolyte disturbances), those who are 65+, or have a weakened immune system are also at a higher risk for sepsis (CDC, 2021). Sepsis is the body's response to an infection (often bacterial), leading to tissue degradation and causing organ dysfunction or failure (Mayo Clinic, 2021). As inflammation throughout the body occurs, the development from sepsis to severe sepsis to septic shock can arise and lead to organ systems shutting down (Schefold et al., 2008).

Emergency departments are often the initial healthcare setting for patients to be diagnosed and treated for sepsis (Wang et al, 2017). Sepsis is diagnosed within a patient based on their symptoms, medical history, and medical tests. Sepsis symptoms include fevers, high heart rate, shortness of breath, low blood pressure, and decreased urine production (Yale Medicine, 2019). Medical tests to identify sepsis can include blood tests, urine tests, and confirmatory tests (protein and bacteria tests); if presence of an infection is suspected, x-rays, sputum samples, CTs, and MRIs may be completed as well (Sepsis Alliance, 2020). Diagnosis of sepsis can be difficult to make as there is not a single gold standard method for detection.

Like many other infections, sepsis diagnosis can vary by season and pathogen. Certain infections are more likely to occur during different times of the year, with the risks of pneumonia greatest in the winter, urinary tract infections greatest in autumn, and surgical infections greatest in summer (Schwab et al., 2020). Seasonality also plays a role in the focus of infection (FOI) area for sepsis diagnosis. Given the health impacts of heat exposure and vulnerabilities of those with underlying medical conditions, it is possible that heat may impact the risk of sepsis. Currently, the literature on heat and ED visits for sepsis is sparse. In one previous study, the risk of hospitalization for adults 65 and older increased during times of heat waves (2+ days with temperatures exceeding the 99^{th} percentile for daily temperatures). Associations with heat waves were observed for patients with septicemia, as well as four other diseases (Bobb et al., 2014).

To further examine the potential for heat to be a risk factor for sepsis, we assessed the association between outdoor heat exposure and ED visits for sepsis in Phoenix, Arizona during 2016-2019; leveraging data acquired as part of the Environmental Exposures and Health Across the Nation (ENVISION) study (Thomas et al., 2021). Of particular interest was identification of seasons and FOI sites in driving the heat-sepsis association.

2. Study Design:

2.1 Emergency Department Visit Data Collection

ED visit and hospitalization billing records that were collected from Phoenix area hospitals from the Arizona Department of Health Services, Bureau of Public Health Statistics, for 2016-2019. Key variables of interest from the records were date of visit, ZIP code of patient residence, primary and secondary International Classification of Diseases, version 10 (ICD-10) discharge diagnosis codes, and 0/1 indicators of whether diagnosis codes were present on arrival (POA) at the ED. Given that sepsis cases can arise during patients' hospital stays and are thus less likely to be influenced by outdoor temperature, we restricted our assessment to only visits with sepsis diagnosis codes recorded at POA to better capture community-acquired sepsis. ED visits were included in the study if the patient resided in a ZIP code that corresponded to a ZIP code tabulation area (ZCTA) with centroid located within the Phoenix metropolitan statistical area (MSA). MSAs are determined by the U.S. Office of Management and Budget based on contiguous counties; the Phoenix MSA consisted of 2 counties (Pinal and Maricopa) for this study.

The main sepsis outcome included visits for severe sepsis and septic shock, and was defined based on ED visit records having a primary or secondary ICD-10 code for one or more of the following diagnoses present on arrival: salmonella sepsis (A021), anthrax sepsis (A227), erysipelothrix sepsis (A267), listerial sepsis (A327), sepsis due to streptococcus (A400, A401, A403, A408, A409), sepsis due to staphylococcus (A4101, A4102, A411, A412), sepsis due to Hemophilus influenzae (A413), sepsis due to anerobes (A414), gram-negative sepsis (A4150, A4159), sepsis due to Escherichia coli (A4151), sepsis due to pseudomonas (A4152), sepsis due to serratia (A4153), sepsis due to Entercoccus (A4181), other specified sepsis (A4189), sepsis from an unspecified organism (A419), actinomycotic sepsis (A427), gonococcal sepsis (A5486), and severe sepsis with and without septic shock (R6521, R6520) (CMS, 2022).

To examine sepsis-related visits by specific focus of infections, we created FOI-specific sub-outcomes that additionally selected ED visit records having a primary or secondary ICD-10 code for one or more of the following diagnoses present on arrival, by FOI: respiratory (A15, A16, J00-J06, J09-J18, J20-J22, J31, J32, J39, J85, J86), urogenital (A18, A51, A54, A56, A59, A60, N30, N39, N41, N45, N49, N70-N77, O23), abdominal (A00-A09, A18, A42, A74, K35-K38, K57, K61, K63, K65, K67, K75, K80, K81, K83), bone/soft tissue (A18, A26, A28, A31, A32, A36, A42, A43, A46, A48, L00-L08, M00, M01, M46, M49, M60, M86), and blood (A19, A40, A49) (Imaeda et al., 2021).

For sepsis and FOI-specific sub-outcomes, we aggregated patient visits by day to obtain the daily counts for ED visits for all outcomes.

2.2 Meteorology Data

The exposure data consisted of population-weighted averages (PWA) for daily average temperature, daily maximum temperature, and daily minimum temperature (degrees Celsius) and vapor pressure (in Pascals) used as a proxy for average dewpoint temperature (Sensirion, 2006). All exposure data were obtained through the Daily Surface Weather and Climatological Summaries (DayMet). DayMet is a research product of the Environmental Sciences Division at Oak Ridge National Laboratory and provides estimates of weather and climate variables at 1km grid cell resolution (Thorton et al, 2021). Daily population-weighted averages (PWAs) were previously developed for this study (Thomas et al., 2021).

2.3 Statistical Methods/Analysis

Poisson regression was used to assess the main association between daily sepsis-related ED visit counts and daily same-day (lag 0) PWA maximum temperature. To account for potential non-linear relationships between temperature and sepsis-related ED visits, we modeled temperature using cubic terms (i.e., including linear, quadratic, and cubic terms for the daily PWA maximum temperature in the model). The model was adjusted for other time-varying covariates. Long-term time trends were controlled by including variables for month and year and a product term of month*year; day of the week and holidays were controlled for using indicator variables; and average dewpoint temperature was controlled using linear, quadratic, and cubic terms. Rate ratios (RR) and 95% confidence intervals (CI) were estimated for various temperature changes (in degrees C) from 24 degrees Celsius, which represented the 25^{th} percentile of the maximum temperature distribution in Phoenix during the study period.

In the secondary analyses, we stratified the model by season to obtain season-specific RRs for: Spring (March – May), Summer (June – August), Autumn (September – November), and Winter (December – February). We also stratified the model by FOI site to obtain FOI-specific RRs. These secondary models controlled for time-varying covariates the same way as the main model.

Lastly, we conducted a sensitivity analysis to assess the certainty of our results to changes within the model. The main model outcome was daily ED visit counts of sepsis among patients with any ICD-10 code for sepsis on their billing record; we compared these results to those from a model assessing the effect of temperature on daily ED visits for sepsis among patients with sepsis as a primary ICD-10 code on their billing record.

3. Results

3.1 Descriptive Analysis Results

Descriptive statistics (mean, standard deviation, minimum, quartile 1, median, quartile 3, maximum, and quartile range) for the exposure data (temperature metrics) are included in Table 1. The average daily PWA maximum temperature for Phoenix during 2016-2019 was 30.5 degrees Celsius throughout the four-year study period across all seasons.

Variable	Mean	Std Dev	Minimum	Lower Quartile	Median	Upper Quartile	Maximum	Quartile Range
Maximum Temperature	30.5	8.6	8.3	23.6	30.7	38	47.8	14.4
Minimum Temperature	15.3	7.9	-2.6	8.9	14.5	22.3	31.7	13.5
Average Temperature	22.9	8.1	4.4	16	22.5	30.4	38	14.4
Vapor Pressure	1046.1	439	235.6	717.4	967.2	1351.4	2555.2	634

Table 1. Descriptive statistics for temperature exposure data, in degrees Celsius. Vapor pressure is a dew point temperature proxy, in Pascals.

The outcome data for this study consisted of 141,822 sepsis-related ED visits for Phoenix, with an average daily sepsis count of 97.1. Of those ED visits, 131,360 (92.6%) had sepsis as the primary ICD-10 code. For 127,132 visits, patients also had ICD-10 coding for specific focus of infection sites related to respiratory (500,056 visits), urogenital (33,971 visits), abdominal (18,328 visits), bone/soft tissue (23,517 visits), and blood (1,260 visits). Figure 1 shows the comparison of daily sepsis and FOI-specific ED visit counts over the study period. Total and average ED visit counts for each outcome are presented in Table 2. Correlations between FOI-specific and sepsis ED visit counts are included in Table 3.

Variable	Sum	Mean	Std Dev	Minimum	Lower Quartile	Median	Upper Quartile	Maximum	Quartile Range
Sepsis (Explicit Medicaid/Medicare)	141822	97.1	16.3	3	86	96	107	170	21
(Primary) Sepsis	131360	89.9	15.4	2	80	89	99	159	19
Respiratory FOI	50056	34.3	13.4	1	25	31	41	117	16
Urogenital FOI	33971	23.3	5.1	0	20	23	27	43	7
Abdominal FOI	18328	12.5	3.7	0	10	12	15	25	5
Bone and soft tissue FOI	23517	16.1	4.5	0	13	16	19	34	6
Blood FOI	1260	0.9	0.9	0	0	1	1	6	1

Table 2. Descriptive statistics for sepsis and focus of infection outcome data. Sum is the total number of daily ED visit counts and mean is the average daily count.

	Sepsis	Respiratory FOI	Urogential FOI	Abdominal FOI	Bone/Soft Tissue FOI	Blood FOI
Sepsis	1	0.77714 <0.0001	0.43984 <0.0001	0.31762 <0.0001	0.40545 <0.0001	0.15825 <0.0001
Respiratory FOI	0.77714 <0.0001	1	0.16479 <0.0001	0.06611 0.0115	0.05564 0.0335	0.1224 <0.0001
Urogenital FOI	0.43984 <0.0001	0.16479 <0.0001	1	0.17988 <0.0001	0.16008 <0.0001	0.05205 0.0467
Abdominal FOI	0.31762 <0.0001	0.06611 0.0115	0.17988 <0.0001	1	0.13384 <0.0001	0.0494 0.059
Bone/Soft Tissue FOI	0.40545 <0.0001	0.05564 0.0335	0.16008 <0.0001	0.13384 <0.0001	1	0.16064 <0.0001
Blood FOI	0.15825 <0.0001	0.1224 <0.0001	0.05205 <0.0001	0.0494 0.059	0.16064 <0.0001	1

Table 3. Correlation of daily counts between sepsis and different focus of infection sites.

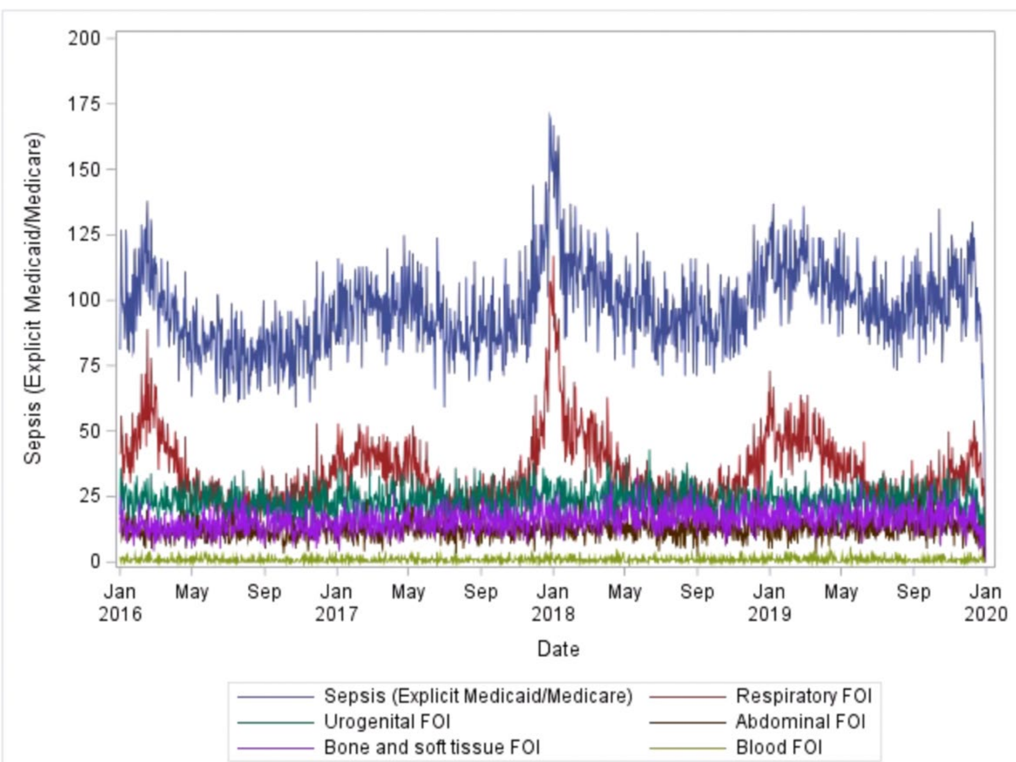

Figure 1. Comparison of daily counts of outcomes over time.

Descriptive statistics for sepsis-related ED visits by season are shown in Table 4. Winter had the highest average sepsis-related ED visit counts at 107.7 within the months December – February. This was followed by Spring and Autumn. The lowest average sepsis-related ED visit counts were in Summer with 89.3 counts. Figure 2 shows the comparative histograms of sepsis-related ED visits count distributions across seasons.

Season	Number Obs	Mean	Std Dev	Minimum	Lower Quartile	Median	Upper Quartile	Maximum	Quartile Range
Spring	368	99.4	12.4	63	91	100	108	129	17
Summer	368	89.3	11.9	59	82	89	97	124	15
Autumn	364	92	13.2	59	83	91	101	144	18
Winter	361	107.7	19.8	3	96	107	119	170	23

Table 4. Descriptive statistics for daily counts of sepsis-related ED visits stratified by season.

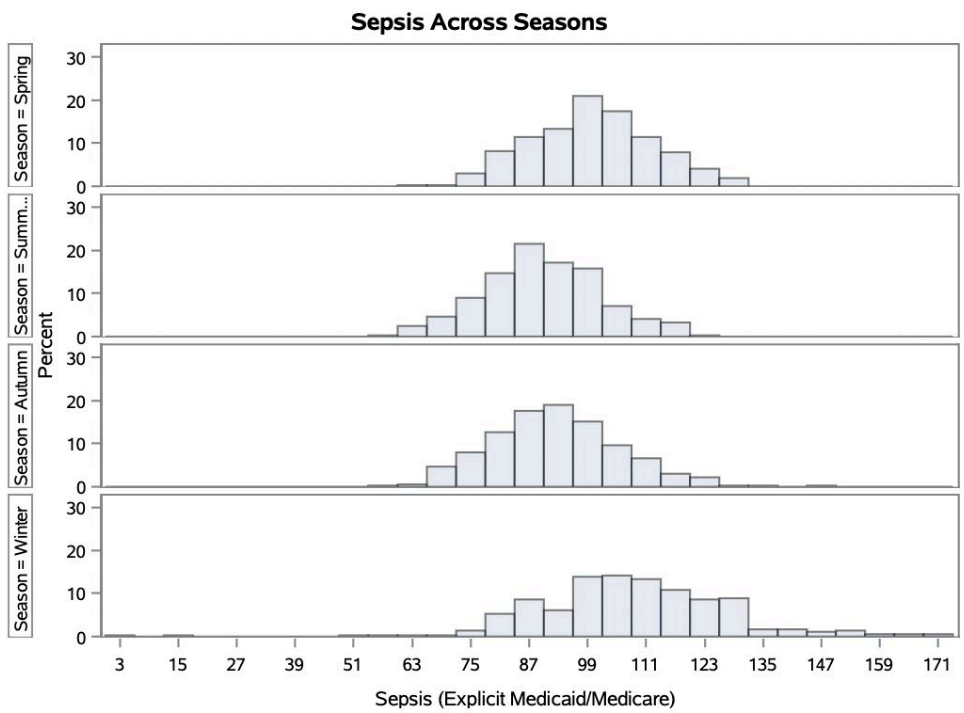

Figure 2. Daily counts of sepsis-related ED visits across seasons from 2016-2019.

3.2 Main Model Results

Estimates for the association between sepsis-related ED visits and PWA maximum temperature were assessed between 13 to 45 degrees Celsius, corresponding to the range of daily maximum temperatures from the 1st to 99th percentiles observed during the study period.

Throughout the temperature range, we observed a positive association between sepsis-related ED visits (for those with sepsis as the primary or secondary outcome) and daily temperature as shown in Figure 3. Holding the 25th percentile (24 degrees) as the reference, RRs were protective for decrease in temperature from the reference (e.g., RR of 0.975 (95% CI (0.963 – 0.987) for the change from 24 degrees C to 19 degrees C); and RRs were positive for increases in temperature compared to the reference (e.g., RR of 1.014 (95% CI 1.000-1.028) for the change from 24 degrees C to 29 degrees C).

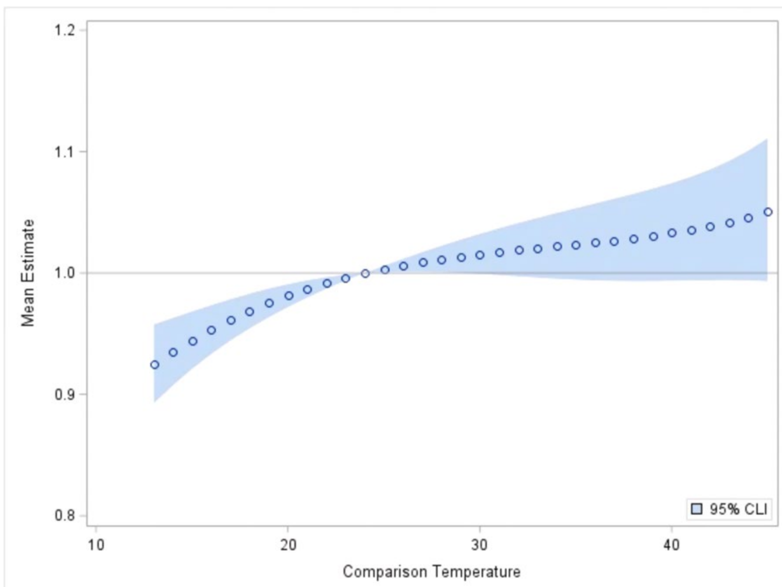

Figure 3. Rate ratios (RRs) for sepsis-related ED visits across comparison temperatures, reference to 24 degrees C.

3.3 Secondary Analysis Results

Estimates for the secondary analysis considered the association between focus of infection sites (consisting of respiratory, urogenital, abdominal, bone/soft tissue, and blood) and PWA maximum temperature between 13 to 45 degrees Celsius, also from the 1st to the 99th percentiles. For those with respiratory FOIs, we observed an overall null or decreased risk of ED visits with increasing maximum temperature as shown in Figure 4A. Given that the daily counts of respiratory FOIs were highest in the Winter season (Figure 1), these results may be expected given the lower temperature range in the winter. Shown in Figure 4B, we observed a positive association between maximum temperature and ED visits for urogenital FOIs and sepsis, similar to the main model. For example, RRs were protective for a decrease in all temperatures below the reference (e.g., RR of 0.970 (95% CI (0.947 – 0.992)) for the change from 24 degrees C to 19 degrees C); and RRs were positive for increases in all temperatures above the reference (e.g., RR of 1.018 (95% CI (0.993 – 1.044)) for the change from 24 degrees C to 29 degrees C). For those with abdominal FOIs (Figure 4C), there was a decreased risk of sepsis-related ED visits across all temperatures compared to 24 degrees (e.g., RR of 0.976 (95% CI 0.946 – 1.007) and RR of 0.989 (95% CI 0.956 – 1.023)) for a decrease and increase in 5 degrees C respectively. Bone and soft tissue FOIs had a null association with sepsis-related ED visits, as shown at the fairly flat curve in Figure 4D. RRs were slightly protective for decrease in temperature from the reference (e.g., RR of 0.977 (95% CI (0.949 – 1.004)) for the change from 24 degrees C to 19 degrees C); and RRs were positive for increases in temperature compared to the reference (e.g., RR of 1.010 (95% CI (0.979 – 1.04)) for the change from 24 degrees C to 29 degrees C). Sepsis-related ED visits for those with blood FOIs had a negative association for all RRs. There was an increased risk across all temperatures (e.g., RR of 1.023 (95% CI 0.913 – 1.148) and RR of 0.944 (95% CI 0.832 – 1.071) for a decrease and increase in 5 degrees C respectively. As shown in Figure 4E, the confidence intervals indicate the uncertainty of this association. Note, the change in the y axis interval for Figure 4E in comparison with the others in Figure 4 to encompass the large CIs.

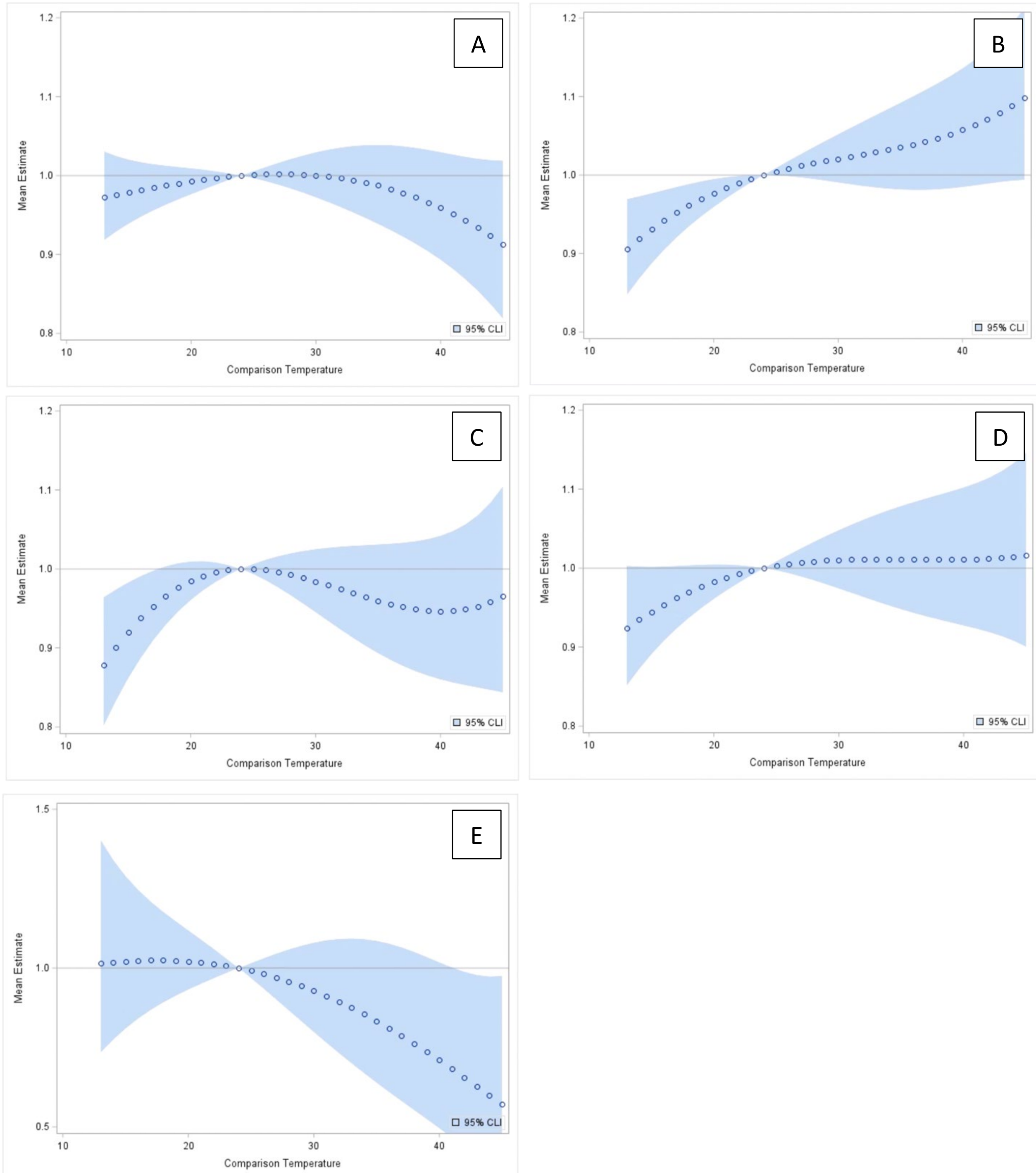

Figure 4. Rate ratios (RR) for focus of infection (FOI) sites across comparison temperatures, reference to 24 degrees C. 4A: respiratory FOI, 4B: urogenital FOI, 4C: abdominal FOI, 4D: bone and soft tissue FOI, and 4E: blood FOI.

In addition to the secondary analysis for FOI, we additionally completed an analysis to determine an association between sepsis-related ED visits and temperature, stratified across seasons throughout the 4-year period. During the Spring season (March-May), there was a slight positive association between sepsis-related ED visits and temperature as shown in Figure 5A. RRs were protective for a decrease in all temperatures below the reference (e.g., RR of 0.963 (95% CI (0.923 – 1.004)) for a change from 24 degrees C to 19 degrees C). RRs were positive for increases in all temperatures above the reference (e.g., RR of 1.021 (95% CI (1.001 – 1.042)) for the change from 24 degrees C to 29 degrees C). For the Summer season (June – August), there was a positive association between sepsis-related ED visits and temperature; however, Summer had wider confidence intervals compared to other seasons seen in Figure 5B. RRs were protective for all temperatures below the reference (e.g., RR of 0.667 (95% CI (0.200 – 2.225)) for a change from 24 degrees C to 19 degrees C). RRs were positive for increases in all temperatures above the reference (e.g., RR of 1.162 (95% CI (0.609 – 2.215)) for the change from 24 degrees C to 29 degrees C). In Figure 5C, results for Autumn (September – November) were very similar to Spring, with having a slight positive association across temperatures. RRs were protective for a decrease in all temperatures below the reference (e.g., RR of 0.992 (95% CI (0.962 – 1.023)) for a change from 24 degrees C to 19 degrees C). RRs were positive for increases in all temperatures above the reference (e.g., RR of 1.015 (95% CI (0.987 – 1.045)) for the change from 24 degrees C to 29 degrees C). Across Winter months (December – February), the association was generally negative shown in Figure 5D. RRs were protective for a decrease in all temperatures below the reference (e.g., RR of 0.956 (95% CI (0.926 – 0.988)) for a change from 24 degrees C to 19 degrees C). However, unlike the other seasons, RRs were positive for increases in temperatures only at 25- and 26-degrees C. For the remaining temperatures, RRs were negative, (e.g., RR of 0.969 (95% CI (0.890 – 1.055)) for the change from 24 degrees C to 29 degrees C). Results across the stratified models were generally like that of the primary model, with a positive association across temperatures, except for the Winter season. This is in agreeance with our hypothesis of heat impacts on sepsis-related ED visits, as the risk decreased within the Winter months when temperatures were not as high as the other seasons.

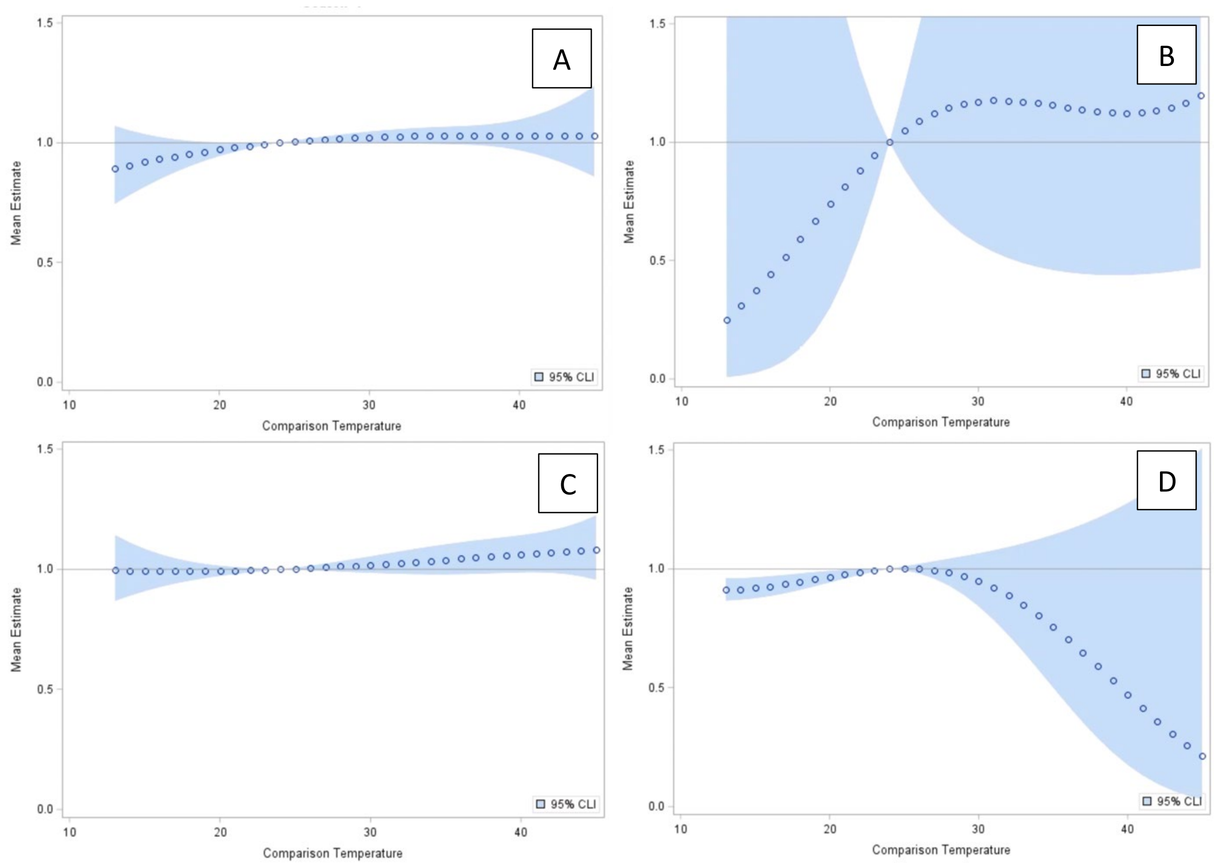

Figure 5. Rate ratios (RR) for sepsis across comparison temperatures, reference to 24 degrees C, stratified by season. 5A: Spring, 5B: Summer, 5C: Autumn, 5D: Winter.

In sensitivity analyses, associations of maximum temperature and sepsis-related ED visits for patients whose primary outcome was sepsis were very similar to main model associations, in which the outcome included patients with either a primary or secondary code for sepsis.

4. Discussion

In this study, we conducted a time-series analysis to determine the association between heat exposure on sepsis-related ED visits during the 2016-2019 period in the Phoenix, Arizona metropolitan area. We found a positive association between the daily PWA maximum temperature and overall sepsis-related ED visits for Phoenix. The rate ratios for change in the PWA maximum temperature from the 1^{st} to the 99^{th} percentile for the sepsis outcome were lowest at lower temperatures and were higher as temperatures increased. In general, relative to our reference temperature of 24 degrees C, RRs for temperatures under 32 degrees C were statistically significant, which may be due to sparser data temperatures higher than 32 degrees C.

The positive association we found agrees with previous studies that found heat exposure (heat waves, high outdoor temperature) can lead to increased hospital visits for certain diseases and disorders, such as septicemia (Bobb et al., 2014), and blood stream infections (BSIs) (Schwab et al., 2020). However, while BSIs cause roughly 25-30% of sepsis cases, not all BSIs will result in sepsis occurrence (Huerta & Rice, 2019). There are many pathways in which death or disease can occur due to heat. One possible mechanism for the positive association with sepsis-related ED visits and temperature is through heat cytotoxicity. Heat cytotoxicity is a heat damaging mechanism that occurs when someone is exposed to heat and their body temperature passes the threshold of cell thermal tolerance. Heat cytotoxicity can break down cell membranes and lead to cell damage by increasing permeability of cells and tissues. Ultimately, heat cytotoxicity can lead to neurological damage, sepsis, inflammatory responses, disseminated intravascular coagulation, tubular necrosis, and rhabdomyolysis (Mora et al., 2017). With heat cytotoxicity, pathogens and toxins can be more readily adsorbed into the body due to the increased cell and tissue permeability, causing membrane breakdown and ultimately organ disfunction or failure. During heat cytotoxicity, sepsis risk is increased as the destruction of cells and tissues can cause holes in mucosal membranes in which bacteria and endotoxins can then leak into the blood system, causing sepsis and ultimately activating a systemic inflammatory response (SIR) (Mora et al., 2017).

To our knowledge, this is the first study to examine the effects of outdoor heat on FOI-specific sepsis-related ED visits. Our overall visit counts agree with other studies that have assessed common infection sites for sepsis. Abe et al. (2019), found that the most common infection sites for sepsis include lungs (respiratory), intra-abdomen, urinary tract, soft tissue, and bloodstream. The Abe et al. (2019) study also considered undifferentiated sepsis as well as the central nervous system as an FOI, but the majority of cases fell into the first 5 FOI groups as determined in the current study. Among the FOI subgroups, we observed the strongest positive associations of heat with urogenital FOIs. This makes sense based on the organs that are a part of the urogenital system. The urogenital system consists of two groups: the urinary tract and the genital tract; the kidneys are included within the urinary tract and play a large role in protecting the body from heat and dehydration (Johnson et al., 2019). Heat stress and dehydration can lead to heatstroke leading to acute kidney injury, chronic kidney disease, kidney stone formation and increase the risk of urinary tract infections (Johnson et al., 2019). We observed the strongest negative association of heat with the blood FOI; however, this may be due to low daily counts (1,260 daily total counts) of FOIs for blood across the study period. This is interesting as infections get worse, they can travel through the bloodstream and impact other areas of the body, so we would expect to see more counts of blood FOI as sepsis becomes more severe.

Across the four seasons, we observed that Winter had the highest counts of sepsis-related ED visits (n=38,869) over the 4-year period, followed by Spring (36,597), Autumn (33,505), and Summer (32,851). The larger numbers of visits in the Winter compared to other seasons is similar to previous studies. McNevin et al. (2019) found an increased sepsis-related ED visit prevalence in Winter compared to Summer in Ireland. In agreeance, Danai et al. (2007) found that cases of sepsis were highest during the Winter and largely related to respiratory infections. Despite higher sepsis-related ED visits in winter, our epidemiologic results indicate that short-term changes in temperature were more associated with sepsis visits during the warmer seasons of Spring, Summer, and Autumn. During Winter, there was an increased risk of ED visits at low temperatures of 13 degrees C up to the reference temperature (24 degrees C); associations above the reference temperature appeared protective but also uncertain, which may be due to sparse data at high temperatures especially in the Winter period. In general, the large CIs for summer- and winter-specific associations suggest large uncertainty in the model results; this may be due in part to low power and may also be indicative of needing tighter temporal controls for these season-specific models.

This study had a number of strengths including analysis of a multi-year period in an arid and hot region, of Phoenix, Arizona. In Phoenix, heat exposure is a concern as approximately 3,000 people visit the ED every summer due to heat (National Weather Service, 2021). Data included a multi-year period with high outcome visit counts that provided sufficient power to detect associations of interest, in particular for the overall analyses (Winquist et al., 2012). Power was naturally weaker for analyses stratified by some FOIs (e.g., blood, which had <1 visit/day) and seasons. We also acknowledge several limitations. First, the definition of sepsis has much variability and there is not a gold standard to diagnosis it (Singer et al., 2016). This can lead to both over and underdiagnosis depending on the medical center and physicians' definition of sepsis. Therefore, with our outcome definition, we may have counted sepsis cases that were not in fact sepsis, or we may have missed cases that were truly sepsis. Previous studies have found that coding for sepsis greatly varies across individual studies and ICD diagnosis code definitions used (Jolley et al., 2015). Lastly, our results may be impacted by residual confounding or effect modification due to covariates that we could not consider directly within our study. Age and place of residence were not provided within this study. Previous studies have found that sepsis incidence increases with age and can be associated with high mortality rates (Martin-Loeches et al., 2019). Since Arizona could be considered a snow-bird state, especially for older individuals, this could have led to an increase in sepsis ED visits during the winter months as individuals from colder environments live in Phoenix for the winter.

As our study was focused in Phoenix, which often is warm even in the cold months and has a low humidity in comparison to other U.S. states, our study may not be generalizable to other states/cities due to environmental differences (World Population Review, 2022). Not only can environmental differences change the sepsis-related ED visits, but the use of air conditioning in high temperature regions can also impact health outcomes. Air conditioning could impact the body's response to heat so the threshold of cell thermal tolerance in the body is not passed. This could lead to a decrease in sepsis-related ED visits because heat cytotoxicity would not occur in individuals. A previous study found that owning and using an air conditioner can significantly reduce the impact of temperature on health outcomes (Ostro et al., 2010). No data was available on an individual's use of air conditioning throughout the year-long time frame from 2016-2019. Although we are looking at community acquired sepsis in this study, Saran et al. (2020) noted that the heating, ventilation, and air-conditioning (HVAC) systems within EDs and hospitals is important to maintain in order to ensure that hospital acquired infections (like those that can lead to sepsis) are being prevented (Saran et al., 2020).

5. Conclusions

Overall, we observed a positive association between heat exposure (PWA maximum temperature) and sepsis-related ED visits. Positive associations were also found within the urogenital FOI, as well as the Spring, Summer, and Autumn seasons. We found negative associations for visits with a blood FOI and for visits occurring within the Winter season, although these associations had high uncertainty. Overall, our results could lead to important changes and support being made during times of high heat for emergency department preparedness and protecting the health of patients, especially of those with adverse health outcomes. As the world continues to become warmer, these results could provide insight into health impacts due to climate change.

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