

Journal Pre-proof



Associations Between Ambient Extreme Heat Exposure and Emergency Department Visits Related to Kidney Disease

Yanji Qu, MD, PhD, Wangjian Zhang, MD, PhD, Asi-Yahola M. Boutelle, MS, MDS, Ian Ryan, PhD, Xinlei Deng, PhD, Xiaoqing Liu, MD, Shao Lin, MD, PhD

PII: S0272-6386(22)00918-0

DOI: <https://doi.org/10.1053/j.ajkd.2022.09.005>

Reference: YAJKD 57778

To appear in: *American Journal of Kidney Diseases*

Received Date: 5 February 2022

Accepted Date: 5 September 2022

Please cite this article as: Qu Y, Zhang W, Boutelle AYM, Ryan I, Deng X, Liu X, Lin S, Associations Between Ambient Extreme Heat Exposure and Emergency Department Visits Related to Kidney Disease, *American Journal of Kidney Diseases* (2022), doi: <https://doi.org/10.1053/j.ajkd.2022.09.005>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2022 Published by Elsevier Inc. on behalf of the National Kidney Foundation, Inc.

**Associations Between Ambient Extreme Heat Exposure and Emergency Department Visits
Related to Kidney Disease**

Yanji Qu, MD, PhD ^{1,2,3}, Wangjian Zhang, MD, PhD ^{2,3}, Asi-Yahola M Boutelle, MS, MDS ²,

Ian Ryan, PhD ², Xinlei Deng, PhD ², Xiaoqing Liu, MD ¹, Shao Lin, MD, PhD ^{2,*}

¹ Guangdong Cardiovascular Institute, Guangdong Provincial People's Hospital, Guangdong

Academy of Medical Sciences;

² Department of Environmental Health Sciences, School of Public Health, University at Albany,

State University of New York;

³ Y.Q. and W.Z. contributed equally to this work.

* Address for Correspondence: Shao Lin, MD, PhD, Department of Environmental Health

Sciences, School of Public Health, University at Albany, State University of New York, One

University Place, Rensselaer, Albany, NY 12144, USA. E-mail: slin@albany.edu

Abstract

Rationale & Objective: Extreme heat exposure (EHE) is associated with multiple diseases.

However, our current understanding of the specific impact of extreme heat exposure on kidney disease is limited.

Study Design: Case-crossover study.

Setting & Participants: 1,114,322 emergency department (ED) visits with a principal diagnosis of kidney disease were identified in New York state, 2005-2013.

Exposure: EHE was defined as when the daily temperature exceeded the 90th percentile temperature of that month during the study period in the county.

Outcomes: ED visits with a principal diagnosis of kidney disease and its subtypes (International Classification of Diseases 9 (ICD-9): 580-599, 788).

Analytical Approach: EHE on the ED visit days was compared to EHE on control days using a conditional logistic regression model, controlling for humidity, air pollutants, and holidays. The excess risk of kidney disease was calculated for a week (0-6 lag days) after EHE during the warm season (May- September). We also stratified our estimates by socio-demographic characteristics.

Results: EHE was associated with a 1.7% (lag day 0) to 3.1% (lag day 2) higher risk of ED visits related to kidney disease, with a stronger association with a greater number of EHE days in the

previous week. The association with EHE lasted for an entire week and was stronger in the transitional months (i.e., May and September; excess rates ranged from 1.8% to 5.1%) rather than the summer months (June through August; excess rates ranged from 1.5% to 2.7%). The strength of association was greater among those with ED visits related to acute kidney injury, kidney stones, and urinary tract infections. Age and gender may modify the association between EHE and ED visits.

Limitations: Individual exposure to heat, i.e., how long people were outside or if they had access to air conditioning, was unknown.

Conclusions: Extreme heat exposure was significantly associated with a dose-dependent increased risk of ED visits for kidney disease.

Keywords: heatwave, renal disease, ambient temperature, climate change, warm season, heat stress, acute kidney injury (AKI), global warming, environmental health,

PLAIN LANGUAGE SUMMARY

Given the increasing frequency and intensity of extreme heat exposure due to climate change and the growing prevalence of kidney disease worldwide, we examined their association with one another. We examined the association between extreme heat exposure and kidney disease–related emergency department (ED) visits based on seasons and disease subtypes in New York state. Extreme heat exposure was significantly associated with an increased risk of ED visits for multiple types of kidney disease (mainly acute kidney injury, kidney stones, and urinary tract infections). Furthermore, the impact of extreme heat exposure lasted a week and was stronger in the transitional months (May and September) than the summer months.

Introduction

Excess death and morbidity due to kidney disease pose substantial public health and economic burdens around the globe.^{1,2,3} Additionally, kidney disease is a key determinant of poor outcomes for other important non-communicable diseases (NCDs).⁴ In fact, 7.6% of the 1.4 million annual cardiovascular disease (CVD) deaths worldwide can be attributed to impaired kidney function.¹ Together, kidney disease, diabetes, hypertension, and CVD profoundly impact global morbidity and mortality trends,⁴ but kidney disease receives far less attention in research on the treatment and etiology of NCDs. While many important NCDs have declined in recent years, kidney disease has experienced a slower rate of decline and even increased in some regions.⁴ Thus, the prevention of kidney disease in high-risk groups warrants greater prominence on the global public health agenda.⁴

In recent decades, climate change has played an increasing role in the world's growing burden of kidney disease.² The unprecedented elevation of ambient temperatures worldwide substantially impacts human health.⁵ Previous studies have demonstrated associations between extreme heat exposure and increased incidence,⁶ morbidity,⁷ and hospital admission rates for kidney disease.⁸⁻¹² Various studies have assessed the associations between extreme heat exposure and emergency department (ED) visits for kidney disease overall¹³⁻¹⁸ and various subtypes, including acute kidney injury (AKI),^{13,14,17,19-21} chronic kidney disease (CKD),^{13,20}

kidney stones,^{22,23} urinary tract infections (UTIs), and renal colic.¹⁸ However, the collective results are inconclusive. There are still multiple knowledge gaps in substantiating the associations between extreme heat exposure and renal ED visits, including a lack of studies assessing 1) lag and dose-dependent effects; 2) impacts of extreme heat exposure in transitional months before and after summer (May and September); 3) associations between extreme heat exposure and kidney disease subtypes; and 4) risks among populations with existing kidney disease who are highly vulnerable to extreme heat exposure.

Our study fills existing knowledge gaps by assessing the associations between extreme heat exposure and ED visits related to kidney disease overall and by subtype in summer and transitional months in New York state. In addition, we stratified our data by socio-demographic characteristics to further uncover associations between extreme heat exposure and renal ED visits. Given the increasing frequency and intensity of extreme heat in weather patterns due to climate change and the growing prevalence of kidney disease worldwide, it is imperative to elucidate the association between extreme heat exposure and the various subtypes of kidney disease.

Methods

Study design and health outcome

We used a time-stratified case-crossover design to study the association of extreme heat exposure with the transient acute and severe exacerbation of kidney diseases by using ED visit data.^{24–26} The case-crossover design contrasts extreme heat exposure immediately before the ED visits due to kidney disease (case days) to other times when the individual did not go to the ED (control days). We defined control days as the same days of the week in the same calendar month as the corresponding case day, resulting in 3 or 4 control days for each case day. We also examined the associations on lag days 0–6 (the 7 days following the extreme heat exposure). Compared to more conventional study designs, cases serve as their own controls in a case-crossover analysis. Therefore, inherited confounders, such as age, gender, unchanged lifestyle, and some time-varying factors, were automatically controlled.²⁷ We used health data from the New York Statewide Planning and Research Cooperative System (SPARCS), a legislatively mandated database covering over 95% of hospital records in New York state.²⁵ We obtained ED visits reported with a principal diagnosis of acute and chronic kidney diseases (International Classification of Diseases 9 (ICD-9): 580–599, 788) from January 1, 2005 through December 31, 2013. As in our previous research²⁸, we included the following eight major kidney disease subtypes: AKI (code 584), CKD (code 585), UTI (code 599), kidney stone (code 592), lower urinary tract calculi (code 594), nephritis and nephrosis (codes 580–583, 590, 591), other kidney and ureter disorders (codes 586–589, 593), and other lower urinary tract disorders (codes 595–

598, 788). We included acute exacerbations of all kidney diseases to properly assess the acute and transient effects according to the assumption of a case-crossover design. In addition, previous literature found that acute onset or exacerbation of many chronic conditions, such as CKD^{13,20} and kidney stones^{22,23}, are significantly related to extreme heat exposure. To ensure a valid outcome definition, we used the principal diagnosis (or discharge diagnosis) confirmed by laboratory testing and clinical examination. Using the principal diagnosis allowed us to identify situations where kidney disease was the leading cause of the ED visit rather than being a morbidity noted in the medical record of uncertain origin and relevance. Furthermore, using ED data for acute kidney disease outcomes was appropriate as these conditions require immediate medical attention. Patients with multiple ED visits were included and treated as independent individual cases. However, we assumed that readmission did not affect the results because the percentage of patients with multiple renal ED visits occurring within 30 days was low (~5%), and we focused on acute exacerbation events rather than incident cases.

This study was approved by the Institutional Review Board (IRB) at the University at Albany, State University of New York (approval number 17X189). Individual-level informed consent was waived by the IRB as the data was statistically de-identified except for residential address, which was deleted after being geocoded to the longitude and latitude coordinates and linked with the meteorological data.

Exposure data and definition

Daily weather data were obtained from the US Environmental Protection Agency (EPA)²⁹ and National Oceanic and Atmospheric Administration (NOAA).³⁰ We assigned the county-level (62 counties in New York state) temperature and humidity exposure to the individual level since ambient temperature and humidity were not likely to change significantly within a county. We used the 90th percentile of daily temperature in each month over the entire study period in each county as the threshold to define extreme heat exposure (a binary variable) based on previous extreme heat exposure health research.^{11,31-35}

As air pollution is related to both EHE and kidney disease,³⁶ and previous studies have identified specific pollutants as confounders,³⁷⁻³⁹ we added PM_{2.5} and ozone, the two pollutants commonly occurring during the warm season, to our analysis as confounders. In addition, our data showed a 6-35% difference in the excess rate when running the regression models with and without adjustments for these two pollutants. We found more than a 15% difference in the risk estimation for most lag days (**Table S1**). We used daily PM_{2.5} and ozone concentrations simulations from the EPA's Community Multiscale Air Quality Modeling System (CMAQ).⁴⁰ CMAQ output represents volume-average pollutant concentrations for every 1-mile x 1-mile grid cell and vertical layer in the model domain. For each census tract, we determined the simulation grids of CMAQ data located in the area using the FIPS.names function in the rSPARCS package.

We then computed the average air pollution concentration across the simulation grids within the census tract. By geocoding the individual residential address of each case to the street level and assigning the exposures to each case, we obtained individual daily PM_{2.5} and ozone exposure estimates.

Statistical analysis

Our analysis focused on ED visits due to kidney disease in summer (June through August) and in the transitional months (May and September), as prior studies found stronger effects of extreme heat exposure on many health outcomes during these transitional months.^{41,42} Other studies on associations between extreme heat exposure and kidney disease included May and September as part of the warm season.^{15,43} We first drew a plot to present the overall relationship between continuous temperature, extreme heat exposure, and the number of renal ED visits over time. We also conducted a sensitivity analysis to fit the relationship between continuous temperature levels and risks of kidney disease (ORs) using the distributed lag non-linear model (DLNM). We then used a conditional logistic model to regress the outcome (i.e., the case/control indicator) against the extreme heat exposure while controlling for multiple confounders on 0-6 lag days. Specifically, we controlled for humidity, holiday, and the concentration of PM_{2.5} and ozone on the same lag day as the extreme heat exposure. Odds ratios (ORs) were first estimated, then excess rate was calculated as $(OR - 1) * 100\%$. We used excess rate because it removes the

baseline change and was commonly used in previous studies.⁴³ We first ran an overall model including all cases in different seasons (i.e., May vs. June-August vs. September) and then a separate model for each kidney disease subtype in the warm season. Afterward, we examined the modifying effects of socio-demographic factors such as age, gender, race, ethnicity, and insurance status on the associations by calculating the *P*-value for the factor *exposure interaction term.²⁵ Finally, stratified analyses were conducted among those factors with significant modification effects (*P* for interaction <0.05). In addition, we calculated the number of extreme heat exposure days within the week before the admission day for each participant and evaluated the potential dose-dependent effect on ED visits.

Results

We identified 1,114,322 ED visits due to kidney disease in New York state during the study period. The basic characteristics of our study population are described in **Table 1**. **Figure S1** shows a plot over time of continuous temperature and the number of renal ED visits; overall, temperature and ED visit volume were highly correlated. As shown in **Figure S2**, we observed a monotonically increasing risk of renal ED visits as temperatures increase during the warm season (May to September). **Figure 1** displays the excess rate of renal ED visits attributable to extreme heat exposure among New York residents. Depending on the day, we found that extreme heat exposure was associated with a 1.7% (95% CI: 0.9-2.5%) to 3.1% (95% CI: 2.3-4.0%) higher

risk of a renal ED visit during the week following the exposure (i.e., lag days 0-6). The impact of extreme heat exposure on renal ED visits increased from lag day 0 to lag day 2, weakening after the strongest effect on lag day 2.

Figure 2 represents the excess rate of renal ED visits associated with extreme heat exposure in the transitional months and summer. Generally, the association between extreme heat exposure and ED was stronger in the transitional months (ERs ranged from 1.8% to 5.1%) than in summer (ERs ranged from 1.5% to 2.7%). In May, the association of extreme heat exposure with renal ED visits lasted for a whole week following the exposure, with the strongest association occurring on lag day 2 [ER = 5.1% (3.4-6.8%)]. In September, the association was strongest on lag day 0 [ER = 4.2% (2.6-5.8%)], but a statistically significant association was lost by lag day 4. During the summer months, the association of extreme heat exposure with renal ED admissions lasted for the whole week of observation, but the magnitude never surpassed the strength of association observed in May.

The associations between extreme heat exposure and ED visits by kidney disease subtypes are presented in **Table 2**. We found that extreme heat exposure was significantly associated with increased ED visits due to AKI, kidney stones, UTIs, other kidney and ureter disorders, and other lower urinary tract disorders. The association was strongest for AKI and lasted for 4 days after the extreme heat exposure (ERs monotonically decreased from 16.5% on

lag day 0 to 4.3% on lag day 4). The association between extreme heat exposure and kidney stones persisted for the whole week (ERs ranged from 3.8% on lag day 6 to 8.2% on lag day 2).

The association of extreme heat exposure with UTI was transient and lasted from lag day 0 to lag day 2. The association with other kidney and ureter disorders was observed 1 day later (lag day 1) and lasted to lag day 3 (ERs ranged from 7.0% to 9.5%), while the association with other lower urinary tract disorders began on lag day 4 and ended on lag day 6 (ERs ranged from 1.8% to 2.9%).

In **Table 3**, we present the modification effect of socio-demographic characteristics on the associations between extreme heat exposure and renal ED visits. Age and gender modified the association significantly. Results of stratification analyses showed that older individuals (aged >65 years) experienced more renal ED visits during the short-term period after extreme heat exposure (from lag days 0 to 3). However, for participants aged 18-65 and 5-18 years, extreme heat exposure was associated with excess risk of renal ED visits during the whole week from lag day 0 to lag day 6. Notably, we found that the association was stronger for male than female participants. Race, ethnicity, and insurance did not significantly modify the associations.

To detect a potential dose dependence in the association between extreme heat exposure and renal ED visits, we assessed excess rates according to the number of days of extreme heat exposure during the previous week (**Figure 3**). The association between extreme heat exposure

and renal ED visits showed a dose-dependent trend from 1 to 5 days of exposure in the previous week. However, the trend did not persist beyond 5 days of exposure.

Discussion

Our analyses found that extreme heat exposure was significantly associated with excess ED visits related to kidney disease (1.7% to 3.1%) in the warm season (May through September), with a significant dose-dependent relationship. A prior systematic review and meta-analysis revealed that high temperature was associated with a 30% increase in kidney disease morbidity; specifically, heat stress/strain increased the risk of kidney disease by 16%.⁷ Similarly, Ogbomo et al. (2017) found that hospitalization rates for kidney disease in Michigan increased significantly (OR=1.14) during extreme-heat periods (daily mean temperature $\geq 95^{\text{th}}$ percentile).⁹ A retrospective cohort study in South Korea found that temperatures above the 90th and 95th percentiles were associated with an overall cumulative relative risk of 1.18-1.23 and 1.23-1.29, respectively, for ED admissions related to kidney disease compared to minimum morbidity percentiles.¹³ A time series analysis in Washington state found a 1.57-fold greater risk of hospital admissions related to kidney disease on a 99th percentile (36.2 °C) heat day compared to days without extreme heat.¹⁰ In addition, Borg et al. (2017) in Australia and Chen et al. (2017) in Atlanta found that a 1°C increase in daily minimum temperature or heatwave average temperature was associated with a 1.003 to 1.009 increase in ED admissions for kidney disease

overall and selected subtypes.^{6,17} In general, our study found a weaker association between extreme heat exposure and renal ED visits than in previous studies, which may be due to differences in study design, exposure definitions, and health outcome categorization. For example, we defined extreme heat exposure as when the daily temperature exceeded the 90th percentile temperature of that month over the entire study period in the county. Since there is no standard definition, researchers have previously elected to use the 90th, 95th, 97th, and 99th percentiles to define extreme heat exposure.^{7,9,10,13} Unsurprisingly, using a higher percentile to define extreme heat exposure tends to yield stronger associations.⁹ Furthermore, we exclusively focused on ED visits, but most prior studies used hospitalizations,^{9,10} which included more severe kidney disease cases, and thus the risks were higher. To our knowledge, we are the first to examine dose dependence in the association of extreme heat exposure with renal ED visits. The limited number of instances in which extreme heat persisted for 6-7 days may explain why excess rates of renal ED visits were not significantly associated with having 6 or 7 extreme heat days in the week preceding a visit.

We also found that the association of extreme heat exposure with renal ED visits was detectable by lag day 0, was greatest on lag day 2, and remained statistically significantly for the whole week. These associations were also significantly stronger in transitional months, especially in May, than in summer. Similar to our results, Ogbomo et al. (2017) reported that

extreme heat exposure had the strongest association with kidney disease on the day of exposure and remained statistically significant for 1 to 5 subsequent days.⁹ Although the association of extreme heat exposure and kidney disease during transitional months and in summer has seldom been studied separately, our recent research found stronger associations between extreme heat exposure and pregnancy complications during transitional months than in summer.⁴² Kidney disease patients may be more prone to the effect of extreme heat exposure in transitional months due to their potential lack of physical and behavioral preparation or adaptations to sudden temperature changes (not using fans or air conditioners, more outdoor activities, and no early heat warning systems).^{41,44,45}

The specific kidney disease subtypes significantly associated with extreme heat exposure in this study included AKI, kidney stones, UTIs, and other kidney and lower urinary tract disorders. AKI had the highest risks (ER ranged from 4.3% to 16.5%), similar to previous studies.^{8,10,12,17} Our results were consistent with previous studies indicating that elevated temperature was mainly associated with AKI,^{6,8,10,12-14,17,19-21} kidney stones,^{22,23} and UTIs.^{6,12}

The exact biological mechanisms by which extreme heat exposure contributes to kidney disease are unclear. However, it is increasingly evident that, while the kidney has a major role in protecting the body from heat stress, it is also a target for heat stress-related injury.²⁰ Heat stress can lead to increased core temperatures, dehydration, hypovolemia, blood hyperosmolality, and

electrolyte imbalance, which can lead to AKI^{13,46} and the formation of kidney stones and renal colic,⁴⁷ and can facilitate the progression of localized infections to sepsis and shock.¹² The adverse effects of vasopressin⁴⁸ and the fructokinase system⁴⁹ on renal tubules from extreme heat exposure can also lead to AKI.¹³ Meanwhile, increased circulating markers of inflammation and oxidative stress associated with elevated ambient temperatures may contribute to kidney disease exacerbation.^{50–52} Additionally, the medications commonly used to treat kidney disease, such as diuretics, may impair thermoregulatory responses and aggravate syndromes related to extreme heat exposure.⁹

Our study found varied associations among populations of different ages and genders, i.e., older adults (aged >65 years) and males had slightly higher extreme heat exposure–associated renal ED risks than other groups. Previous studies found that the groups vulnerable to extreme heat exposure varied depending on health outcomes, geographic regions, and type of diseases. However, most studies agree that older adults are most vulnerable to the renal effects of extreme heat exposure.^{9,53,54} Similar to our results, previous studies also found a higher risk of hospitalization and ED visits due to kidney disease in males than in females.^{16,43}

Our results indicate several implications: 1) everyone, especially those with pre-existing kidney disease, are recommended to avoid extreme heat exposure in summer and especially transitional months to prevent AKI and disease exacerbation; 2) the prevention and treatment of

heat-related kidney disease may be prepared during heatwaves and may last week-long; 3) the public health benefit of avoiding extreme heat exposure is potentially significant due to the high prevalence of kidney disease, the growing frequency of extreme heat exposure due to climate change, and the significant excess risk of extreme heat exposure related kidney disease; and 4) the real impacts of EHE on RD could be larger than what we found in the current study because we only included some severe cases (ED visits) and omitted more moderate and hospitalization cases.

Our study has several strengths. First, we included a large sample size of over one million ED visits related to kidney disease. Furthermore, we compared the risks for renal ED visits by different lag days, and between summer and transitional months. Additionally, our detailed classification of kidney disease enabled us to assess the association of extreme heat exposure with specific subtypes as well as by socio-demographic characteristics. Finally, we used a case-crossover design, which controls most interindividual confounders.

However, several limitations should be considered when interpreting our results. First, the sample size may be a concern when evaluating the associations of extreme heat exposure with kidney disease subtypes. However, we collected multiple years of data from one of the largest states in the United States. Second, confounders may be a concern. However, we used the case-crossover design. Each case was self-compared regarding the exposure to control all

individually inherited confounders. We further controlled for air pollutants, humidity, and various time-related variables (holidays). Third, we exclusively considered ED visits in our case selection, limiting our analysis to the severe cases of kidney disease. However, this may be less of a problem for the kidney diseases studied as patients with AKI, kidney stones, and UTI may be more likely to present to an ED to get urgent medical care than other patients. Fourth, we did not evaluate individual exposure to heat or access to air conditioning. Future studies with more accurate measurements of individual exposures are needed to verify our findings. Finally, cases within a county were assigned the same temperature values for a specific day due to data limits, which likely resulted in exposure misclassification. However, we assigned weather data at the level of county (n = 62 in New York), which is more granular than the data from limited monitoring sites (n = 14 in New York). The temperature variance across New York state was limited in our study (SD: 4.17-9.74 °F from month to month; <10% change). Thus, we assumed that the ambient temperature was not likely to change each day significantly within a much smaller area, i.e., within a county. In addition, using a case-crossover design, we compared extreme heat exposure on the case and control days, i.e., exposure was compared at different times but in the same residence. Therefore, if exposure misclassification occurs, the bias would be non-differential between the case and control days.^{25,55}

In conclusion, extreme heat exposure was significantly associated with increased risk of ED visits related to multiple kidney disease types and displayed a dose-dependent relationship. This association lasted a week after exposure and was stronger during transitional months (especially May) than in summer. The kidney disease subtype showing the strongest association was AKI, although kidney stones and UTIs also showed strong associations. Age and gender may modify observed associations. The association of extreme heat exposure and kidney disease was observed not only in summer but also in transitional months.

Supplementary Material

Table S1. Excess rate (%) of emergency department visits due to renal diseases associated with extreme heat exposure, with and without adjusting for air pollutants.

Figure S1. Overall relationship between temperature and the number of emergency department visits due to renal disease over time.

Figure S2. Relationship between continuous temperature levels and risk of ED visits due to RD (ORs).

Article Information

Authors' Contributions: Study design/concept: YJQ, SL, AYMB; data acquisition/analysis: WJZ, YJQ, XLD, IR; mentorship and data interpretation: SL, XQL, WJZ, YJQ. Each author contributed important intellectual content during manuscript drafting or revision and agreed to be personally accountable for the individual's contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

Support: This work was supported by the NYS Energy Research and Development Authority (grant number 137487), the National Institute of Environmental Health Science (grant number 1R15ES02800001A1), and the Environmental Protection Agency (grant number 83563602). The funding sources were not involved in the study design, data collection, analysis, reporting, conduction, or preparation of this article, nor the decision to submit it for publication.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Peer Review: Received February 5, 2022. Evaluated by 2 external peer reviewers, with direct editorial input from a Statistics/Methods Editor, an Associate Editor, and the Editor-in-Chief.

Accepted in revised form September 5, 2022.

References

1. Carney EF. The impact of chronic kidney disease on global health. *Nat Rev Nephrol.* 2020 May;16(5):251. doi: 10.1038/s41581-020-0268-7
2. Bikbov B, Purcell CA, Levey AS, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* 2020 Feb 29;395(10225):709-733. doi: 10.1016/S0140-6736(20)30045-3.
3. World Kidney Day: Chronic Kidney Disease. Published 2015. <http://www.worldkidneyday.org/faqs/chronic-kidney-disease/> .
4. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney Int.* 2011 Dec;80(12):1258-70. doi: 10.1038/ki.2011.368.
5. Patz JA, Frumkin H, Holloway T, Vimont DJ, Haines A. Climate change: challenges and opportunities for global health. *JAMA.* 2014 Oct 15;312(15):1565-80. doi: 10.1001/jama.2014.13186.
6. Borg M, Bi P, Nitschke M, Williams S, McDonald S. The impact of daily temperature on renal disease incidence: an ecological study. *Environ Health.* 2017 Oct 27;16(1):114. doi: 10.1186/s12940-017-0331-4.
7. Lee WS, Kim WS, Lim YH, Hong YC. High Temperatures and Kidney Disease Morbidity: A Systematic Review and Meta-analysis. *J Prev Med Public Health.* 2019 Jan;52(1):1-13. doi: 10.3961/jpmph.18.149.
8. Hopp S, Dominici F, Bobb JF. Medical diagnoses of heat wave-related hospital admissions in older adults. *Prev Med.* 2018 May;110:81-85. doi: 10.1016/j.ypmed.2018.02.001.
9. Ogbomo AS, Gronlund CJ, O'Neill MS, Konen T, Cameron L, Wahl R. Vulnerability to extreme-heat-associated hospitalization in three counties in Michigan, USA, 2000-2009. *Int J Biometeorol.* 2017 May;61(5):833-843. doi: 10.1007/s00484-016-1261-5
10. Isaksen TB, Yost MG, Hom EK, Ren Y, Lyons H, Fenske RA. Increased hospital admissions associated with extreme-heat exposure in King County, Washington, 1990-2010. *Rev Environ Health.* 2015;30(1):51-64. doi: 10.1515/reveh-2014-0050.
11. Gronlund CJ, Zanobetti A, Schwartz JD, Wellenius GA, O'Neill MS. Heat, heat waves, and hospital admissions among the elderly in the United States, 1992-2006. *Environ Health Perspect.* 2014 Nov;122(11):1187-92. doi: 10.1289/ehp.1206132.
12. Bobb JF, Obermeyer Z, Wang Y, Dominici F. Cause-specific risk of hospital admission related to extreme heat in older adults. *JAMA.* 2014 Dec 24-31;312(24):2659-67. doi: 10.1001/jama.2014.15715.

13. Kim E, Kim H, Kim YC, Lee JP. Association between extreme temperature and kidney disease in South Korea, 2003-2013: Stratified by sex and age groups. *Sci Total Environ*. 2018 Nov 15;642:800-808. doi: 10.1016/j.scitotenv.2018.06.055.
14. Kim SE, Lee H, Kim J, Lee YK, Kang M, Hijioka Y, Kim H. Temperature as a risk factor of emergency department visits for acute kidney injury: a case-crossover study in Seoul, South Korea. *Environ Health*. 2019 Jun 14;18(1):55. doi: 10.1186/s12940-019-0491-5.
15. Winquist A, Grundstein A, Chang HH, Hess J, Sarnat SE. Warm season temperatures and emergency department visits in Atlanta, Georgia. *Environ Res*. 2016 May;147:314-23. doi: 10.1016/j.envres.2016.02.022.
16. Heidari L, Winquist A, Klein M, O'Lenick C, Grundstein A, Ebel Sarnat S. Susceptibility to Heat-Related Fluid and Electrolyte Imbalance Emergency Department Visits in Atlanta, Georgia, USA. *Int J Environ Res Public Health*. 2016 Oct 2;13(10):982. doi: 10.3390/ijerph13100982.
17. Chen T, Sarnat SE, Grundstein AJ, Winquist A, Chang HH. Time-series Analysis of Heat Waves and Emergency Department Visits in Atlanta, 1993 to 2012. *Environ Health Perspect*. 2017 May 31;125(5):057009. doi: 10.1289/EHP44.
18. Cervellin G, Comelli I, Comelli D, Meschi T, Lippi G, Borghi L. Mean temperature and humidity variations, along with patient age, predict the number of visits for renal colic in a large urban Emergency Department: results of a 9-year survey. *J Epidemiol Glob Health*. 2012 Mar;2(1):31-8. doi: 10.1016/j.jegh.2012.01.001.
19. Honda T, Manjourides J, Suh H. Daily ambient temperature is associated with biomarkers of kidney injury in older Americans. *Environ Res*. 2019 Dec;179(Pt A):108790. doi: 10.1016/j.envres.2019.108790.
20. Johnson RJ, Sánchez-Lozada LG, Newman LS, Lanaspa MA, Diaz HF, Lemery J, Rodriguez-Iturbe B, Tolan DR, Butler-Dawson J, Sato Y, Garcia G, Hernando AA, Roncal-Jimenez CA. Climate Change and the Kidney. *Ann Nutr Metab*. 2019;74 Suppl 3:38-44. doi: 10.1159/000500344.
21. McTavish RK, Richard L, McArthur E, et al. Association Between High Environmental Heat and Risk of Acute Kidney Injury Among Older Adults in a Northern Climate: A Matched Case-Control Study. *Am J kidney Dis Off J Natl Kidney Found*. 2018;71(2):200-208. doi:10.1053/j.ajkd.2017.07.011
22. Ross ME, Vicedo-Cabrera AM, Kopp RE, Song L, Goldfarb DS, Pulido J, Warner S, Furth SL, Tasian GE. Assessment of the combination of temperature and relative humidity on kidney stone presentations. *Environ Res*. 2018 Apr;162:97-105. doi: 10.1016/j.envres.2017.12.020.

23. Tasian GE, Pulido JE, Gasparrini A, Saigal CS, Horton BP, Landis JR, Madison R, Keren R; Urologic Diseases in America Project. Daily mean temperature and clinical kidney stone presentation in five U.S. metropolitan areas: a time-series analysis. *Environ Health Perspect.* 2014 Oct;122(10):1081-7. doi: 10.1289/ehp.1307703.
24. Maclure M. The case-crossover design: a method for studying transient effects on the risk of acute events. *Am J Epidemiol.* 1991 Jan 15;133(2):144-53. doi: 10.1093/oxfordjournals.aje.a115853.
25. Zhang W, Lin S, Hopke PK, Thurston SW, van Wijngaarden E, Croft D, Squizzato S, Masiol M, Rich DQ. Triggering of cardiovascular hospital admissions by fine particle concentrations in New York state: Before, during, and after implementation of multiple environmental policies and a recession. *Environ Pollut.* 2018 Nov;242(Pt B):1404-1416. doi: 10.1016/j.envpol.2018.08.030.
26. Rich DQ, Zhang W, Lin S, Squizzato S, Thurston SW, van Wijngaarden E, Croft D, Masiol M, Hopke PK. Triggering of cardiovascular hospital admissions by source specific fine particle concentrations in urban centers of New York State. *Environ Int.* 2019 May;126:387-394. doi: 10.1016/j.envint.2019.02.018.
27. Lin S, Bell EM, Liu W, Walker RJ, Kim NK, Hwang SA. Ambient ozone concentration and hospital admissions due to childhood respiratory diseases in New York State, 1991-2001. *Environ Res.* 2008 Sep;108(1):42-7. doi: 10.1016/j.envres.2008.06.007.
28. Fletcher BA, Lin S, Fitzgerald EF, Hwang SA. Association of summer temperatures with hospital admissions for renal diseases in New York state: A case-crossover study. *Am J Epidemiol.* 2012;175(9):907-916. doi:10.1093/aje/kwr417
29. EPA. Daily Summary Data.
https://aqs.epa.gov/aqsweb/airdata/download_files.html#Daily
30. NOAA. <https://www.ncdc.noaa.gov/isd/data-access>
31. D'Ippoliti D, Michelozzi P, Marino C, de'Donato F, Menne B, Katsouyanni K, Kirchmayer U, Analitis A, Medina-Ramón M, Paldy A, Atkinson R, Kovats S, Bisanti L, Schneider A, Lefranc A, Iñiguez C, Perucci CA. The impact of heat waves on mortality in 9 European cities: results from the EuroHEAT project. *Environ Health.* 2010 Jul 16;9:37. doi: 10.1186/1476-069X-9-37.
32. Ha S, Liu D, Zhu Y, Soo Kim S, Sherman S, Grantz KL, Mendola P. Ambient Temperature and Stillbirth: A Multi-Center Retrospective Cohort Study. *Environ Health Perspect.* 2017 Jun 22;125(6):067011. doi: 10.1289/EHP945.
33. Ha S, Liu D, Zhu Y, Kim SS, Sherman S, Mendola P. Ambient Temperature and Early Delivery of Singleton Pregnancies. *Environ Health Perspect.* 2017 Mar;125(3):453-459. doi: 10.1289/EHP97.

34. Heo S, Bell ML, Lee JT. Comparison of health risks by heat wave definition: Applicability of wet-bulb globe temperature for heat wave criteria. *Environ Res.* 2019 Jan;168:158-170. doi: 10.1016/j.envres.2018.09.032.
35. Tobías A, Armstrong B, Gasparini A, Diaz J. Effects of high summer temperatures on mortality in 50 Spanish cities. *Environ Health.* 2014 Jun 9;13(1):48. doi: 10.1186/1476-069X-13-48.
36. Remigio RV, He H, Raimann JG, Kotanko P, Maddux FW, Sapkota AR, Liang XZ, Puett R, He X, Sapkota A. Combined effects of air pollution and extreme heat events among ESKD patients within the Northeastern United States. *Sci Total Environ.* 2022 Mar 15;812:152481. doi: 10.1016/j.scitotenv.2021.152481.
37. Bekkar B, Pacheco S, Basu R, DeNicola N. Association of Air Pollution and Heat Exposure With Preterm Birth, Low Birth Weight, and Stillbirth in the US: A Systematic Review. *JAMA Netw open.* 2020;3(6):e208243. doi:10.1001/jamanetworkopen.2020.8243
38. Chiu PF, Chang CH, Wu CL, et al. High particulate matter 2.5 levels and ambient temperature are associated with acute lung edema in patients with nondialysis Stage 5 chronic kidney disease. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* 2019;34(8):1354-1360. doi:10.1093/ndt/gfy144
39. Hoffmann B, Luttmann-Gibson H, Cohen A, et al. Opposing effects of particle pollution, ozone, and ambient temperature on arterial blood pressure. *Environ Health Perspect.* 2012;120(2):241-246. doi:10.1289/ehp.1103647
40. EPA. CMAQ: The Community Multiscale Air Quality Modeling System. <https://www.epa.gov/cmaq>
41. Lin S, Lin Z, Ou Y, Soim A, Shrestha S, Lu Y, Sheridan S, Luben TJ, Fitzgerald E, Bell E, Shaw GM, Reefhuis J, Langlois PH, Romitti P, Feldkamp ML, Malik S, Pantea C, Nayak S, Hwang SA, Browne M; National Birth Defects Prevention Study. Maternal ambient heat exposure during early pregnancy in summer and spring and congenital heart defects - A large US population-based, case-control study. *Environ Int.* 2018 Sep;118:211-221. doi: 10.1016/j.envint.2018.04.043.
42. Qu Y, Zhang W, Ryan I, et al. Ambient extreme heat exposure in summer and transitional months and emergency department visits and hospital admissions due to pregnancy complications. *Sci Total Environ.* 2021;777:146134. doi:10.1016/j.scitotenv.2021.146134
43. Sun S, Weinberger KR, Nori-Sarma A, et al. Ambient heat and risks of emergency department visits among adults in the United States: time stratified case crossover study. *BMJ.* 2021;375:e065653. doi:10.1136/bmj-2021-065653
44. Loughnan M, Tapper N, Loughnan T. The impact of "unseasonably" warm spring temperatures on acute myocardial infarction hospital admissions in Melbourne, Australia:

- a city with a temperate climate. *J Environ Public Health*. 2014;2014:483785. doi: 10.1155/2014/483785.
45. Schifano P, Leone M, De Sario M, de'Donato F, Bargagli AM, D'Ippoliti D, Marino C, Michelozzi P. Changes in the effects of heat on mortality among the elderly from 1998-2010: results from a multicenter time series study in Italy. *Environ Health*. 2012 Sep 3;11:58. doi: 10.1186/1476-069X-11-58.
 46. Knowlton K, Rotkin-Ellman M, King G, et al. The 2006 California heat wave: impacts on hospitalizations and emergency department visits. *Environ Health Perspect*. 2009;117(1):61-67. doi:10.1289/ehp.11594
 47. Borghi L, Meschi T, Amato F, Novarini A, Romanelli A, Cigala F. Hot occupation and nephrolithiasis. *J Urol*. 1993;150(6):1757-1760. doi:10.1016/s0022-5347(17)35887-1
 48. Bankir L, Bouby N, Ritz E. Vasopressin: a novel target for the prevention and retardation of kidney disease? *Nat Rev Nephrol*. 2013;9(4):223-239. doi:10.1038/nrneph.2013.22
 49. Roncal Jimenez CA, Ishimoto T, Lanaspa MA, et al. Fructokinase activity mediates dehydration-induced renal injury. *Kidney Int*. 2014;86(2):294-302. doi:10.1038/ki.2013.492
 50. Wu S, Yang D, Pan L, et al. Ambient temperature and cardiovascular biomarkers in a repeated-measure study in healthy adults: A novel biomarker index approach. *Environ Res*. 2017;156:231-238. doi:10.1016/j.envres.2017.02.036
 51. Halonen JI, Zanobetti A, Sparrow D, Vokonas PS, Schwartz J. Associations between outdoor temperature and markers of inflammation: a cohort study. *Environ Health*. 2010;9:42. doi:10.1186/1476-069X-9-42
 52. Kahle JJ, Neas LM, Devlin RB, et al. Interaction effects of temperature and ozone on lung function and markers of systemic inflammation, coagulation, and fibrinolysis: a crossover study of healthy young volunteers. *Environ Health Perspect*. 2015;123(4):310-316. doi:10.1289/ehp.1307986
 53. Gronlund CJ, Zanobetti A, Wellenius GA, Schwartz JD, O'Neill MS. Vulnerability to Renal, Heat and Respiratory Hospitalizations During Extreme Heat Among U.S. Elderly. *Clim Change*. 2016;136(3):631-645. doi:10.1007/s10584-016-1638-9
 54. Kravchenko J, Abernethy AP, Fawzy M, Lysterly HK. Minimization of heatwave morbidity and mortality. *Am J Prev Med*. 2013;44(3):274-282. doi:10.1016/j.amepre.2012.11.015
 55. Zeger SL, Thomas D, Dominici F, et al. Exposure measurement error in time-series studies of air pollution: concepts and consequences. *Environ Health Perspect*. 2000;108(5):419-426. doi:10.1289/ehp.00108419

Figure Legends

Figure 1. Excess rate (%) of emergency department visits due to renal diseases associated with extreme heat exposure

Figure 2. Excess rate (%) of emergency department visit due to renal diseases associated with extreme heat exposure by month

Figure 3. Excess rate (%) of emergency department visit due to renal diseases associated with the number of days during the past week exposed to extreme heat

Table 1. Basic characteristics of the study population in New York State

Basic characteristics	Number	Proportion (%)
Age		
<5	91,581	8.2
5-18	444,034	39.8
18-65	267,641	24.0
>65	311,066	27.9
Gender		
Female	679,307	61.0
Male	435,003	39.0
Unknown	12	0.0
Race		
African American	216,301	19.4
Non- African American	898,021	80.6
Ethnicity		
Hispanic	185,815	18.0
Non-Hispanic	843,920	82.0
Insurance		
Medicaid	109,845	9.9
Self-pay	120,696	10.8
Other insurance	883,781	79.3
Renal diseases subtypes		
Acute kidney disease	86,194	7.7
Chronic kidney disease	9,053	0.8
Lower urinary tract calculi	3,189	0.3
Nephritis and nephrosis	79,754	7.2
Kidney stone	182,779	16.4
Urinary tract infections	497,055	44.6
Other kidney and ureter disorders	12,040	1.1
Other lower urinary tract disorders	244,258	21.9

Table 2. Excess rate (%) of emergency department visit due to renal diseases associated with extreme heat exposure, by subtypes

Lag days	AKI	CKD	Lower urinary tract calculi	Nephritis and nephrosis	Kidney stone	UTI	Other kidney and ureter disorders	Other lower urinary tract disorders
Lag 0	16.5 (13.9, 19.2)	1.2 (-5.8, 8.7)	0.0 (-11.4, 12.9)	-0.2 (-2.7, 2.3)	4.2 (2.5, 5.9)	2.4 (1.3, 3.5)	5.3 (-1.0, 12.0)	-3.4 (-4.9, -2.0)
Lag 1	17.8 (15.1, 20.5)	-1.1 (-8.1, 6.3)	0.2 (-11.1, 12.9)	-2.1 (-4.5, 0.4)	7.3 (5.6, 9.1)	2.4 (1.3, 3.5)	7.0 (0.6, 13.9)	-3.3 (-4.8, -1.9)
Lag 2	12.6 (10.0, 15.2)	-6.4 (-13.2, 0.9)	-4.4 (-15.5, 8.2)	-0.4 (-2.8, 2.2)	8.2 (6.5, 10.0)	1.4 (0.3, 2.5)	9.5 (2.8, 16.5)	0.9 (-0.6, 2.4)
Lag 3	8.6 (6.1, 11.2)	-0.6 (-7.7, 7.1)	-3.0 (-14.4, 9.8)	-0.1 (-2.6, 2.4)	5.5 (3.8, 7.3)	0.9 (-0.2, 2.0)	8.6 (2.0, 15.6)	1.5 (0.0, 3.0)
Lag 4	4.3 (1.9, 6.9)	0.6 (-6.7, 8.4)	-3.6 (-15.1, 9.4)	0.4 (-2.1, 2.9)	5.4 (3.7, 7.2)	0.8 (-0.3, 1.9)	4.8 (-1.7, 11.8)	1.8 (0.3, 3.3)
Lag 5	1.1 (-1.4, 3.5)	-1.9 (-9.0, 5.8)	-1.1 (-12.8, 12.2)	0.5 (-2.0, 3.0)	3.9 (2.2, 5.7)	1.6 (0.5, 2.7)	1.2 (-5.1, 8.0)	1.9 (0.4, 3.4)
Lag 6	-0.9 (-3.2, 1.6)	-3.9 (-10.9, 3.5)	-3.7 (-15.2, 9.4)	1.5 (-1.0, 4.1)	3.8 (2.1, 5.5)	0.9 (-0.2, 2.0)	3.5 (-2.9, 10.3)	2.9 (1.3, 4.4)

Abbreviations: AKI, acute kidney disease; CKD, chronic kidney disease; UTI, urinary tract infections.

Table 3. Excess rate (%) of emergency department visit due to renal diseases associated with extreme heat exposure, effect modification, and stratification by socio-demographic characteristics

Socio-demographic characteristics	Lag 0	Lag 1	Lag 2	Lag 3	Lag 4	Lag 5	Lag 6
Age							
<5	1.1 (-1.2, 3.4)	1.7 (-0.7, 4.1)	-0.7 (-3.0, 1.7)	-0.6 (-2.9, 1.8)	0.8 (-1.5, 3.2)	1.0 (-1.3, 3.4)	-1.5 (-3.8, 0.9)
5-18	1.1 (-0.0, 2.3)	2.5 (1.3, 3.7)	3.6 (2.4, 4.8)	2.5 (1.3, 3.6)	2.2 (1.0, 3.4)	2.1 (0.9, 3.2)	2.0 (0.8, 3.1)
18-65	2.8 (1.3, 4.2)	3.0 (1.5, 4.4)	4.7 (3.3, 6.2)	3.9 (2.4, 5.3)	4.1 (2.7, 5.6)	2.9 (1.5, 4.4)	3.0 (1.6, 4.5)
>65	3.9 (2.6, 5.3)	3.4 (2.0, 4.8)	2.3 (0.9, 3.6)	1.8 (0.4, 3.1)	0.4 (-0.9, 1.8)	1.0 (-0.3, 2.3)	1.1 (-0.3, 2.4)
<i>P for interaction</i>	0.005*	0.545	<0.001*	0.009*	0.001*	0.193	0.008*
Gender							
Female	1.5 (0.5, 2.4)	1.7 (0.8, 2.7)	2.3 (1.4, 3.3)	1.6 (0.7, 2.6)	1.4 (0.5, 2.4)	1.6 (0.6, 2.5)	1.6 (0.6, 2.5)
Male	3.5 (2.4, 4.7)	4.4 (3.3, 5.6)	4.4 (3.2, 5.6)	3.5 (2.4, 4.7)	3.1 (1.9, 4.2)	2.4 (1.2, 3.6)	1.9 (0.7, 3.1)
<i>P for interaction</i>	0.005*	<0.001*	0.004*	0.014*	0.021*	0.325	0.773
Race							
African American	1.6 (0.1, 3.2)	1.8 (0.2, 3.4)	2.9 (1.3, 4.5)	1.7 (0.1, 3.3)	1.2 (-0.4, 2.8)	1.8 (0.2, 3.4)	0.9 (-0.6, 2.5)
Non- African American	2.4 (1.6, 3.3)	3.0 (2.2, 3.9)	3.2 (2.3, 4.1)	2.5 (1.7, 3.4)	2.3 (1.4, 3.1)	1.9 (1.0, 2.8)	1.9 (1.0, 2.8)
<i>P for interaction</i>	0.331	0.146	0.757	0.311	0.211	0.882	0.278
Ethnicity							
Hispanic	1.1 (-0.5, 2.8)	3.2 (1.5, 4.9)	3.3 (1.6, 5.0)	3.1 (1.4, 4.8)	2.3 (0.6, 4.0)	2.4 (0.7, 4.1)	3.0 (1.3, 4.8)
Non-Hispanic	2.4 (1.5, 3.3)	2.6 (1.7, 3.5)	3.1 (2.2, 4.0)	2.1 (1.2, 3.0)	2.0 (1.1, 2.9)	1.8 (0.9, 2.7)	1.5 (0.6, 2.4)
<i>P for interaction</i>	0.192	0.561	0.953	0.434	0.841	0.742	0.200
Insurance							
Medicaid	3.7 (1.6, 5.9)	4.2 (2.0, 6.4)	3.4 (1.2, 5.6)	3.3 (1.1, 5.5)	3.4 (1.2, 5.6)	2.3 (0.2, 4.5)	1.0 (-1.2, 3.2)
Self-pay	1.6 (-0.5, 3.6)	0.8 (-1.3, 2.9)	2.1 (0.1, 4.3)	1.9 (-0.2, 4.1)	1.1 (-0.9, 3.3)	0.7 (-1.4, 2.8)	1.1 (-1.0, 3.2)
Other insurance	2.2 (1.3, 3.1)	2.9 (2.0, 3.8)	3.2 (2.4, 4.1)	2.3 (1.4, 3.2)	2.0 (1.1, 2.9)	2.0 (1.1, 2.9)	1.9 (1.0, 2.8)
<i>P for interaction</i>	0.307	0.065	0.599	0.638	0.315	0.487	0.623





