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# Assessment of the combination of temperature and relative humidity on kidney stone presentations

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## ABSTRACT

Temperature and relative humidity have opposing effects on evaporative water loss, the likely mediator of the temperature-dependence of nephrolithiasis. However, prior studies considered only dry-bulb temperatures when estimating the temperature-dependence of nephrolithiasis.

We used distributed lag non-linear models and repeated 10-fold cross-validation to determine the daily temperature metric and corresponding adjustment for relative humidity that most accurately predicted kidney stone presentations during hot and cold periods in South Carolina from 1997 to 2015. We examined three metrics for wet-bulb temperatures and heat index, both of which measure the combination of temperature and humidity, and for dry-bulb temperatures: (1) daytime mean temperature; (2) 24-h mean temperature; and (3) most extreme 24-h temperature. For models using dry-bulb temperatures, we considered four treatments of relative humidity.

Among 188,531 patients who presented with kidney stones, 24-h wet bulb temperature best predicted kidney stone presentation during summer. Mean cross-validated residuals were generally lower in summer for wet-bulb temperatures and heat index than the corresponding dry-bulb temperature metric, regardless of type of adjustment for relative humidity. Those dry-bulb models that additionally adjusted for relative humidity had higher mean residuals than other temperature metrics. The relative risk of kidney stone presentations at the 99th percentile of each temperature metric compared to the respective median temperature in summer months differed by temperature metric and relative humidity adjustment, and ranged from an excess risk of 8–14%. All metrics performed similarly in winter.

The combination of temperature and relative humidity determine the risk of kidney stone presentations, particularly during periods of high heat and humidity. These results suggest that metrics that measure moist heat stress should be used to estimate the temperature-dependence of kidney stone presentations, but that the particular metric is relatively unimportant.

## 1. Introduction

Nephrolithiasis (kidney stone disease), which affects 9% of the population in the United States and is estimated to cost $10 billion per year, is punctuated by acute, painful presentations caused by growth and detachment of stones from the renal papillae (Litwin and Saigal, 2012; Scales et al., 2012). Although the cause of kidney stone detachment is unknown, prior epidemiologic studies reported that high and

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low daily temperatures are associated with an increased risk of kidney stone presentations. The increase in kidney stone presentations following hot and cold days is likely mediated by increased evaporative water loss through sweating, and respiration (Masterson et al., 2013; Parks et al., 2003). The resultant low urine volume increases urinary supersaturation of calcium, oxalate, and phosphate, which leads to stone growth in susceptible patients.

During the hours to days during which the risk of kidney stone presentations increase following hot and cold days (Tasian et al., 2014), evaporative water loss is determined by the difference in water vapor concentration between the body surface and ambient air (Withers and Cooper, 2014). Evaporative water loss increases exponentially as temperature increases and is inversely related to relative humidity. Metrics that measure the complex thermodynamic relationship between temperature and humidity, such as wet-bulb temperatures and heat index, may be considered a proxy for the combined effect of temperature and humidity on human physiology (Sherwood and Huber, 2010). However, prior studies considered only dry-bulb temperatures when estimating the temperature-dependence of nephrolithiasis. Whether the combined effect of temperature and relative humidity better predicts kidney stone presentations, and other temperature-dependent health outcomes, such as mortality, is unclear (Gasparrini et al., 2010; Gronlund et al., 2014; Hondula and Barnett, 2014; Oudin Astrom et al., 2016; Zheng et al., 2016). Although prior studies have reported that no one temperature metric best predicts mortality (Barnett et al., 2010), the association between temperature extremes and kidney stone presentations is likely mediated by a single process that is dependent on both temperature and relative humidity (evaporative water loss), whereas there are many potential causal pathways for temperature and mortality.

Identifying the temperature metric(s) that best predict kidney stone presentations will help identify the temperatures and times during which vulnerable populations are at greatest risk. This knowledge would also have implications for improving projections of the effect of climate change on nephrolithiasis, which have thus far only used dry-bulb temperatures (Brikowski et al., 2008). In this study, we used a time series design with distributed lag non-linear models (DLNMs) and repeated 10-fold cross-validation to estimate the differences between predicted and observed kidney stone presentations for different daily temperature metrics and adjustment for relative humidity during hot and cold periods in South Carolina from 1997 to 2015. We identified the daily temperature metrics that most accurately predicted kidney stone presentations.

## 2. Methods

### 2.1. Study setting

We conducted this study using South Carolina Medical Encounter Data and Financial Reports. We included all patients aged 20–65 years who lived in South Carolina and presented to hospitals in South Carolina with kidney stones from January 1, 1997 to September 30, 2015. These age limits reflect the group of patients with the highest incidence of nephrolithiasis, ensuring sufficient power for the analyses, and limited potential imprecision that could be introduced by including patients at the extremes of life, who are more vulnerable to temperature extremes. We chose South Carolina because of its hot summers and cool winters and high prevalence of kidney stones, (Soucie et al., 1994) and because it is the largest of a few states with an all-payer claims database that captures all points of care where patients with symptomatic kidney stones present.

By law, South Carolina Medical Encounter Data records all Emergency Department visits, surgeries, and hospital admissions for South Carolina's population, including those who are uninsured or have governmental insurance. Data are sent by all healthcare facilities in the state on a monthly basis. By law, all data must be 99.9% accurate (valid codes) and 99.5% complete. Routine audits are performed to ensure

**Table 1**
Characteristics of patients who presented with kidney stones and the population of South Carolina.

| Characteristics | | Cohort (n = 188,531) | Census 2010 (n = 4,625,364) |
|---|---|---|---|
| Male (%) | | 114,100 (60.5) | 2,250,101 (48.6) |
| Urban (%) | | 143,201(76.0) | 3,067,809 (66.3) |
| Race/Ethnicity (%) | White | 159,468(84.6) | 2,962,740 (64.1) |
| | African-American | 23,391(12.4) | 1,279,998 (27.7) |
| | Asian | 673 (0.4) | 58,307 (1.3) |
| | Native American | 265 (0.1) | 18,727 (0.4) |
| | Other | 4734 (2.5) | 69,910 (1.5) |
| Age group (%) | < 10 y/o | n/a | 598,150 (12.9) |
| | 10–14 y/o | n/a | 297,286 (6.4) |
| | 15–19 y/o | n/a | 328,989 (7.1) |
| | 20–24 y/o | 12,089 (6.4) | 332,494 (7.2) |
| | 25–34 y/o | 33,486 (17.8) | 592,056 (12.8) |
| | 35–44 y/o | 39,181 (20.8) | 601,292 (13.0) |
| | 45–64 y/o | 68,354 (36.3) | 1243,223 (27.0) |
| | > = 65 y/o | 27,414 (14.5) | 631,874 (13.6) |
| Insurance (%) | Public | 49,852 (26.4) | |
| | Private | 107,231(56.9) | |
| | Self-pay | 30,470 (16.2) | |
| | No insurance | 978 ( 0.5) | |

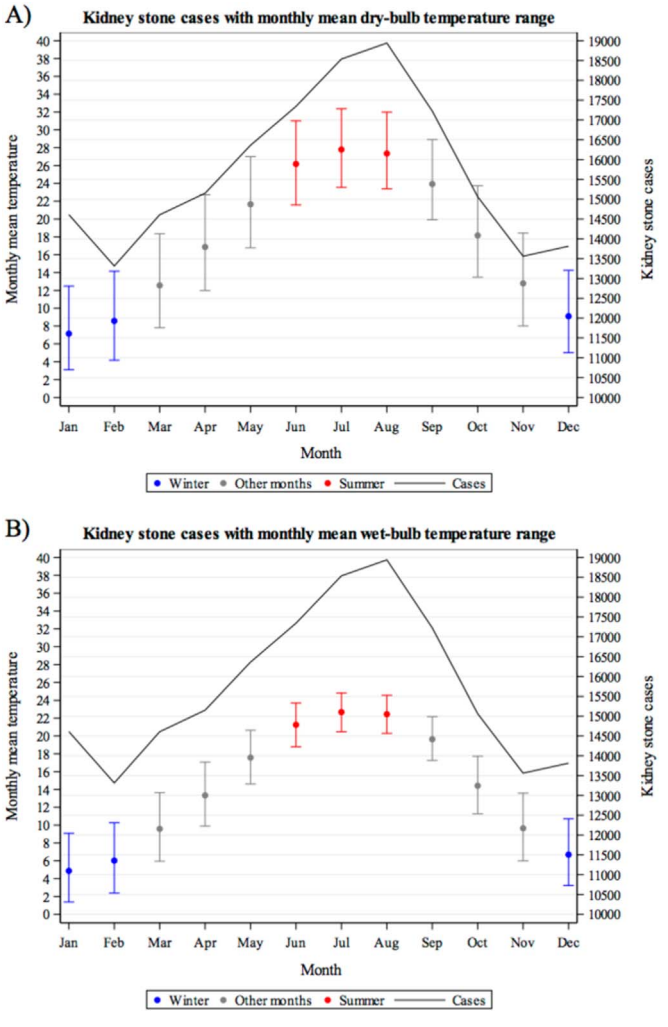


**Fig. 1.** Monthly mean temperature and frequency of kidney stone presentations in South Carolina from 1997 to 2015. The limits of the temperature ranges for A) dry-bulb and B) wet-bulb temperatures are the averages of the monthly maximum and minimum temperature across the study period.