Climate-related increase in the prevalence of urolithiasis in the United States

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An unanticipated result of global warming is the likely northward expansion of the present-day southeastern U.S. kidney stone "belt." The fraction of the U.S. population living in high-risk zones for nephrolithiasis will grow from 40% in 2000 to 56% by 2050, and to 70% by 2095. Predictions based on a climate model of intermediate severity warming (SRESa1b) indicate a climate-related increase of 1.6–2.2 million lifetime cases of nephrolithiasis by 2050, representing up to a 30% increase in some climate divisions. Nationwide, the cost increase associated with this rise in nephrolithiasis would be $0.9–1.3 billion annually (year-2000 dollars), representing a 25% increase over current expenditures. The impact of these changes will be geographically concentrated, depending on the precise relationship between temperature and stone risk. Stone risk may abruptly increase at a threshold temperature (nonlinear model) or increase steadily with temperature change (linear model) or some combination thereof. The linear model predicts increases by 2050 that are concentrated in California, Texas, Florida, and the Eastern Seaboard; the nonlinear model predicts concentration in a geographic band stretching from Kansas to Kentucky and Northern California, immediately south of the threshold isotherm.

climate change | epidemiology | kidney stone | medicine | urology

Nephrolithiasis, or kidney stone disease, is a common human affliction, with a lifetime prevalence of ≈12% in men and 7% in women in the U.S (1). Kidney stones form in response to environmental and/or metabolic risk factors. Low urine volume, an important environmental factor, reflects low fluid intake or excessive fluid loss and directly increases stone risk by increasing urinary saturation of stone-forming salts.

Stone disease in the U.S. shows marked geographic variability; the Southeast has been found in several studies to have as much as a 50% higher prevalence of stone disease than the Northwest (2–4). Because of its influence on fluid status and urine volume, mean annual temperature (MAT) has been estimated to account for 70% or more of this variability (MAT is 8°C higher in the Southeast), whereas other risk factors such as age, gender, race, diuretic use, and sunlight index account for the remainder (3, 4).

In addition to regional variation in stone disease, evidence is mounting that in Western societies the overall prevalence of stone disease is increasing (2, 5, 6). In the U.S., an increase in the prevalence of stone disease from 3.6 to 5.2% between the time periods 1976–1980 and 1988–1994 has been reported (2). Interestingly, between these two time periods, U.S. MAT increased by 0.5°C, suggesting a potential but unproven correlation between the rise in temperature and the increased prevalence of nephrolithiasis.

Transient variations in stone prevalence, such as seen with desert military deployments (7–9) and seasonal cyclicity (10–14), can also be accounted for by temperature changes. The physiologic response time to these climate changes is generally rapid; in one study, the peak time for stone development occurred 90 days after military deployment into a hot, arid climate (15).

Prediction of global warming in this century indicates that MAT will rise significantly in much of the U.S. (16). Consequently, the prevalence of nephrolithiasis is likely to increase as the present-day "kidney stone belt," currently comprising primarily the Southeast, expands north- and westward in response to warming. We hypothesize that predicted climate change will result in an increase in kidney stone disease and stone-related health care costs. This work evaluates the predicted spatial distribution of the increase in prevalence and cost of nephrolithiasis in the U.S. by 2050 by using estimates of the temperature dependence (3) and cost (1) of nephrolithiasis, along with global climate predictions (16). We limited our analysis to upper-tract stones because the formation of kidney stones is responsive to environmental change, whereas lower-urinary tract (bladder) stones are thought to be temperature-independent and instead form as a result of infection, obstruction, and other factors. We also restricted our quantitative predictions to the next 50 years because unpredictable changes in demographics, internal migration, and diet may predominate over climate effects over longer periods.

Results

Given projected warming (e.g., histograms; Fig. 1), the two temperature-response models (lines, top of Fig. 1) clearly indicate that the risk of nephrolithiasis will increase. The predicted distribution of climate-related changes in urolithiasis strongly depends on the form of the temperature-dependence model. In the linear model, stone risk depends on baseline risk and rise in temperature, and therefore risk increase is concentrated in the midcontinent and West (Fig. 2). Arbitrarily defining the stone belt as those areas with a risk ratio ≥1.2 relative to the Northeast, the net effect of warming on stone risk is most easily visualized as a northward expansion of this belt from the Southeast into the Midwest (Fig. 3) This newly expanded stone belt occupies the southeastern half of the nation and all of California by 2050 and significantly beyond that by 2095.

In contrast, the nonlinear model theorizes a steeper rate of increase in stone risk between 10 and 15°C (i.e., a threshold value) and a small risk decrease above those temperatures (Fig. 1). Consequently, the nonlinear model predicts little change in stone risk with warming in the traditional Southeastern stone belt where MAT already exceeds 15°C; however, just north of that belt, a significant increase in risk is predicted in areas where 2050 temperatures rise above 13.4°C (i.e., trailing the northward movement of the threshold isotherm, red area, Fig. 4). Likewise, where 2050 temperatures rise above 17.2°C, a narrow zone of decreased risk is predicted, extending from Southern California to South Carolina (green, Fig. 4). The net effect predicted by the nonlinear model is similar to the linear model, where the present southeastern zone of elevated stone risk expands northward to include a band of states from Kansas to Virginia and Northern California, but prevalence increase is sharply concentrated immediately south of the threshold isotherm.

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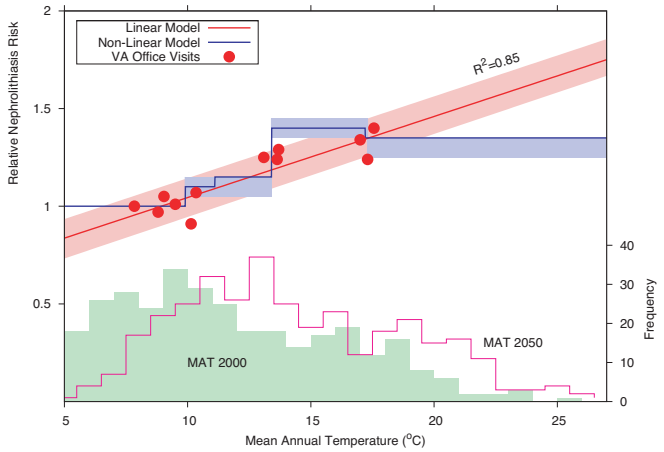

Fig. 1. Temperature-dependence models for nephrolithiasis risk relative to the Northeast (*Upper*) and current and projected MAT for U.S. climate divisions (*Lower*). Linear model 80% prediction interval and non-linear model 95% confidence interval is shown by shading. Original VA data were grouped by U.S. census region, temperature is the value for nearest corresponding National Oceanic and Atmospheric Administration (NOAA) climate region. Nonlinear risk model [1983 data, age- and gender-corrected (3)] exhibits peaked temperature dependence. Heating will drive many climate divisions to higher risk of urolithiasis, regardless of choice of nephrolithiasis model.

The epidemiological and economic impact of climate-related changes in temperature on stone risk depends on the distribution of risk as plotted in Figs. 3 and 4 modified (multiplied) by the distribution of population. Warming in general is moderated by proximity to the oceans in the coastal states. In the linear model, changes in prevalence are solely a function of warming; consequently, inland populations compared with coastal populations of approximately the same size exhibit larger prevalence changes (Fig. 5*a*). For example, Florida is projected to incur a 7.5% increased risk by 2050 [80% confidence interval (C.I.) 4.4–10.6%], whereas Illinois is anticipated to incur an 11.2% increased risk (C.I. 6.3–16.9%). Other examples of states predicted to have proportionately higher prevalence are Colorado, Michigan, and Wisconsin compared with similar-sized states Alabama, Georgia, and Washington, respectively. In the nonlinear model, the steep increase in risk associated with the temperature range of 10–15°C means that climate divisions warming into this range will incur the maximum climate-related risk increase. In general, population centers lying in the latitude range 37–42°N fit this criterion, including New York, Detroit, Chicago, Salt Lake City, and Sacramento (Fig. 5*b*). South of this band lies the zone predicted to experience risk reduction by the nonlinear model, and population centers lying in latitudes 32–36°N fit this criterion, including Atlanta, Oklahoma City, Phoenix, and Los Angeles.

In the linear model, the increase in number of cases (prevalence times population) is relatively uniformly distributed between census regions, although slightly smaller in the Northeast because of lesser warming in high-population coastal climate divisions. In the nonlinear model, new cases are strongly concentrated in the Midwest, whereas the number of new cases in the South and West are reduced by the predicted decrease in risk for temperatures >17.2°C. Nationwide, 1.6–2.3 million new lifetime cases are predicted by the models by 2050 (80% C.I. nonlinear model 0.3–3.1 million, linear model 1.3–3.3 million). Annual direct costs related to the treatment of climate-related nephrolithiasis are projected to increase by $1.3 billion by 2050 (year 2000 dollars) for the linear model (C.I. $0.72–1.84 billion). The nonlinear model predicts an annual increase of $900 million (C.I. $0.3–1.6 billion).

Discussion

The nationwide impact of climate-related increases in stone disease based on these two models of temperature dependence of stone risk is significant (Table 1, right columns). We predict a nationwide increase in prevalence of nephrolithiasis of 10.4% (linear model) and 7% (nonlinear) and an increase in annual cost of nephrolithiasis of 25% [compared with $5.3 billion for 2000 (17)], of which approximately two-thirds is accounted for by the consequences of warming and the remainder from growth in the population exposed to warming, concentrated predominantly in the higher-cost regions of the U.S. (Table 2). These changes in risk are somewhat larger than projected indirect climate-change effects on human health, e.g., the climate-related increase in vector-borne diseases such as malaria in tropical areas (18).

Similar climate-related changes in the prevalence of nephrolithiasis can be expected worldwide given the well established dependence of nephrolithiasis on MAT and predictions of long-term climate warming. This phenomenon will be manifest primarily as expansion of recognized kidney stone belts in the southern portions

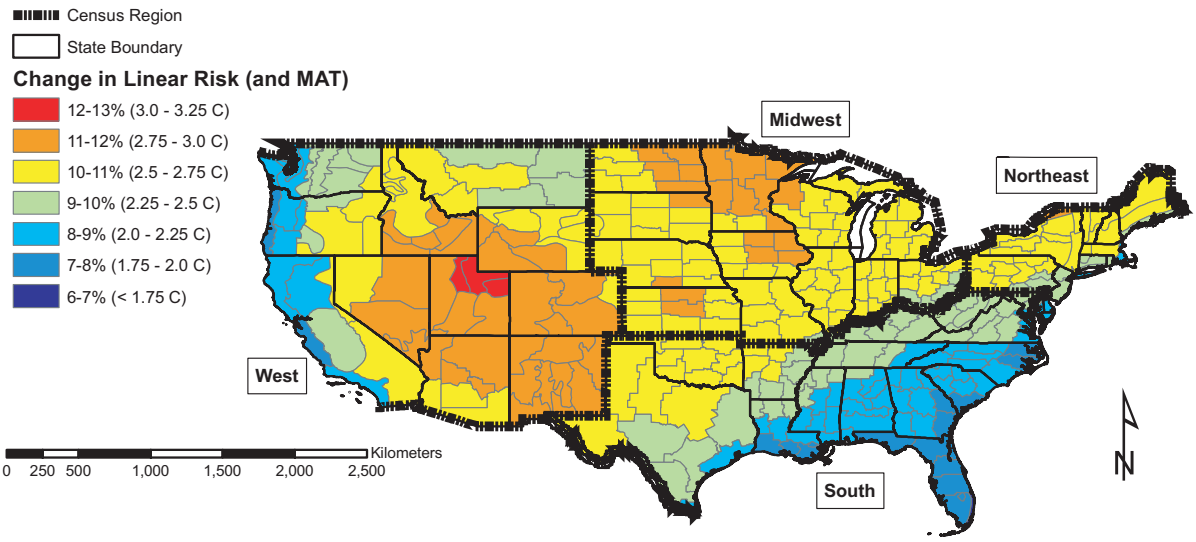

Fig. 2. Predicted warming and linear model nephrolithiasis risk change by 2050 for U.S. Strongest warming is in the midcontinent and upper Midwest. Heavy lines show the four U.S. census regions, and light gray lines show NOAA climate divisions.

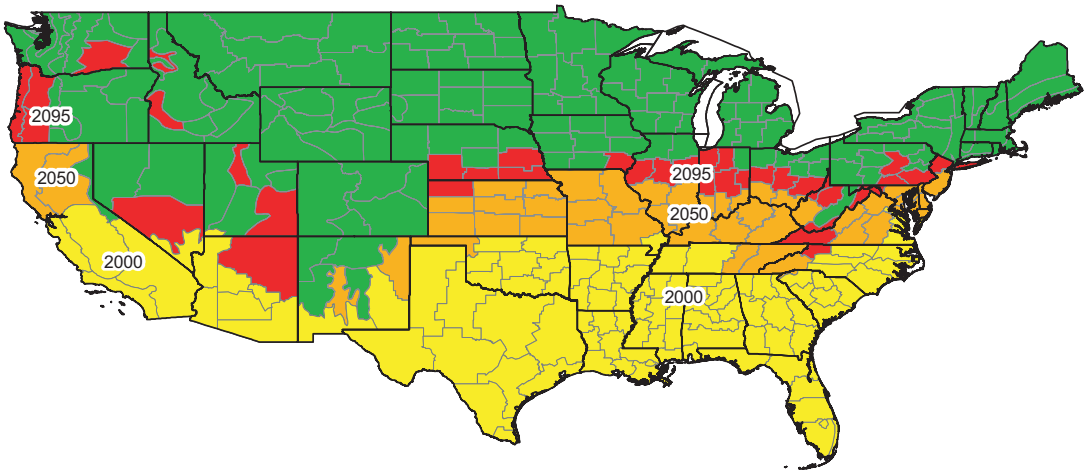

Fig. 3. Predicted growth in high-risk stone area (stone belt; risk ratio ≥1.2) vs. time, for 2000 (yellow), 2050 (orange), and 2095 (red); linear model. At 2000, 41% of the population is within a high-risk zone, 56% at 2050, and 70% at 2095, based on year 2000 population distribution.

of the U.S., Europe, and Asia (19, 20). Although a precise understanding of the temperature dependence of stone disease remains to be established, published reports consistent with a nonlinear relationship imply that the upper Midwest of the U.S. would be most heavily impacted. For example Kansas, Missouri, Maryland, and Kentucky are predicted to sustain 25% increases in stone prevalence by 2050 under the nonlinear model. The linear model developed here yields a more uniform distribution of increased prevalence, but the number of cases and increased annual costs will be concentrated in warm, high-population states such as California and Texas, which, by 2050, would each realize an annual cost increase of $110 million in year 2000 dollars.

This work used data primarily developed for other purposes, and as such our results are subject to a number of limitations. Perhaps foremost is that the precise relationship between ambient temperature and stone risk remains unknown, chiefly because it was of little importance to management of stone disease in the past. Clearly with the likelihood of long-term temperature changes, this importance is now greatly enhanced, and the issue warrants careful study. Of the two models discussed here, we favor the linear model because the Veterans Affairs (VA) data on which estimates of stone prevalence are based were derived from actual outpatient visits for stone disease rather than on surveys eliciting a self-reported history of stones (3). It is also consistent with our own observation of seasonal variation despite a high MAT. Although it is possible that individuals might reduce their environmental exposure during "hot" seasons, thereby decreasing stone risk at high temperature as suggested by the nonlinear model, a compensatory increase in stone risk during "cooler" seasons might also be expected. More accurate models will require detailed analysis of spatial and temporal variations in nephrolithiasis by using climate-based, rather than population-based divisions. Given the likely mechanism of nephrolithiasis response to climate change (i.e., fluid balance), derived climate variables such as mean annual heat stress [apparent temperature, akin to heat index (21)] may provide a better correlation. For example, the year 2000 distribution of elevated risk as defined by the linear model (Fig. 3) appears to overestimate present risk in the Southwest (compare with ref. 22). Heat stress falls off from east to west in the U.S., and its distribution more closely mimics the known stone belt.

Considerable uncertainty is present in the underlying climate models obtained from the Fourth Climate Assessment of the

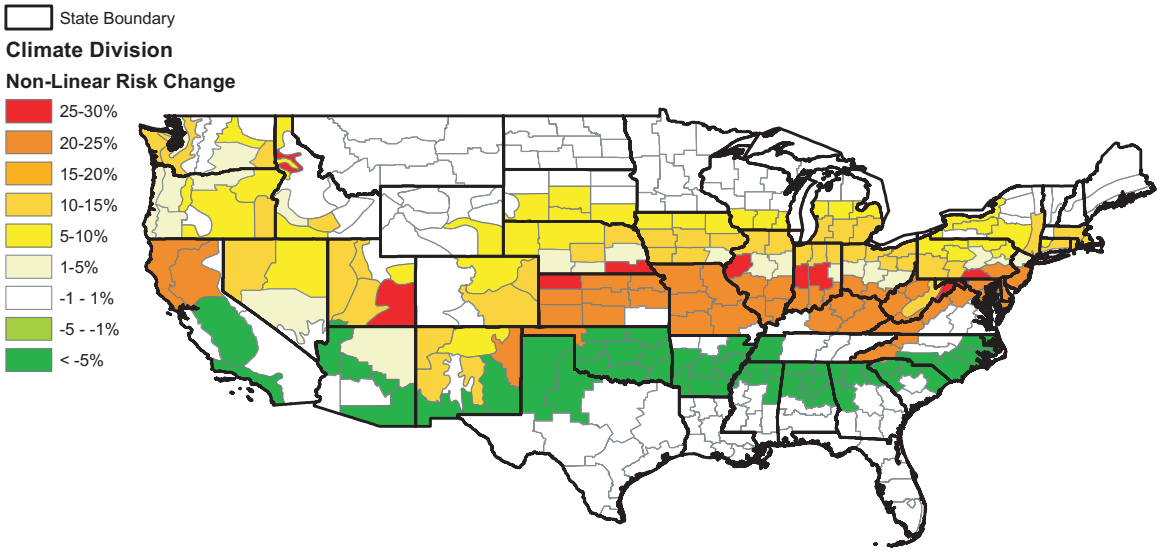

Fig. 4. Predicted changes in stone risk by 2050, nonlinear model (3). Peaked risk vs. temperature model (Fig. 1) concentrates risk change at northern edge of the present-day stone belt (yellow, Fig. 3). Trailing that to the south is a zone of reduced risk (green).

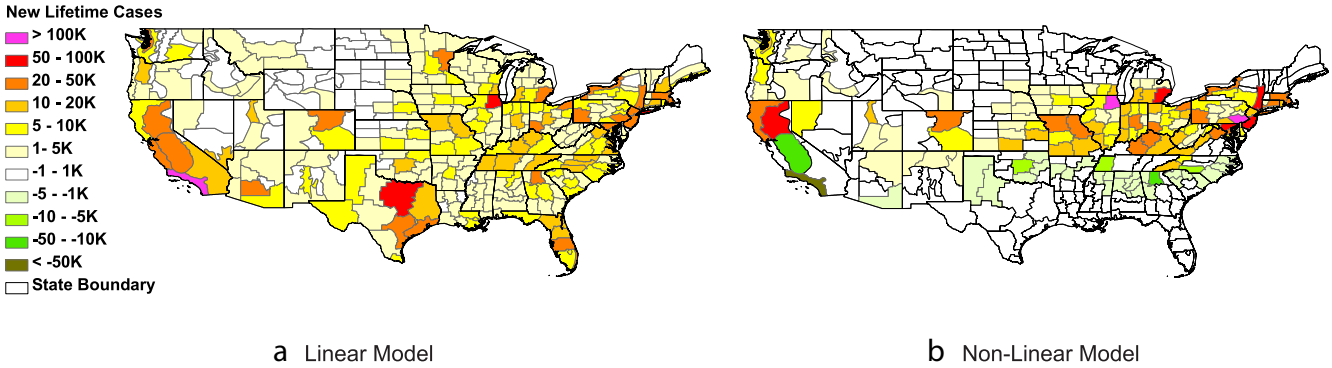

Fig. 5. Impact of climate-related increase in nephrolithiasis prevalence by 2050 for the linear (*a*) and nonlinear (*b*) models. Data are represented as the number of new climate-related cases (predicted 2050 nephrolithiasis prevalence times 2050 estimated population).

Intergovernmental Panel on Climate Change (IPCC4). We considered the intermediate warming scenarios (A1B) as defined in the Special Report on Emissions Scenarios (SRES). For example, a U.S. contribution to this model set is the National Center for Atmospheric Research Parallel Climate Model (NCAR-PCM), which predicts an additional degree of warming, for a total of 4°C in the midcontinent by 2050. More severe warming scenarios, e.g., SRESa2, predict significantly greater warming after 2050. Given this level of warming, the nationwide increase in the prevalence of stone disease would be 15–20% and the annual cost increase up to 40% by 2050. With the nonlinear model, this amount of warming would yield a 40–50% increase in prevalence and cost in some Midwest climate divisions such as Chicago.

We acknowledge additional limitations in this work. The temperature-dependence models presume an accurate understanding of current stone prevalence; however, such data are problematic for a variety of reasons. Unlike some diseases that are readily diagnosed as present or not, such as appendicitis, stone disease occurs intermittently and is not always readily apparent. Many patients harbor undiagnosed, asymptomatic stones, whereas others require repeated hospitalizations for recurrent stone events. Whereas virtually all patients with appendicitis come to medical attention and can be accounted for by hospital discharges and confirmed with pathology reports, patients with stone disease may or may not come to medical attention, and consequently some remain unaccounted for, and others involve repeated use of health care resources for the same or different stone events. Consequently, true stone prevalence is difficult to determine and is likely routinely underestimated but also occasionally overestimated. The baseline prevalence of stone disease assumed here reflects the most current published data (2) but could be as much as 35% higher today, based on trend projection. For the linear model, this would yield a matching percentage increase in nephrolithiasis prevalence and cost.

When using national and regional datasets, a variety of surrogate markers are used to estimate stone prevalence, including hospital discharges, physician office visits, emergency room visits, or procedures related to a primary diagnosis of stone disease, or a self-reported history of stones (17, 23). All of these surrogates are compromised in that they likely underestimate the prevalence of disease either because a patient may pass a stone without requiring any health care resources or because a patient may report a history of stones based on unsubstantiated symptoms or not report a history of stones because a stone was never collected despite classic symptoms of renal colic.

In the linear model that we derived using VA data, prevalence was derived from inpatient and outpatient hospital visits, which provide an accurate estimate of health care resource utilization in this population during the specified time; however, because the data were not acquired by using unique identifiers, all encounters, not only unique patients, were captured, thereby likely overestimating prevalence. However, because this dataset relies on resource utilization, individuals who passed stones without accessing the health care system were not captured, potentially leading to an underestimate of prevalence.

When determining regional differences in stone risk, these systematic errors affect the entire population and should not affect the calculated relative regional risks of stone disease. However, error in stone prevalence can have a profound impact on estimates of economic consequences of increased stone prevalence in that the increase in health care dollars depends on a precise estimate of the burden of disease. In the future, we plan to use other national datasets that use population-based estimates of stone prevalence (i.e., self-reported history) or that use claims data for a much greater and more inclusive sampled population, allowing a more accurate estimate of current and future stone prevalence.

Finally, this analysis cannot take into account potential dramatic changes in the care of patients with kidney stones that might result in significant and unexpected changes in the future cost of care of these patients. Although dramatic changes in technology are possible, small changes with minimal impact on cost are more likely. Health care-related costs have been increasing at a rate that surpasses inflation. Most surgical procedures for stone removal

Table 1. Predicted change in stone prevalence and cost by 2050 attributable to climate change, by census region

	Warming (°C)		Risk change, %		New cases		Annual costs, $	
Region	Mean	80% C.I.	Linear	Nonlinear	Linear	Nonlinear	Linear	Nonlinear
Northeast	2.43	1.43–3.58	10.6	8.1	414,107	487,717	243,586,285	286,885,204
Midwest	2.64	1.48–3.94	11.0	9.9	601,383	739,938	353,746,067	435,246,747
South	2.19	1.31–3.27	9.3	4.7	697,366	277,469	435,231,996	141,965,298
West	2.34	1.27–3.25	10.7	5.3	542,068	151,146	296,604,853	296,604,853
Mean	2.38		10.4	7.0				
Total					2.25M	1.61M	1.33B	947M
80% C.I.	1.36–3.48		6–15	3–11	1.29M–3.30M	500K–2.83M	761M–1.9B	301M–1.7B

Table 2. Costs of stone-related interventions ($) by region per 100,000 population, based on utilization rates in Table 3

Region	Inpatient hospitalization, $	Physician office visits, $	Ambulatory surgery, $	Total, $
Midwest	91,350	97,805	2,751,965	3,246,977
Northeast	103,034	106,330	2,377,794	2,893,016
South	91,350	114,855	2,933,015	3,445,078
West	46,737	98,037	2,045,868	2,496,501

Total for each region includes $104,244 for emergency room, $150,875 for inpatient procedures, and $50,738 for outpatient hospital visits (only nationwide data available).

(ureteroscopy and shock wave lithotripsy) are minimally invasive and are already performed on an outpatient basis. Furthermore, newer generation shock wave lithotripters are rarely less costly but are less effective than the original lithotripter, the Dornier HM-3, which was introduced >20 years ago (24). Whereas medications have been shown to reduce the risk of stone recurrence, they are not currently in widespread use by patients because of high cost, frequent side effects, and poor patient compliance (25). Furthermore, the cost-effectiveness of medications aimed at stone prevention has been questioned because of low yearly recurrence rates in first-time stone formers and the high cost of current medications (26). Although recurrent stone formers have a greater potential benefit from medication, current medications are still not cost-effective despite their therapeutic effectiveness. It is possible that new medications will be developed that will be more effective or less costly than ones currently available, and this change could impact overall cost, both by increasing medication use and by decreasing utilization of health care resources. Unfortunately, there have been no new medications that have come to market for stone prevention in the last few decades, and therefore this is unlikely to have a significant impact on cost in the near future. Overall, the future estimates of health care costs are limited by our inability to predict future changes in medical care and health care delivery.

Regardless of these limitations, climate-related increases in the prevalence of nephrolithiasis in the U.S. appear likely, and the impact of changes in stone disease will be nonuniformly distributed. The nephrolithiasis-response models used here indicate that the impact will either be concentrated in the southern half of the U.S. (linear model) or the upper Midwest (nonlinear model). These changes are likely to cause notable perturbations in the magnitude of stone interventions, with corresponding stresses in health care delivery and economics. Although less well characterized, stone belts worldwide will be similarly affected, with much greater impact on morbidity in developing nations. This direct link between climate change and human health adds yet another challenge to the task of adapting to climate change this century.

Materials and Methods

Dependence of Stone Risk on Temperature. Although evidence strongly supports a positive correlation between temperature and stone risk, the precise relationship between these factors has not been elucidated. One possibility is that stone risk rises with increasing temperature, perhaps abruptly at some threshold value, until a point at which it plateaus or even declines (nonlinear model). Alternatively, stone risk may continue to rise with increasing temperature (e.g., a linear model).

The nonlinear model is based primarily on data derived from the Second Cancer Prevention Survey of 1982, in which a history of stone disease was elicited from >1 million subjects (3). This cross-sectional study revealed a peaked (nonlinear) distribution of stone risk with a maximum raw odds ratio of 1.9 (or 1.4 when adjusted for gender, age, and personal risk factors; Fig. 1) for persons living in areas with a MAT of 13.4–17.2°C. For reasons that are unclear, the risk of nephrolithiasis declined slightly for those living in areas with MAT exceeding 17.2°C, perhaps because at higher temperatures individuals are more likely to avoid outdoor activities, thereby limiting their environmental exposure and reducing their stone risk. The most prominent feature of this model is the indication of a threshold value of MAT at which stone risk rises rapidly (13.4°C; Fig. 1).

An alternative linear model describing the temperature dependence of stone prevalence is supported by evidence that even in high-MAT locales increases in temperature continue to raise stone risk, i.e., there is still a ''stone season'' [e.g., Saudi Arabia (10), Taiwan (14), with monthly temperatures ranging from 24 to 34°C]. Indeed, a study of spinal cord injury patients in the U.S. revealed a linear 10% increase in stone risk per 1°C increase in MAT (4). We derived a linear model of temperature dependence of stone disease by using a VA dataset from the Urologic Diseases in America project (UDA; ref. 1). Stone prevalence, estimated from physician office visits for a diagnosis of upper-tract urolithiasis, was correlated with MAT for the four U.S. census regions. A strong linear relationship was found between the two (points and linear fit; Fig. 1) with a 4.2% increase in stone risk per degree Celsius temperature increase.

This work considers both models of temperature dependence of nephrolithiasis, the nonlinear distribution (3) and the linear model fit to the VA dataset.

Projected Temperature Change. Over the last 30 years, global temperature increases have been steadily accelerating, and increases in MAT of nearly 1°C have been recorded in the U.S. Projections of future climate are best represented in the results of global circulation models (GCMs). The most comprehensive of these are coordinated by the IPCC4 (16). From these results, predicted temperature increases resulting from CO_2 already added to the atmosphere (''committed'') will add another 1–2°C rise in the U.S. MAT by 2100. Future emissions are predicted to cause a 3–5°C rise in MAT in midcontinent regions by 2100 (16), depending on greenhouse gas emissions scenario (27). The global mean of all IPCC4 scenario models is quite similar to the mean of the intermediate scenario models (SRESa1b), and therefore the latter was chosen for this work to predict U.S. temperature changes. In simplest terms, the degree of modeled warming correlates primarily with atmospheric CO_2, and predicted CO_2 for all scenarios by 2100 ranges from 600 to 1,500 ppm (27); current levels are ≈380 ppm. Atmospheric CO_2 concentration for the SRESa1b scenario by 2100 is 850 ppm, thereby constituting the closest specific scenario to the mean value for all scenarios modeled in IPCC4. Current rates of emission (2.5% increase per year in atmospheric CO_2 since 2000) (28) are consistent with the SRESa1b scenario, although they would exceed SRESa1b-envisioned emissions if continued beyond 2025.

The predicted change in annual MAT across the U.S. was determined from the mean of 19 IPCC4 SRESa1b scenario GCM results. Mean monthly surface air temperatures (TAS) were computed for each model and regridded to a $0.5 \times 0.5°$ mesh over North America. To minimize GCM bias, monthly model increments of TAS (model departure from the mean of 20th-century model, 20c3m, results) were determined, and the annual average increment was calculated for each model. These were downscaled to U.S. climate divisions (1–10 of these per state) by using intersection–area weighting, and future TAS values were computed by adding the increment to observed temperature normals (1895–2006) for each division. The climate normals represent an instrumental record that is effectively population weighted within each division (weather stations are near people) and therefore most closely indicate the temperature experienced by the population. This can be important in areas with significant topographic relief. For example, Las Vegas, NV, has an observed divisional normal TAS of 17.4°C. A direct average of SRESa1b TAS for that division at 2050 predicts an unreasonably low 15.4°C, which reflects an average of mountain and desert temperatures. The 2050 mean TAS increment of 2.8°C added to the normal gives a predicted MAT of 20.2°C, more consistent with expected temperatures in the populated desert valleys in that climate division. Mean, 90th- and 10th-percentile values over the 19 models were computed for each division for each year and were the basis for the central projection and uncertainty ranges described below.

Current Costs of Urolithiasis. There are two factors that influence the overall financial burden of stone disease: cost of service and rate of utilization. The direct cost of stone disease comprises emergency room visits, outpatient physician and hospital visits, inpatient hospital care, and procedure costs for both inpatient and outpatient care. The indirect costs include primarily loss of work and are less objectively defined, although the UDA project estimated these costs at $775 million per year currently (17).

The UDA project obtained information from a variety of national datasets, including the Healthcare Cost and Utilization Project (HCUP), Centers for Medicare and Medicaid Services (CMS), National Hospital Ambulatory Medical Care Survey (NHAMCS), National Ambulatory Medical Care Survey (NAMCS), and Center for Health Care Policy and Evaluation (CHCPE), to identify regional rates of stone-related interventions (Table 3), and these data were used to determine rates of utilization.

Specific health care costs related to patients with stone disease were obtained from two large metropolitan hospitals in Dallas, Texas. We used cost rather than charge data to capture relative resource utilization more accurately because charge data include profit margins that are variable for different cost centers

Table 3. Rates of stone-related interventions by region per 100,000 population

Region*	Inpatient hospitalization HCUP†	Physician office visits		Ambulatory surgery		
		CMS‡	Total§	CHCPE¶	CMS	Total
Midwest	86	594	1262	237	219	456
Northeast	97	704	1372	197	197	394
South	86	814	1482	271	215	486
West	44	597	1265	188	151	339

Region boundaries shown by heavy line in Fig. 2.

*Regional rates unavailable for the following, therefore, the national average was included in the category totals: emergency room (national average, 226 visits based on NHAMCS); outpatient hospital visits, 110 visits based on NHAMCS; inpatient procedure (national average, 25 from CHCPE).

†Healthcare Cost and Utilization Project.

‡Centers for Medicare and Medicaid Services.

§CMS + NAMCS (National Ambulatory Medical Care Survey, national average 668 visits.

¶Center for Health Care Policy and Evaluation.

within an institution and among institutions. These individual costs were aggregated into costs per population for the four U.S. census regions (Table 2).

Emergency room visits. Data for emergency room visits were obtained from the NHAMCS dataset and were estimated at 226 per 100,000 population (Table 3). The cost of an emergency room visit was estimated by the cumulative cost of nursing, medication (i.v. fluids, pain medication, and antiemetics), radiology (computed tomography of the abdomen), and laboratory along with physician fees for a level III visit based on 2007 Texas Medicare reimbursement fees; it averaged $461.

Inpatient hospitalization. By using the HCUP dataset for the year 2000, the mean inpatient hospital length of stay was determined to be 2.2 days, and rates of utilization varied by region from 44 to 97 per 100,000 population (Table 3). The cost of an average hospital stay, based on the cumulative cost of room and board, nursing, medication (i.v. fluids, pain medication and antiemetics), radiology and laboratory and physician fees, was estimated at $1062.

Outpatient hospital visits. Outpatient hospitalization rates were obtained from NHAMCS for the year 2000. No regional data were available for this dataset, but the overall rate was 110 visits per 100,000 population (Table 3). The cost of an outpatient hospital visit was assumed to be the same as an emergency room visit (see above) at $461.

Physician office visits. Outpatient office visit rates were obtained from NAMCS and CMS and ranged from 1262 to 1482 per 100,000 population (Table 3). Physician fees for a level III visit based on 2007 Texas Medicare reimbursement fees for new and established patients averaged $77.50 per visit.

Procedure costs. The number and distribution of procedures, including both inpatient- and ambulatory-based procedures, were obtained from the CHCPE and CMS datasets. The distribution of procedures for stones was comparable for CMS and CHCPE: shock wave lithotripsy (SWL) 54% for both; ureteroscopy (URS) 41% and 42% for CMS and CHCPE, respectively, and percutaneous nephrostolithotomy (PCNL) 4% and 6% for CMS and CHCPE, respectively. For our model, we used procedure rates from CMS. The estimated cost of each procedure was obtained from the mean cost of >100 cases performed at a large, metropolitan county hospital. The mean costs of SWL, URS, and PCNL were $6,620, $4,773, and $11,530, respectively. Cost centers included the operating room, operating room supplies, day surgery, recovery room, laboratory costs, and anesthesia along with professional fees. Professional fees were obtained from 2007 Medicare reimbursement rates in Texas rather than from charge data. SWL and URS were assumed to be outpatient procedures, whereas PCNL was considered an inpatient procedure.

Total direct costs. Table 2 summarizes the total costs for each geographic region taking into account procedure/intervention costs and rates of utilization. Costs are highest in the Southeast, primarily reflecting the elevated incidence of nephrolithiasis in the stone belt. Indirect costs such as those associated with lost work time were not considered but would add an additional 15–20% to the computed cost (17).

Projecting Climate Change Impact on Nephrolithiasis. ***Prevalence.*** To project the likely changes in the expected prevalence of stone disease and associated health care cost, we combine the predicted temperature changes and the quantitative relationship between ambient temperature and stone risk. Warming-related change in stone risk was calculated by using the predicted TAS (nonlinear model) or TAS increments (linear model). These risk changes multiplied by a base risk of 5.2% [representing age- and gender-corrected stone prevalence for the Northeast between 1988 and 1994 (2)] and by the estimated population in 2050 [assuming uniform 48% growth (29)] yield the climate-related change in number of lifetime stone cases incurred by 2050.

Cost. The change in annual cost associated with the warming-related change in stone disease for each climate division was computed by using current regional cost rates (Table 2, converted to per capita) multiplied by risk change and estimated 2050 population. Stated C.I. values for the nonlinear model and computed prediction interval for the linear model regression were combined with the temperature C.I. to compute an 80% C.I. for the number of cases and costs (Fig. 1 and Table 1).

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