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Warmer Weather as a Risk Factor for Cellulitis: A Population-based Investigation

Ryan A. Peterson,[1] Linnea A. Polgreen,[2] Daniel K. Sewell,[1] and Philip M. Polgreen[3,4]

Departments of [1]Biostatistics and [2]Pharmacy Practice and Science, University of Iowa, [3]Departments of Internal Medicine and Epidemiology, University of Iowa, and [4]The University of Iowa Health Ventures' Signal Center for Health Innovation, Iowa City

Background. The incidence of cellulitis is highly seasonal and this seasonality may be explained by changes in the weather, specifically, temperature.

Methods. Using data from the Nationwide Inpatient Sample (years 1998 to 2011), we identified the geographic location for 773 719 admissions with the primary diagnosis (ICD-9-CM code) of cellulitis and abscess of finger and toe (681.XX) and other cellulitis and abscess (682.XX). Next, we used data from the National Climatic Data Center to estimate the monthly average temperature for each of these different locations. We modeled the odds of an admission having a primary diagnosis of cellulitis as a function of demographics, payer, location, patient severity, admission month, year, and the average temperature in the month of admission.

Results. We found that the odds of an admission with a primary diagnosis of cellulitis increase with higher temperatures in a dose-response fashion. For example, relative to a cold February with average temperatures under 40° F, an admission in a hot July with an average temperature exceeding 90°F has 66.63% higher odds of being diagnosed with cellulitis (95% confidence interval [CI]: [61.2, 72.3]). After controlling for temperature, the estimated amplitude of seasonality of cellulitis decreased by approximately 71%.

Conclusion. At a population level, admissions to the hospital for cellulitis risk are strongly associated with warmer weather.

Keywords. cellulitis; skin and soft tissue infection; weather; temperature; seasonality; climate change.

Cellulitis is an infection of the skin associated with discomfort, erythema, swelling, and warmth of the affected area [1, 2]. Cellulitis is common and represents an important cause of morbidity [2–6]. Although minor cases can be treated on an outpatient basis, more severe cases frequently require an admission to a hospital and intravenous antimicrobial therapy. The disease generated an estimated 537 000 hospitalizations in 2013 and is a major driver of healthcare costs, $3.74 billion in 2013 [6]. Although cellulitis most commonly affects the lower extremities, it can also affect other anatomic areas (e.g., the face, hands) [1–3, 7, 8]. Risk factors for developing cellulitis include skin trauma [8, 9], venous insufficiency [8], and lymphedema [8, 10, 11]. Cellulitis is commonly associated with trauma (e.g., cuts, bites) [1], and in many cases even very minor trauma. For example, small breaks between the toes associated with fungal infections are associated with cellulitis of the lower extremities [8, 9]. In addition, specific therapies can increase the risk for developing cellulitis: prior surgery [12–14] and radiation therapy [14–16] can increase the risk of cellulitis.

Beyond individual-level risk factors, environmental risk factors for cellulitis may also exist. A majority of cases of cellulitis are caused by Gram positive organisms (e.g., beta-hemolytic streptococci and also *Staphylococcus aureus*) [1, 2, 17]. However, exposure to water can increase the risk of cellulitis caused by more unusual pathogens, for example, *Aeromonas hydrophila* [1]. In addition, a few studies demonstrate a seasonal increase in cellulitis and skin and soft tissue infections, with cases peaking in warmer months [18–21]. The same seasonal pattern has been reported for surgical site infections [22–26]. Although the seasonal pattern in the incidence of cellulitis cases strongly suggests the role of environmental risk factors for developing cellulitis [6], the reason for the seasonality of cellulitis is not clear. Weather affects the seasonality of a wide range of infectious diseases [27], and it is likely that weather patterns are also related to the seasonal pattern in the incidence of cellulitis.

The purpose of this study is to determine the effects of weather on the risk for cellulitis over large geographic regions. For this investigation we use a population-based sample of US hospital discharges from 1998 to 2011 representing multiple different geographic regions combined with weather data from the National Oceanic and Atmospheric Administration.

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Correspondence: P. M. Polgreen, University of Iowa, Departments of Internal Medicine, Division of Infectious Diseases, 200 Hawkins Dr, Iowa City, IA 52242 (philip-polgreen@uiowa.edu).

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METHODS

Discharge data were extracted from the Nationwide Inpatient Sample (NIS), the largest all-payer database of national discharges in the United States. The database is maintained as part of the Healthcare Cost and Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (AHRQ) and contains data from a 20% stratified sample of nonfederal acute-care hospitals. This sample includes academic medical centers, community hospitals, general hospitals, and specialty hospitals. However, it excludes long-term care facilities and rehabilitation hospitals. To adjust for yearly changes in the sampling design, we applied the weights provided by AHRQ.

We identified every adult hospitalization for which the primary diagnosis was cellulitis over the period from January 1998 to November 2011. For case ascertainment, we used the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 681.00–681.02, 681.10, 681.11, 681.9 (cellulitis and abscess of finger and toe), and 682.0–682.9 (other cellulitis and abscess). There are no codes for cellulitis exclusively, but here we refer to these codes collectively as cellulitis. All records without a primary diagnosis of cellulitis were considered as controls. Hospitals in the study were geolocated using the Google Maps Geocoding API [28] using the American Hospital Association (AHA) identification number when available. Weather data were obtained from the Unedited Local Climatological Data (1998–2004) and the Quality Controlled Local Climatological Data (2005–2011). Both data sets were reported by the National Climatic Data Center (NCDC) of the National Oceanic and Atmospheric Administration (NOAA).

Using each hospital's longitude and latitude, we found all weather stations within 100 km of the hospital and then extracted the following monthly summary statistics for these stations: average temperature, minimum temperature, maximum temperature, total precipitation, average dew point, average wet bulb temperature, average heating degree days, average cooling degree days, resultant wind speed, and total monthly precipitation. The summary statistics for hospitals with multiple nearby stations were averaged across stations, whereas the summary statistics for hospitals with no nearby stations (1.9%) were imputed using a k-nearest-neighbor approach with k = 5.

We used logistic regression to estimate the odds of an inpatient visit having a primary diagnosis of cellulitis and considered 2 candidate models. Our first model is a "demographics model," which controls for the following patient-level covariates: age (grouped by decade), sex, primary payer, length-of-stay, Elixhauser comorbidity index (29 categories) [29, 30], admission month, and admission year. These patient-level coefficients can be interpreted as potential risk factors for cellulitis admissions. The demographics model also contains hospital-level variables: region (Northeast, Midwest, West, and South), longitude and latitude. Our second model is a "weather model" including both weather data and the same factors as the demographics model. Specifically, the weather model includes average monthly temperature (in 5 degree steps from <40 to 90+). Other weather variables were not included in either model; they were either highly correlated with average monthly temperature or did not lead to any clinically significant change in the model estimates. In addition, to assess whether the effect of temperature differed by region, we examined the effects of interaction terms between (linear) temperature and region and plotted them against the overall model's temperature effect.

For both models, the cyclic seasonal nature of cellulitis admissions was captured through the fixed month effects; the ratio between the nadir month's odds and the peak month's odds can be interpreted as the "average amplitude of seasonality," adjusted for the other covariates in the model. To determine how much of the seasonality of cellulitis is attributable to weather, we compared the average amplitude of seasonality for both models.

RESULTS

Before applying discharge weights, over the course of our study period, the NIS contains 108 595 896 hospitalizations (1.313% with a primary diagnosis of cellulitis). We excluded 27 410 478 observations because they were missing key variables: admission month, age, sex, payer, or length of stay. Because several states do not report an AHA geocodable variable, we omitted an additional 25 508 342 discharges for which we were not able to assign a location. This left a total of 55 665 828 total hospitalizations to be used in our final analysis (1.39% cellulitis cases). Table 1 includes a summary of the included and excluded records.

Descriptive statistics for our sample are presented in Table 2. Cellulitis cases were generally similar to the control group (noncellulitis discharges) in terms of mean age, latitude, and longitude. However, cases were admitted during a month with a higher mean temperature than the control group (55.91° F vs 54.37° F). Cellulitis patients had a slightly shorter mean length of stay than did the controls (4.79 days vs 4.84 days), but they had a higher mean Elixhauser comorbidity sum than the controls (2.14 vs 1.77). Although the control group had more women than men (60.8% to 39.2%), in the case group this difference was less pronounced (47.8% to 52.2%). Patients in their 40s and 50s are much more common in the case group than the control group.

Results from the weather model logistic regression are presented in Table 3. After controlling for temperature and other covariates, patients in the Midwest, South, and West were less likely to be a cellulitis admission than patients in the Northeast. Also, patients who have private insurance were 13.8% less likely to be a cellulitis admission than patients on Medicare (95% confidence interval [CI]: [12.2, 14.4]). Patients in their 40s were 80.4% more likely to be a cellulitis admission

Table 1. Summary of Sample Size Included After Applying Necessary Filters

Filter	Sample Size	Percent of Initial Sample
None	108 595 896	100%
Nonmissing:		
Admission month	98 435 410	90.64%
Sex	98 252 484	90.48%
Length of stay	98 246 157	90.47%
Payer	97 971 752	90.22%
Age	97 957 295	90.20%
Age ≥18	81 174 170	74.75%
Address listed	55 665 828	51.26%

(95% CI: [78.6, 82.1]), compared to the baseline group of 18- to 30-year-old patients. There was also a significant time trend over the course of the study; holding all else equal, the odds of a cellulitis admission grew by 2.8% per year (95% CI: [2.8, 2.9]) under our model. Several comorbidities were strongly associated with higher odds of a cellulitis admission: for example, the odds of a cellulitis admission were 146% higher for patients with diabetes (95% CI: [143, 148]), and 122% higher for patients labeled as obese (95% CI: [121, 124]). Longitude and latitude were statistically significant, but the odds ratios were small.

Seasonal changes in cellulitis admissions for both the demographics-only and the weather models are presented in Figure 1, and the unadjusted and adjusted odds ratios are presented in Table 4. In the demographics-only model, the amplitude of seasonality is markedly greater: the odds of a cellulitis admission are 36.0% higher in July than in February (95% CI: [34.5, 37.6]). However, the average amplitude of seasonality (February to July) when temperature is added to the model is 10.4% (95% CI: [8.1, 12.8]). This indicates that after controlling for the effects of temperature and demographics, the odds of a cellulitis admission are about 10.4% higher during July than February. Comparing the 2 models, we find that adding temperature to the model decreased the February–July amplitude by approximately 71%.

The effect of temperature on the odds of cellulitis admission was strong. The odds of cellulitis admission increase by roughly 3.55% per 5°F increment in temperature. Specifically, the highest temperature group, 90°F+, was associated with an increase in the odds of a cellulitis admission of 50.9% (95% CI: [45.1, 56.9]) when compared to temperatures below 40°F. Combining this with the residual seasonality effect, this means that relative to a cold February with average temperatures under 40°F, an admission in a hot July with an average temperature exceeding 90°F has 66.63% higher odds of being diagnosed with cellulitis (95% CI: [61.2, 72.3]). This temperature effect was similar for all census regions, as shown in Figure 2.

DISCUSSION

Our results show that the vast majority of the observed seasonality in the incidence of admissions for cellulitis can be explained by the weather, specifically by changes in temperature. We found that as average monthly temperatures increase, so does the risk for admissions due to cellulitis. This increased risk for cellulitis is associated with warmer temperatures and it persisted even after controlling for patient age, sex, type of payer, length of stay, comorbidities, geographic region, latitude, and longitude. With respect to the increased risk associated with warmer weather, we observed a dose-dependent relationship between temperature and the odds of admission for cellulitis. For example, for every 5°F increase in temperature, the odds of a cellulitis admission increased by roughly 3.55%.

The incidence of several different types of infectious diseases is seasonal [27]. Although many infections increase in incidence in during winter months (e.g., respiratory and some gastrointestinal infections) [31–35], others, especially tick-borne infections, peak during warmer summer months [36]. Thus, although the seasonality of several different diseases is well described, much less attention has been focused on the seasonality of cellulitis. The few existing reports of seasonality are consistent with our results and describe an increase in the

Table 2. Descriptive Statistics (Continuous on Top, Categorical on Bottom)

Variable	Cellulitis Mean (± SD)	Control Mean (± SD)
Age (years)	56.8 (± 19.2)	56.88 (± 21.1)
Length of stay	4.79 (± 4.8)	4.84 (± 6.8)
Latitude	39.63 (± 3.4)	39.61 (± 3.4)
Longitude	-90.65 (± 18.2)	-91.28 (± 18)
Avg monthly temp	55.91 (± 16)	54.37 (± 16.1)
Elixhauser Sum	2.14 (± 1.7)	1.77 (± 1.6)
Variable	**Cellulitis % of Sample**	**Control % of Sample**
Sex		
Female	47.8%	60.8%
Male	52.2%	39.2%
Payer		
Medicare	42.1%	43.6%
Medicaid	14.5%	14.3%
Private insurance	29.2%	34.4%
Self-pay	8.9%	4.3%
No charge	0.4%	0.2%
Other	4.8%	3.2%
Region		
Northeast	34.4%	31.2%
Midwest	19.9%	21.5%
South	17.5%	18.2%
West	28.2%	29.2%
Age group		
(18, 30)	8.5%	13.7%
(30, 40)	11.9%	12.6%
(40, 50)	18.1%	11.8%
(50, 60)	18.2%	13.4%
(60, 70)	14.2%	14.4%
(70, 80)	13.7%	16.9%
80+	15.5%	17.3%

Abbreviation: SD, standard deviation.

Table 3. Logistic Regression Results for "Weather Model"

Covariate	Odds Ratio (95% CI)	Covariate	Odds Ratio (95% CI)
Month effects		**Payer**	
January	Baseline	Medicare	Baseline
February	0.975 (0.963, 0.987)	Medicaid	1.010 (1.002, 1.019)
March	1.010 (0.998, 1.022)	Private insurance	0.862 (0.856, 0.868)
April	0.997 (0.983, 1.011)	Self-pay	1.863 (1.845, 1.881)
May	1.022 (1.005, 1.039)	No charge	1.886 (1.822, 1.952)
June	1.032 (1.012, 1.052)	Other	1.404 (1.388, 1.421)
July	1.076 (1.054, 1.099)		
August	1.068 (1.046, 1.090)	**Age Group**	
September	1.057 (1.037, 1.076)	(18, 30)	Baseline
October	1.052 (1.037, 1.067)	(30, 40)	1.390 (1.376, 1.404)
November	1.065 (1.051, 1.078)	(40, 50)	1.804 (1.786, 1.821)
December	1.065 (1.053, 1.078)	(50, 60)	1.533 (1.518, 1.548)
		(60, 70)	1.125 (1.113, 1.138)
Average Temperature		(70, 80)	0.991 (0.980, 1.003)
<40	Baseline	80+	1.216 (1.202, 1.231)
(40, 45)	1.046 (1.034, 1.057)		
(45, 50)	1.072 (1.060, 1.084)	**Region**	
(50, 55)	1.106 (1.093, 1.119)	Northeast	Baseline
(55, 60)	1.128 (1.112, 1.143)	Midwest	0.824 (0.814, 0.834)
(60, 65)	1.172 (1.153, 1.191)	South	0.810 (0.803, 0.816)
(65, 70)	1.207 (1.185, 1.229)	West	0.710 (0.690, 0.731)
(70, 75)	1.258 (1.233, 1.283)		
(75, 80)	1.282 (1.254, 1.310)	**Sex**	
(80, 85)	1.279 (1.243, 1.315)	Male	Baseline
(85, 90)	1.434 (1.379, 1.491)	Female	0.636 (0.633, 0.639)
90+	1.509 (1.451, 1.569)		
		Continuous Variables	
Comorbidities[a]		Time Trend (years)	1.028 (1.028, 1.029)
None	Baseline	Length of Stay	0.995 (0.995, 0.996)
DM w/complications	2.456 (2.434, 2.479)	Latitude (scaled)	1.013 (1.009, 1.017)
Obese	2.225 (2.209, 2.240)	Longitude (scaled)	0.926 (0.916, 0.937)

Abbreviations: CI, confidence interval; DM, diabetes mellitus.

[a]All 29 Elixhauser comorbidities are included in the model as indicator variables, but only those for "DM with complications" and "Obese" are presented here.

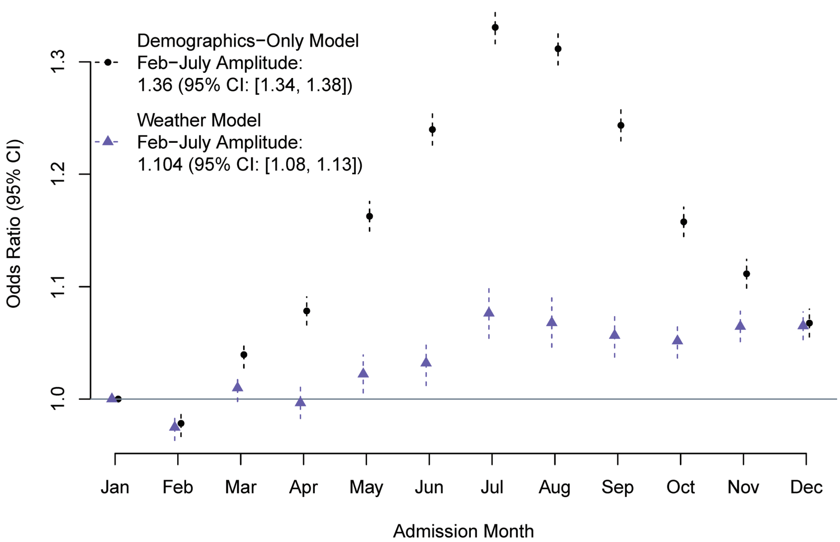

Figure 1. Comparing the seasonality of the odds of a primary cellulitis admission with and without considering temperature in the model. Abbreviation: CI, confidence interval.

Table 4. Odds Ratios for Monthly Fixed Effects in Demographics-only Model (Unadjusted for Average Monthly Temperature) and Weather Model (Adjusted for Average Monthly Temperature)

Month	Unadjusted Odds Ratios	Adjusted Odds Ratios
January	Baseline	Baseline
February	0.978 (0.967, 0.990)	0.975 (0.963, 0.987)
March	1.040 (1.028, 1.052)	1.010 (0.998, 1.022)
April	1.078 (1.066, 1.091)	0.997 (0.983, 1.011)
May	1.163 (1.150, 1.176)	1.022 (1.005, 1.039)
June	1.240 (1.226, 1.254)	1.032 (1.012, 1.052)
July	1.331 (1.316, 1.345)	1.076 (1.054, 1.099)
August	1.312 (1.297, 1.326)	1.068 (1.046, 1.090)
September	1.243 (1.230, 1.257)	1.057 (1.037, 1.076)
October	1.158 (1.145, 1.171)	1.052 (1.037, 1.067)
November	1.111 (1.099, 1.124)	1.065 (1.051, 1.078)
December	1.068 (1.055, 1.080)	1.065 (1.053, 1.078)
Feb–July contrast (i.e., seasonal amplitude)	1.360 (1.345, 1.376)	1.104 (1.081, 1.128)

incidence of cellulitis and skin and soft tissue infections during summer or warmer months [18–21, 37, 38]. Interestingly, some studies have also demonstrated an increased incidence of surgical site infections for surgeries performed during summer months [22–26]. Although there are many possible reasons for the seasonal incidence of infectious diseases [27], our results indicate that seasonal patterns in the incidence of cellulitis are driven by weather, specifically by higher temperatures. In fact, in our model we can explain 71% of the observed seasonality by considering average monthly temperature. In contrast to other reports concerning the seasonality of cellulitis and skin and soft-tissue infections, our investigation is based on a large geographically dispersed population, a 20% sample of all hospital discharges in the United States across many different seasons.

Given that 29% of the seasonality of cellulitis admissions was still unexplained after accounting for temperature, there may be other drivers of the observed seasonal incidence. Alternatively, by using more granular data (day of admission rather than month of admission) we might be able to explain more of the observed seasonality. However, the NIS provides data on a monthly time scale; thus we aggregated both the disease series and the weather series at the monthly level. Future work should focus on using more granular (i.e., daily) data. In addition, we also considered incorporating additional weather variables (e.g., humidity) into our models, though this did not make a difference in the average amplitude of seasonality. More granular data and analyses could be used to identify the importance of other weather variables.

In addition, future work needs to move toward estimating the actual weather exposure at the individual level. For example, a differential exposure of air conditioning may alter the individual exposure to heat in patients living in the same location experiencing the same weather conditions. Considering the temperatures that the patient is actually experiencing at an individual level may help define possible temperature effects on the host and pathogen. For example, warmer weather may alter host response, increasing the susceptibility of a host to skin infections. Elevated levels of bacteria may be found in certain anatomic locations in climates with higher temperature and humidity compared to climates that are cooler and drier [39], and the concentration of bacteria colonizing human skin may contribute to the seasonal pattern of disease that we observed. Alternatively, warmer weather may have effects on pathogens. However, regardless of the specific mechanism for warmer weather increasing risk for cellulitis, our results should help increase the clinical suspicion for cellulitis during warmer months, especially because the diagnosis of cellulitis can be confused with other syndromes not requiring antibiotics [40]. Ultimately, a better understanding of why warmer weather increases the risk for cellulitis may help inform preventive approaches or target early treatment as early treatment with the appropriate antimicrobials can improve cellulitis

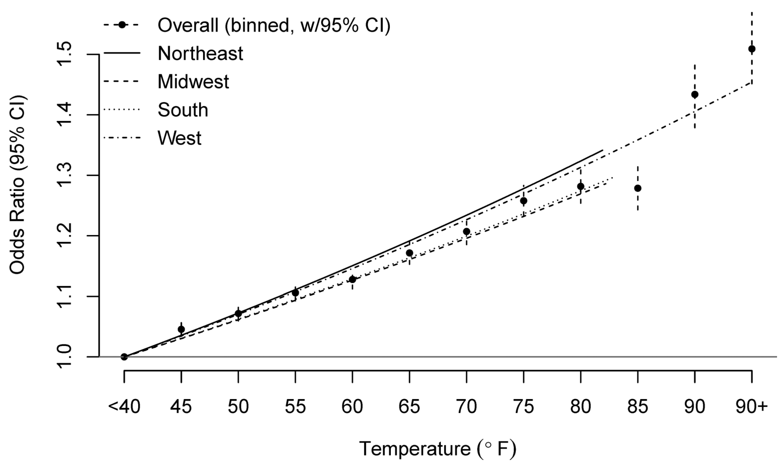

Figure 2. Effect of temperature in the final model (temperature binned in groups of 5°F), overlaid with a linear temperature effect estimated separately (via interaction terms) for each census region. The length of the diagonal lines corresponds to the range of temperatures witnessed by each region over the course of the study. Abbreviation: CI,confidence interval.

outcomes. Preventive strategies for cellulitis are most promising for patients with recurrent cases. Thus, future work will need to determine if and how warmer temperatures affect patients with recurrent episodes of cellulitis.

Our analysis also revealed additional risk factors for admissions for cellulitis besides warmer weather and summer months. Similar to other work, we found that older age [3] and obesity were risk factors [8, 10, 41]. We found that diabetes was a risk factor for cellulitis, in contrast to other studies [8, 41, 42]. We also found payer status (i.e., self-pay and no charge) to be a risk factor. We presume that payer status is a marker for socioeconomic status, and another study found socioeconomic status (e.g., homelessness [43]) as a risk factor for cellulitis. Future work should focus on understanding how weather interacts with traditional risk factors for cellulitis. For example, lymphatic insufficiency is a known risk factor [8, 41, 42], and weather may contribute to the incidence of lymphatic insufficiency if, for example, lymphatic insufficiency or other causes of lower extremity swelling were seasonal, peaking in the summer. We investigated admissions with a primary and secondary diagnosis of stasis (ICD-9-CM 459.81) and found no evidence of seasonality (data not shown). However, a recent report that showed that internet searches for a collection of searches including the terms "swollen ankle," "ankle swelling," "swollen feet," or "swollen legs" peaked during the summer months in the United States [44]. Interestingly, the same collection of search terms was also seasonal in Australia, but the seasonal peak was shifted by approximately 6 months coinciding with Australian summer months [44]. Thus, it is possible that warmer weather may lead to lower extremity swelling. Indeed, extracellular water content was found to be seasonal among patients undergoing hemodialysis [45], and among nondialysis patients, some research suggests that total body water and extracellular fluid volume increases during summer months [46]. In addition, it is conceivable that warmer weather can lead to changes in behavior that increase the risk for cellulitis. For example, skin trauma, even minor trauma, and skin lesions are risk factors for cellulitis [2, 8, 10], and warmer weather may change behavior that increases the risk for skin trauma (e.g., wearing open toed footwear). Also, animal bites, insect bites, and water exposure may all increase during summer months, and these increased exposures might help increase the risk of cellulitis during warmer months.

Our work is subject to several limitations. First, our clinical information is based exclusively on administrative data and we do not have access to laboratory records. We cannot do chart reviews to confirm the accuracy of the diagnosis of cellulitis or to accurately determine the anatomic site of the infection. In addition, ICD-9-CM codes were used to identify cases, and there are no ICD-9-CM codes that refer exclusively to cellulitis, so skin abscesses were included in our analysis. Also, these codes may not be specific to cellulitis or skin abscesses as venous stasis or penetrating injuries are sometimes mistakenly coded as cellulitis [40]. Future work should incorporate alternative approaches for identifying cases of cellulitis that do not rely exclusively on administrative data (e.g., data from electronic medical records). Second, the NIS does not include pharmacy data, so we are unable to examine treatment approaches for cellulitis. Third, because our data do not include patient identifiers, we are unable to determine if patients have been readmitted, as patients with cellulitis often suffer from repeated episodes. Fourth, our data are restricted to inpatients, and thus our results may not be generalizable to less severe cases of cellulitis treated on an outpatient basis. Finally, our analysis does not allow us to include the temperature that subjects actually experienced or take into account use of air-conditioning or other factors which might affect subjects' exposures to the outdoor versus the indoor environment.

Despite the limitations of our work, we demonstrate a strong dose-dependent relationship between average monthly temperature and the risk for cellulitis. Our results may help inform future pathogenesis studies from either the host's or pathogen's perspective. In recent years, much attention has been focused on global warming or climate change [47–51], and many have speculated that warmer temperatures could increase many different infections [48–50, 52]. Our results indicate that if temperatures consistently increase, the odds of cellulitis may also increase in regions exposed to warmer temperatures.

Notes

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References

1. Swartz MN. Clinical practice. cellulitis. N Engl J Med **2004**; 350:904–12.
2. Raff AB, Kroshinsky D. Cellulitis: a review. JAMA **2016**; 316:325–37.
3. McNamara DR, Tleyjeh IM, Berbari EF, et al. Incidence of lower-extremity cellulitis: a population-based study in Olmsted county, Minnesota. Mayo Clinic proceedings **2007**; 82:817–21.
4. Ellis Simonsen SM, van Orman ER, Hatch BE, et al. Cellulitis incidence in a defined population. Epidemiol Infect **2006**; 134:293–9.
5. Christensen KL, Holman RC, Steiner CA, Sejvar JJ, Stoll BJ, Schonberger LB. Infectious disease hospitalizations in the United States. Clin Infect Dis **2009**; 49:1025–35.
6. Peterson RA, Polgreen LA, Cavanaugh JE, Polgreen PM. Increasing incidence, cost, and seasonality in patients hospitalized for cellulitis. Open Forum Infect Dis **2017**; 4:ofx008.
7. Hirschmann JV, Raugi GJ. Lower limb cellulitis and its mimics: part I. Lower limb cellulitis. J Am Acad Dermatol **2012**; 67:163.e1-12; quiz 75–6.
8. Dupuy A, Benchikhi H, Roujeau JC, et al. Risk factors for erysipelas of the leg (cellulitis): case-control study. BMJ **1999**; 318:1591–4.
9. Semel JD, Goldin H. Association of athlete's foot with cellulitis of the lower extremities: diagnostic value of bacterial cultures of ipsilateral interdigital space samples. Clin Infect Dis **1996**; 23:1162–4.
10. Björnsdóttir S, Gottfredsson M, Thórisdóttir AS, et al. Risk factors for acute cellulitis of the lower limb: a prospective case-control study. Clin Infect Dis **2005**; 41:1416–22.
11. Baddour LM, Bisno AL. Non-group A beta-hemolytic streptococcal cellulitis: association with venous and lymphatic compromise. Am J Med **1985**; 79:155–9.

12. Dan M, Heller K, Shapira I, Vidne B, Shibolet S. Incidence of erysipelas following venectomy for coronary artery bypass surgery. Infection **1987**; 15:107–8.
13. Baddour LM, Bisno AL. Recurrent cellulitis after saphenous venectomy for coronary bypass surgery. Ann Intern Med **1982**; 97:493–6.
14. Baddour LM. Breast cellulitis complicating breast conservation therapy. J Intern Med **1999**; 245:5–9.
15. Indelicato DJ, Grobmyer SR, Newlin H, et al. Delayed breast cellulitis: an evolving complication of breast conservation. Int J Radiat Oncol Biol Phys **2006**; 66:1339–46.
16. Jawad H, Hodson NA, Nixon PJ. A review of dental treatment of head and neck cancer patients, before, during and after radiotherapy: part 1. Br Dent J **2015**; 218:65–8.
17. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis **2014**; 59:147–59.
18. Ronnen M, Suster S, Schewach-Millet M, Modan M. Erysipelas. Int J Dermatol **1985**; 24:169–72.
19. Haydock SF, Bornshin S, Wall EC, Connick RM. Admissions to a U.K. teaching hospital with nonnecrotizing lower limb cellulitis show a marked seasonal variation. Br J Dermatol **2007**; 157:1047–8.
20. Macario-Barrel A, Zeghnoun A, Young P, et al. Influence of environmental temperature on the occurrence of non-necrotizing cellulitis of the leg. Br J Dermatol **2004**; 150:155–6.
21. Wang X, Towers S, Panchanathan S, Chowell G. A population based study of seasonality of skin and soft tissue infections: implications for the spread of CA-MRSA. PLoS One **2013**; 8:e60872.
22. Anthony CA, Peterson RA, Polgreen LA, Sewell DK, Polgreen PM. The seasonal variability in surgical site infections and the association with warmer weather: a population-based investigation. Infect Control Hosp Epidemiol **2017**, forthcoming.
23. Durkin MJ, Dicks KV, Baker AW, et al. Seasonal variation of common surgical site infections: does season matter? Infect Control Hosp Epidemiol **2015**; 36:1011–6.
24. Durkin MJ, Dicks KV, Baker AW, et al. Postoperative infection in spine surgery: does the month matter? J Neurosurg Spine **2015**; 23:128–34.
25. Kane P, Chen C, Post Z, Radcliff K, Orozco F, Ong A. Seasonality of infection rates after total joint arthroplasty. Orthopedics **2014**; 37:e182–6.
26. Sagi HC, Cooper S, Donahue D, Marberry S, Steverson B. Seasonal variations in posttraumatic wound infections after open extremity fractures. J Trauma Acute Care Surg **2015**; 79:1073–8.
27. Fisman DN. Seasonality of infectious diseases. Annu Rev Public Health **2007**; 28:127–43.
28. Kahle D, Wickham H. ggmap: Spatial Visualization with ggplot2. The R Journal **2013**; 5:144–61.
29. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. Med Care **1998**; 36:8–27.
30. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. Med Care **2009**; 47:626–33.
31. Patel MM, Pitzer VE, Alonso WJ, et al. Global seasonality of rotavirus disease. Pediatr Infect Dis J **2013**; 32:e134–47.
32. Azziz Baumgartner E, Dao CN, Nasreen S, et al. Seasonality, timing, and climate drivers of influenza activity worldwide. J Infect Dis **2012**; 206:838–46.
33. Monto AS. The seasonality of rhinovirus infections and its implications for clinical recognition. Clin Ther **2002**; 24:1987–97.
34. Gilca R, Fortin E, Frenette C, Longtin Y, Gourdeau M. Seasonal variations in *Clostridium difficile* infections are associated with influenza and respiratory syncytial virus activity independently of antibiotic prescriptions: a time series analysis in Quebec, Canada. Antimicrob Agents Chemother **2012**; 56:639–46.
35. Polgreen PM, Yang M, Bohnett LC, Cavanaugh JE. A time-series analysis of *Clostridium difficile* and its seasonal association with influenza. Infect Control Hosp Epidemiol **2010**; 31:382–7.
36. Moore SM, Eisen RJ, Monaghan A, Mead P. Meteorological influences on the seasonality of Lyme disease in the United States. Am J Trop Med Hyg **2014**; 90:486–96.
37. Mermel LA, Machan JT, Parenteau S. Seasonality of MRSA infections. PLoS One **2011**; 6:e17925.
38. Leekha S, Diekema DJ, Perencevich EN. Seasonality of staphylococcal infections. Clin Microbiol Infect **2012**; 18:927–33.
39. McBride ME, Duncan WC, Knox JM. The environment and the microbial ecology of human skin. Appl Environ Microbiol **1977**; 33:603–8.
40. Friedman DN, Pollard J, Huffam S, et al. Randomized controlled trial of short course intravenous therapy for cellulitis and erysipelas of the lower limb (Switch): study protocol and pilot trial results. J Clin Trials **2014**; 4: doi:10.4172/2167-0870.1000200.
41. Karppelin M, Siljander T, Vuopio-Varkila J, et al. Factors predisposing to acute and recurrent bacterial non-necrotizing cellulitis in hospitalized patients: a prospective case-control study. Clin Microbiol Infect **2010**; 16:729–34.
42. Halpern J, Holder R, Langford NJ. Ethnicity and other risk factors for acute lower limb cellulitis: a U.K.-based prospective case-control study. Br J Dermatol **2008**; 158:1288–92.
43. Eells SJ, Chira S, David CG, Craft N, Miller LG. Non-suppurative cellulitis: risk factors and its association with *Staphylococcus aureus* colonization in an area of endemic community-associated methicillin-resistant *S. aureus* infections. Epidemiol Infect **2011**; 139:606–12.
44. Liu F, Allan GM, Korownyk C, et al. Seasonality of ankle swelling: population symptom reporting using google trends. Ann Fam Med **2016**; 14:356–8.
45. Broers NJ, Usvyat LA, Marcelli D, et al.; on behalf the MONitoring Dialysis Outcomes (MONDO) Consortium. Season affects body composition and estimation of fluid overload in haemodialysis patients: variations in body composition; a survey from the European MONDO database. Nephrol Dial Transplant **2015**; 30:676–81.
46. Yoshimura H. Seasonal changes in human body fluids. Jpn J Physiol **1958**; 8:165–79.
47. De Souza DK, Owusu PN, Wilson MD. Impact of climate change on the geographic scope of diseases. **2012**.
48. Greer A, Ng V, Fisman D. Climate change and infectious diseases in North America: the road ahead. CMAJ **2008**; 178:715–22.
49. Hay SI, Cox J, Rogers DJ, et al. Climate change and the resurgence of malaria in the East African highlands. Nature **2002**; 415:905–9.
50. Ogden NH, Maarouf A, Barker IK, et al. Climate change and the potential for range expansion of the Lyme disease vector *Ixodes scapularis* in Canada. Int J Parasitol **2006**; 36:63–70.
51. Rohayem J. Norovirus seasonality and the potential impact of climate change. Clin Microbiol Infect **2009**; 15:524–7.
52. Gubler DJ, Reiter P, Ebi KL, Yap W, Nasci R, Patz JA. Climate variability and change in the United States: potential impacts on vector- and rodent-borne diseases. Environ Health Perspect **2001**; 109 Suppl 2:223–33.