

## Report

# Atopic dermatitis: the relationship to temperature and seasonality in the United States

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**Introduction**

Atopic dermatitis (AD) represents a complex itching inflammatory condition with both genetic and environmental factors that seem capable of induction and exacerbation.<sup>1–5</sup> Patients do manifest seasonal exacerbation, and winter weather with low ambient humidity and cold temperatures exacerbates disease.<sup>6–9</sup> A number of studies have been performed in similarly geographically localized areas including northern India,<sup>10</sup> Japan,<sup>11</sup> Turkey,<sup>12</sup> and Korea<sup>13</sup> in which winter AD seasonality was reported. In their detailed study, Krämer and colleagues examined AD symptom severity in a cohort of 39 children in Augsburg, Germany, over the course of 6 months.<sup>14</sup> They found evidence for seasonal phenotypes of AD including a “winter type” and a “summer type” according to the season in which there was exacerbation. These two phenotypes influence

**Abstract**

**Background** Climatologic factors may affect atopic dermatitis (AD), and there have been few explorations into this topic. Because of its size, the United States (US) has a broad range of climates. The objective of this study is to assess the relationship between ambulatory office visits physicians for AD with temperature and season.

**Methods** US region-specific satellite-derived data air temperature from the North America Land Data Assimilation System from 1993 to 2011 were studied in relation with ambulatory AD visits to all physicians from the National Ambulatory Medical Care Survey.

**Results** Over the 19-year study period, in no regional location in the US is there clear evidence of a winter flare of AD. The greatest numbers of visits occur in May and June, and smaller peaks also occur in January and October. As the ambient air temperature increases, the likelihood of an AD visit rises ( $P < .0001$ ). In the South, the hottest US climate, summer is responsible for substantially more AD visits. In every other region and the US overall, the largest number of AD visits occur in spring. AD visits appear to display regional variation in comparing the Northeast, South, Midwest, and West.

**Conclusions** Increased temperatures predict increased likelihood of AD office visits.

symptom severity and treatment patterns. Moreover, Krämer and colleagues found that temperature increases in the “winter type” AD decreased symptoms. These aforementioned studies all take place in geographically limited areas.

The United States (US) is the fourth largest country by area at 9.8 million square kilometers,<sup>15</sup> with wide observed variability in climatic factors between different geographic regions. Moreover, in the US, a large amount of climatologic data including land surface temperature are available from the Centers for Disease Control and Prevention (CDC).<sup>16</sup> Analysis of the combination of nationwide climatologic data with related diseases has begun to be investigated.<sup>17</sup>

The current study investigates the relationships between US ambulatory office visits for AD and seasonality and temperature. Are the same patterns of winter exacerbation evident in the US? Can temperature inform us of the risk of AD visits and/or

exacerbations? In a previous more limited study, our group found no evidence of seasonality to AD visits.<sup>18</sup>

## Materials and methods

This study uses the North America Land Data Assimilation System (NLDAS) climate data on CDC WONDER (Wide-ranging Online Data for Epidemiologic Research). These are satellite-based collaborations between many governmental agencies and universities, including: the National Oceanic and Atmospheric Administration National Centers for Environmental Prediction Environmental Modeling Center, the National Aeronautics and Space Administration Goddard Space Flight Center, Land Processes Distributed Active Archive Center, Environmental Modeling Center, Universities Space Research Association, National Weather Service Office of Hydrological Development, and others.<sup>19</sup> Specifically, the author queried and downloaded climatologic data for 1993–2011, the most recent years in which satellite-based maximum air temperature and minimum air temperature were available.<sup>17</sup> These data were stratified by year, month, and geographic region (Northeast, Midwest, South, and West) for the 48 States of the Continental US and the District of Columbia. More precise information is available and can be assessed by exact date, county, state, and geographic division.

Data from the 1993 to 2011 National Ambulatory Medical Care Survey (NAMCS) were used to characterize outpatient AD visits (International Classification of Diagnoses, 9th Edition, Clinical Modification 691.8<sup>19</sup>) made to all healthcare providers. This survey is developed and implemented on a yearly basis by the CDC,<sup>20</sup> and all data are publicly accessible.<sup>21</sup> Results from this survey provide nationally representative estimates of

outpatient healthcare utilization. As a brief overview of how the survey data are collected, using a list of all medical doctors and doctors of osteopathy, a sample of physicians are selected and invited to participate in the annual survey. For participating physicians, data were recorded for a sample of their visits for a random week of the year. Visits to physicians were identified and isolated, and stratified by year, month, and geographic region. Note that after the present study interval beginning in 2012, more precise NAMCS geographic location for the most populous US states becomes available on these public use datasets.<sup>22</sup> NAMCS datasets were merged with climatologic data to create the average daily temperature for each year, month, and region. The mean of the minimum air temperature and maximum air temperature was calculated and used in all analyses.

To account for the variability in healthcare utilization as well as for the variability in the US population rising from 255 million in 1993<sup>23</sup> to 313 million in 2011,<sup>24</sup> visits with the diagnosis of AD were compared with all visits at which AD was not diagnosed. All data from this study were analyzed using SAS University Edition (SAS Institute Inc., Cary, NC, USA). To account for the variance caused by the complex survey design, survey weights were employed for all analyses. Analyses were performed using the SURVEY procedures, and all hypothesis testing was performed with SURVEYFREQ and SURVEYLOGISTIC. Significance was defined as being achieved when  $P < .05$ .

## Results

For the entire 19-year study period, there were 546,990 ambulatory office visits, estimating the experience of 16.5 (95%

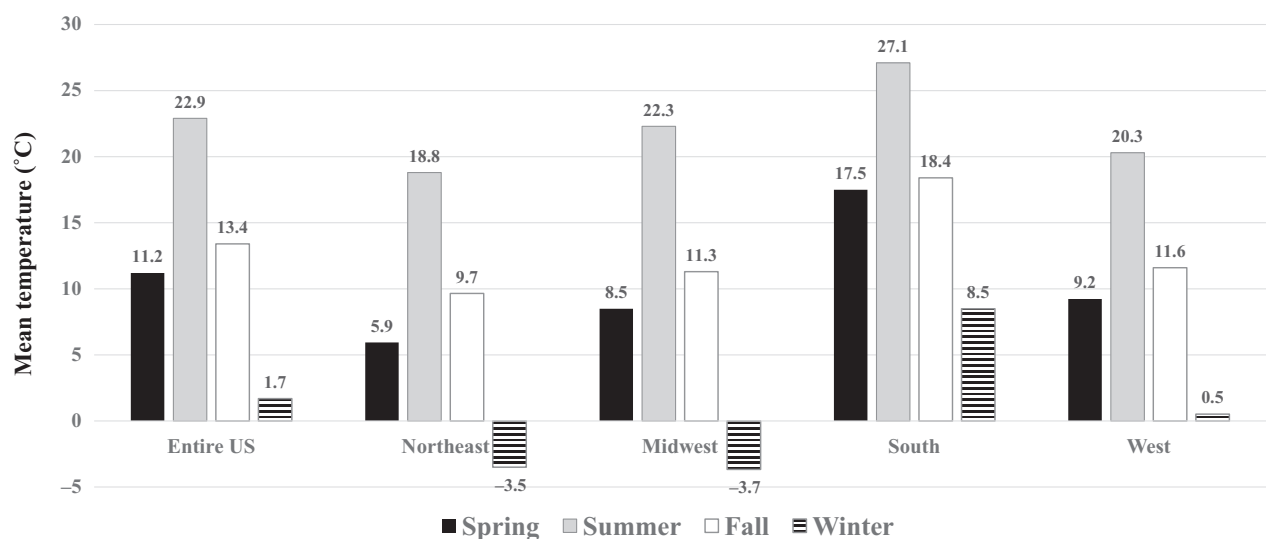


**Figure 1** This figure depicts the relationship between geographic region and season as it relates to temperature and variability across the US

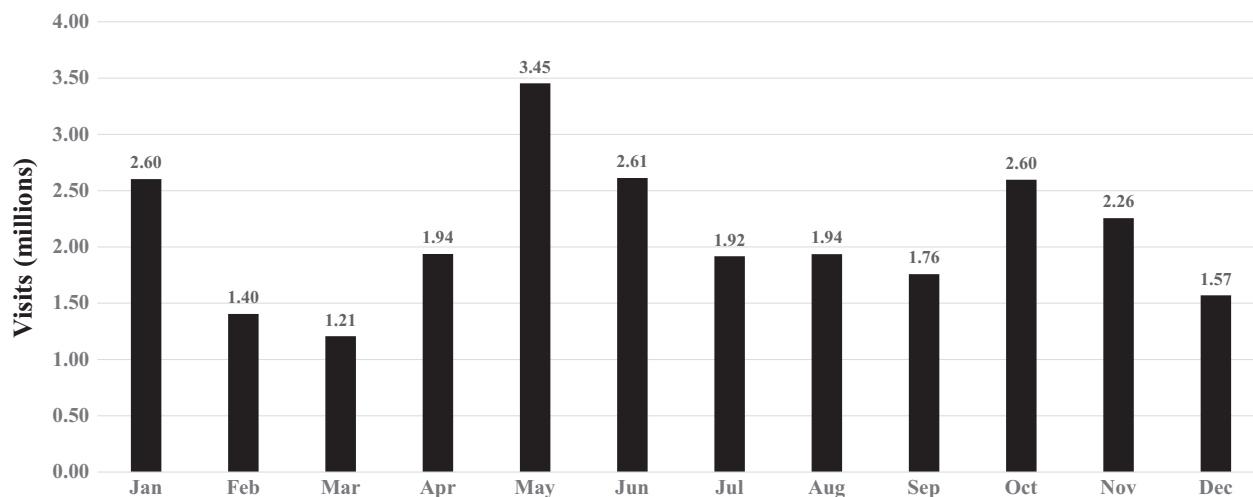


**Figure 2** This figure shows the estimated number of atopic dermatitis visits per month

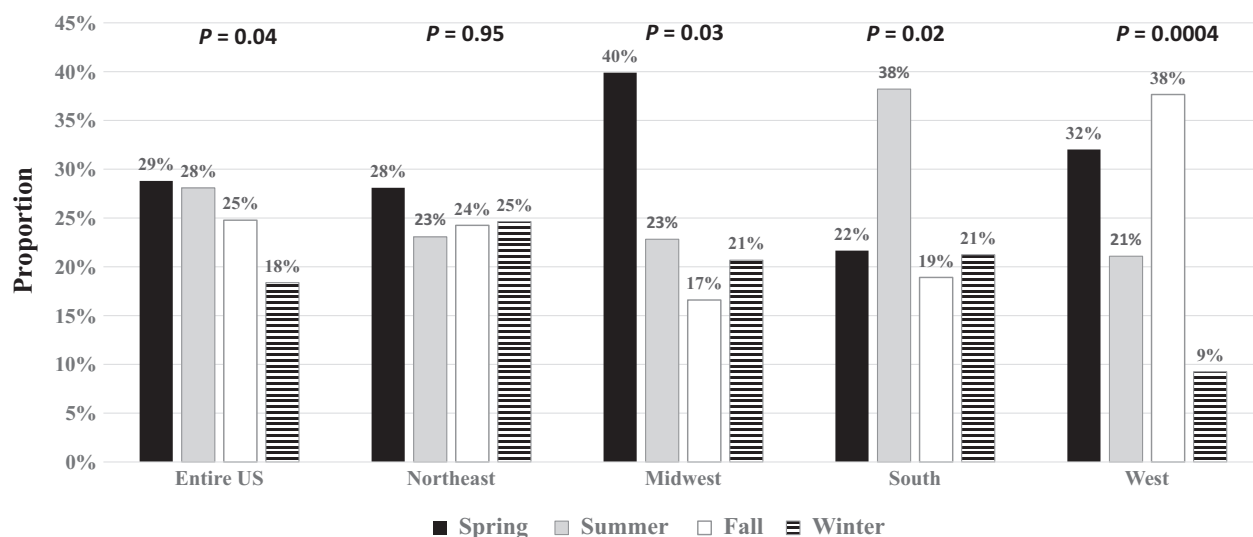


**Figure 3** This figure shows the seasonal differences in atopic dermatitis (AD) visits for the entire United States and for the individual regions. There is no evidence of AD seasonality in the Northeast, but such seasonality is present for the entire country and every other region

confidence interval 16.4, 16.5) billion visits. For AD, there were 869 visits, estimating 25.3 (23.1, 27.5) million visits. This represents approximately 1.3 million visits per year.

The mean temperature of all US visits for all medical conditions was 12.3 (12.3, 12.4) °C. The regions differed in temperature since the Northeast mean was 7.94 (7.87, 8.01) °C, the Midwest mean 7.79 (9.71, 9.86) °C, the South mean 17.8 (17.7, 17.8) °C, and the West mean 10.1 (10.1, 10.2) °C ( $P < .0001$ ). Between geographic regions, the South has the highest mean temperatures whereas the Midwest and Northeast the lowest (Fig. 1). In addition to overall temperature data, these regions suggest substantially heterogeneity in climates.

Over the study interval, the mean temperature at the time of all US ambulatory office visits increased by .034 (0.032, 0.036) °C per year ( $P < .0001$ ). This increase was not uniform across the US, and the Northeast had an increase in 0.024 (0.019, 0.029) °C per year, the Midwest increased 0.036 (0.032, 0.040) °C per year, the South increased 0.035 (0.031, 0.040) °C per year, whereas the West had a decline of -0.009 (-0.014, -0.004) °C per year (all  $P \leq .0003$ ).

When examining the monthly number of visits for AD, there is a complex relationship between the number of AD visits and month (Fig. 2). Although the greatest numbers of visits occur in May and June, smaller peaks also occur in January and

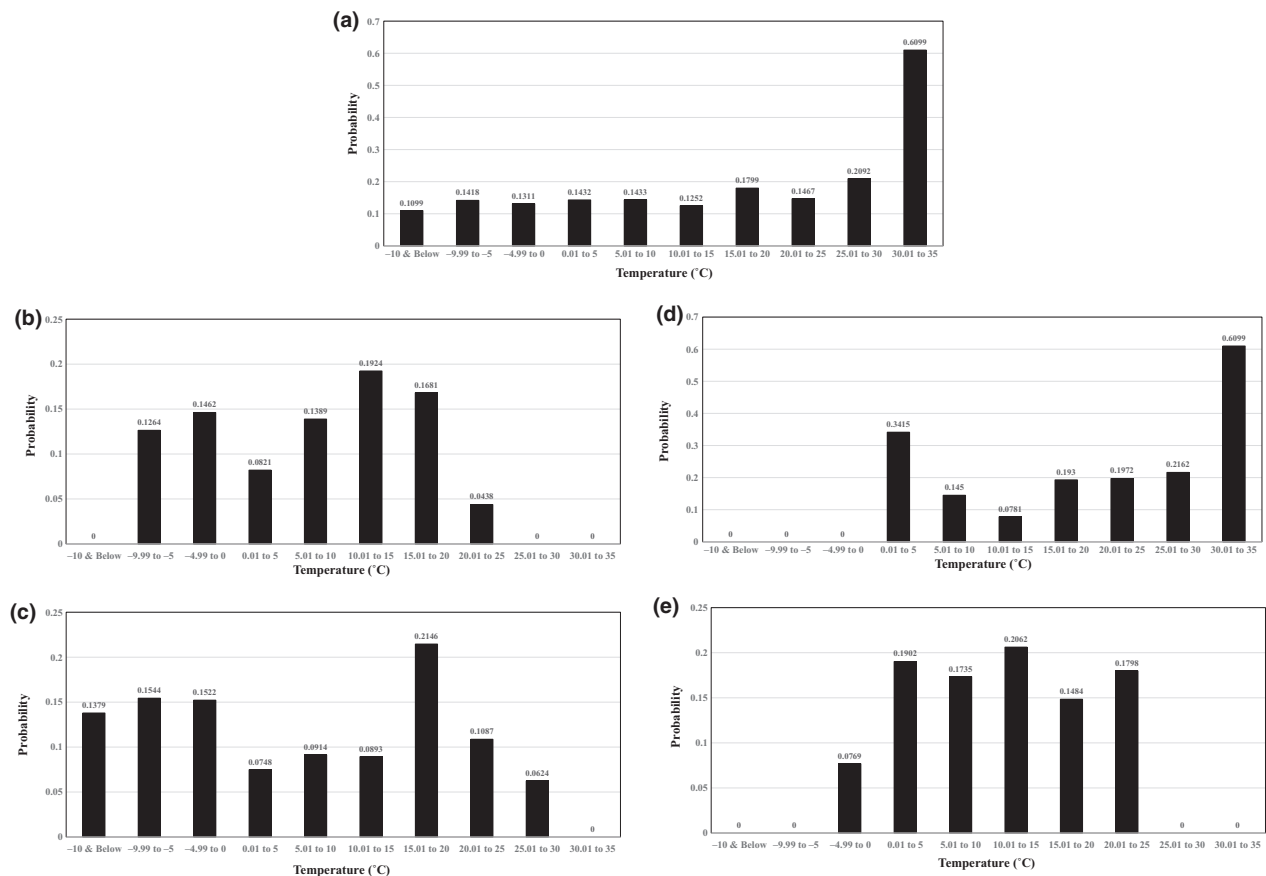


**Figure 4** The likelihood of an atopic dermatitis visit controlled by all other office visits for the entire US (a) and for the Northeast (b), Midwest (c), South (d) and West (e). There is considerable variability between the regions

October. Because of the limited numbers of AD visits, subsetting into 12 months as well as further subdivision by four regions was not possible to retain reliability. By combining individual months into seasons, hypothesis testing was possible. Seasonal variation in AD visits for the entire US and by region is interesting (Fig. 3). If each season has an equal likelihood of an AD visit, only the Northeast shows no significant seasonal variation. The other regions show significant variation but not in uniform fashion. In the South, the hottest US climate, summer is responsible for substantially more AD visits. In every other region and the US overall, the largest number of visits occur in spring. Although we saw a smaller peak number of visits in January, there is not a single region which finds a substantial increase in the number of winter visits.

This study models the likelihood of an AD office visit compared with all other visits as a function of temperature. Figure 4 presents the results of this analysis. Overall, for the entire US, as the temperature increases, the likelihood of an AD visit rises ( $P < .0001$ ). Noteworthy is the increased likelihood especially noted above 30 °C. Across the different regions, strikingly different relationships exist. In the West, as the temperature

increases, the likelihood of an AD visit decreases ( $P = .0003$ ). By contrast, in the other three regions, increasing temperature increases the likelihood of an AD visit ( $P < .0001$ ).

## Discussion

Multiple credible sources cite the existence of an AD winter flare and the associated increased medical utilization and/or severity.<sup>11–13,25</sup> Only one study by Krämer *et al.* identified both winter and summer phenotypes, in which the summer season and temperature seemed to be related to disease exacerbation.<sup>14</sup> Unlike many of the previous studies, the current investigation examines AD healthcare utilization across the large and geographically diverse US. As a country with markedly different weather patterns, we observe different AD seasonal and temperature patterns. Especially in the South, the warmest of the regions, the association of summer temperature with summer AD exacerbation is noteworthy. This author has spent nearly all of his practicing career in the American South, the warmest overall region in the US, and had first-hand experience with patient flares occurring in the summer months. Supporting the

notion that summer and/or high temperatures may play a role in disease exacerbation, by examining US healthcare expenditures, Silverberg and colleagues found that hospitalization rates for AD were highest in the Northeast US during the winter and South during the summer.<sup>26</sup>

The current study examines the influence of both seasonality and temperature on AD. However, associated with temperature increases in the southern US, there is an increase in the amount of ambient light levels. Because of the phenomenon of photosensitive AD,<sup>27</sup> our study is not able to distinguish between the effects of solar radiation, seasonality, and temperature. Other possibly atopic-related diseases may also occur in the summer, such as summer prurigo,<sup>28,29</sup> frictional lichenoid dermatitis,<sup>30</sup> and nummular dermatitis.<sup>31</sup> Some have hypothesized that contact allergens could also exacerbate summer disease.<sup>32</sup> Whereas some patients clearly flare in the winter, summer holidays may be responsible for AD improvement and clearance in others.<sup>33</sup>

Interestingly, there is evidence of equine AD flares in the summer.<sup>34–36</sup> There are many similarities between the disease that occurs in humans and animals, and canine AD seems to be the most closely related to human AD.<sup>37</sup> Not surprisingly, canine AD summer flares also occur.<sup>38</sup>

As for evidence of winter flare, the small peak number of visits in January, the third highest month of peak is tempered by the overall lack of evidence of the winter seasonal exacerbation for AD. There are very few visits in December for AD, and other social and holiday events may modulate the number of observed visits in this month. Again, as previously stated, US hospitalization rates for AD were highest in the Northeast US during the winter and south during the summer.<sup>26</sup> However, in Denmark, healthcare utilization was highest in the winter and spring.<sup>39</sup> In healthcare cost studies, a relatively small number of hospitalizations can skew the overall cost structure attributed to seasons or any other disease-related characteristic.<sup>40</sup> Furthermore, Denmark is a relatively small country compared with the US and is also substantially more ethnically homogeneous compared with the US.<sup>41</sup> As a point of interest, note that the highest risk temperature range for AD visits in the Northeast was 15.01–20 °C.

Weiss and colleagues performed an innovative study examining the seasonality of AD subjects into clinical trials.<sup>42</sup> In their review of a topical corticosteroid foam AD trial, enrollment was limited to winter ( $n = 193$ ), spring ( $n = 215$ ) and fall ( $n = 172$ ). Clinical success, a minimum of a two-point improvement in the investigator global assessment, was achieved by 66% of subjects in the spring, whereas in winter success was achieved by 52%, implying a greater severity in the winter. Although this paper does not specifically state that the analysis of the AD study is from the US, segmentation to further north of the 38th parallel, a line which passes through California, Nevada, Utah, Kansas, Missouri, Illinois, Kentucky, West Virginia, and Virginia, was said to be the one that distinguishes more severe winter.

Above this parallel, only 40% achieved success. This again supports that in the US, heterogeneity in climate affects the severity of AD disease. Again, this implies more severe disease in winter. Little may be said about summer since enrollment was not conducted during this season. The results of the present study indicate that excluding summer enrollment in US AD clinical trials may not be evidence-based.

The present study does not examine the disease condition or severity of individuals but does examine the health behavior of an entire population. By controlling for all other visits in the likelihood of AD visits by temperature, this study controls for some of the social and societal factors that influence the overall utilization of healthcare. The surprising finding is the striking increased likelihood in AD visits as the temperature increases.

A major limitation of this study is the difference in the way that the NAMCS and NLDAS data are collected. NAMCS data are collected from the 50 US States and the District of Columbia. By contrast, NLDAS data are restricted to the continental US. The NAMCS in the interval used public use datasets do not allow for exclusion of Alaska or Hawaii. More recent NAMCS data do include some state-level designations for the most populous states. Nevertheless, in 2010, Hawaii ranks 40th and Alaska ranks 47th among the states in terms of population, and the two constitute a total of 0.6% of the US population.<sup>43</sup> The expected small number of AD visits in these two western states is unlikely to affect the analysis. An additional limitation is that this study uses mean temperatures, which do also relate to minimum and maximum temperatures. Perhaps there is a more complex association between AD visits and an additional climatologic variable, such as minimum temperature, or temperature combined with other climatologic outcomes.

The present study takes advantage of the increasing availability of searchable climatologic datasets, indicating that further and more complex analyses into these areas are increasingly possible. The observation of increased temperature as a risk factor for increased AD visits should remind us that a dogmatic belief in winter and only winter disease exacerbations should not be believed. Some large scale clinical trials recruit study subjects only in nonsummer seasons such as the study analyzed by Weiss and colleagues,<sup>42</sup> and the current study suggests that this seasonal restrictive enrollment may not be evidence-based.

The heterogeneous population of the US and the varied climates within this large country may now be explored in other dermatologic and nondermatologic disease states. This investigative area is just beginning to have the surface scratched.

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