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# Association Of Diurnal Temperature Range With Pediatric Influenza Hospitalization Rates In The United States, 2009 – 2019

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**Abstract**

*Introduction:* Climate change may have a negative impact on respiratory illnesses, such as influenza. Diurnal temperature range (DTR), an indicator of climate change, is the difference between the maximum and minimum temperature within a day or a week. As the climate warms, global DTR decreases, though there might be regions where DTR increases instead. Previous literature conducted in non-U.S. regions found both positive and negative associations between DTR and influenza infections. A group especially vulnerable to the effects of DTR are children less than 5 years of age due to their less-developed thermoregulation capability. This study thus aimed to explore the association of DTR with pediatric influenza hospitalization rates in different U.S. states from 2009 to 2019 to further understand this relationship. *Methods:* Utilizing weekly influenza hospitalization rates from the Center for Disease Control and Prevention (CDC)'s FluSurv-NET surveillance system and meteorological data from the National Oceanic and Atmospheric Administration (NOAA), we employed a distributed non-linear lag model and a generalized additive model using a quasi-Poisson distribution to examine the complex non-linear relationship between the two variables, adjusting for relative humidity, mean temperature, and precipitation. *Results:* New York's Albany and Rochester, Michigan, and California exhibited positive associations between DTR and pediatric influenza hospitalization rate (relative risk at maximum DTR was 3.06 (95% confidence interval (CI): 1.532 – 5.893), 1.97 (95% CI: 1.018 – 3.812), 2.07 (95% CI: 1.185 – 3.601), and 1.69 (95% CI: 1.054 – 2.707), respectively). Additionally, there was a respective 1,403% ($p = 0.007$), 475% ($p = 0.045$), 569% ($p = 0.011$), and 344% ($p=0.030$) change in hospitalization rate for every 1°C increase in DTR. *Conclusions:* Our results can be used to inform the development of an early warning system that can alert the potential impact of significant increase in DTRs. With regard to climate change, if global DTR

decreases as the climate warms, then our results suggest that hospitalization rates will decrease as well, though in regions where DTR increases, hospitalization rates might increase. Further research on the relationship between temperature variability and respiratory infections that utilizes more granular data and that considers other important meteorological factors, influenza strain type, and vaccination history is needed.

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**Introduction**

Due to the rise in anthropogenic greenhouse gas emissions, climate change events such as rising temperatures, extreme flood and drought events, and weather variability pose great risks to human health (Pörtner et al., 2022). Specifically, 93 out of 103 primary research articles have found a positive association between a climatological factor (e.g., temperature, precipitation, and relative humidity) and an epidemiological factor (e.g., incidence, mortality, and hospitalization) of influenza infections. At the biological level, studies discovered that virus viability, infectivity, mutation rate, and transmissibility positively correlate with lower temperature and high humidity, though the extent varies for different strains of influenza viruses (Lane et al., 2022). Other studies focus on environmental conditions such as air pollution and UV radiation, but do not relate them to climate change, rendering knowledge in this field largely unexplored.

One important meteorological indicator of climate change is diurnal temperature range (DTR), which refers to the difference between the maximum and minimum temperatures in one day or week (Lu et al., 2022). As global atmospheric warming increases, global DTR decreases because there are larger increases to the daily minimum temperatures compared to the daily maximum temperatures, which has been the trend since early 1950s (Makowski et al., 2008). However, this is global DTR and may not pertain to specific regions, where DTR may actually increase instead. As such, there has been recent interest in examining the relationship between temperature variability as an indicator of climate change and respiratory illnesses, such as influenza. This is mainly because DTR has an impact on human health that is independent of the impacts of other temperature variables such as extreme temperatures (Cheng et al., 2014). Several studies conducted in the United States found that sudden large temperature changes may cause respiratory mortality (Zhang et al., 2017) and may heavily impact the seasonality of influenza (Li et al., 2018) after adjusting for other temperature variables.

The mechanism behind this remains to be studied, although findings have consistently proposed that sudden changes in temperature may cause weakened human immune functions, triggering an immune evasion (Graudenz et al., 2006; Guo et al., 2011; Loh et al., 2013). This may be a result of the human thermoregulation mechanism’s inability to adjust to large and sudden temperature changes (Guo et al., 2016). Contradictorily, Yap et al. (2021) found that larger daily DTR shortens the lifetime of coronaviruses and influenza viruses, posing decreased risks after adjusting for other factors. This means that while humans are more susceptible to risks posed by respiratory viruses due to a compromised immune system with increased DTR, there is also a decreased risk associated with shortened virus lifetime. These findings add to the complexity of the relationship between temperature variability and respiratory infections.

This is also reflected in the current body of literature that examines the relationship between DTR and influenza incidence, as there were mixed findings. Studies in China found a positive association between large DTR and influenza hospitalization and incidence (Lao et al., 2018), though Li et al. (2018) found this to only be true during dry periods and Ma et al. (2022) concluded that the association was negative for Flu-B but positive for Flu-A. Another study in South Korea found that high DTR was associated with an increase in influenza incidence only in temperate regions after controlling for factors like temperature and humidity (Park et al., 2020). As evident from these findings, factors such as seasonality, influenza strain type, and geography all seem to play a big role.

What many of these studies have in common, however, is their focus on locations in the eastern hemisphere, and to our knowledge, there are very few studies conducted in the United

States (Liu et al., 2020; Yap et al.; 2021). The implications that these studies' findings have for public health is very important, but the disagreeing results and the lack of generalizability makes the implications inapplicable in other regions of the world that are also experiencing climate change events at a rapid rate. For this reason, we honed in on the United States to explore the relationship between diurnal temperature range and influenza risks with consideration for seasonality and geography by focusing on just the influenza season and on each individual state. The specific outcome variable examined was pediatric influenza hospitalization rate, specifically among those 0 to 4 years of age, as Li et al. (2018) found that when exposed to large DTR, children less than 5 years of age experienced a 71.35% higher rate of influenza hospitalization than other age groups. Additionally, Basu and Ostro (2008) postulated that their vulnerability to temperature variation may be the result of a less-developed thermoregulation capability.

## Methods

### *Study Design*

Public national datasets from the Center for Disease Control and Prevention (CDC) and the National Oceanic and Atmosphere Administration (NOAA) were utilized to analyze the association between DTR, the predictor variable, and pediatric influenza hospitalization rates, the response variable. Given that these datasets did not have personal identification and that no questionnaires, testing, or interviews were conducted, this study was purely observational and ecological as the data was examined at the population level.

Due to the long-term nature of climate change, the availability of data, and the onset of the COVID-19 pandemic in 2020, the study period was weekly data spanning from 2009 to 2019, with

Sunday being defined as the first day of the week. The target population for the outcome were children in the United States under the age of five.

*Hospitalization Data*

Pediatric influenza hospitalization data was retrieved from the CDC's Influenza Hospitalization Surveillance Network (FluSurv-NET) system. The CDC conducts population-based surveillance using laboratory-confirmed influenza-associated hospitalization data from hospitals in 14 states to produce weekly hospitalization rates, which are calculated as "the number of residents of a defined area who are hospitalized with a positive influenza laboratory test divided by the total population within the defined area" (CDC, 2023). A laboratory-confirmed case is defined as a laboratory-confirmed positive test for influenza within 14 days prior to or during hospitalization. The Influenza-Like Illness Surveillance Network (ILINet), which reports outpatient visits to healthcare providers for influenza-like illnesses, would have offered a more complete picture of influenza activity in all 50 states since it also captures non-severe cases that do not result in hospitalization (CDC, 2022). However, the FluSurv-NET system provided data disaggregated by age, which was necessary for this study since it focused on children ages 0 to 4, and laboratory-confirmed data, so there was no potential for confounding by other respiratory illnesses.

Coverage for the FluSurv-NET system consisted of 13 states that are a part of the Emerging Infections Program (EIP) and the Influenza Hospitalization Surveillance Program (IHSP). States participating in the EIP included: California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, Tennessee. Those participating in the IHSP were Michigan, New Mexico, Ohio, and Utah. A preliminary examination of the data for each state revealed that only

10 contained data from 2009 to 2019, so these states were selected for this study: California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, Tennessee, and Michigan. Data for New York in particular existed in two separate datasets, one representing Albany and the other being Rochester, thereafter simply referred to by their names. While it would have been consistent to aggregate both to represent New York as a whole, such granular data allowed for a better depiction of the association. *Appendix 1* demonstrates the number of participating counties in each state and the percentage of state population represented by the data. *Appendix 2* lists the names of the participating counties in each state.

The FluSurv-NET system only conducts surveillance during flu season, which is from October to April. The CDC reports data by Morbidity and Mortality Weekly Report (MMWR) week, which is defined as the "week of the epidemiologic year for which the National Diseases Surveillance System (NNDSS) disease report is assigned by the reporting local or state health department for the purposes of MMWR disease incidence reporting and publishing" (CDC, 2013). MMWR week 1 is typically the first week of the surveillance year and MMWR week 52 or 53 is the last week. Each flu season within the FluSurv-NET system runs from week 40 of the previous year (October) to week 17 of the adjacent year (April). Though this means that there are gaps in the data, having a 10-year span of data helped to strengthen the statistical validity of the analysis. Furthermore, the focus on just the influenza season accounted for seasonality.

*Meteorological Data*

While the original source of meteorological data was the National Oceanic and Atmospheric Administration (NOAA), datasets were obtained from a third-party provider of weather data called Visual Crossing (Visual Crossing, n.d.). This tool allowed for easy retrieval of multiple meteorological variables from the desired locations all at once. To maintain consistency with the limited data available for hospitalization rates, only meteorological data from each state's catchment area was included. For example, for California, meteorological data only reflected that of Alameda, Contra Costa, and San Francisco counties and not the whole state since these were the counties for which hospitalization data was reported. Additionally, dates for this dataset matched with that of the hospitalization rate dataset by a two-week lag due to a one-week lag in reporting (CDC, 2022) and another week lag to account for the delay in the exposure-outcome relationship (Park, 2019). In other words, when one is exposed, the outcome associated with the exposure is assumed to be 2 weeks later.

Meteorological data used for the analysis included daily maximum, minimum and mean temperature, precipitation (rainfall depth), and relative humidity, all of which were converted to their weekly version (7-day moving average). DTR was derived from the difference between the maximum and minimum temperatures within 1 week.

*Statistical Analysis*

Given that the effects of DTR are lagged and non-linear, analysis required the use of the distributed non-linear lag model (DNLM) with a quasi-Poisson generalized additive model (GAM) (Gasparrini et al., 2010; Gasparrini, 2011; Park et al., 2019). The quasi-Poisson model was chosen over the Poisson model to account for overdispersion and over the negative binomial model due to a lower residual deviance to degree of freedom ratio, which signifies a good fit, and a consideration for the non-linear relationship that can be better depicted by logarithmic functions. The resulting model used for analysis was adapted from previous studies on the same topic (Li et al., 2018; Ma et al., 2022):

$$\log[E(Y_t)] = \alpha + \beta DTR_{0\text{–}2t} + ns(\text{mean temperature}_{0\text{–}2t}, df = 3) + ns(RH_{0\text{-}2t}, df = 3)$$

$$+ ns(\text{precipitation}_{0\text{-}2t}, df = 3) + ns(\text{time}, df = 4/\text{per year}) + \text{week of year}$$

$E(Y_t)$ is the expected pediatric influenza hospitalization rate on week *t.* $\alpha$ denotes the intercept and $\beta$ indicates the coefficient of DTR with a lag of 0-2 weeks. This lag structure was chosen due to a 1-week reporting delay and another 1-week delay between exposure and outcome (CDC, 2023; Park, 2019). The term DTR represents the cross-basis matrix obtained after applying DLNM. To capture the non-linear relationship, a natural cubic spline function (*ns*) accompanies each of the other confounding predictor variables (mean temperature, relative humidity, and precipitation) to capture the flexible and non-linear relationship with the response variable. The degree of freedom (df) of 3 for these variables are consistent with literature that conducted sensitivity analyses in their studies to determine the best value (Gasparrini et al., 2010; Ma et al., 2022). The time term with a df of 4 per year was included as a smoothing function to control for seasonality and long-term trends (Wang et al., 2020). Week of year denotes the categorical week of the year. This was included to account for week-of-year patterns that may be unrelated, such as different hospitalization rates on certain weeks of the year due to factors such as reporting delays or healthcare staffing levels.

The inclusion of vaccination rates was considered for the model, as immunization against influenza plays a major role in preventing flu-associated hospitalizations (Ferdinands et al., 2014; Rondy et al., 2017; Thompson et al., 2018). Unfortunately, the available vaccination data provided by the CDC do not cover the entirety of the study period (CDC, 2022).

All data management and analytical processes were conducted in the statistical programming software R software version 4.1.3 (The R Project for Statistical Computing, Vienna, Austria). Geographical visualizations of results were completed in ArcGIS Pro version 3.0.1 (Esri) using state and county boundaries from the U.S. Census and climate data from NOAA.

## Results

*Table 1* showcases the mean DTR and pediatric influenza hospitalization rate by state. Focusing on DTR, Colorado experienced the highest mean value at 13.08°C, while Oregon had the lowest mean value at 8.59°C. With regard to mean weekly hospitalization rate, Michigan had the highest at 3.61 followed by Colorado (2.65), Maryland (1.99), Minnesota (1.92), Albany (1.81), Rochester (1.57), Connecticut (1.48), California (1.32), Georgia (1.19), Tennessee (1.02), and Oregon (0.95). A more detailed summary statistics of meteorological factors and weekly pediatric influenza hospitalization rates for each state are depicted in *Appendix 3*.

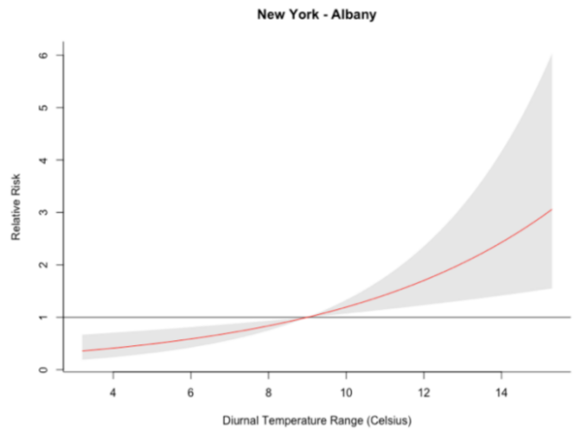
Table 1. Mean DTR and pediatric influenza hospitalization rate in each state by order of highest to lowest DTR

| State | Mean DTR (°C) | Mean Pediatric Influenza Hospitalization Rate |
|---|---|---|
| Colorado | 13.08 | 2.65 |
| Tennessee | 10.85 | 1.02 |
| Georgia | 10.70 | 1.19 |
| California | 9.84 | 1.32 |
| Albany | 8.85 | 1.81 |
| Michigan | 8.77 | 3.61 |
| Maryland | 8.73 | 1.99 |
| Connecticut | 8.65 | 1.48 |
| Minnesota | 8.59 | 1.92 |
| Rochester | 8.29 | 1.81 |
| Oregon | 7.29 | 0.95 |

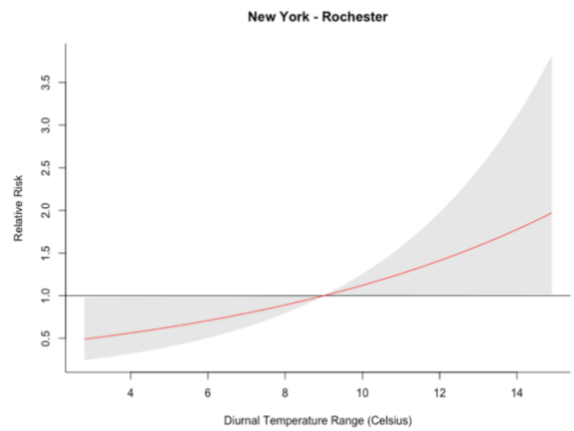
*Relative Risk Associated with DTR*

The regression analysis yielded mixed results. *Figure 1* showcases relative risk (RR) at different DTR values in each state. Relative risk refers to the chance of an event (pediatric influenza hospitalization rate) occurring due to an exposure (DTR) (Tenny & Hoffman, 2023). A relative risk value of 1 indicates no difference between two variables; a value less than 1 means that the event is less likely to result from the exposure; and a value larger than 1 means that the event is more likely to result from the exposure. Present in each plot is a reference DTR value where the associated relative risk value is 1, signifying a change in direction of hospitalization rate after crossing this threshold. An upwards curve indicates increased hospitalization rate among those exposed to the associated values of DTR compared to those exposed to the reference DTR value, and a downwards curve depicts decreased hospitalization rate due to exposure of the DTR value higher than the reference value. For example, a relative risk of 1.16 means that the pediatric influenza hospitalization rate was 16% higher among those exposed to that associated DTR value compared to those who are exposed to the reference DTR value at which the relative risk is 1.

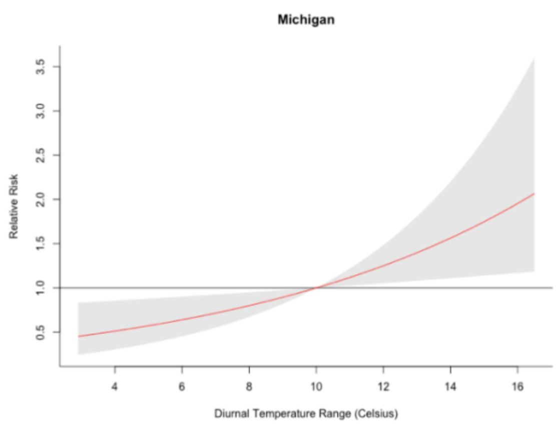
Albany, Rochester, Michigan, California, Georgia, Minnesota, and Colorado experienced an increase in relative risk as DTR increased, with the former four locations having a 95% confidence interval that does not include one, suggesting that the mean difference is statistically significant at the 5% level. Oregon, Tennessee, Connecticut, and Maryland experienced a decrease in relative risk as DTR increased, though all are not statistically significant. The DTR ranged from 3.5°C to 20°C.


New York - Albany
Relative Risk
0 1 2 3 4 5 6
4 6 8 10 12 14
Diurnal Temperature Range (Celsius)

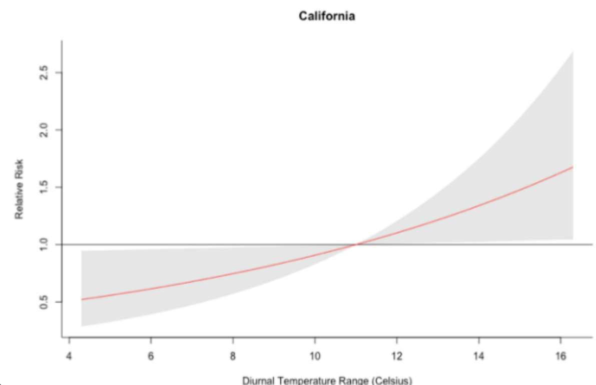
A.


New York - Rochester
Relative Risk
0.5 1.0 1.5 2.0 2.5 3.0 3.5
4 6 8 10 12 14
Diurnal Temperature Range (Celsius)

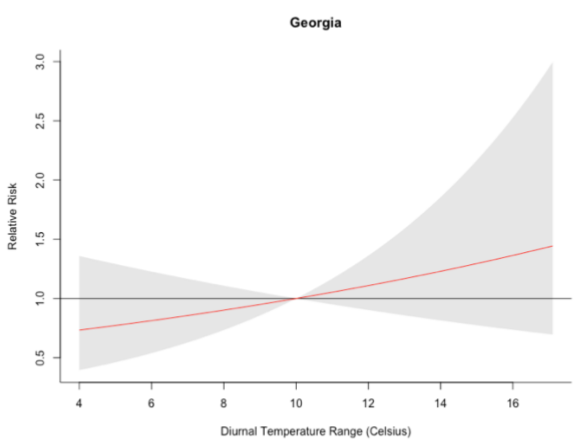
B.


Michigan
Relative Risk
0.5 1.0 1.5 2.0 2.5 3.0 3.5
4 6 8 10 12 14 16
Diurnal Temperature Range (Celsius)

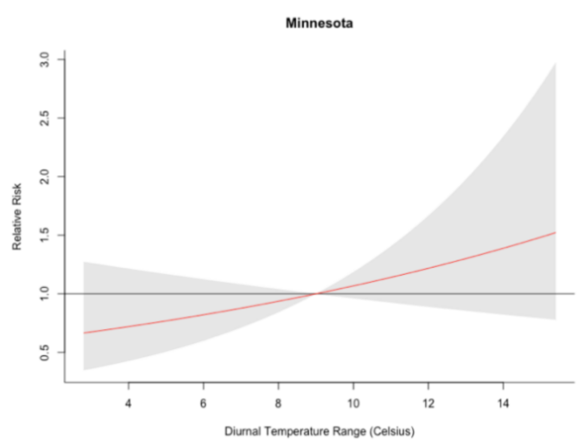
C.


California
Relative Risk
0.5 1.0 1.5 2.0 2.5
4 6 8 10 12 14 16
Diurnal Temperature Range (Celsius)

D.


Georgia
Relative Risk
0.5 1.0 1.5 2.0 2.5 3.0
4 6 8 10 12 14 16
Diurnal Temperature Range (Celsius)

E.


Minnesota
Relative Risk
0.5 1.0 1.5 2.0 2.5 3.0
4 6 8 10 12 14
Diurnal Temperature Range (Celsius)

F.

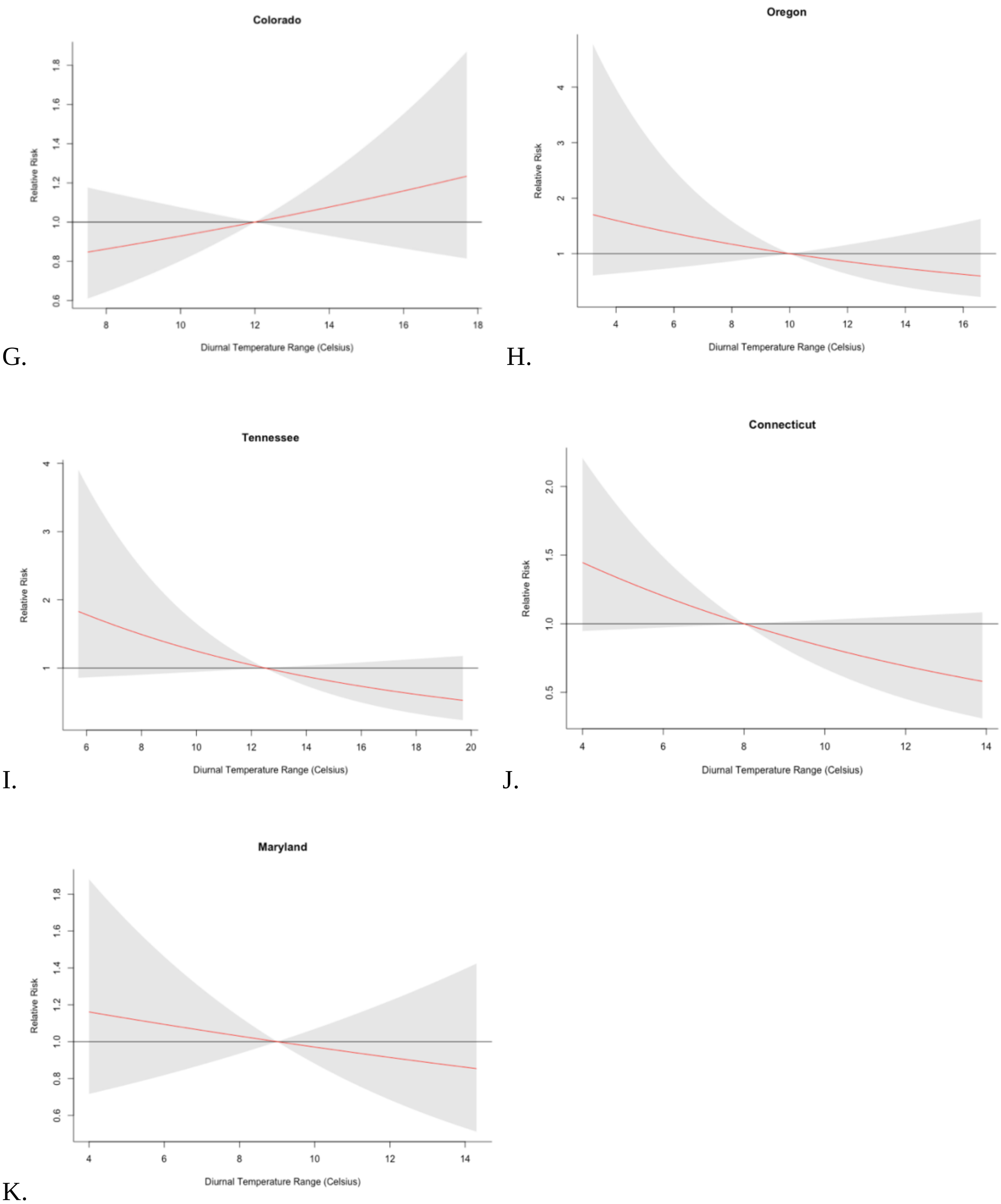



Figure 1. Relative risk for the relationship between DTR and pediatric influenza hospitalization rate. Axes are not on the same scale due to climate differences in each state.

*Figure 2*, which depicts relative risk at minimum DTR, reveals that among those who are exposed to this DTR value in California, Colorado, Georgia, Michigan, Minnesota, Albany, and Rochester, pediatric influenza hospitalization rate was actually lower compared to those who were exposed to higher values of DTR. California, Michigan, Albany, and Rochester all exhibited statistically significant relative risk values of 0.52 (95% CI: 0.284 – 0.936), 0.45 (95% CI: 0.247 – 0.830), 0.36 (95% CI: 0.196 – 0.769), and 0.49 (95% CI: 0.245 – 0.981), respectively. On the other hand, Connecticut, Maryland, Oregon, and Tennessee had relative risk values of 1.45 (95% CI: 0.947 – 2.21), 1.16 (95% CI: 0.717 – 1.880), 1.70 (95% CI: 0.607 – 4.770), and 1.83 (95% CI: 0.857 – 3.906), suggesting that those exposed to the minimum DTR in these states had a higher pediatric influenza hospitalization rate than those who were exposed to higher values of DTR. However, these were not statistically significant results (95% CI crossed 1).

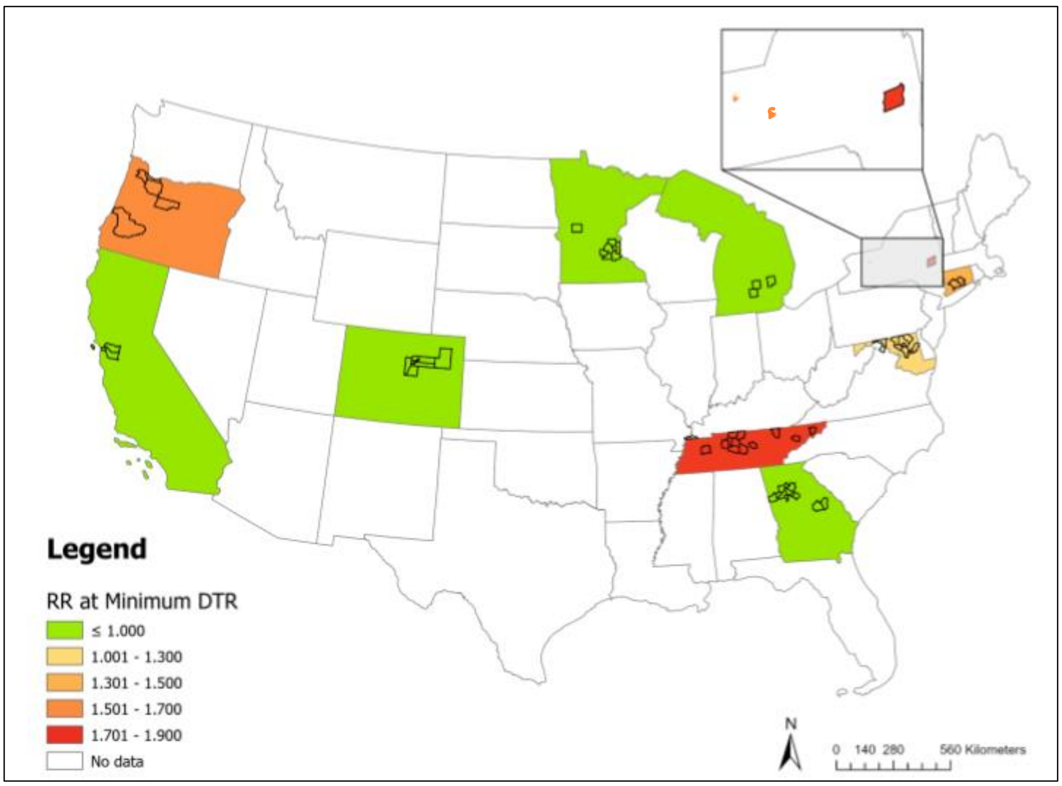



Figure 2. Relative risk at minimum DTR. Black outlines indicate counties that participate in the FluSurv-NET system in each state.

The relative risk at maximum DTR for all states ranged from 0.58 to 2.1. As depicted in *Figure 3*, Connecticut, Maryland, Oregon and Tennessee exhibited a relative risk below 1 at maximum DTR, suggesting that hospitalization rate was lower among those exposed to the maximum DTR compared to those who were exposed to all lower values of DTR. However, these values were not statistically significant (95% CI crossed 1). Locations with the highest relative risk at maximum DTR were Albany, Rochester, and Michigan with statistically significant values of 3.06 (95% CI: 1.532 – 5.893), 1.97 (95% CI: 1.018 – 3.812), and 2.07 (95% CI: 1.185 – 3.601), respectively. California was the only other location with a statistically significant relative risk of 1.69 (95% CI: 1.054 - 2.707). *Appendix 4* provides a complete summary statistic of relative risk at the mean and at different quantiles of DTR.

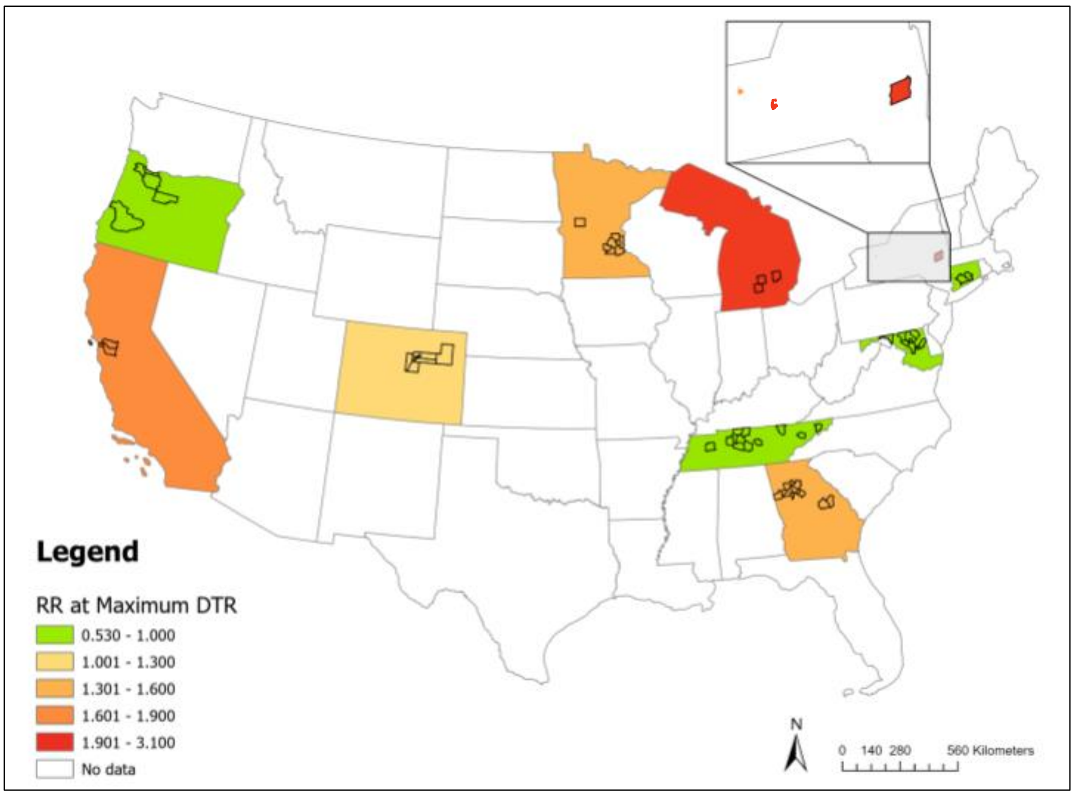



Figure 3. Relative risk at maximum DTR. Black outlines indicate counties that participate in the FluSurv-NET system in each state.

*Regression Coefficient*

Another important component to assess was the regression coefficient of the predictor variable. Regression coefficients (β) in a quasi-Poisson model indicates that for every unit increase in the predictor variable the expected value of the response variable will increase by a factor of $e^{(\beta)}$, adjusting for overdispersion in the data. This can also be depicted as percentage change, or ($e^{(\beta)}$ -1) * 100%, in hospitalization rate for a 1°C increase in DTR. As depicted in *Table 2* and visualized geographically in *Figure 4*, Albany and Rochester had the largest coefficient of the predictor variable DTR of 2.71 ($p = 0.007$) and 1.75 ($p = 0.045$), respectively. This means that in both of these locations, for every 1°C increase in DTR, the pediatric influenza hospitalization rates would increase by 1,403% and 475%, respectively. Michigan followed with a coefficient of 1.90 (569% increase; $p = 0.011$) and California with a coefficient of 1.49 (344% increase; $p = 0.030$). All the aforementioned states possessed p-values less than 0.05, indicating that the results were statistically significant.

While not statistically significant, Connecticut, Maryland, Oregon, and Tennessee exhibited an opposite trend with a respective 69% ($p = 0.089$), 32% ($p = 0.545$), 73% ($p = 0.313$), and 79% ($p = 0.120$) reduction in hospitalization rate for a 1°C increase in DTR.

Table 2. DTR coefficient and percent change in hospitalization for a 1°C increase in DTR

| State | Coefficient | % Change in Hospitalization Rate for a 1°C Increase in DTR | P-value |
|---|---|---|---|
| California | 1.49 | 344 | 0.030* |
| Colorado | 0.47 | 60 | 0.322 |
| Connecticut | -1.16 | -69 | 0.089 |
| Georgia | 0.85 | 134 | 0.325 |
| Maryland | -0.39 | -32 | 0.545 |
| Michigan | 1.90 | 569 | 0.011* |
| Minnesota | 1.04 | 183 | 0.220 |
| New York – Albany | 2.71 | 1403 | 0.007* |
| New York – Rochester | 1.75 | 475 | 0.045* |
| Oregon | -1.31 | -73 | 0.313 |
| Tennessee | -1.57 | -79 | 0.120 |

*P-value < 0.05, indicating statistical significance.

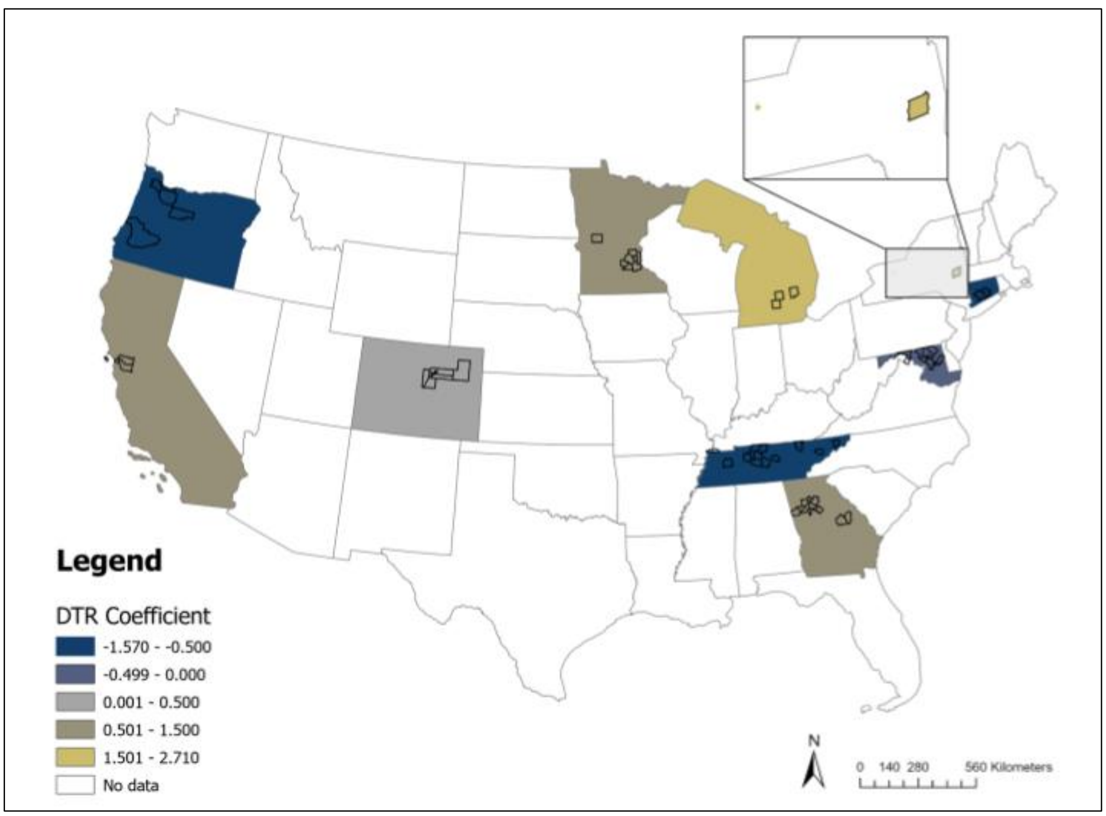



Figure 4. Regression coefficient of DTR. Coefficients for California, Michigan, Albany, and Rochester had p-values < 0.05. Black outlines indicate counties that participate in the FluSurv-NET system in each state.

## Discussion

*Relationship between DTR and Influenza Hospitalization Rate*

This study aimed to examine the association of DTR with pediatric influenza hospitalization rate in the United States from 2009 to 2019. Given the imminent threat posed by various meteorological changes resulting from climate change, it is necessary to discuss how DTR as an indicator of climate change, affects health outcomes, namely influenza hospitalization rates among children less than five years of age.

After adjusting for the effects of relative humidity, precipitation, and mean temperature, all of which contribute to influenza (Tamerius et al., 2013), the results showed conflicting associations between DTR and pediatric influenza hospitalization rate. *Figure 1* reveals that there was a positive association between these two variables in California, Colorado, Georgia, Michigan, Minnesota, Albany, and Rochester while there was a negative association in Connecticut, Maryland, Oregon, and Tennessee. However, statistically significant results from Rochester, Albany, Michigan, and California validates the positive association, suggesting that pediatric influenza hospitalization rate was higher among those exposed to a DTR value above the threshold compared to those who were not exposed. Thus, DTR should be considered in discussions relating to influenza.

These results align with a large body of literature on the topic. Most notably, a similar study conducted in Hong Kong found that among children less than 5 years of age, exposure to a large DTR was associated with a 71.35% higher rate of influenza hospitalization, which was the largest percent change among all age groups (Li et al., 2018). In both Zhang et al. (2020) and Ma et al. (2021), a larger DTR was also found to have a positive relationship with Flu-A. Furthermore, Lao et al. (2018) found a statistically significant association between DTR and influenza incidence among children and the elderly in Beijing with those exposed to the maximum DTR experiencing a 1.2% higher incidence than those who were not exposed. DTR was also positively associated with other respiratory illnesses as well, such as pneumonia (Cicco et al., 2020; Miyayo et al., 2021; Pedder et al., 2021) and chronic respiratory diseases (Liang et al., 2009; Ma et al., 2018; Wang et al., 2020). Although the physiological mechanism for this effect is not widely understood, previous research posits that exposure to a large daily temperature change may negatively affect respiratory and humoral and cellular immunity functions, thereby triggering to the onset of a respiratory outcome (Bull, 1980; Imai et al., 1998).

This study found statistically insignificant negative associations between DTR and pediatric influenza hospitalization rate in some states. There exists some literature with similar results. In two separate studies conducted in China, while a larger DTR was associated with increased Flu-A risk, low DTR did so for Flu-B (Zhang et al., 2020; Ma et al., 2022). Seasonality factors other than the influenza season might make a difference, as another study conducted in China found DTR to have a significant positive association with influenza during dry periods, but had an insignificant negative association during humid periods (Li et al., 2018). The same trend also existed for other respiratory viruses, such as COVID-19, where the relative risk was about 0.9 per 1°C increase in DTR (Islam et al., 2020; Liu et al., 2020).

At the cellular level, Yap et al. (2021) found that higher DTR shortens the lifetime of coronaviruses and influenza viruses, suggesting that there might be a negative association between the magnitude of DTR and influenza incidence. It must be noted, however, that the number of studies supporting the negative association found in this study is far less than that supporting a positive association. This reveals the complex impact DTR has on influenza and suggests that virus strain type, viral characteristics, and regional and seasonal differences might all play a big role in determining the association between these two variables.

### *Climate Change*

In the context of climate change, if the statistically significant positive association of DTR with pediatric influenza hospitalization rate reflect reality, the implications might be a positive one for public health. Since studies reveal that climate change is causing a decrease in DTR (Qu et al., 2014; Guan et al., 2022), then a positive relationship suggests that influenza risks may actually decrease as a result of climate change since a decrease in DTR also means a decrease in the relative risk of hospitalization rate. As illustrated in the plots for Albany, Rochester, Michigan, and California in *figure 1,* if DTR were to decrease to reach values below that of the threshold, then those exposed to these DTR values will have a lower risk compared to those exposed to the reference DTR value. However, this implication must be investigated further, as climate change is a long-term phenomenon, and cannot be adequately evaluated based on just ten years of data (Abbass et al., 2022).

One must also consider that there is a plethora of other meteorological indicators of climate change that may also impact influenza risks. These impacts can affect risks differentially since each location has different permutations of meteorological trends, many of which were not factored into this study. Some examples include air pollution, extreme weather events, and wind speed (Liu et al., 2020). Furthermore, some locations are warming at a different rate than others, especially those in the sub-tropic regions (Stuecker et al., 2020).

We attempted to understand whether there was any geographic or climatological trend that may explain the conflicting associations by visualizing the different states' relative risk values and regression coefficients in *Figures 2-4,* but no such trend seemed to exist. Overlaying the 5 Köppen climates in the U.S. on the participating counties in each state, we found that counties in the four states that exhibited a negative association between DTR and pediatric influenza hospitalization rate (Oregon, Tennessee, Connecticut, and Maryland) fall into regions that have a moist sub-tropical mid-latitude climate (*Figure 5)*. Only two states with positive associations have participating counties that fall in this region. Wang et al. (2017) found that in addition to relative humidity, vapor pressure, and temperature, regional climate heterogeneity also had a significant impact on influenza risks. Had there been available data for other states, we would have been able to better identify any geographic trends. Thus, the relationship is complex, and further exploration with all of the aforementioned confounding factors are necessary for a better understanding.

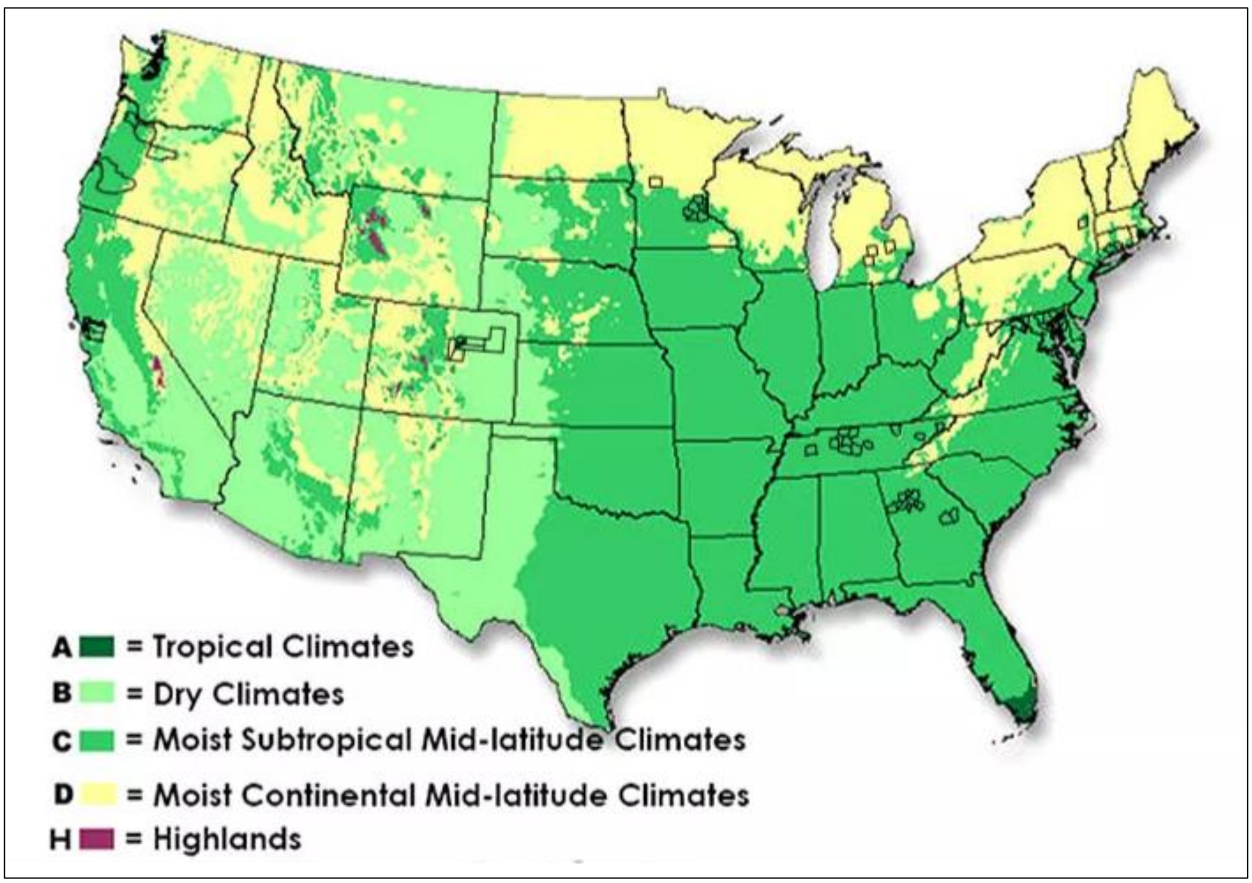



Figure 5. Köppen climates of the United States (NOAA, n.d.). Black outlines indicate counties that participate in the FluSurv-NET system in each state.

*Predictions and Public Health Implications*

Furthermore, this study generated regression coefficient values that could be used to forecast pediatric influenza hospitalization rates in the future. As previously postulated, locations with statistically significant coefficient values were Albany, Rochester, Michigan, and California. This value was used to predict the percent change in hospitalization rate for a 1°C increase in DTR. All four locations yielded a percent change larger than 300%, demonstrating the large effect DTR has on pediatric influenza hospitalization rate.

Such a powerful tool can be used by public health professionals and organizations in various ways. Firstly, this study's results on risk differences among the studied states allow health departments and national government agencies to have a better idea of where efforts should be allocated, whether it be in the form of further research or interventions. Another usage for such results is to set up an early-warning system based on the current ability to predict daily and weekly temperature. For example, one can use the weather forecast system to trigger an alarm when it is predicted that there will be a 1°C increase in DTR from the norm. If such an event were to occur, local governments can send out advisory notices to share with the general population, especially parents with children less than five years of age, the different kinds of measures they can take to protect themselves and their children. Such measures can be in the form of tips like maintaining a constant temperature within the household or work environment to avoid the drastic fluctuations in temperatures. This effort can be implemented in tandem with social programs that aim to address other meteorological factors.

Kapwata et al. (2022) applied the knowledge of such data to create a metric for heatwave detection and an early warning system for heatwaves. With previous literature discovering DTR as one of the most suitable metrics for integration in a Heat-Health Warning System (HHWS) in

South Africa, the researchers employed DTR data from past heatwaves to determine a threshold at which mortality would increase and to predict the differential impacts of DTR on mortality per a 1°C increase. Integration of this knowledge into a HHWS would allow for alerts and recommend measures to be sent out to the public prior to the event to help them combat the negative consequences of heatwaves.

*Limitations and Future Research*

This study was not without limitations. Although the relative risks and coefficients were statistically significant for Albany, Rochester, Michigan, and California, one must proceed with caution as the data from these locations represent less than 10% of their respective state population, whereas data from states with statistically insignificant results represent more than 29% of their state population (*appendix 1*). Furthermore, *Figure 2* reveals that the counties in Michigan and California are very close to each other, whereas those in the other states are generally far apart. This may play a role in the consistency of weather trends and hospitalization surveillance, as counties that are farther apart may experience more distinctive weather trends from each other. However, we do not know for certain why this phenomenon exists as the data is not granular enough. This may also be why Rochester and Albany had such high relative risks and regression coefficients; the data was more granular, and the relationship was therefore more accurately depicted by the model. Thus, these results, though significant, should not be generalized to the whole state.

A major limiting characteristic of the influenza dataset used is that it consists of weekly instead of daily hospitalization rates. As Park et al. (2019) posits, daily influenza data better reflects meteorological factors' impacts. This is especially true for DTR, which has more of an immediate effect on the body day-to-day rather than week-to-week (Park et al., 2019). Many studies on this topic have used daily data, but we were limited by the lack of available data that would allow us to investigate influenza by age group. Our study did, however, compensate for this limitation by analyzing the trend over the course of ten years, which provided a sufficient number of data points. Additionally, because the CDC only reports influenza data seasonally for MWWR weeks 40 to 52 and weeks 1 to 17 of the adjacent year, we did not get a full picture of influenza trends over the course of a whole year. The availability of such data would have also allowed us to use results from the non-influenza season as a comparison.

Vaccination has a major impact on influenza risks but was not included due to limited data availability. Although flu vaccines' effectiveness depends on multiple factors and can vary each season, it can still significantly reduce risks of hospitalizations (Campbell et al., 2020) and deaths (Flannery et al., 2017) among children. However, the current influenza vaccination surveillance system does not have available data spanning the entirety of the study period, so this type of data was not included (CDC, 2022). Inclusion of vaccination rates in the model may help to explain the complex relationship between DTR and pediatric influenza hospitalization. For example, Connecticut and Maryland, two of the states exhibiting a negative association, consistently had the higher vaccination coverage at 75% and above among children between 6 months to 4 years old, whereas California and Michigan, the two states that demonstrated a statistically significant positive association, had lower vaccination coverage at about 60 to 70 percent (CDC, 2022). Although superficial, these observations suggest that vaccination coverage may play a role in this relationship. Thus, future research should incorporate this important variable into the model.

Our study was one of the first to explore this relationship in the United States. For this reason, it served a peripheral purpose of identifying states that may potentially exhibit higher influenza risks due to DTR. As such, future research should focus on a single state and examine the variables on an even smaller scale. For example, both Zhang et al. (2020) and Ma et al. (2021) investigated the relationship between DTR and Flu-A and Flu-B cases in Shanghai and Shenzhen, China, respectively, and found significant but contrasting associations between the two types of influenza. This may reveal whether a particular strain of flu might be more sensitive to DTR. Human behaviors and virus pathogenicity are also two variables to consider for future research, as humans and viruses will continue to adapt to the changing climate in various ways.

## Conclusion

Climate change may have a negative impact on respiratory illnesses, such as influenza, which this study aimed to investigate through an associated meteorological variable, diurnal temperature range (DTR). Specifically, the relationship between DTR and pediatric influenza hospitalization rates in different U.S. states between 2009 and 2019 was examined. To achieve this, the study integrated available government datasets with a robust non-linear lag regression model that had been consistently used by previous literature on this topic.

Being one of the first of its kind to explore this relationship in the United States, our study found a statistically significant positive association between these two variables in Albany, Rochester, Michigan, and California. This finding can be used to inform the development of early warning systems and adaptation strategies and to inspire further research in these regions. Variables to consider in future research include other climate-related meteorological factors, vaccination history, and influenza strain type, all of which may illuminate this complex non-linear relationship. Although other regions show statistically insignificant results, it may also be worth to investigate them if more granular data became available so that the field of public health can benefit from the implications of a more accurate picture of the relationship.

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**Appendix**

*Appendix 1. State characteristics.*

Table 1. Number of participating counties in each state and the percentage of state population represented by the data (CDC, 2023; Census Bureau, 2020).

| State | % of State Population Represented | Number of Participating Counties |
|---|---|---|
| California | 9.00% | 3 |
| Colorado | 49.00% | 5 |
| Connecticut | 29.00% | 2 |
| Georgia | 39.00% | 8 |
| Maryland | 46.00% | 6 |
| Michigan | 13.00% | 5 |
| Minnesota | 55.00% | 7 |
| New York - Albany | 1.56% | 1 |
| New York - Rochester | 1.05% | 1 |
| Oregon | 44.00% | 3 |
| Tennessee | 26.00% | 8 |

*Appendix 2. Participating counties in each state (CDC, 2023).*

California: Alameda, Contra Costa, San Francisco

Connecticut: New Haven, Middlesex

Colorado: Adams, Arapahoe, Denver, Douglas, Jefferson

Georgia: Fulton, DeKalb, Clayton, Cobb, Douglas, Gwinnett, Rockdale, Newton

Maryland: Baltimore, Howard, Anne Arundel, Harford, Carroll, Queen Anne's

Minnesota: Anoka, Carver, Dakota, Hennepin, Ramsey, Scott, Washington

Michigan: Clinton, Eaton, Genesee, Ingham, Washtenaw

New York – Albany

New York – Rochester

Oregon: Clackamas, Multnomah, Washington

Tennessee: Cheatham, Davidson, Dickson, Robertson, Rutherford, Sumner, Williamson, Wilson

*Appendix 3. Summary statistics of weekly meteorological factors and weekly influenza hospitalization rates for each state.*

Table 1. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in California

| **Variables** | **Mean** | **Minimum** | **25th** | **50th** | **75th** | **Maximum** |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 9.84 | 4.23 | 8.03 | 9.89 | 11.69 | 16.31 |
| Mean Temperature (°C) | 12.82 | 5.32 | 10.31 | 12.47 | 15 | 22.18 |
| Relative Humidity (%) | 69.37 | 41.91 | 63.37 | 70.26 | 75.52 | 88.71 |
| Precipitation (mm) | 1.75 | 0 | 0.01 | 0.53 | 2.49 | 12.74 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.32 | 0 | 0 | 0.9 | 2 | 6.9 |

Table 2. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Colorado

| **Variables** | **Mean** | **Minimum** | **25th** | **50th** | **75th** | **Maximum** |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 13.08 | 7.41 | 11.69 | 13.13 | 14.63 | 17.73 |
| Mean Temperature (°C) | 4.29 | -11.47 | 0.17 | 3.66 | 8.54 | 21.26 |
| Relative Humidity (%) | 51.78 | 23.21 | 43.28 | 52.12 | 59.25 | 83.76 |
| Precipitation (mm) | 0.58 | 0.00 | 0.03 | 0.19 | 0.78 | 7.04 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 2.65 | 0.00 | 0.50 | 1.70 | 4.00 | 17.7 |

Table 3. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Connecticut

| **Variables** | **Mean** | **Minimum** | **25th** | **50th** | **75th** | **Maximum** |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 8.65 | 3.94 | 7.31 | 8.49 | 10.00 | 13.99 |
| Mean Temperature (°C) | 5.43 | -10.39 | 0.71 | 4.54 | 9.51 | 21.94 |
| Relative Humidity (%) | 65.83 | 44.45 | 59.95 | 66.59 | 71.21 | 84.29 |
| Precipitation (mm) | 2.51 | 0.00 | 0.48 | 1.72 | 3.52 | 15.02 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.48 | 0.00 | 0 | 0 | 1.9 | 24.6 |

Table 4. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Georgia

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 10.70 | 3.91 | 8.97 | 10.84 | 12.21 | 17.11 |
| Mean Temperature (°C) | 11.41 | -4.04 | 7.52 | 11.50 | 15.69 | 24.38 |
| Relative Humidity (%) | 66.68 | 42.5 | 59.92 | 65.99 | 73.70 | 92.62 |
| Precipitation (mm) | 3.31 | 0 | 0.51 | 2.10 | 5.02 | 18.91 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.19 | 0 | 0 | 0.4 | 1.5 | 12 |

Table 5. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Maryland

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 8.73 | 3.99 | 7.5 | 8.61 | 10.03 | 14.33 |
| Mean Temperature (°C) | 7.23 | -9.5 | 3.05 | 6.87 | 11.5 | 21.56 |
| Relative Humidity (%) | 66.88 | 44.84 | 61.05 | 66.78 | 72.8 | 89.52 |
| Precipitation (mm) | 2.02 | 0 | 0.45 | 1.44 | 2.89 | 16.73 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.99 | 0 | 0 | 1.2 | 2.9 | 16.3 |

Table 6. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Minnesota

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 8.59 | 2.77 | 7.03 | 8.56 | 10.11 | 15.47 |
| Mean Temperature (°C) | -0.22 | -19.28 | -6.5 | -0.56 | 6.55 | 20.03 |
| Relative Humidity (%) | 70.44 | 42.63 | 65.61 | 71.36 | 76.76 | 89.3 |
| Precipitation (mm) | 0.98 | 0 | 0.06 | 0.31 | 1.29 | 9.9 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.92 | 0 | 0 | 1 | 2.5 | 19.6 |

Table 7. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Oregon

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 7.29 | 3.19 | 5.47 | 6.57 | 8.37 | 16.67 |
| Mean Temperature (°C) | 7.83 | -3.38 | 5.48 | 7.8 | 10.2 | 17.38 |
| Relative Humidity (%) | 78.95 | 45.09 | 74.58 | 80.58 | 84.68 | 92.74 |
| Precipitation (mm) | 3.86 | 0 | 1.44 | 2.97 | 5.34 | 25.76 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 0.95 | 0 | 0 | 0 | 1 | 16.1 |

Table 8. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Tennessee

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 10.85 | 5.61 | 8.91 | 10.64 | 12.47 | 19.77 |
| Mean Temperature (°C) | 9.32 | -8.03 | 4.83 | 9.5 | 14.04 | 23.69 |
| Relative Humidity (%) | 68.86 | 46.84 | 62.59 | 68.53 | 75.21 | 90.92 |
| Precipitation (mm) | 2.98 | 0 | 0.78 | 2.2 | 4.38 | 17.45 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.02 | 0 | 0 | 0 | 1.8 | 7.7 |

Table 9. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in New York – Albany

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 8.85 | 2.97 | 7.29 | 8.71 | 10.157 | 16.37 |
| Mean Temperature (°C) | 2.75 | -13.67 | -1.84 | 2.21 | 7.47 | 16.47 |
| Relative Humidity (%) | 65.74 | 44.16 | 60.16 | 66.04 | 71.81 | 87.07 |
| Precipitation (mm) | 2.32 | 0 | 0.69 | 1.7 | 3.52 | 13.01 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.81 | 0 | 0 | 0 | 3.7 | 12.6 |

Table 10. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in New York – Rochester

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 8.29 | 2.73 | 6.67 | 7.91 | 9.54 | 14.91 |
| Mean Temperature (°C) | 2.95 | -14.59 | -1.59 | 2.64 | 7.37 | 17.43 |
| Relative Humidity (%) | 70.67 | 47.51 | 66.6 | 71.33 | 75.71 | 89.4 |
| Precipitation (mm) | 2.08 | 0 | 0.68 | 1.68 | 2.81 | 12.91 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 1.57 | 0 | 0 | 0 | 1.6 | 15.4 |

Table 11. Summary Statistics of Weekly Meteorological Factors and Weekly Influenza Hospitalization Rate in Michigan

| Variables | Mean | Minimum | 25th | 50th | 75th | Maximum |
|---|---|---|---|---|---|---|
| **Weekly Meteorology** | | | | | | |
| DTR (°C) | 8.77 | 2.9 | 6.84 | 8.53 | 10.56 | 16.57 |
| Mean Temperature (°C) | 2.37 | -15.43 | -2 | 2.14 | 7.43 | 17.95 |
| Relative Humidity (%) | 72.64 | 49.99 | 6.67 | 73.75 | 78.13 | 90.63 |
| Precipitation (mm) | 1.66 | 0 | 0.42 | 1.12 | 2.24 | 9.78 |
| **Weekly Hospitalization Rate** | | | | | | |
| Influenza | 3.61 | 0 | 0 | 1.9 | 5.8 | 59.8 |

*Appendix 4. Relative risk*

Table 1. Relative risk of pediatric influenza hospitalization at the mean and at different quantiles of DTR

| | **Relative Risk at Mean and Different Quantiles of DTR** | | | | | |
|---|---|---|---|---|---|---|
| **State** | **Mean** | **Minimum** | **25th** | **50th** | **75th** | **Maximum** |
| California* | 0.99 | 0.52 | 0.69 | 0.93 | 1.26 | 1.69 |
| Colorado | 1.03 | 0.85 | 0.93 | 1.02 | 1.12 | 1.23 |
| Connecticut | 0.95 | 1.45 | 1.15 | 0.92 | 0.73 | 0.58 |
| Georgia | 1.05 | 0.73 | 0.87 | 1.03 | 1.22 | 1.44 |
| Maryland | 1.00 | 1.16 | 1.08 | 1.00 | 0.92 | 0.85 |
| Michigan* | 1.06 | 0.45 | 0.66 | 0.97 | 1.41 | 2.07 |
| Minnesota | 1.04 | 0.67 | 0.82 | 1.01 | 1.24 | 1.52 |
| New York – Albany* | 1.27 | 0.36 | 0.61 | 1.05 | 1.79 | 3.06 |
| New York – Rochester* | 1.07 | 0.49 | 0.69 | 0.98 | 1.39 | 1.97 |
| Oregon | 1.06 | 1.70 | 1.31 | 1.01 | 0.78 | 0.60 |
| Tennessee | 1.05 | 1.83 | 1.34 | 0.98 | 0.72 | 0.53 |

*95% CI for RR does not cross 1 for all values of DTR, indicating statistical significance.