GeoHealth

RESEARCH ARTICLE
10.1029/2021GH000469

Key Points:
- Humidity thresholds that signal the onset of seasonal outbreaks vary by state when using state-level humidity and influenza case estimates
- The humidity thresholds that were identified as signaling outbreaks have a linear relationship with average annual humidity of the location

Supporting Information:

Supporting Information may be found in the online version of this article.

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Citation:

Serman, E., Thrastarson, H. Th., Franklin, M., & Teixeira, J. (2022). Spatial variation in humidity and the onset of seasonal influenza across the contiguous United States. *GeoHealth*, *6*, e2021GH000469. https://doi.org/10.1029/2021GH000469

Received 2 JUN 2021
Accepted 6 DEC 2021

Spatial Variation in Humidity and the Onset of Seasonal Influenza Across the Contiguous United States

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Abstract In recent years, environmental factors, particularly humidity, have been used to inform influenza prediction models. This study aims to quantify the relationship between humidity and influenza incidence at the state-level in the contiguous United States. Piecewise segmented regressions were performed on specific humidity data from NASA's Atmospheric Infrared Sounder (AIRS) and incident influenza estimates from Google Flu Trends to identify threshold values of humidity that signal the onset of an influenza outbreak. Our results suggest that influenza incidence increases after reaching a humidity threshold that is state-specific. A linear regression showed that the state-specific thresholds were associated with annual average humidity conditions ($R^2 = 0.9$). Threshold values statistically significantly varied by region (F-statistic = 8.274, $p < 0.001$) and of their 36 pairwise combinations, 13 pairs had at least marginally statistically significant differences in their means. All of the significant comparisons included either the South or Southeast region, which had higher humidity threshold values. Results from this study improve our understanding of the significance of humidity in the transmission of influenza and reinforce the need for local and regional conditions to be considered in this relationship. Ultimately this could help researchers to produce more accurate forecasts of seasonal influenza onset and provide health officials with better information prior to outbreaks.

Plain Language Summary The influenza, or flu, virus is a contagious respiratory illness that infects millions of people in the United States each year. Scientists from multiple disciplines have been using complex models to try and predict the start of seasonal outbreaks using a variety of information. Humidity has been shown in laboratory experiments to be a potentially important component of influenza transmission. This study uses historical estimates of influenza case numbers as well as humidity data to investigate the relationship between the two at the state-level across the contiguous United States. We found the humidity values that seemed to signal the onset of seasonal influenza differed by state and that in states with higher average annual humidity, the humidity value that "signaled" seasonal onset was also higher. Additionally, we found that there were regional patterns in our results. This work could improve our understanding of how humidity impacts influenza transmission and how we use humidity in models that aim to predict seasonal outbreaks.

1. Introduction

Every year, millions of people in the United States are infected with the contagious respiratory illness known as the influenza, or flu, virus. Symptoms of influenza range from mild to severe, and in some cases require hospitalization that can even lead to death. In the United States, seasonal influenza outbreaks generally begin in fall and peak over the course of the winter or into the spring months (CDC, 2016). However, the driving factors behind this seasonality are not well understood. There are several hypotheses about possible influences on the transmission cycle including: changes in host immune capability, melatonin and vitamin D levels in winter, behavior (e.g., staying indoors and the effect of HVAC systems in winter), as well as environmental conditions like temperature, humidity, and UV irradiation (Lowen & Steel, 2014). Studies focused on the relationship between seasonal influenza and environmental conditions have found the strongest associations with temperature and humidity in temperate regions of the world (Dalziel et al., 2018; Lowen et al., 2007; Lowen & Steel, 2014; Shaman et al., 2017; Soebiyanto & Kiang, 2014; Tamerius et al., 2019). This study focuses on the role of humidity as a driving factor of state-level seasonal influenza outbreaks in the contiguous United States.

It is theorized that the relationship between humidity and influenza might be explained by all or some the following three mechanisms: (a) virus survival increases as humidity levels decrease; (b) droplet size decreases with decreasing humidity, allowing particles to travel farther and remain suspended in the air for longer; and (c) low humidity dries out the mucous membranes of the nose leaving the subject more susceptible to infection when they encounter the virus (Lowen & Steel, 2014; Lowen et al., 2007). However, a more recent study by Kudo et al. (2019) presented further evidence for impaired host responses to influenza virus when in low humidity conditions. They found that mice exposed to low relative humidity conditions had more severe influenza infections compared to those kept in high relative humidity environments and were not able to clear the virus from their bodies' due to impaired physical mechanisms and immune systems responses. Not only did the mice in low humidity have difficulties in mucociliary clearance, they also showed signs of impaired tissue repair in their airways, and had lower production of interferon-stimulated genes that block virus spread.

While laboratory experiments on animals have utilized relative humidity to better understand the physical and immunological responses to influenza exposure (Kudo et al., 2019; Lowen & Steel, 2014; Lowen et al., 2007), from a modeling perspective, absolute humidity seems a better proxy for human conditions (Shaman et al., 2010, 2017). Absolute humidity is the mass of water vapor divided by the total volume of air, while relative humidity is the ratio of the vapor pressure to the saturation vapor pressure with respect to water and, perhaps most importantly, is influenced by temperature. Shaman et al. (2017) describe several reasons why absolute humidity is the more appropriate measure for modeling in human populations. For example, outdoors, relative humidity is highest in the winter time, while absolute humidity is at its lowest (Lowen & Steel, 2014; Shaman et al., 2010, 2017). However, indoors, where people in high income countries such as the United States, spend the majority of their time in the winter months, both absolute and relative humidity are low (Lowen & Steel, 2014; Shaman et al., 2010, 2017). Therefore, outdoor absolute humidity is easily used to approximate indoor conditions, where the virus is more likely transmitted from person to person (Shaman et al., 2017). It is common for specific humidity to be used, in the context of meteorology and climate, as a replacement for absolute humidity, and this analysis, like Tamerius et al. (2019), follows that precedent. Specific humidity is the mass of water vapor divided by the total mass of air.

The analysis presented here contributes to the understanding of how local environmental conditions influence influenza transmission. While other studies have considered the impact of humidity on the magnitude and seasonality of influenza outbreaks (Dalziel et al., 2018; Soebiyanto & Kiang, 2014; Tamerius et al., 2019), this work specifically investigates the onset of outbreaks. In turn, this can improve the use of variables such as humidity in models that attempt to predict the timing of seasonal epidemics (Shaman et al., 2010, 2017). Given that the best method for influenza prevention is an annual vaccine, an early warning system would allow local health workers and community members to be better prepared for the start of seasonal transmission. This study analyzes weekly averages from a decade of data to estimate the relationship between humidity and influenza at the state level for the contiguous United States and relates the patterns found to location specific average annual humidity conditions. This study uses a novel combination of datasets including humidity from NASA's Atmospheric Infrared Sounder (AIRS) and incident influenza estimates from Google Flu Trends (GFT).

2. Data

The AIRS instrument on-board NASA's Earth Observing System Aqua satellite, launched in 2002, provides profiles of atmospheric conditions including temperature and humidity (e.g., Tian et al., 2013, 2017). Version 6 (V6) Level 3 AIRS observations are available twice daily from an ascending (daytime, ~1:30p.m. local time) and descending (nighttime, ~1:30a.m. local time) path in a 1-degree by 1-degree grid (AIRS Science Team/Joao Teixeira, 2013). This study uses water vapor Mass Mixing Ratio (MMR) at the near-surface level as a substitute for specific humidity values. Water vapor MMR is the ratio of the mass of water vapor in an air parcel to the mass of dry air for the same parcel (i.e., g/kg dry air) and near surface MMR is a close proxy to specific humidity (Camuffo, 2014).

In 2008, Google launched the GFT product, which aggregated Google search queries on influenza activity for more than 25 countries (Olson et al., 2013). The data provide an estimated number of Influenza-Like-Illness (ILI) related physicians visits per 100,000 people for each week of the year (Ginsberg et al., 2009). In this context, a "case" is defined as a query for phrases and keywords such as "flu-like symptoms" or "influenza remedies" in a Google search engine (Ginsberg et al., 2009). These data are available as weekly estimates from the start of the 2003 influenza season through the end of the 2015 season for select cities, the lower 48 contiguous states, and for all 10 Health and Human Services regions. This study focuses on the state-level data.

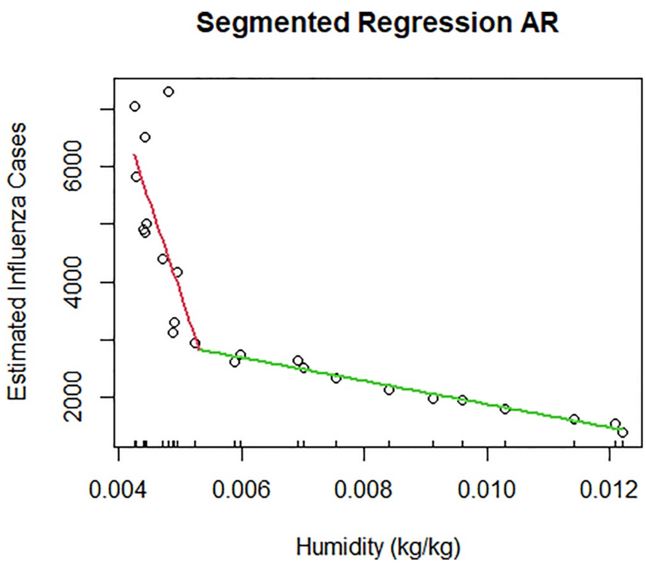

Figure 1. Average weekly humidity versus average weekly incidence for Arkansas (2003–2015). The red and green lines represent the results of the segmented regression, their intersection is the breakpoint.

There has been some discussion about the utility and accuracy of GFT data as an estimation for influenza incidence. In particular, there are arguments that GFT overestimates the burden of influenza infections, with the 2012–2013 season being noted as a particularly extreme occurrence of this (Kandula & Shaman, 2019; Olson et al., 2013). This analysis acknowledges the limitations of GFT as an estimation of influenza in the US and excludes data from the 2009–2010 pandemic and the documented overestimation of the 2012–2013 to reduce the influence of these extreme conditions. Additionally, it should be noted that this is an analysis of weekly averages over several seasons which may also reduce the impact of inconsistencies in the data.

3. Methods

3.1. Data Processing

AIRS 1-degree by 1-degree grid cells were averaged for the 48 contiguous states to generate state-specific MMR. For a given cell, the location of its center was used to pair the cell (as a whole) with a state. As mentioned previously, the daily AIRS data contains both an ascending and descending humidity reading. These readings were averaged together to produce a single measurement for each day and then aggregated to the weekly time scale over the period 2003–2015 to complement the GFT data.

The GFT data is provided as weekly incidence estimates for each state. Not all states have data for the entire time period of interest (2003–2015), but this study processed what was available. In order to avoid skewing from extreme conditions and estimations, the H1N1 pandemic of 2009–2010 and the documented overestimation of GFT data for the 2012–2013 influenza season (Olson et al., 2013) were excluded from this analysis.

Both the AIRS and GFT datasets for each state were aggregated once more to find the average humidity and influenza conditions by week of the year over the 2003–2015 time period. Since the aim of this analysis is to better understand the humidity conditions leading up to and at the start of the influenza season, the weekly averages were restricted to the period from week 36, the beginning of September, to the peak average week for each state. "Peak average week" refers to the week of the year with the highest average influenza over the course of the time series. These averages were plotted versus influenza incidence and a segmented linear regression was fit to the data in order to estimate the breakpoint humidity value.

3.2. Segmented Regression

This analysis used segmented regression (Muggeo, 2008) to assess the association between humidity and ILI. Segmented regression is essentially a piecewise linear regression (Equation 1) whereby breakpoints (or knots, ψ) are determined iteratively given a starting value. We estimate a one-breakpoint model with the following form:

$$y = \beta_0 + \beta_1 x + \beta_2 (x - \tilde{\psi})^+ + \gamma I(x > \tilde{\psi})^- \quad (1)$$

where y is the dependent variable, ILI, x is the independent variable, humidity, β_0 is the intercept, β_1 is the slope describing the association between humidity and ILI before the breakpoint ψ, β_2 is the slope describing the association between humidity and ILI after breakpoint ψ, and I is the indicator function (equal to 1 when true). To obtain the optimal estimate of the breakpoint, $\hat{\psi}$, the linear model is fit iteratively. Through $\gamma I(x > \tilde{\psi})^-$ the breakpoint is updated by $\hat{\psi} = \tilde{\psi} + \hat{\gamma}/\hat{\beta}_2$. Additional details are available in Muggeo (2003) and Muggeo (2008).

Breakpoints indicate the intersection of parts of the line segment that have different slopes. In the context of this analysis, the "breakpoint humidity value" is the humidity level which precedes a sharp increase in influenza cases. An example of this plot, for the state of Arkansas, can be seen in Figure 1 where the breakpoint approximation, located where the red and green colored segments intersect, is 0.0052 (note that the units are kg/kg because of the use of MMR as a humidity proxy, and because it is a ratio, units are not included from this point forward). This study suggests that the breakpoint signals the onset of an influenza outbreak and, for the example of Arkansas,

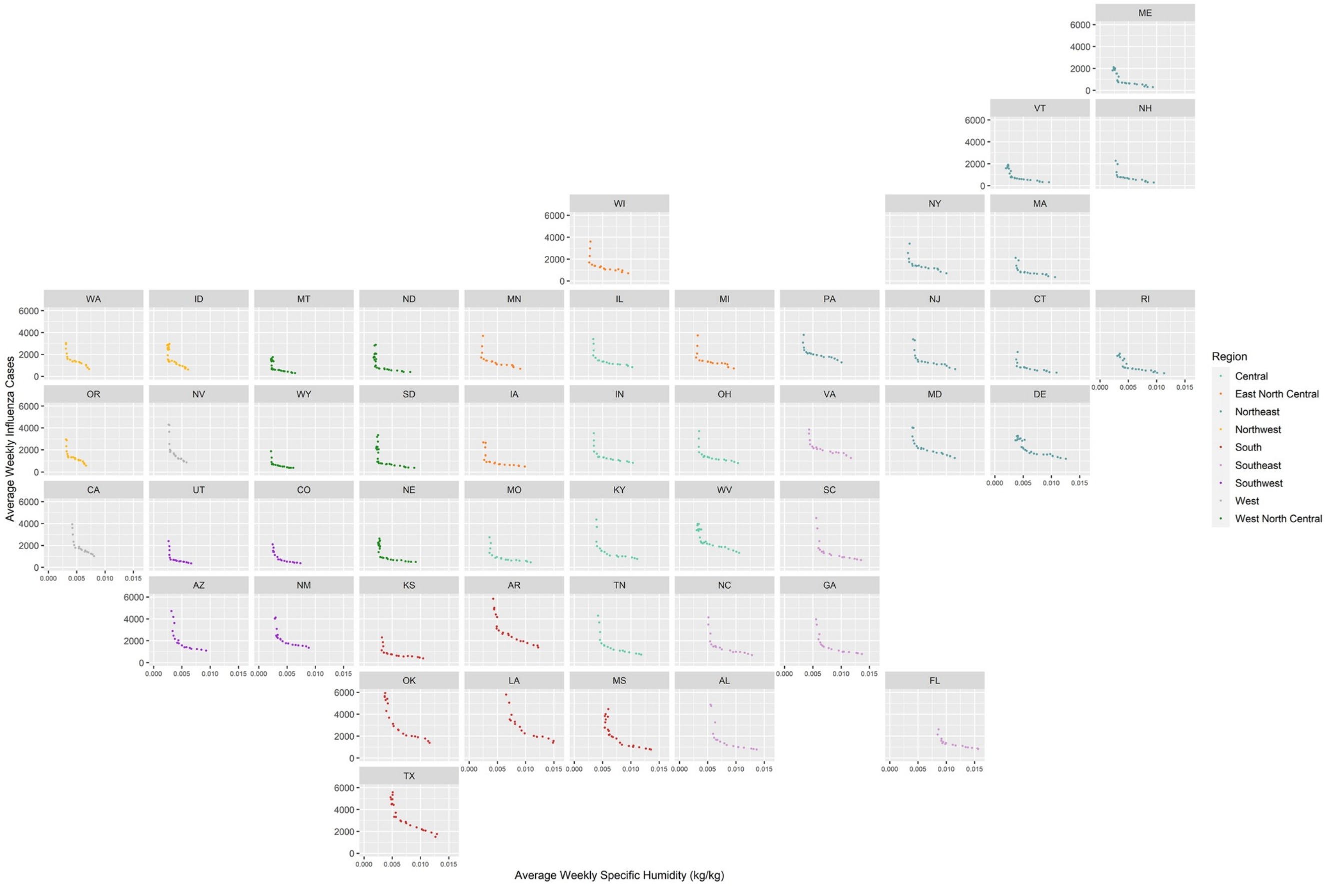

Figure 2. Observed average weekly humidity (kg/kg) versus average Influenza-Like-Illness count for each state. The scatter plots for each state are colored by the corresponding NOAA region they were assigned for the ANOVA analysis and are arranged in their approximate geographic location.

once the local humidity conditions reach approximately 0.0052, the number of influenza cases could be expected to rise

3.3. ANOVA Analysis

We tested for regional differences in the extracted breakpoint values using an ANOVA regression. States were grouped according to the nine climatological regions previously defined by the National Centers for Environmental Information (Karl & Koss, 1984). Since the ANOVA analysis provides only an overall association, a Tukey Honest Significant Differences (HSD) test was used to determine which of the pairwise regional combinations had statistically significant differences.

4. Results

Figure 1 shows the 2003–2015 average weekly humidity versus the average weekly influenza incidence for the state of Arkansas. The one-breakpoint segmented regression is displayed by its piecewise linear shape (red and green lines) separated by the estimated breakpoint $\hat{\psi}$. For Arkansas, $\hat{\psi} = 0.0052$.

Scatter plots of weekly humidity climatology versus the average weekly influenza incidence, as seen in Figure 1, were created for each individual state and can be found in the Supporting Information S1. The scatter plots, without the overlaying regressions, are also shown colored by their climatological region and arranged in their approximate geographic position in the United States in Figure 2. Viewing the state-level plots in this manner reveals how this relationship varies over space by making clear the similarities in the "shape" of the onset of seasonal outbreaks, as well as highlighting potential limitations of the NOAA climatic groupings in this context. States in the West and Northwest regions (California and Nevada; Oregon, Washington, and Idaho, respectively) have similarly steep increases in influenza cases at both higher and lower humidity values. In the Northeast region, the scatterplots show a smaller increase at higher humidity values and a generally lower increase in cases than the rest of the country at humidity values lower than the breakpoint. Finally, the "rounded" less distinct breaks, as compared to the West and Northwest, in the incidence/humidity relationship found in the South and Southeast regions are noted. The inclusion of Kansas in the South region is the most notable potential misfit of the NOAA regional classifications. Kansas appears to have the steeper more distinct slopes more similar to its northern neighbors Missouri, Nebraska, and Iowa than the more rounded shape and higher incidence rates seen in states to its south such as Oklahoma, Arkansas, and Texas. The adjusted R^2 values, indicating how well the segmented regression model fit, range from 0.51 for the state of Michigan to 0.99 for California with a standard deviation of 0.13. The complete list of adjusted R^2 values can be found in Table 1 along with each states' estimated breakpoint values, all of which are grouped by climate region. These breakpoint values, $\hat{\psi}$, are displayed by state in Figure 3. In this figure, each state is represented by a box, once again displayed in its approximate geographic position in the US, and the color corresponds with the humidity value extracted at the breakpoint. States in the Southeast and Southern regions had generally higher breakpoint values and Florida and Wyoming have the highest and lowest breakpoints, respectively. The extracted humidity breakpoint values for each state were also plotted versus each states' average annual specific humidity and fitted with a linear regression (Figure 4). The overall relationship between these two humidity values has an R^2 of 0.90 and the trend is highly linear.

In addition to spatial variation in the breakpoint, we also considered variation in the slopes of the piecewise regression as well as the week of the year that the breakpoint occurred. However, despite regional similarities in the "shapes" of the epidemic curves, there was little variation in these values between states and no distinct relationships with annual average humidity conditions as were seen with the breakpoint. Results from these tests can be seen in Figures S50–S53 in Supporting Information S1.

Finally, we have the results of the ANOVA regression and Tukey HSD test. State breakpoint values statistically significantly varied by region (F-statistic = 8.274, $p < 0.001$). All possible regional pairwise combinations from the Tukey HSD test are listed in Table 2 along with their differences in mean, upper and lower limits and the associated adjusted p-value. Of the 36 possible combinations, 13 of them were at least marginally statistically significant. All of the significant pairs included one of either the South or Southeast regions. These results can be seen graphically in the Supporting Information S1, which depicts the significant pairings in red.

5. Conclusions

The purpose of this analysis is to build upon previous works relating humidity to seasonal influenza outbreaks (Barreca & Shimshack, 2012; Chattopadhyay et al., 2018; Dalziel et al., 2018; Shaman & Kohn, 2009; Shaman et al., 2010; Soebiyanto & Kiang, 2014; Tamerius et al., 2019) by considering how the climate-influenza interaction at the onset of seasonal outbreaks varies over space. Our findings are generally aligned with previous studies, in that they support humidity and influenza interaction theories (Barreca & Shimshack, 2012; Dalziel et al., 2018; Shaman & Kohn, 2009; Shaman et al., 2010; Tamerius et al., 2019). In contrast to the other findings, but similar to Tamerius et al. (2019), the analysis described here provides evidence that this interaction is relative to local annual humidity (Figure 4). This finding may have important implications for identifying the mechanism that drives the humidity and influenza interaction, as well as the use of humidity as a driver in influenza prediction models.

As stated in the introduction, there were three early explanations for the importance of low humidity in influenza transmission. Of these three, it would be expected that the virus' survival threshold and the impact of humidity on particle size would be related to a humidity range that would apply in all locations, regardless of average local conditions. However, this study and the work presented by Kudo et al. (2019), show evidence that supports the third mechanism involving the role of the mucous membranes of the nasal cavity in protecting individuals from viruses, which are impacted by average local environmental conditions. Figures 2 and 3 both provide evidence of spatial variability in both incidence trends during an average influenza season and the breakpoint humidity values. The ANOVA and Tukey HSD test provide additional support for distinct regional trends, particularly in the South and Southeast regions as compared to the rest of the country (Table 2).

Table 1
The Resulting Breakpoint Values Estimated From the Segmented Linear Regression Analysis, as Well as the Adjusted R^2 Values for the Regressions

Region	State	Abbreviation	Estimated breakpoint (kg/kg)	Adjusted R-squared value
Central	Illinois	IL	0.00389	0.799
	Indiana	IN	0.00350	0.973
	Kentucky	KY	0.00463	0.735
	Missouri	MO	0.00431	0.744
	Ohio	OH	0.00406	0.718
	Tennessee	TN	0.00474	0.960
	West Virginia	WV	0.00420	0.847
East North Central	Iowa	IA	0.00345	0.630
	Michigan	MI	0.00410	0.506
	Minnesota	MN	0.00325	0.545
	Wisconsin	WI	0.00366	0.613
Northeast	Connecticut	CT	0.00462	0.589
	Delaware	DE	0.00614	0.875
	Massachusetts	MA	0.00384	0.717
	Maryland	MD	0.00452	0.877
	Maine	ME	0.00346	0.908
	New Hampshire	NH	0.00296	0.716
	New Jersey	NJ	0.00470	0.865
	New York	NY	0.00407	0.660
	Pennsylvania	PA	0.00360	0.827
	Rhode Island	RI	0.00485	0.862
	Vermont	VT	0.00310	0.893
Northwest	Idaho	ID	0.00342	0.654
	Oregon	OR	0.00339	0.881
	Washington	WA	0.00336	0.947
South	Arkansas	AR	0.00532	0.793
	Kansas	KS	0.00387	0.697
	Louisiana	LA	0.00769	0.915
	Mississippi	MS	0.00724	0.772
	Oklahoma	OK	0.00545	0.916
	Texas	TX	0.00587	0.914
Southeast	Alabama	AL	0.00601	0.885
	Florida	FL	0.00937	0.911
	Georgia	GA	0.00644	0.955
	North Carolina	NC	0.00567	0.933
	South Carolina	SC	0.00604	0.938
	Virginia	VA	0.00455	0.969
Southwest	Arizona	AZ	0.00404	0.797
	Colorado	CO	0.00295	0.941
	New Mexico	NM	0.00326	0.913
	Utah	UT	0.00291	0.918

Table 1
Continued

Region	State	Abbreviation	Estimated breakpoint (kg/kg)	Adjusted R-squared value
West	California	CA	0.00446	0.994
	Nevada	NV	0.00293	0.899
West North Central	Montana	MT	0.00294	0.631
	North Dakota	ND	0.00274	0.609
	Nebraska	NE	0.00339	0.792
	South Dakota	SD	0.00306	0.588
	Wyoming	WY	0.00233	0.893

Note. The states are grouped into the NOAA regions used for the ANOVA analysis.

We believe that our results are consistent with that of Kudo et al. (2019) and that the impact of humidity might be better considered at the individual or more localized level. For example, populations adapted to more humid environments with large ranges of seasonal humidity may not be as susceptible to slight changes in humidity levels as those who live in drier climates with little seasonal variability. What is considered "low" humidity for a state such as Florida would still feel quite "high" for inhabitants of a state that is very dry, such as Wyoming, especially given that even the lowest seasonal ranges of humidity in Florida exceed the highest ranges of seasonal humidity in Wyoming. This is particularly notable given the significance of the impact of low humidity not only on the mucous membranes of the nasal passage but also immunological function outlined by Kudo et al. (2019), both of which have substantial impact on transmission and susceptibility. The linear regression of the estimated breakpoints versus annual average humidity shown in Figure 4 further supports this argument. In locations where the annual average humidity is higher, the humidity values associated with the breakpoints, that this analysis argues signal the onset of the highest weeks of influenza incidence, is also higher. This linear relationship and insight into potential local thresholds could be used to enhance current prediction models. Additionally, it could

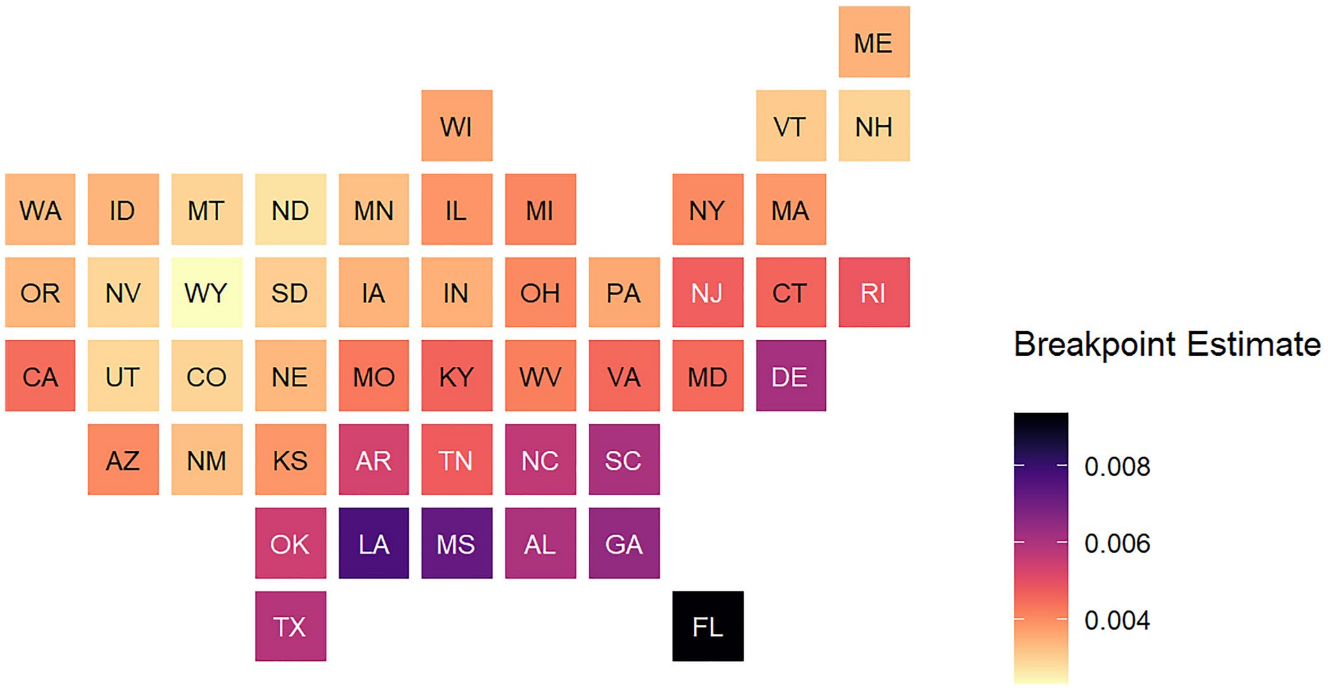

Figure 3. Each box represents a state, denoted by its state abbreviation (state abbreviations are listed in Table 1 for reference), and is colored according to the humidity value (kg/kg) at the breakpoint which was determined with segmented regression. Wyoming has the lowest breakpoint humidity value and Florida has the highest.

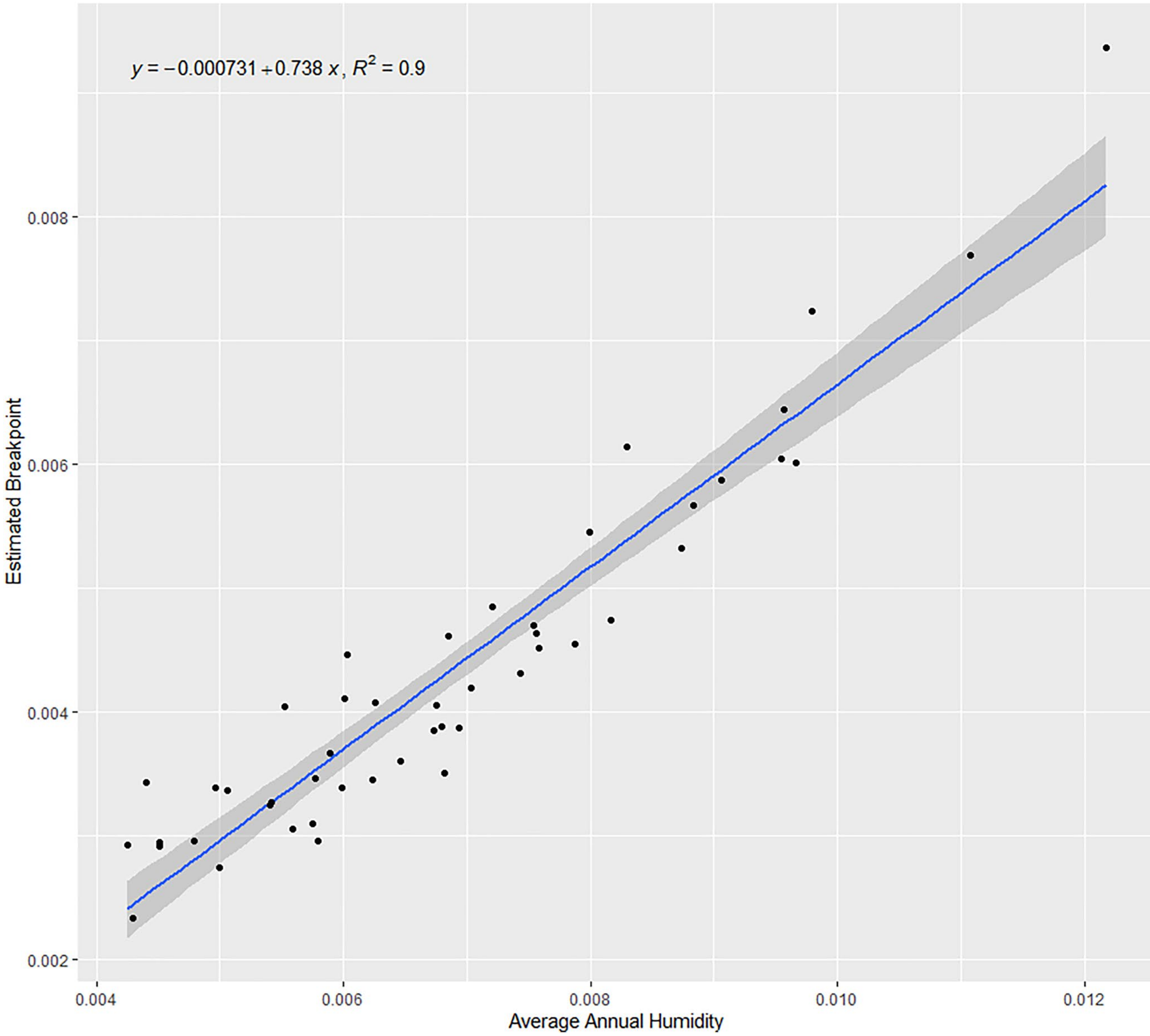

Figure 4. Average annual humidity values (kg/kg) for each state (x) versus the extracted breakpoint for humidity (y) with a simple linear association (blue line).

be used to identify a more precise "environmental flu season" that is dictated by real-time humidity conditions as opposed to a general time period of October to March.

This finding is partially in agreement with the work of Barreca and Shimshack (2012). Barreca and Shimshack (2012) performed a regression analysis for 30 years of humidity and influenza mortality data for a collection of urban counties in the US. They found that the strength of the association with humidity and temperature depended on the counties' average humidity conditions over the course of the year. Specifically, they found that for counties that were considered to have "high" average humidity during the year, associations were stronger between mortality and low winter humidity. In "low" average humidity counties and those that were generally colder, mortality was more strongly correlated with temperature. While we are not considering mortality data, the differences between "high" average humidity versus "low" average humidity counties is notable.

Furthermore, Tamerius et al. (2019) also suggest that seasonal characteristics of influenza vary by regional climatological characteristics across the US. Their investigation of "cross-seasonal," or summer transmission, found

Table 2
Results From the Tukey Honest Significant Difference Test on All of the Possible Regional Pairwise Combinations

Region comparison	Difference In means	95% confidence interval Lower	95% confidence interval Upper	Adjusted p-value	
East North Central-Central	−0.00057	−0.00253	0.00139	0.988	
Northeast-Central	−0.00002	−0.00153	0.00149	1.000	
Northwest-Central	−0.00080	−0.00295	0.00136	0.949	
South-Central	0.00172	−0.00002	0.00346	0.054	.
Southeast-Central	0.00216	0.00042	0.00390	0.006	**
Southwest-Central	−0.00090	−0.00285	0.00106	0.847	
West-Central	−0.00050	−0.00300	0.00201	0.999	
West North Central-Central	−0.00130	−0.00312	0.00053	0.352	
Northeast-East North Central	0.00055	−0.00127	0.00238	0.984	
Northwest-East North Central	−0.00023	−0.00261	0.00216	1.000	
South-East North Central	0.00229	0.00027	0.00430	0.016	*
Southeast-East North Central	0.00273	0.00072	0.00475	0.002	**
Southwest-East North Central	−0.00033	−0.00253	0.00188	1.000	
West-East North Central	0.00008	−0.00263	0.00278	1.000	
West North Central-East North Central	−0.00073	−0.00282	0.00137	0.964	
Northwest-Northeast	−0.00078	−0.00281	0.00125	0.937	
South-Northeast	0.00174	0.00015	0.00332	0.023	*
Southeast-Northeast	0.00218	0.00059	0.00376	0.002	**
Southwest-Northeast	−0.00088	−0.00270	0.00094	0.808	
West-Northeast	−0.00048	−0.00288	0.00192	0.999	
West North Central-Northeast	−0.00128	−0.00296	0.00041	0.267	
South-Northwest	0.00252	0.00031	0.00472	0.015	*
Southeast-Northwest	0.00296	0.00075	0.00516	0.002	**
Southwest-Northwest	−0.00010	−0.00248	0.00228	1.000	
West-Northwest	0.00030	−0.00255	0.00315	1.000	
West North Central-Northwest	−0.00050	−0.00278	0.00178	0.998	
Southeast-South	0.00044	−0.00136	0.00224	0.996	
Southwest-South	−0.00262	−0.00463	−0.00060	0.004	**
West-South	−0.00221	−0.00476	0.00034	0.134	
West North Central-South	−0.00301	−0.00491	−0.00112	<0.001	***
Southwest-Southeast	−0.00306	−0.00507	−0.00104	<0.001	***
West-Southeast	−0.00266	−0.00520	−0.00011	0.036	*
West North Central-Southeast	−0.00346	−0.00535	−0.00157	0.000	***
West-Southwest	0.00040	−0.00230	0.00311	1.000	
West North Central-Southwest	−0.00040	−0.00249	0.00170	0.999	
West North Central-West	−0.00080	−0.00341	0.00181	0.983	

Note. Significance codes: 0 "***" 0.001 "**" 0.01 "*" 0.05 "." 0.1 " " 1. The differences in mean breakpoints between pairwise combinations, lower and upper limits of the 95% confidence interval, as well as the statistical significance of the comparisons are listed.

that the country's more tropical locales, such as Florida and Hawaii, had higher cross-seasonal transmission and lower seasonal transmission. This may explain the low incidence values seen for peak weeks in our analysis for Florida and the more gradual increases in slope as the influenza seasons progress in the South and Southeast when compared with the West coast of the country where there are sharp increases in slope at humidity levels lower than the breakpoint (Figure 2). Generally, our results are in agreement with the suggestion that there is a regional or localized trend to the influenza-climate interaction. This finding is important as it could ultimately lead to an opportunity for more generalized regional predictions in addition to more localized state predictions. Identifying these regional transmission patterns could better inform public health campaigns and the distribution bulletins about increased influenza activity.

Further work is needed to determine whether the trends seen in this analysis are influenced by population characteristics or additional underlying climatic conditions. Although there is increasing evidence for the impacts of local climate (Barreca & Shimshack, 2012; Dalziel et al., 2018; Shaman et al., 2010; Soebiyanto & Kiang, 2014; Tamerius et al., 2019; Towers et al., 2013), interdisciplinary research has also shown network and mobility functions (Brownstein et al., 2006; Chao et al., 2010; Gao et al., 2015; Grais & Ellis, 2004; Maliszewski & Wei, 2011; Pei et al., 2018), demographics (Chitnis et al., 2010; Gounder et al., 2014; Kwan-Ghett et al., 2009; Placzek & Madoff, 2014; Suryaprasad et al., 2013; Thompson et al., 2011; Wegner & Naumova, 2011), antigenic characteristics (Du et al., 2017; Towers et al., 2013), as well as socioeconomic status (Chandrasekhar et al., 2017; Hadler et al., 2016; Kumar et al., 2015; Ponnambalam et al., 2011; Sloan et al., 2015; Tam et al., 2014) impact our vulnerability to contracting influenza, our prevention behaviors, and our perception of risk. Additional interdisciplinary work, similar to that of Chattopadhyay et al. (2018), is needed to parse out the complex, non-linear transmission dynamics of the timing, magnitude, and spatial distribution of influenza outbreaks, which are not addressed by the regression framework used in this analysis. Additionally, more flexible, polynomial regressions may improve upon the results presented here. Future studies should also consider the spatial scale at which this analysis may be applicable, as another limitation of this study is its use of data aggregated at the state-level. State-level data, particularly for humidity, can not address intrastate variability in environmental conditions.

Results from this study improve our understanding of the significance of humidity in the transmission of influenza. They also reinforce the need for local and regional conditions to be considered in this relationship. Understanding the variations in this interaction at multiple levels of spatial and temporal resolution, as well as for varying locales, will help researchers to produce more accurate forecasts of seasonal influenza onset and provide health officials with better information prior to outbreaks.

Conflict of Interest

The authors declare no conflicts of interest relevant to this study.

Data Availability Statement

More information about AIRS and how to download its data products, including those used in this study (AIRS Science Team/Joao Teixeira, 2013) can be found on the AIRS mission homepage (https://airs.jpl.nasa.gov/data/get-data/standard-data/). Archived GFT data can be found through Google's Public Data Explorer in Google, 2015 (https://www.google.com/publicdata/explore?ds=z3bsqef7ki44ac_&ctype=l&met_y=flu_index).

Acknowledgments
The authors would like to acknowledge and thank the anonymous reviewer of this analysis for their constructive feedback. Part of this research was carried out at the Jet Propulsion Laboratory, California Institute of Technology, under a contract with the National Aeronautics and Space Administration.

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