A County Level Cross-Over Approach to Examining Weather Prior to Influenza Surges: 2003 Pennsylvania H3N2
V Dato

Citation

Abstract
This paper utilizes a county-level cross over approach to examine weather conditions during a hazard period just before an influenza spike and a control period just prior to the hazard period where most other conditions – population immunity, circulation of viral strains, latitude, travel were the same or similar. For the seven counties with a December spike, temperatures and dew points just above freezing were more likely to be seen in this hazard period (days 1 through 3) then in the control period (days 4 through 8). Two counties with a November surge were warmer in the control period with temperatures as high as an average of 12.6 degrees C, nevertheless the temperatures and dew points seen during the hazard period in the November spike counties are very similar to the December spike counties. Other recent studies also support the plausibility of optimal influenza transmission at temperatures just above freezing.

INTRODUCTION
Although it is well known that influenza mortality surges at varying times mostly during winter [1] the factors responsible for this are not fully understand [1] and the timing cannot reliably be predicted. Predicting the time of a surge in influenza is important for the timely implementation of preventive control measures.

A number of factors play a role in the timing of influenza surges including population immunity (through immunization or prior infection), domestic airline travel over Thanksgiving[4], international airline travel in September[4], circulating viral clades [5,6], seasonal factors [3] and latitude [7]. None of these predict the time of the surge.

In late November and December of 2003, the US experienced an outbreak of influenza A (H3N2) [8,9]. In terms of mortality the 2003-2004 season was the most severe between the 2001-2002[4] season and the 2006-2007 season[10] and the peak in mortality surpassed even the 2007-2008 season[11].

The Real-time Outbreak and Disease Surveillance (RODS) system[12] was functional in many Pennsylvanian hospitals by October 2003. The system monitors the chief complaints provided by individuals upon admission to emergency rooms and parses them into syndromes. The constitutional syndrome includes complaints such as fever, flu, congestion, weakness, chills, and dizziness and has been shown to correlate with influenza laboratory reporting (Personal communication - T.H. Chen 10/24/2007). RODS provided an ideal tool to determine the beginning of an influenza surge in individual counties.

Method
A case cross-over design was successfully used by Fisman et al to demonstrate the relationship of legionellosis cases with humidity 6 to 10 days earlier. [13] This paper utilizes a similar approach to examine weather conditions during a hazard period just before an H3N2 influenza spike (as determined by the RODS constitutional syndrome) and a control period (the days prior to the hazard period where most other conditions – population immunity, circulation of viral strains, latitude, travel were the same or similar but which did not result in a spike).

METHODS
RODS normalized constitutional graphs were plotted for all 67 counties in Pennsylvania for the 2003-2004 influenza season. Only ten counties had sufficient resident chief complaints in the system to create a credible graph. (Other counties’ populations were extremely small or the dominant hospitals were not participating in the system as of...
November 2003). The nine counties with a spike which met the RODS moving average algorithm threshold of 4.08 are shown in Table 1. Allegheny County’s (containing the city of Pittsburgh) chart is shown (Figure 1)

Table 1. Counties with a spike which met the RODS moving average algorithm threshold of 4.08

<table>
<thead>
<tr>
<th>County</th>
<th>Date of Spike</th>
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<tbody>
<tr>
<td>Allegheny</td>
<td>November 26</td>
</tr>
<tr>
<td>Blair</td>
<td>November 26</td>
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<tr>
<td>Cambria</td>
<td>November 26</td>
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<tr>
<td>Clearfield</td>
<td>November 26</td>
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<td>Dauphin</td>
<td>November 26</td>
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<td>Erie</td>
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<td>Lackawanna</td>
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<tr>
<td>Montgomery</td>
<td>November 26</td>
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<tr>
<td>Washington</td>
<td>November 26</td>
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Hourly weather data including dew point, temperature and cloud coverage was obtained from the National Climatic Data System [14] for the nine counties (Allegheny, Blair, Cambria, Clearfield, Dauphin, Erie Lackawanna, Montgomery and Washington) that had both a first flu spike in November or December and a weather station in or near the border of the county. (The most central weather station was chosen for Allegheny, the only county with two stations.) Although the data set is called the hourly data, there were sometimes two or three measurements (at different fractions of an hour) in the data set for a given hour.

Epi Info 3.4 was used for graphs and analysis. Only counties with December spikes were used in the cross over analysis because of predicted confounding from Thanksgiving for the two counties with November spikes. Days 1, 2 and 3 before the spike were chosen as the weather hazard period. The control period was chosen as days 4, 5, 6, 7, and 8 before a spike. Weather conditions during hours when individuals are unlikely to be outside (Monday through Friday before 7 AM; Saturday, Sunday and Thanksgiving before 9 AM; Sunday through Thursday after 10 PM) were excluded to eliminate the late evening and early morning hours when few individuals could be infected even if airborne viral survival were possible.

RESULTS

Figure 2 is a scatter plot comparing temperature and dew point on the 8 days before an influenza spike.

For the seven counties selected for the cross over analysis, the mean temperature on hazard days (days 1, 2 and 3 after the spike) was 1.3 degrees Celsius with a standard deviation of 6.5 and the mean temperature on control days was -2.4 C with a standard deviation of 2.9. (Kruskal-Wallis H p<0.005). The mean temperature for the counties by day is available in Table 2. The mean temperature for the counties by day is available in Table 2. The mean dew point on hazard days was a mean of -2.5 with a standard deviation of 6.8 significantly higher than the mean on control days of -6.6 with a standard deviation of 3.2 (Kruskal-Wallis H p<0.005)

Table 2 contains the mean temperatures for all days for the 7 counties used in the cross-over analysis as well as the two counties with November spikes. Both of the November spikes occurred during the Thanksgiving weekend. These two counties were not included in the cross-over analysis because November 26th, the traditional largest travel day of the year would have been in either the control or hazard period. Nevertheless the temperatures and dew points seen during the hazard period in the two November spike counties are very similar to the December spike counties. (Figure 2). Of the nine counties only Cambria did not have temperatures above 3°C with dew points at 0 degrees or higher in the first, second or third day prior to an influenza spike. Cambria had similar temperatures on the day of the spike.

DISCUSSION

In order to find weather conditions permissive for airborne transmission of influenza, this study looked at the temperature and dew point in the three days just prior to a surge of influenza (as indicated by a significant increase in emergency room visits of individuals with chief complaints consistent with influenza). Temperatures and dew points just above freezing were more likely to be seen in this hazard period then in the control period days 4 through 8.

Temperatures that were just above freezing in the hazard period were not the a priori hypothesis. A lower temperature was expected because of the winter season association of influenza. A lower relative humidity was expected based upon historical studies documenting airborne transmission at low relative humidity [15,16,17]. However, in hindsight these studies were all indoors and at higher temperatures.

Recent studies support the plausibility of optimal transmission at temperatures just above freezing. Lowen et. al [18] used guinea pigs to study influenza transmission. They found that transmission at 5 degrees C (41 degrees F) was efficient with 50 % transmission at a relative humidity of 80% (dew point equivalent of 2 degrees). These conditions are similar to conditions seen in the hazard period but not in the control period But they also found that transmission was more efficient (100%) at 35 and 50 percent relative humidity
(dew point equivalent of -9 and -5 degrees C respectively) a range that occurred to a limited extent in our control period without triggering a spike.

Polozov et.al \(^1\) studied the phospholipids layer of the influenza virus. They found that ordered fraction of lipids increased as the temperature decreased until approximately 1 degree C. They suggest that “lipid ordering may contribute to viral stability at lower temperatures, which has recently been found to be critical for airborne transmission.”

These recent studies might explain why airborne transmission was possible at temperatures just above freezing. They do not explain why airborne transmission did not occur with the lower temperatures seen in the counties with December surges during the control period.

Viral stability is not sufficient to guarantee airborne transmission. Virus must also retain the ability to infect the human. Temperatures below freezing may adversely affect the ability of the influenza virus to infect humans either because of structural changes from too little water or from water molecules in the solid state.

Despite the hundreds of data points, this is a study of just 7 counties all during the same year when an influenza A H3N2 virus was predominant. Weather conditions found during the hazard period may be correlated with some other factor (such as increased viral shedding \(p_i\)) which is the true cause of a flu spike. It is also possible that this is a statistical aberration and there is no true relationship between hourly weather conditions and flu spikes. Even if these combinations of temperature and dew point are permissive for airborne transmission for the 2003 circulating strain, the 2003 circulating strain may not be representative of other strains.

Nevertheless, the question of which weather conditions if any are permissive of airborne transmission is important and worthy of additional epidemiologic and experimental research. If specific zones of transmission are found, flu days (or hours) could join ozone action days as times when outdoor activity patterns are changed for the short term goal of preventing morbidity and mortality.

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References

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