Associations of Seasonal Influenza Activity with Meteorological Parameters in Temperate and Subtropical Climates: Germany, Israel, Slovenia and Spain

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Seasonal Influenza

- Respiratory illness caused by influenza viruses
  - Influenza virus types: A, B and C
- Influenza viruses undergo frequent evolutionary changes
  - *Antigenic drift* results in a strain that is not recognizable by the body, may lead to a loss of immunity or vaccine mismatch
  - *Antigenic shift* results in a novel strain for human, causing pandemic
- Transmission: aerosol-borne, direct contact with infected, contact with contaminated objects
- Vaccination is the most effective method for prevention
Spatiotemporal Pattern

- Varies with latitude
- Temperate regions
  - Distinct annual oscillation with winter peak
- Tropics
  - Less distinct seasonality
  - Often more than 1 peak in a year
- Southward migration in Brazil from low-population area near equator to dense area with temperate climate [Alonso et al. 2007, Am. J Epi]
- Role of environmental and climatic factors
Environmental & Sociological Factors Affecting Human Influenza Transmissions

Change in Transmission with Increase in Factor

<table>
<thead>
<tr>
<th>Virus SURVIVORSHIP</th>
<th>Temperature ↓</th>
<th>Humidity ↓</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vapor pressure ↓</td>
<td>Solar irradiance ↓</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Host SUSCEPTIBILITY</th>
<th>Sunlight exposure ↓ ↓</th>
<th>Nutrition varies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Previous infections ↓ ↓</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Transmission EFFICIENCY</th>
<th>Temperature ↓ ↓</th>
<th>Humidity varies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vapor pressure ↓ ↓</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Precipitation ↑ ↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ENSO ↑ ↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Air travel ↑ ↑</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Holidays ↑ ↑</td>
<td></td>
</tr>
</tbody>
</table>

Biological Evidence
Empirical Evidence

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Study Objective

- Identify meteorological parameters associated with influenza activity

- Understanding influenza seasonality provides a basis on how pandemic influenza may behave

- Develop capabilities for short-term forecast of influenza activity as warranted by meteorological condition
Study Areas
Köppen-Geiger Climate Classification

- **Cfb**: Maritime Temperate, or Oceanic
  - Narrow annual temperature range
  - Wet all year (lacks dry season)

- **Csa**: Dry-Summer Subtropical, or Mediterranean
  - Summer month precipitation < 30 mm
  - $Csa$: Hot summer, $T > 22^\circ$
  - $Csb$: Warm summer, $T < 22^\circ$

- **BSH**: Hot Semi-Arid, or Steppe
  - Annual temperature $\geq 18^\circ$C

- **BWh**: Hot Desert, or Arid
  - Annual precipitation < 250 mm

10/25/2013
Meteorological Data

NASA’s assimilated data

With Giovanni’s data sets and user friendly analysis tools available on the World Wide Web to the whole world, it is possible for an increasing and broader audience to address issues in earth science without having a detailed knowledge of digital image processing and programming techniques - a Giovanni user.

- It is a hands-on tutorial.
- Bring your own laptop and learn it on the spot.
- Start your own project.
Brief Description on Humidity

- Measure of water content in the air
- Previous studies indicated
  - Bimodal relationship between influenza activity and relative humidity
  - Absolute humidity is a better predictor for influenza than relative humidity
- Relative Humidity
  Amount of water vapor in the air compared to the maximum amount of vapor that can exist in the air at the given temperature
- Absolute Humidity
  Mass of water vapor per unite volume of air
- Specific Humidity
  Ratio between mass of water vapor and the mass of air

[Lowens et al., 2007]
Influenza Data

- Sentinel Surveillance
  Robert Koch Institute, Berlin, Germany
  Israel Center for Disease Control, Israel
  National Institute of Public Health Slovenia, Ljubljana, Slovenia
  Health Directorate, Health Department, Valladolid, Spain

- Clinical Data
  - Influenza-Like-Illness (ILI), and/or Acute Respiratory Infection (ARI)
  - Case definition varies by country
  - ILI case definition recommended by WHO: acute respiratory illness with onset (the last 7 days) of fever (≥38°C) AND cough

- Virological Data (Laboratory test)
  - ILI or SARI samples tested for influenza virus
Influenza Data

Weekly Influenza activity was estimated using:

\[ y_t = \frac{\text{Influenza-positive samples}}{\text{Number of samples tested}} \times \frac{\text{ILI}}{\text{Population}} \]

- For Berlin, influenza activity was estimated from ARI data
Regression Model

Generalized Additive Model (GAM)

Estimated influenza activity at week \( t \) (\( y_t \)):

\[
\ln(y_t) = \beta_0 + s(\ln(y_{t-2})) + s(sh_{1-4}) + s(rf_{1-4}) + s(srad_{1-4})
\]

- \( y_t \): Estimated influenza activity at week \( t \) calculated from
- \( \beta_0 \): Intercept
- \( s(x) \): Smoothed spline function of independent variable, \( x \)
- \( sh_{1-4} \): Specific humidity (in g/kg) averaged from the previous 4 weeks of \( t \)
- \( rf_{1-4} \): Precipitation (in mm) averaged from the previous 4 weeks of \( t \)
- \( srad_{1-4} \): Solar radiation (in W/m\(^2\)) averaged from the previous 4 weeks of \( t \)

- Temperature was excluded due to high correlation with specific humidity and solar radiation
Modeled Influenza Activity

Training data (year < 2010)

- All observations except for the final year was used to parameterize (or train) the model
- Excluded data during H1N1 pandemic year (May 2009 to May 2010)
- Model was trained individually to each area
- Inputs:
  - Specific humidity, rainfall and solar radiation (averaged over the previous 4 weeks)
  - Previous 1 or 2 weeks of influenza activity
Modeled Influenza Activity

Predicted 2010/2011 Season

- The models closely followed the rise and fall of the epidemic curves in 6 out of the 9 study areas
- Peak timing could be predicted within 3 weeks of the observation (excluding Ljubljana)
  - Accurate prediction in Jerusalem and South
- Underestimated the amplitude of influenza activity in most areas
**Model Performance**

### Goodness of fit

- **% Deviance Explained**
  - Berlin
  - Ljubljana
  - Castilla Y Leon
  - North
  - Haifa
  - Center
  - Tel Aviv
  - Jerusalem
  - South

<table>
<thead>
<tr>
<th>Location</th>
<th>Adjusted R-squared</th>
<th>% Deviance Explained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berlin</td>
<td>0.8</td>
<td>100</td>
</tr>
<tr>
<td>Ljubljana</td>
<td>0.5</td>
<td>63%</td>
</tr>
<tr>
<td>Castilla Y Leon</td>
<td>0.7</td>
<td>50%</td>
</tr>
<tr>
<td>North</td>
<td>0.4</td>
<td>26%</td>
</tr>
<tr>
<td>Haifa</td>
<td>0.6</td>
<td>38%</td>
</tr>
<tr>
<td>Center</td>
<td>0.7</td>
<td>47%</td>
</tr>
<tr>
<td>Tel Aviv</td>
<td>0.9</td>
<td>88%</td>
</tr>
<tr>
<td>Jerusalem</td>
<td>0.8</td>
<td>75%</td>
</tr>
<tr>
<td>South</td>
<td>0.6</td>
<td>25%</td>
</tr>
</tbody>
</table>

### Accuracy of Peak Week Prediction

- Adjusted R2 ranged from 0.26 to 0.8 (mean = 0.55)
- 63% to 88% of deviance explained
- Predicted peak timing for training data was within 0 to 6 weeks of observation
- Lower model performance in Ljubljana and Haifa, where total number of specimens tested were lower as well

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Meteorological Determinants

- Specific humidity is significantly associated with influenza activity in ALL regions
  - Inversed linear relationship
  - Highest contributor among meteorological variables (except for Spain)
- Influenza activity association with rainfall and solar radiation is region-specific. In general:
  - Nonlinear relationship with rainfall; inversed linear relationship with solar radiation

**Meteorological variables effective degrees of freedom**

(Effective number of parameters of the cubic spline smoother. A value of 1 typically indicates linear relationship)

<table>
<thead>
<tr>
<th></th>
<th>Specific Humidity</th>
<th>Rainfall</th>
<th>Solar Radiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berlin</td>
<td>1.66*</td>
<td>1</td>
<td>2.13*</td>
</tr>
<tr>
<td>Ljubljana</td>
<td>1*</td>
<td>1.35*</td>
<td>1</td>
</tr>
<tr>
<td>Castilla y León</td>
<td>1*</td>
<td>3.89*</td>
<td>2.57*</td>
</tr>
<tr>
<td>North</td>
<td>1*</td>
<td>2.95*</td>
<td>1*</td>
</tr>
<tr>
<td>Haifa</td>
<td>1*</td>
<td>1.02</td>
<td>1.68</td>
</tr>
<tr>
<td>Tel Aviv</td>
<td>1*</td>
<td>2.65*</td>
<td>1*</td>
</tr>
<tr>
<td>Center</td>
<td>1*</td>
<td>1</td>
<td>1.87*</td>
</tr>
<tr>
<td>Jerusalem</td>
<td>1*</td>
<td>2.18*</td>
<td>2.95*</td>
</tr>
<tr>
<td>South</td>
<td>1*</td>
<td>2.88*</td>
<td>1.89</td>
</tr>
</tbody>
</table>

* Indicates significance (p-value < 0.05)

**Meteorological variables Contribution to the model**

(Calculated based on change in the explained deviance when the specified variable was removed)

Smoothed function for each meteorological variable
Improvement to Base Model

- Model determinants
  - Base model: Previous week(s) influenza activity
  - Full model: Previous week(s) influenza activity + meteorological variables
- Performance of full model is better than the base model as measured by Akaike’s Information Criterion (AIC)

<table>
<thead>
<tr>
<th>City</th>
<th>Adj. R²</th>
<th>% Dev. Explained</th>
<th>AIC</th>
<th>Adj. R²</th>
<th>% Dev. Explained</th>
<th>AIC</th>
<th>% AIC Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berlin</td>
<td>0.569</td>
<td>61</td>
<td>57708</td>
<td>0.743</td>
<td>78</td>
<td>32506</td>
<td>43.67</td>
</tr>
<tr>
<td>Ljubljana</td>
<td>0.111</td>
<td>23</td>
<td>1221</td>
<td>0.256</td>
<td>63</td>
<td>620</td>
<td>49.22</td>
</tr>
<tr>
<td>Castilla y León</td>
<td>0.441</td>
<td>57</td>
<td>25508</td>
<td>0.568</td>
<td>72</td>
<td>16926</td>
<td>33.64</td>
</tr>
<tr>
<td>North</td>
<td>0.183</td>
<td>30</td>
<td>3391</td>
<td>0.445</td>
<td>74</td>
<td>1350</td>
<td>60.19</td>
</tr>
<tr>
<td>Haifa</td>
<td>0.264</td>
<td>48</td>
<td>1932</td>
<td>0.375</td>
<td>66</td>
<td>1298</td>
<td>32.82</td>
</tr>
<tr>
<td>Tel Aviv</td>
<td>0.344</td>
<td>51</td>
<td>3834</td>
<td>0.597</td>
<td>79</td>
<td>1762</td>
<td>54.04</td>
</tr>
<tr>
<td>Center</td>
<td>0.56</td>
<td>76</td>
<td>1956</td>
<td>0.616</td>
<td>85</td>
<td>1306</td>
<td>33.23</td>
</tr>
<tr>
<td>Jerusalem</td>
<td>0.688</td>
<td>82</td>
<td>1511</td>
<td>0.802</td>
<td>90</td>
<td>980</td>
<td>35.14</td>
</tr>
<tr>
<td>South</td>
<td>0.499</td>
<td>62</td>
<td>2401</td>
<td>0.562</td>
<td>79</td>
<td>1431</td>
<td>40.4</td>
</tr>
</tbody>
</table>

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Conclusion

- Significant association between influenza activity and specific humidity across temperate and subtropical climates
- Associations with precipitation and solar radiation were region-specific
- Results are consistent with other studies in the temperate regions
- Adding meteorological covariates improved historical data-based model performance
  - Could be used to enhance influenza surveillance system
  - Influenza activity can be predicted 2 weeks ahead
Acknowledgments

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