Predicting Seasonal Influenza Hospitalizations using Simple Statistical Models

Kevin W. McConeghy, Jason R. Gantenberg, Andrew R. Zullo, Chanelle J. Howe, …

Compiled: 2019-07-29

Purpose

To determine which of a set of simple candidate statistical models (CSM) most closely fits a series of hypothetical influenza hospitalization curves (HIHC), stratified by season severity (Centers for Disease Control and Prevention, 2016).

Which of these simple CSMs would provide the best severity forecast at the beginning of the flu season (i.e., epiweek 40) based purely on fit to the HIHCs described below?

Subquestion: Which model best predicts the proportion of flu-attributable hospitalizations?

General approach

1. Fit a quadratic trend filter model (Brooks et al., 2015) to FluSurv-NET hospitalization data for the seasons 2003–2004 through 2017–2018, based in part on the approach described by Brooks et al. (Brooks et al., 2015).
2. Simulate 3,000 HIHCs using the empirical Bayes model as a "generative model".
3. Stratify these HIHCs into groups representing High/Moderate and Mild severity HIHCs, based on the CDC's categorization (Biggerstaff et al., 2018; Centers for Disease Control and Prevention, 2018).
4. Fit each CSM within each severity stratum and test for goodness of fit. Systematically alter the functional form of epiweek indicators as in Wang et al.'s study of influenza mortality (Wang et al., 2012).

Forecasting targets

All weeks will be specified using the *MMWR* Week convention (Centers for Disease Control and Prevention, a):

1. Peak week
2. Peak number of hospitalizations
3. Total hospitalizations

These targets follow in part from (Brooks et al., 2015).

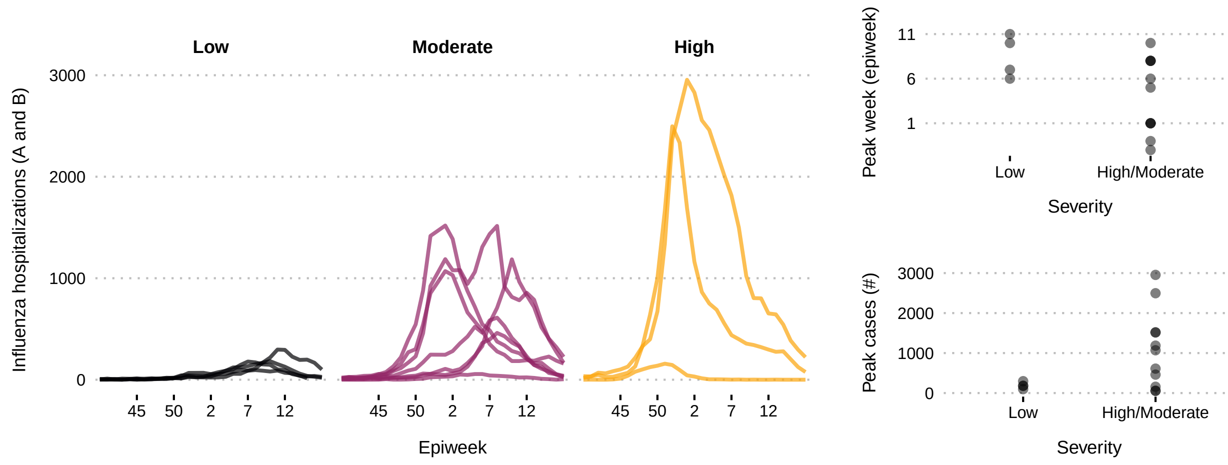

Figure 1: Empirical hospitalization curves, peak weeks, and peak number of cases — 2003–2017 (Source: FluSurv-NET, CDC). Data excludes 2009–2010 pandemic influenza season and 2017–2018 due to no official severity designation.

Curve fitting and simulation

We will simulate HIHCs using a modified version of the curve-fitting approach described by Brooks et al. (Brooks et al., 2015).

First, we fit a quadratic trend filter to historical hospitalization curves released by the CDC (beginning with the 2003–2004 season), using the R package `glmgen` (Brooks et al., 2015; Centers for Disease Control and Prevention, 2016). This model is fit within flu severity group (Mild, High/Moderate).

For each season s and each week i, Brooks et al. conceptualize a seasonal influenza curve as some function plus noise:

$$y_i^s = f^s(i) + \epsilon_i^s, \epsilon \sim N(0, \tau^s),$$

where

$$f^s(i) = b + \frac{\theta - b}{\max_j f(j) - b}\left[f\left(\frac{i-u}{v} + \underset{f}{\text{arg max } j}(j)\right) - b\right]$$

and b represents a seasonal "baseline" increase in cases which is used to designate officially the week of season onset.

To account for natural variation in b across flu seasons, we will sweep a plausible range of values (to be determined) during curve simulation. [1]

Based on fitting the quadratic trend filtering model to empirical data (i.e., historical CDC flu hospitalization data), we estimate error τ^s:

$$(\hat{\tau}^s)^2 = \underset{i}{\text{avg}}\left[y_i^s - \hat{f}^s(i)\right]^2$$

and then sample from the model, introducing noise for each weekly observation based this estimate of τ^2.

[1] In Brook et al., the authors use their framework to forecast a current flu season, where b represents the current season's epidemic threshold. Because we are interested in model fitting, we will sample from a range of plausible "hospitalization thresholds" to account for seasonal variation.

Parameters in quadratic trend filtering model

The quadratic trend filter is fit using the following sampling scheme for each parameter represented in the model for hospitalization count (y_i^s) at each week. Note that all equations are either adapted from or appear in (Brooks et al., 2015).

$$\langle f, o, \nu, \theta, \mu \rangle$$

Shape (f)

$$f \sim U\{\hat{f} : \text{historical season } s\}$$

Noise (σ)

$$\sigma \sim U\{\hat{\tau}^s : \text{historical season } s\}$$

Peak height (θ)

$$\theta \sim U\left[\theta_m, \theta_M\right]$$

Results in the following curve:

$$f_3(i) = f_2(i - \mu + \text{arg max}_j f_2(j))$$

Pacing (ν)

Curve-stretching around peak week:

$$\nu \sim U[0.75, 1.25]$$

Results in following curve:

$$f_4(i) = f_3\left(\frac{i - \text{arg max}_j\ f_3(j)}{\nu} + \text{arg max}_j\ f_3(j)\right)$$

Candidate models

Incidence-rate difference models

- Generate a set of predicted flu-related hospitalizations based on a standard incidence rate difference model typically used to model flu cases. Implement in flumodelr based on (Izurieta et al., 2000; Thompson et al., 2009).
- Thresholds: 0.1 and 0.15 as in (Thompson et al., 2009).

Serfling model (least squares)

Modified from (McConeghy et al.):

$$Y = \beta_0\alpha + \beta_1 t + \beta_r X_r + ... + \beta_p cos\left(\frac{2\pi t}{52}\right) + \beta_q sin\left(\frac{2\pi t}{52}\right)$$

Where t = time (epiweek), subscript r denotes a vector of β coefficients and variables, and subscripts p and q take on particular numbers based on the length of r.

Modified Serfling model

Modified (McConeghy et al.):

$$y = \alpha_0 + \beta_1 t + \beta_2 Flu_t + \beta_p X_p + ... + sin\left(\frac{2\pi t}{period}\right) + cos\left(\frac{2\pi t}{period}\right) + u$$

Where t = time (epiweek) and subscript p denotes a vector of $beta$ coefficients and variables.

Generalized additive model (Prophet)

This model will be implemented using Facebook's R package *prophet* (Taylor and Letham, 2017). Exact specifications TBD upon consultation with Kevin.

Model terms

The following model terms will be entered into the vector of covariates considered for each model (see Serfling and modified Serfling equations):

a) Cyclical terms (Serfling, Fourier, etc.)

b) Historical (empirical) flu hospitalizations

c) Historical data on viral activity (NREVSS), outpatient surveillance (ILI-Net)

d) Average weekly temperature

e) Climate factors (e.g., prior summer temperatures)

f) Lags and leads of c or d

g) Indicators for weeks of Thanksgiving and/or Christmas (Brooks et al., 2015; Taylor and Letham, 2017)

Goodness of fit

- Root mean squared error (RMSE)
- Bayesian information criterion (BIC)
- Relative bias
- Cross-validation, sample-splitting?

Sensitivity analysis

Challenge

The composition of institutions reflected in the FluSurv-NET has changed over time (Centers for Disease Control and Prevention, b; Kandula et al., 2019), meaning the FluSurv-NET estimates for influenza-related hospitalizations may not be comparable across time.

Response

Redo the analysis three times: one for each set of years in which the same participating institutions reported flu data to CDC. See (Centers for Disease Control and Prevention, b) for more information.

Limitations

Brooks et al. showed that their empirical Bayes model improved upon standard lagged CDC predictions for several forecasting targets of the overall influenza curves (season onset, peak week, peak rate/count, duration of season). In adapting their approach to hospitalizations, we should ensure we can achieve similar accuracy.

References

Matthew Biggerstaff, Krista Kniss, Daniel B Jernigan, Lynnette Brammer, Joseph Bresee, Shikha Garg, Erin Burns, and Carrie Reed. Systematic assessment of multiple routine and near Real-Time indicators to classify the severity of influenza seasons and pandemics in the united states, 2003-2004 through 2015-2016. *Am. J. Epidemiol.*, 187(5):1040–1050, May 2018. ISSN 0002-9262, 1476-6256. DOI: 10.1093/aje/kwx334.

Logan C Brooks, David C Farrow, Sangwon Hyun, Ryan J Tibshirani, and Roni Rosenfeld. Flexible modeling of epidemics with an empirical bayes framework. *PLoS Comput. Biol.*, 11(8):e1004382, August 2015. ISSN 1553-734X, 1553-7358. DOI: 10.1371/journal.pcbi.1004382.

Centers for Disease Control and Prevention. MMWR week overview. `https://wwwn.cdc.gov/nndss/document/MMWR_Week_overview.pdf`, a. Accessed: 2019-7-9.

Centers for Disease Control and Prevention. Flu view phase 3 quick reference guide, b.

Centers for Disease Control and Prevention. Laboratory-confirmed influenza hospitalizations. `https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html`, 2016. Accessed: 2019-7-1.

Centers for Disease Control and Prevention. How CDC classifies flu severity. `https://www.cdc.gov/flu/about/classifies-flu-severity.htm`, September 2018. Accessed: 2019-7-9.

H S Izurieta, W W Thompson, P Kramarz, D K Shay, R L Davis, F DeStefano, S Black, H Shinefield, and K Fukuda. Influenza and the rates of hospitalization for respiratory disease among infants and young children. *N. Engl. J. Med.*, 342(4):232–239, January 2000. ISSN 0028-4793. DOI: 10.1056/NEJM200001273420402.

Sasikiran Kandula, Sen Pei, and Jeffrey Shaman. Improved forecasts of influenza-associated hospitalization rates with google search trends. *J. R. Soc. Interface*, 16(155):20190080, June 2019. ISSN 1742-5689, 1742-5662. DOI: 10.1098/rsif.2019.0080.

Kevin W McConeghy, Rob van Aalst, Andrew R Zullo, and Nina Joyce. An R package for estimating attributable influenza morbidity and mortality. https://kmcconeghy.github.io/flumodelr/. Accessed: 2019-7-1.

Sean J Taylor and Benjamin Letham. Forecasting at scale. September 2017.

William W Thompson, Eric Weintraub, Praveen Dhankhar, Po-Yung Cheng, Lynnette Brammer, Martin I Meltzer, Joseph S Bresee, and David K Shay. Estimates of US influenza-associated deaths made using four different methods. *Influenza Other Respi. Viruses*, 3(1):37–49, January 2009. ISSN 1750-2640, 1750-2659. DOI: 10.1111/j.1750-2659.2009.00073.x.

Xi-Ling Wang, Lin Yang, King-Pan Chan, Susan S Chiu, Kwok-Hung Chan, J S Malik Peiris, and Chit-Ming Wong. Model selection in time series studies of influenza-associated mortality. *PLoS One*, 7(6):e39423, June 2012. ISSN 1932-6203. DOI: 10.1371/journal.pone.0039423.