Predicting Seasonal Influenza Hospitalizations using Simple Statistical Models

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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 sets of HIHCs, based on the CDC's categorization (Biggerstaff et al., 2018; Centers for Disease Control and Prevention, 2018).

4. Fit each CSM to each severity set and test for goodness of fit. Systematically alter the functional form of epiweek independent predictors 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. Season onset week
2. Peak week
3. Peak count
4. Total hospitalization counts
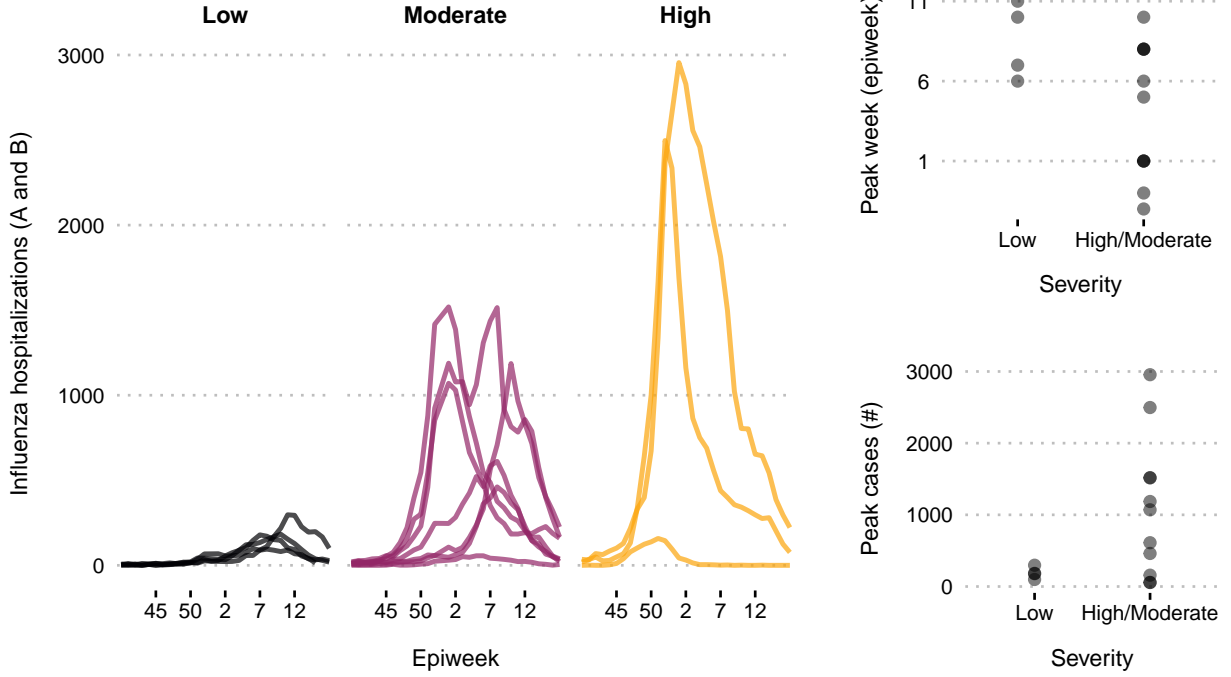
These targets follow from (Brooks et al., 2015).

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.

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 as 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 (Low, 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

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

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:

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

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

Parameters in quadratic trend filtering model

The quadratice 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:

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

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:

$$f_3(i) = f_2(i - \mu + \arg\max_j f_2(j))$$

Pacing (ν)

Curve-stretching around peak week:

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

Results in following curve:

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

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)

As presented in (McConeghy et al.):

$$Y = \beta_0\alpha + \beta_1 t + \beta_6 cos\left(\frac{2\pi t}{52}\right) + \beta_7 sin\left(\frac{2\pi t}{52}\right)$$

Modified Serfling model

As presented in (McConeghy et al.):

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

Generalized additive model (Prophet)

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

Seasonal - ARIMA (?)

Neural net (?) See *Forecast* package.

Model terms

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

b) Historical (empirical) flu hospitalizations

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

- Average weekly temperature

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

- Lags and leads of c or d

- 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.

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