Abstract

We investigate the potential for Electronic Health Records (EHR) to replace ILI as the target of forecasting. In comparison to ILI, EHR-derived signals can be available in near-real-time, can track lab-confirmed influenza, and are obtainable at a much finer geographic resolution than ILI. Through a retrospective study, we investigate the performance of current-week nowcasting for both ILI and EHR signals via the sensor fusion algorithm based on the Kalman filter, and show that the two data sources produce comparably accurate estimates.
1 Introduction

Seasonal influenza (flu) is one of the most common infectious disease worldwide. Estimates by the World Health Organization (WHO) indicate that each yearly epidemic results in up to five million cases and approximately 290,000 to 600,000 deaths [16]. During the 2017–18 season, the United States Centers for Disease Control and Prevention (CDC) approximate that the flu factored in 900,000 hospitalizations and 80,000 deaths [2]. The annual occurrence of flu is also a substantial economic burden, and costs an estimated average of $11.2 billion [11, 2, 9].

One idealistic goal of flu forecasting is to create a decision-support system that informs hospitals and individuals about local flu intensities. The aim is to increase public awareness and preparedness, which can prevent illness and inform medicine allocations. Put more concretely, one can imagine a system that outputs current and short-term forecasts of local flu levels similar to how weather forecasts are available. This is a demanding task; forming such a system calls for real-time, local-level flu data that, in its current state, is inaccessible to the public. In this project, we explore the potential for electronic health records to produce a nearly-real-time system by benchmarking its predictive accuracy to the widely accepted standards via a state-of-the-art “nowcasting” (forecasting current-time) algorithm.

The current standard of flu levels used within the forecasting community is measured through incidents of influenza-like illnesses (ILI). This is considered the gold standard metric, and is provided by the CDC. ILI is monitored through a network of healthcare providers called the Outpatient Influenza-Like Illness Surveillance Program (ILINet), run by its National Center for Immunization and Respiratory Diseases (NCIRD) branch. ILINet consists of reports of patient visits for ILI from more than 2,800 providers reporting 39+ million visits every year. These reports are curated and publicly published each week with a 1 week delay.

Electronic health records (EHR) have long been considered as potential substitutes for these traditional flu surveillance systems [13, 5]. EHRs have many advantages; records have little or negligible lag and can measured at the (in the worst case) 5-digit zip-code. Moreover, electronic records typically contain clinical diagnosis codes rather than syndromic data, which is useful in informing resource allocations for hospitals. The primary drawback of EHR data, and a major reason for their lack of popularity, is that such data is proprietary and highly-restricted. In the hopes that such data would become more widely available, we study the predictive performance of using EHR signals as the ground truth for flu incidence, compared to the traditional measure of ILI.

Digital Surveillance In 2009, [Ginsberg et al.] [6] proposed an innovative search-query driven method to track flu levels in near real-time. Though initially promising, this system known as Google Flu Trends struggled to adapt to changing flu dynamics. Nonetheless, this work has inspired other research to consider digital sources as proxies to flu prevalence [8, 10, 17]. In particular, [Santillana et al.] [12] employed ensemble method combining traditional and digital sources, [Guo et al.] [7] proposed an ensemble penalized regression via bagging, and [Farrow] [5] constructed a “nowcasting” (current-time forecasting) system called sensor fusion, which draws from the Kalman filter. We base this analysis on [Farrow’s work].
Sensor fusion  Sensor fusion is a filtering method that fuses (combines) various “sensors” to make a stronger prediction. A sensor refers to a covariate trained to predict the response. Sensor fusion builds on a special case of the Kalman filter, which can be thought of as solving a tracking problem, but assumes no mechanistic model of the flu process. The structure of sensor fusion is reminiscent of ensemble methods [3], such as a stacked regression where the entire training data is used and without a non-negativity constraint. It has been shown that sensor fusion is identical to a special form of constrained regression. Our analysis will draw from these equalities.

In this report, we aim to check the feasibility in using EHR data as a ground truth measure of the current-time flu. To this end, we perform a retrospective simulation to nowcast flu levels using either ILI or EHR data as the response, and digital surveillance sources as the covariates. We first describe the construction of flu signals from the ILI and EHR datasets, as well as the curation of digital surveillance sources. We then give a background of the sensor fusion algorithm and Kalman filter, and state the useful equivalences. With these in place, we structure the study and give details on several issues and interpretations of our approach.

2 Description of Data

2.1 ILI-derived signals

Since 1997, the CDC has collected the reports of influenza-like illnesses (ILI) through its voluntary network ILINet. ILI is defined as a high temperature fever and a cough or sore throat that has not been attributed to a known cause other than influenza. Each week, reports of ILI are gathered and the counts are weighted by state populations to produce estimates of flu intensity at the national (1), regional (20), and state (50 plus District of Columbia) levels. The weighted estimate, wILI, is available for use after a 1-2 week reporting delay. Within the epidemiological forecasting community wILI is considered the gold standard indicator for flu levels in the US.

It is important to note that ILI is often revised due to incomplete reports. This can cause significant adjustments to previously published ILI counts, with values typically stabilizing after three weeks. Figure 1 shows the general shape of finalized weighted ILI visits.
2.2 EHR-derived signals

We compare ILI to a batch of EHRs received from a large private health insurance provider. The records contain daily historical counts of flu-related ICD (International Classification of Diseases) diagnosis codes spanning from January 1, 1993 to December 31, 2017. There are three measures contained in this dataset. Each consists of the number of ICD codes pertaining to three sets:

1. Influenza only codes (EHR\textsubscript{1}). Most commonly used in literature (alongside sets (2) and (3)) to show how a model might undercount flu activity.

2. Influenza or pneumonia (EHR\textsubscript{2}), a superset of EHR\textsubscript{1} that also includes the set of codes corresponding to pneumonia. This is a popular choice in literature to assess flu activity levels and burden estimation.

3. Influenza or pneumonia or influenza-like illness or acute respiratory infection codes (EHR\textsubscript{3}), a superset of EHR\textsubscript{2}. This measure is useful in assessing the burden of influenza.

The counts are divided by the total number of office visits, then weighted by state population. Figure 2 demonstrates the difference in scale among the three weighted measures. Noticeably, EHR\textsubscript{3} is much larger than both EHR\textsubscript{2} and EHR\textsubscript{1}, and is more variable. These nested code sets were selected to measure general influenza prevalence in different ways. Success in nowcasting EHR\textsubscript{1} or EHR\textsubscript{2} can be useful for targeting “true” flu prevalence, while accurate predictions of EHR\textsubscript{3} help hospital preparedness. We will consider the predictive performance across all three measures.

**Revision fairness** It is a bit unfair to directly compare ILI to EHR data since initial reports of ILI can be unstable, and are usually revised for at least three weeks. The private company releasing the EHRs did not inform us if the data had any revisions or instability issues. Because of this and in the effort of fairness, we make all of our comparisons to finalized ILI reports. For the purposes for this initial analysis, we aggregate the date into weeks, zip-codes to states, and age group to all. Though we lose much of the granular information that makes EHR advantageous, these adjustments make it comparable to ILI signal as defined by the CDC.
Relationship to ILI  As our goal is to estimate flu intensity, we check the relationship between the EHR measures and ILI (keeping in mind that ILI is not ground truth, though we treat it as such). Figure 3 visually demonstrates that EHR follows the general cyclic trend, but the scale is much different – wILI falls between the scales of EHR\(_2\) and EHR\(_3\). However, there is a systemic difference. Regressing wILI onto wILI is better than regressing wILI onto the various EHR signals, i.e. EHR is not simply a less noisy version of ILI. This implies there is potentially useful information in EHR that can be explored, even when the data is aggregated to the week-state granularity.

2.3 Digital surveillance sources
Digital surveillance data streams are (generally weak) signals of flu trends transmitted through online mediums. For example, individuals experiencing early symptoms of the flu might use a search engine to find more information about their symptoms, or post to social media. The corresponding data might then be the number of flu-related searches or hashtags for flu. There are several potential snags in taking this approach. For one, there may be false alarms–for example, a media spike for a flu vaccine may wrongly indicate an increase in flu levels. Another issue is that these signals can be easily overfit to seasonal indicators–e.g. basketball season. Thus, the system becomes a monitor for both the flu and winter season. These complications are accounted for when training the base predictors.

Throughout this report, we will refer to the raw data as sources, and the output predictions from

<table>
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<th>States</th>
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<td></td>
<td>✓</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>Seasonal Autoregression (SAR3)</td>
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<td>✓</td>
<td></td>
</tr>
<tr>
<td>The Archetype (ARCH)</td>
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<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4: Source availability by geographic levels. Epicast predictions are only done for certain selected states. Sources were curated by the DELPHI group at Carnegie Mellon and Farrow\,[5]\]
sources fitted to predict a flu signal as sensors. Each source can be trained to predict a signal independently—all that is needed is an (approximately unbiased) prediction for the flu level. Because the system we consider is input agnostic, we can also include non-digital surveillance sources—such as forecasts made via time series models. Farrow [5] has developed several models adjusted for each source, which we directly use for ILI, and replicate for EHR-derived signals. Table 4 lists all the sources we consider, and indicates the locations for which each is available.

Sensors can also be unavailable at certain timepoints. For example, the HealthTweets system is only available starting in 2011, while Google Flu Trends (GFT) was retired in 2015. Figure 5 shows the pattern of missing national-level sensors from 2010 through 2017. The regularly missing blocks of data are from sources that only produced predictions during the flu season. This missing data problem will be addressed in Section 4.2.

3 Sensor Fusion

3.1 The Kalman filter

Sensor fusion is based on the Kalman filter as developed by Farrow [5]. The Kalman filter (KF) itself is a recursive algorithm used to estimate the state and covariance of a dynamical system. For linear systems, KF is the optimal unbiased estimator minimizing the mean squared error \( \mathbb{E} \| \hat{x}_t - x_t \|^2 \) \([1, 14]\).

Let \( x \in \mathbb{R}^k \) be the state vector, and \( z \in \mathbb{R}^d \) be the vector of observed measurements. KF models
the state at time $t$ according to

$$x_t = F x_{t-1} + \delta_t \quad (3.1)$$
$$z_t = H x_t + \epsilon_t \quad (3.2)$$

where $F$ is the stationary process matrix relating $x_{t-1}$ to $x_t$, and $H$ is the noiseless matrix mapping state space onto measurement space. The process and measurement noise vectors, $\delta_t$ and $\epsilon_t$ respectively, are assumed to be mutually independent with Gaussian distributions $\delta_t \sim N(0, Q_t)$, $\epsilon_t \sim N(0, R_t)$. Given past estimates $\hat{x}_1, \ldots, \hat{x}_{t-1}$, and observed measurements $z_1, \ldots, z_t$, KF predicts the state using the process model and prior estimate $\bar{x}_{t-1}$

$$\bar{x}_t = F \hat{x}_{t-1} \quad \text{State prediction (3.3)}$$
$$\bar{P}_t = F P_{t-1} F^\top + Q_t \quad \text{Covariance prediction (3.4)}$$

We update (or correct) the intermediate prediction $\bar{x}_t$ with the observed measurement $z_t$ and measurement map $H$

$$\hat{x}_t = \bar{x}_t + K_t (z_t - H \bar{x}_t) \quad \text{State correction (3.5)}$$
$$\hat{P}_t = (I - K_t H) \bar{P}_t \quad \text{Covariance correction (3.6)}$$
$$K_t = \bar{P}_t H^\top (H \bar{P}_t H^\top + R_t)^{-1}. \quad \text{Kalman gain (3.7)}$$

where $K$ is the Kalman gain indicating the relative weight balanced between the measurement and process models.

### 3.2 Sensor fusion

Within many settings, such as flu nowcasting, we do not have an established process model describing the state transition over time. To show our distrust in the process model $F$, we can reformulate the KF estimate to a process-agnostic (i.e. non-mechanistic) estimator called sensor fusion. This is done by setting $Q$, the process noise covariance to infinity. Intuitively, $Q$ measures the uncertainty in the process model due to noise; if we let $Q \to \infty$ (say $\text{tr}(Q) \to \infty$), then $\bar{P}_{t-1} \to 0$. This can also be understood by examining the case where the error distributions are Gaussian—then the KF is the Bayes estimator, and we approach a flat prior.

We can now simplify equations (3.3)-(3.7), and rewrite the Kalman gain as

$$K_t = (\bar{P}_t^{-1} + H^\top R^{-1} H)^{-1} H^\top R^{-1} \quad (3.8)$$

Details on the derivation can be found in [5]. The simplified equations form what we call the sensor fusion estimator,

$$\hat{x}_t = (H^\top R^{-1} H)^{-1} H^\top R^{-1} z_t \quad (3.9)$$
$$\hat{P}_t = (H^\top R^{-1} H)^{-1}, \quad (3.10)$$

where the measurements $z_t$ at all timepoints $t = 1, 2, 3, \ldots$ are referred to as sensors.
Equivalence to regression   An interesting note is that sensor fusion is equivalent to a form of constrained regression [4]. If we take the measurement error covariance to be the empirical covariance, then the sensor fusion estimate (3.9) is equivalent to $\hat{\beta}^T z_t$, where we define the estimator $\hat{\beta} \in \mathbb{R}^{d \times k}$ as the solution to the problem

$$\begin{align*}
\minimize_{\beta \in \mathbb{R}^{d \times k}} & & ||X - Z \beta||_F^2 \\
\text{subject to} & & H^T \beta = I
\end{align*}$$

(3.11)

where $X \in \mathbb{R}^{t \times k}$ is the state matrix where rows are the states across time, $Z \in \mathbb{R}^{t \times d}$ is the sensor matrix stacking sensors across time, and $I$ is the identity matrix. This equivalence can be a useful tool to improve sensor fusion estimates by leveraging well-established regression methodology.

4 Retrospective analysis

While our overarching goal is to produce estimates of the flu as close as possible to real-time, our first step is to answer the question “Can we get comparably accurate nowcasts using EHR data?” To this end, we perform a retrospective study nowcasting weekly flu levels using both ILI– and EHR–derived signals in the US from 2014 to 2017 ($T = 162$ weeks). We consider each of the three weighted EHR signals, and the finalized weighted ILI signal as a potential ground truth value for our response. For each week, and for each US state and Washington DC, we produce an estimate of the flu level given by $\hat{x}_t \in \mathbb{R}^{51}$ by iteratively training the sensors and applying sensor fusion.

Figure 6: Overview of training-nowcast cycle, which is repeated every week, for each flu signal independently.
Figure 6 gives the structure for one iteration for a single response. An overview of sensor training process is described below, with an overview of the process given by the top portion (yellow). Once the sensors are trained, the nowcasting portion fuses the sensors to produce \( \hat{x}_t \) as given by the bottom (blue) portion.

4.1 Sensor training

We use the 5 digital surveillance sources as described in Section 2.3, as well as two forecasting models. The predictions made from forecasting models, SAR3 and ARCH, can be used as sensor fusion is rather agnostic to its inputs. Recall that each source can be observed at different locations, and at different times. In general, during a flu season we observe approximately 308 source-location pairs. Occasionally, fewer data pairs can be gathered due to unreliable digital surveillance sources. In sensor fusion, we take the value of each sensor to be the predictions of the response (flu level), using the sources as our covariates. We then fit different models, primarily regression based, to produce predictions (sensors) for the current week, \( z_t \in \mathbb{R}^{308} \).

The model-fitting procedure is flexible; each source-location pair can be fitted independently (or jointly), with the only restriction being that the output prediction is approximately unbiased. Specifics of the fitted models for each of the sources in Table 4 is given in [5]. In this analysis, we replicate the procedures to produce predictions for both ILI and EHR measures (with concessions for unavailable data), for each location, and ensure that at each timepoint we retrain the models.

4.2 Missing sensors and covariance estimation

In sensor fusion, missing data becomes a problem when estimating the measurement error precision matrix \( R^{-1} \). Estimation of \( R^{-1} \) is straightforward when all sensors are observed at each time point. However, digital surveillance signals can often be missing during non-peak flu season weeks or unavailable in certain regions.

In fact, we can use the intermediate KF predictions as a sensor, and reintegrate the process model itself. This shown that the equivalence between KF and the constrained regression is fully general.
The naïve approach would be simply to only use data from weeks where all source-locations pairs are observed. Clearly, this considerably reduces the amount of viable data. Instead, an effective solution is to take the empirical pairwise covariance matrix using the average of the observed entries \( [5] \), and refine by shrinking the estimate towards the identity until it is at least positive semidefinite \( [15] \). This procedure conveniently side-steps the issue of imputing missing values in the sensors.

4.3 Geographical interpretation of \( H \) map

Recall that in sensor fusion, \( H \) is a matrix mapping state space onto measurement space. In our setting, each row of \( H \) is a sensor and each column is a state (which are coincidentally US states). Sensors are observed at all levels of the US hierarchy: state, regional, and national. Therefore, each entry in \( H \) corresponds to the populational weight of a source-location pair for a state

\[
H_{ij} = \begin{cases} 
\text{population,} & j \in i \\
0, & \text{otherwise}
\end{cases}
\]

By virtue of the US hierarchy, the rows of \( H \) sum to 1.

The underlying assumption in this configuration is that we only want to consider hierarchically-related sensors for each state’s prediction. Consider a sensor \( z \) predicting state \( s \), then the row of \( H \) corresponding to \( z \) is 0 everywhere except for state \( s \). If \( z \) was a sensor for region \( r \), then that row is 0 everywhere except for those states within region \( r \). It follows that the row is non-zero everywhere for a national-level sensor, as all US states are nested within. By choosing \( H \) in this manner, we restrain the contribution of sensors that are not hierarchically related.

5 Results

Performance on nowcasting ILI via digital surveillance nowcasting has been previously studied \( [5] \), and has proven to yield state-of-the-art estimates. Figure 8 shows that the nowcasts closely trace the ground truth (either finalized ILI or EHR signal) very well. To make a numeric comparison, we consider three metrics: Mean Absolute Error (MAE), Mean Absolute Scaled Error (MASE), and Mean Directional Accuracy (MDA). MAE is defined in the standard manner, where the averaging is done over the \( T = 162 \) weeks and across all 51 locations. MASE is an interpretable variant of MAE, formally defined as

\[
\text{MASE} = \frac{\sum_{t=1}^{T} |x_t - \hat{x}_t|}{\sum_{t=2}^{T} |x_t - x_{t-1}|}
\]

where \( x_t \) is the ground truth signal at time \( t \) and \( \hat{x}_t \) is the sensor fusion estimate. The denominator translates to a naïve one-step forecast, so if the value is smaller than 1, the predictive accuracy of

\(^2\)If the shrinkage is done by taking a convex combination, then in the regression equivalence it is the same as imposing a ridge penalty. The shrinkage parameter \( \lambda \) can be chosen to produce exact equivalence \( [4] \).
Table 1 gives the results for the US national and Pennsylvania flu levels across the $T = 162$ weeks. Figures 9, 10 show the distribution across all states. From this we see two trends. First, broader signals such as EHR$_3$ tend to have highest predictive accuracies. Second, larger geographies (national or regional levels) have smaller errors than more specific locations (US states).

<table>
<thead>
<tr>
<th>Location</th>
<th>Signal</th>
<th>MAE</th>
<th>MASE</th>
<th>MDA</th>
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<tr>
<td>National</td>
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<td>0.7339</td>
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<tr>
<td></td>
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Table 1: Numerical performances of sensor fusion applied to weighted ILI and EHR data.
Effect of signal resolution  The first observation is somewhat unsatisfying. It is good news for informing general resource allocation, as we see that it is easier to nowcast the level and direction of approximate flu. However, our objective is to capture the true flu intensities, and this proves to be more difficult at the EHR$_2$ scale — recall that EHR$_2$ is a popular choice in literature to reflect flu activity — and even harder for EHR$_3$. We see empirically that wILI performance falls somewhat in EHR$_2$ and EHR$_3$ at the national level and distributionally across all states. For Pennsylvania in particular, it seems that EHR$_2$ is easier to predict than wILI, both in terms of MASE and MDA. It is reassuring to note that, overall, EHR and ILI perform comparatively well at both the national, regional, and state level.

From the EHR standpoint, one encouraging caveat is that the sensor training models were adapted to digital surveillance sources chosen to optimize performance for ILI data. It is certainly plausible that with several adjustments, EHR performance could significantly improve. Another noteworthy aside is that the regularization parameter for the covariance estimation was chosen adaptively (but still somewhat empirically) at each timepoint. This tuning knob can have significant impact on predictive performance, and could have different optimal tradeoff curves when considering EHR data.

Effect of geographic resolution  Sensor fusion performs worse at the state-level than at the regional or national level. This is attributed to the additional noisiness of the data as we have smaller counts (and less digital surveillance data available). However, this phenomena seems to be balanced by observing that coarser geographies are in fact, convolutions of more specific geographies. We speculate that, in theory, the specific trends at a zip-code level should be more straightforward to predict. Preliminary experiments in nowcasting a specific 5 digit zip-code location have shown promising results, with better predictive performance than at the state-level. This opens a entirely new avenue to explore: daily nowcasting, which is accompanied with a whole host of issues to ad-
6 Discussion

We performed a retrospective study which nowcasts various ground truth approximations of flu intensities given by two datasets: ILI as provided by the CDC, and diagnostic codes found in EHRs. To produce estimates across the United States, we iteratively applied sensor fusion to combine near-real-time digital surveillance sources into weekly estimates of flu levels. Numerical results show that predictive performance across both datasets are comparable, with broader (more general) flu signals having smaller error.

To be explicitly clear, this study has demonstrated that EHR data is of proportional quality to ILI data, and can be used to produce reasonably accurate nowcasts—but we have not yet shown that it is a practical substitute for ILI. The primary obstacle lies in the proprietary nature of EHRs, and the difficulty in structuring a publically available, real-time system to leverage them. However, we have successfully shown that the EHR dataset merits further investigation, and is an exciting resource as it can be used to produce nowcasts at more finer geographic (zip-code) and temporal (daily) resolutions. These attributes of EHR are necessary to achieve the aforementioned idealistic decision-support system.

There are certain reservations to our analysis; we made several assumptions about the availability of EHR, such as the time delay in collecting and transmitting counts, and if there were any revisions made post-release. To make a good faith comparison, we then used only the finalized ILI data, which is typically stable after 3 weeks. These changes could skew the comparison, more likely favoring EHR performance. It is worth restating that ILI itself is not a perfect representation
of true flu intensity, and as such, our analysis only serves as a check to the feasibility of EHRs.

The equivalence between sensor fusion and regression given in Section 3.2 allows us to refer to well-established regression methodology to improve our estimates. One idea for future exploration is to reassess the models for sensor training, and determine the optimal way to construct the sensors from the sources. Conceptually, sensor fusion is similar to stacking (with some difference in constraints) and can be more generally viewed as an ensemble method combining weak, highly correlated predictors into a single strong prediction. These ideas have deep roots in statistical literature, and can be drawn upon to improve our nowcasts.

References


