# Flusion:

Integrating multiple data sources for accurate influenza predictions

**Evan L. Ray**, Yijin Wang, Russel D. Wolfinger, Nicholas G. Reich University of Massachusetts, Amherst

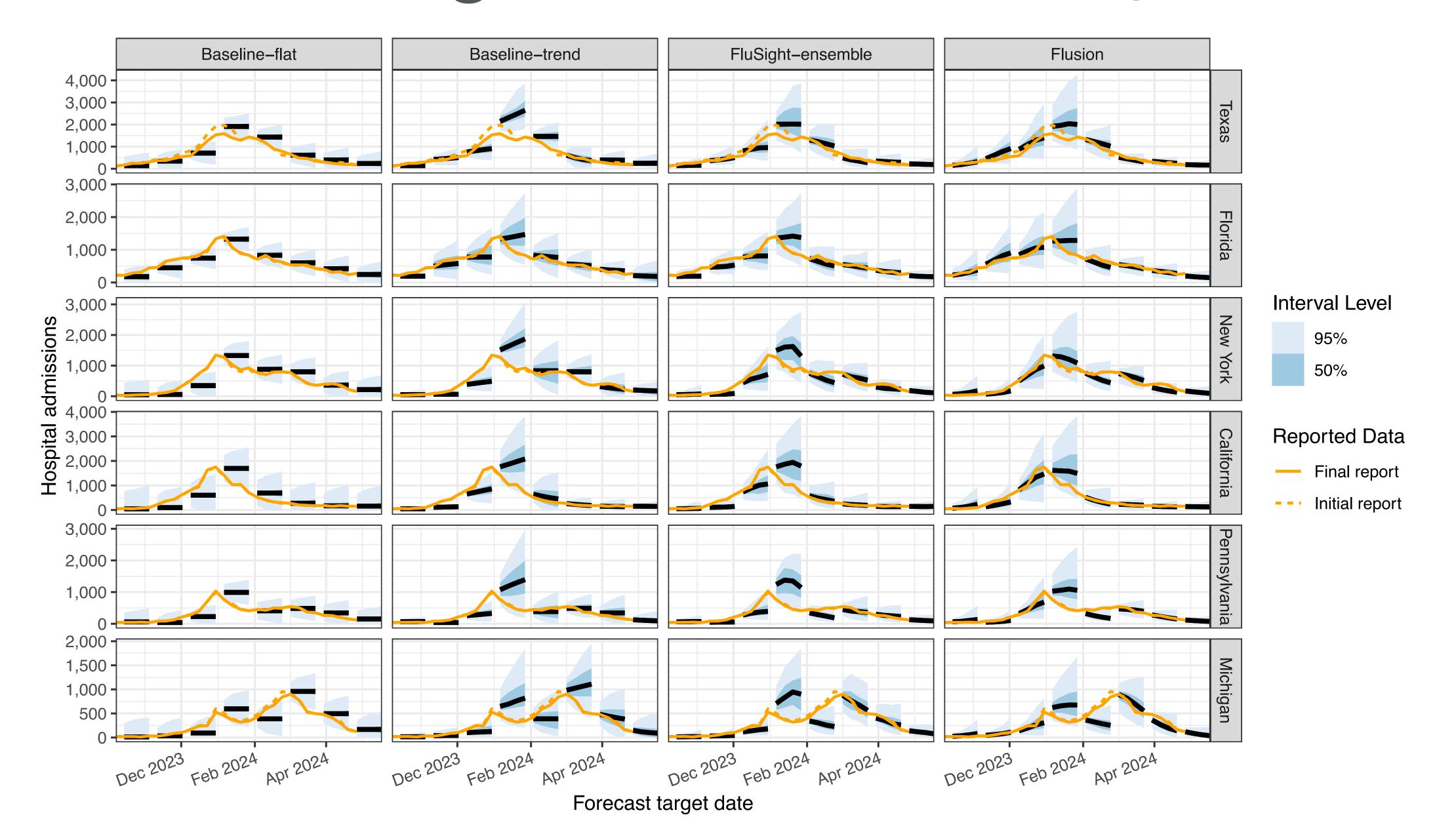
Yale Biostatistics Seminar November 12, 2024



### Overview of this talk

- Motivation, preview of results
- Modeling approaches
  - Model 1
  - Model 2
- Conclusions

### First look: FluSight forecasts, 2023/24 season



### Overall Results: FluSight 2023/24 season

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Model	% Submitted	MWIS	m rMWIS	MAE	rMAE	50% Cov.	95% Cov.
Flusion	99.9	29.6	0.610	45.6	0.670	0.583	0.967
FluSight-ensemble	100.0	35.5	0.731	55.4	0.814	0.516	0.926
Other Model #1	100.0	35.6	0.731	54.0	0.792	0.558	0.940
Other Model #2	89.1	40.4	0.773	61.5	0.840	0.479	0.908
Other Model #3	97.8	39.9	0.806	59.3	0.857	0.363	0.793
Other Model #4	100.0	40.0	0.823	60.5	0.890	$\boldsymbol{0.497}$	0.884
Other Model #5	67.3	45.0	0.827	68.7	0.899	0.487	0.866
Other Model #6	100.0	41.5	0.851	64.4	0.945	0.466	0.903
Other Model #7	85.5	45.7	0.852	66.1	0.878	0.418	0.824
Other Model #8	100.0	41.6	0.856	60.7	0.893	0.460	0.855
Other Model #9	100.0	42.1	0.865	60.9	0.894	0.442	0.827
Other Model $#10$	98.8	44.3	0.901	67.7	0.986	0.456	0.939
Baseline-trend	99.9	43.9	0.906	67.0	0.990	0.618	0.922
Other Model $#11$	95.7	45.0	0.908	66.2	0.956	0.554	0.870
Other Model $#12$	87.0	45.0	0.936	70.7	1.050	0.449	0.929
Other Model #13	96.4	42.4	0.948	64.2	1.030	0.429	0.896
Other Model #14	93.6	48.7	0.980	70.8	1.020	0.473	0.838
Other Model #15	99.2	47.3	0.993	58.1	0.870	0.596	0.793
Baseline-flat	100.0	48.5	1.000	67.9	1.000	0.282	0.888

(Results for 11 lower-ranked models are suppressed for brevity)

### Why Forecast Infectious Disease?

• Situational awareness for the public and stakeholders like health care providers.

https://www.cdc.gov/flu-forecasting/data-vis/04242024-flu-forecasts.html



APRIL 26, 2024

#### Flu Hospital Admission as of May 11, 2024

#### **PURPOSE**

This week's ensemble predicts that the number of new weekly laboratory confirmed influenza hospital admissions will likely decrease nationally, with 520 to 4,700 laboratory confirmed influenza hospital admissions likely reported in the week ending May 11, 2024.

#### Interpretation of forecasts

- Reported and forecasted new influenza hospital admissions as of April 24, 2024
- This week, 24 modeling groups contributed 29 forecasts that were eligible for inclusion in the ensemble forecasts for at least one jurisdiction. Contributing teams are listed below.

ON THIS PAGE

Interpretation of forecasts

**State Forecasts** 

Contributing Teams and Models

### Why Forecast Infectious Disease?

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- Allocation of resources such as
  - antiviral treatments
  - hospital care staff
  - hospital beds

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Health Care Management Science (2021) 24:253–272 https://doi.org/10.1007/s10729-020-09542-0

#### From predictions to prescriptions: A data-driven response to COVID-19

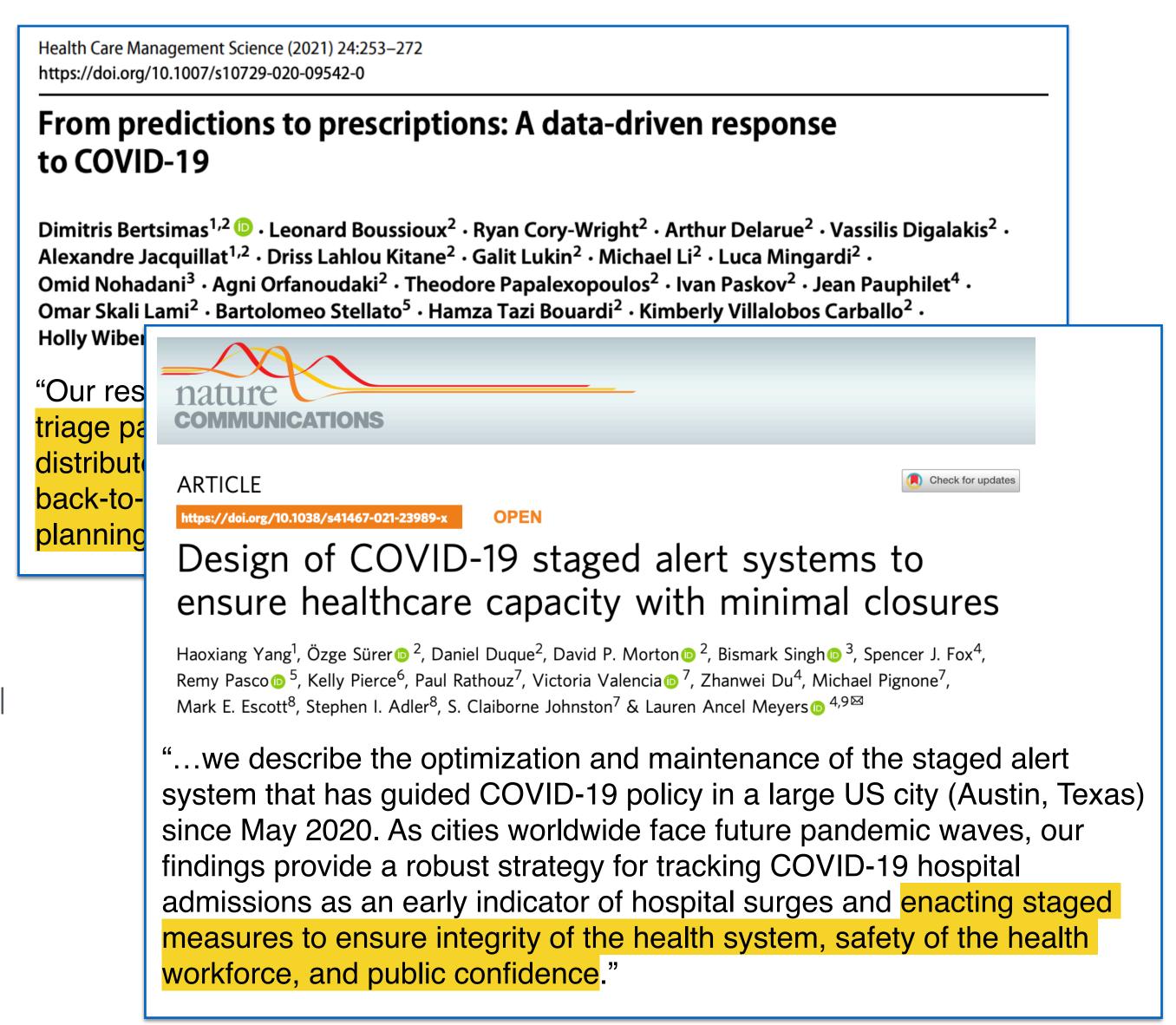
Dimitris Bertsimas<sup>1,2</sup> • Leonard Boussioux<sup>2</sup> · Ryan Cory-Wright<sup>2</sup> · Arthur Delarue<sup>2</sup> · Vassilis Digalakis<sup>2</sup> · Alexandre Jacquillat<sup>1,2</sup> · Driss Lahlou Kitane<sup>2</sup> · Galit Lukin<sup>2</sup> · Michael Li<sup>2</sup> · Luca Mingardi<sup>2</sup> · Omid Nohadani<sup>3</sup> · Agni Orfanoudaki<sup>2</sup> · Theodore Papalexopoulos<sup>2</sup> · Ivan Paskov<sup>2</sup> · Jean Pauphilet<sup>4</sup> · Omar Skali Lami<sup>2</sup> · Bartolomeo Stellato<sup>5</sup> · Hamza Tazi Bouardi<sup>2</sup> · Kimberly Villalobos Carballo<sup>2</sup> · Holly Wiberg<sup>2</sup> · Cynthia Zeng<sup>2</sup>

"Our results have been used at the clinical level by several hospitals to triage patients, guide care management, plan ICU capacity, and redistribute ventilators. At the policy level, they are currently supporting safe back-to-work policies at a major institution and vaccine trial location planning at Janssen Pharmaceuticals..."

### Why Forecast Infectious Disease?

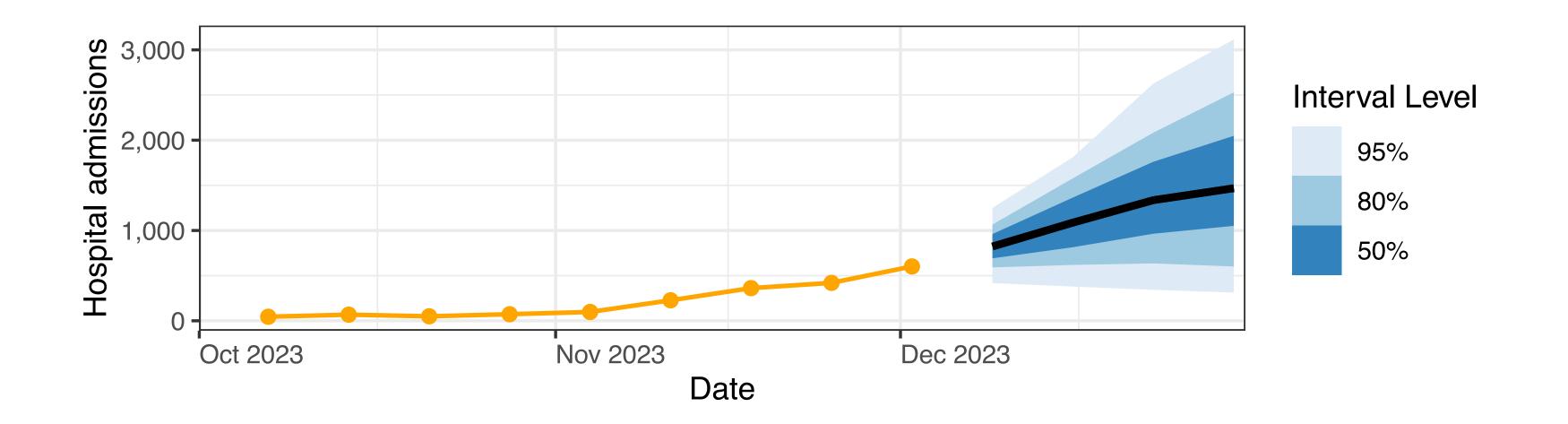
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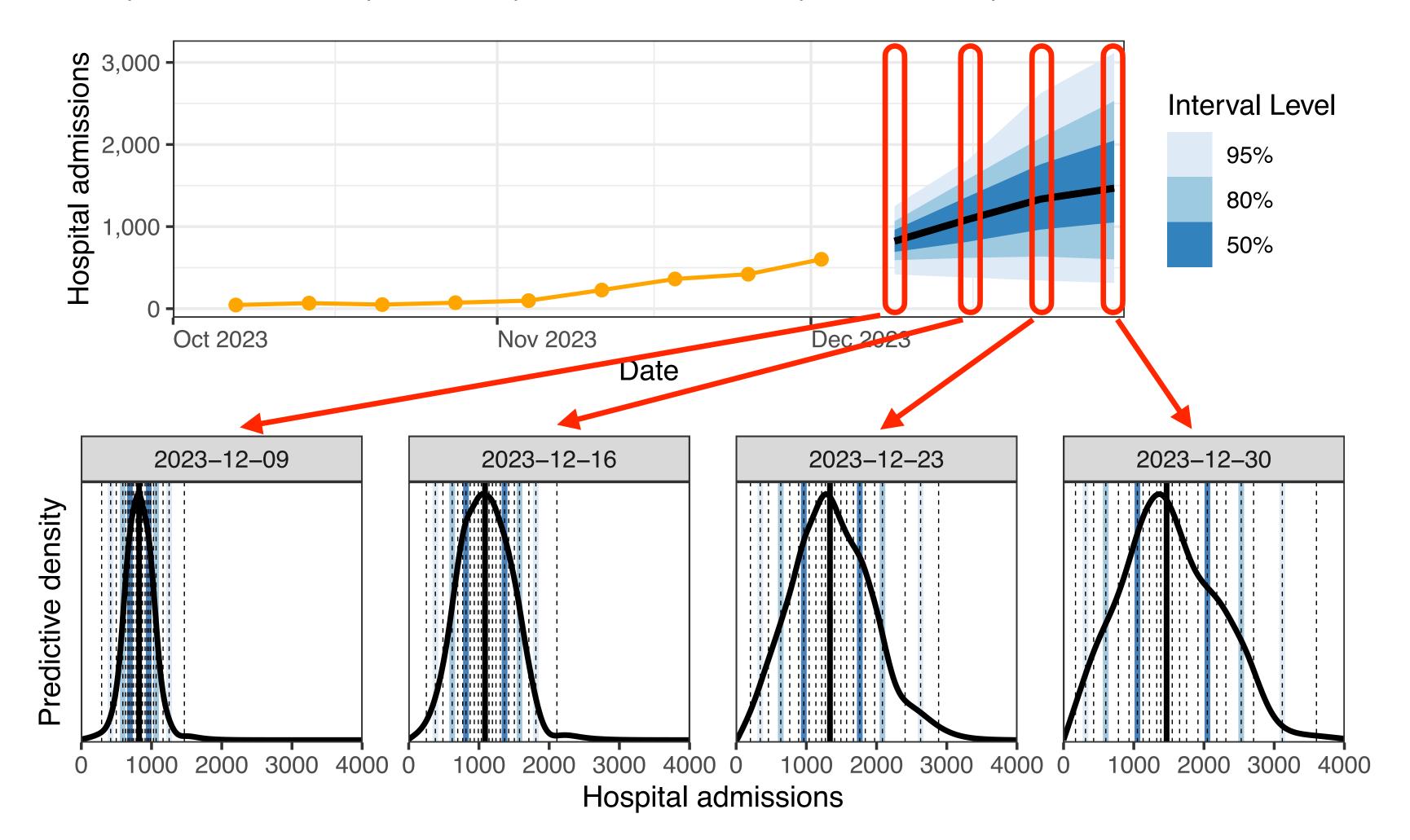
### Anatomy of a forecast

- •On each week (time index t), available data report on weekly hospitalizations up to t-1
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- We submit predictive distributions for weeks t through t+3
- Distributions are represented by their quantiles at 23 probability levels: 0.01, 0.025, 0.05, ..., 0.99

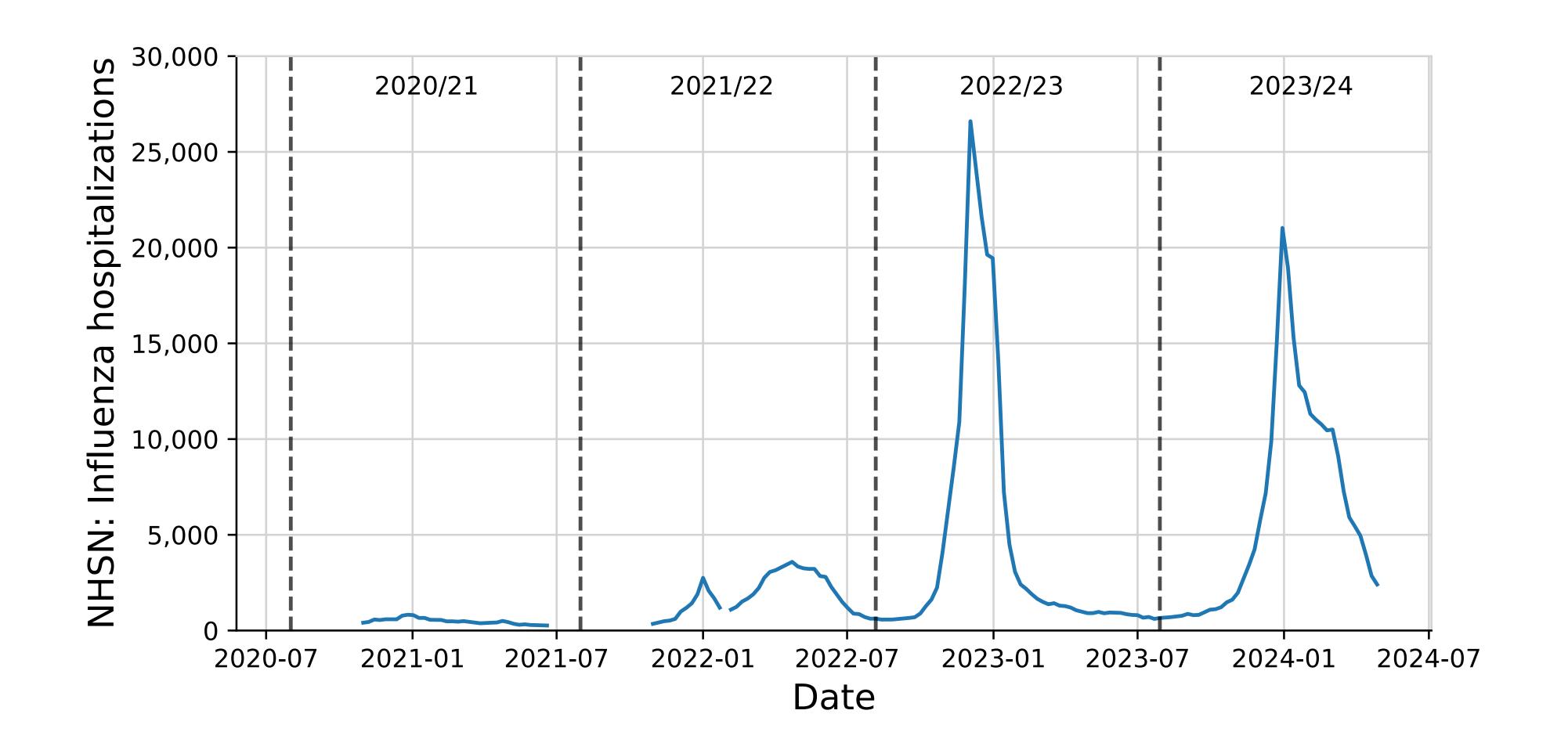


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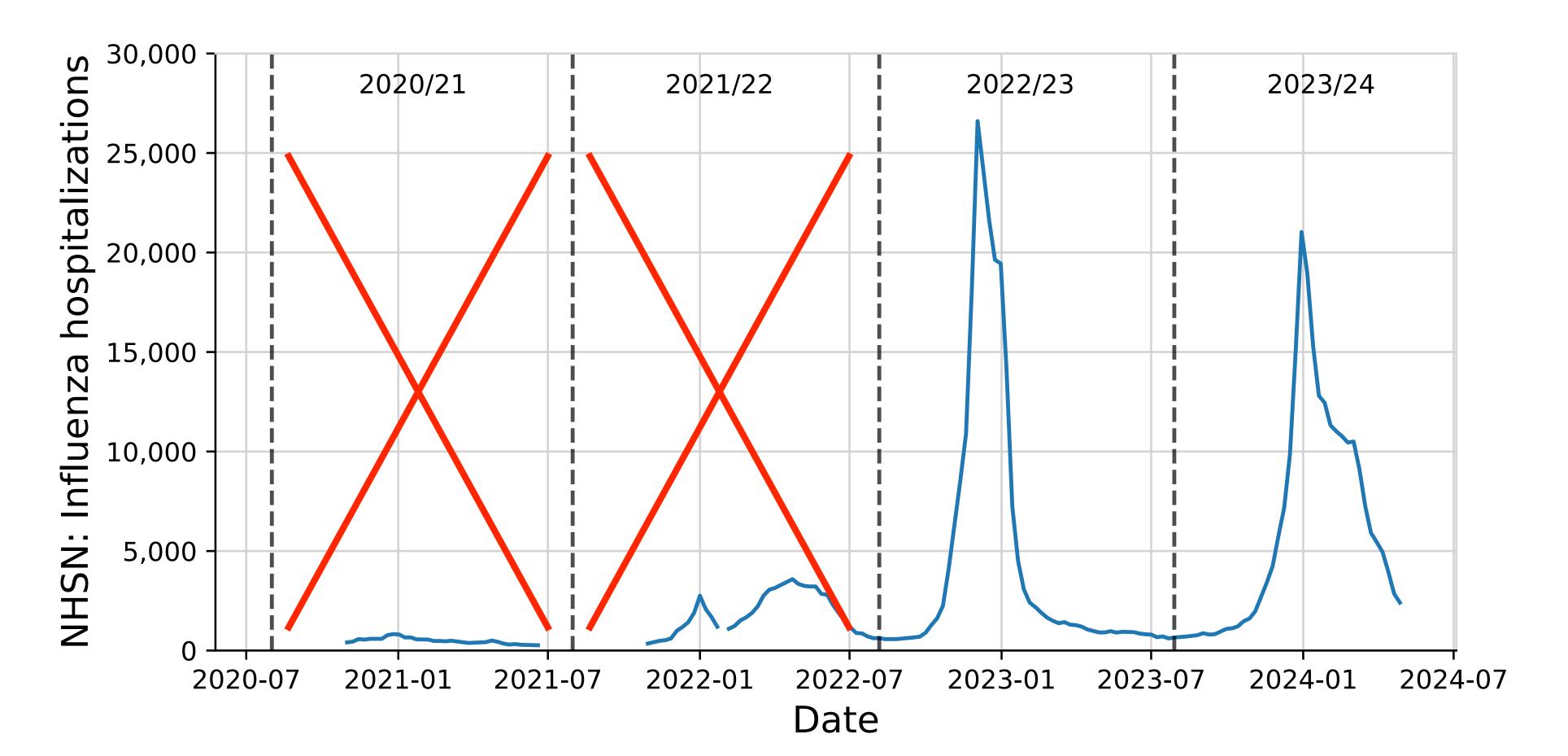
### A central data challenge

- Since the COVID-19 pandemic, FluSight is based on a new data stream:
- Hospitalizations with influenza as reported in National Healthcare Safety Network (NHSN)



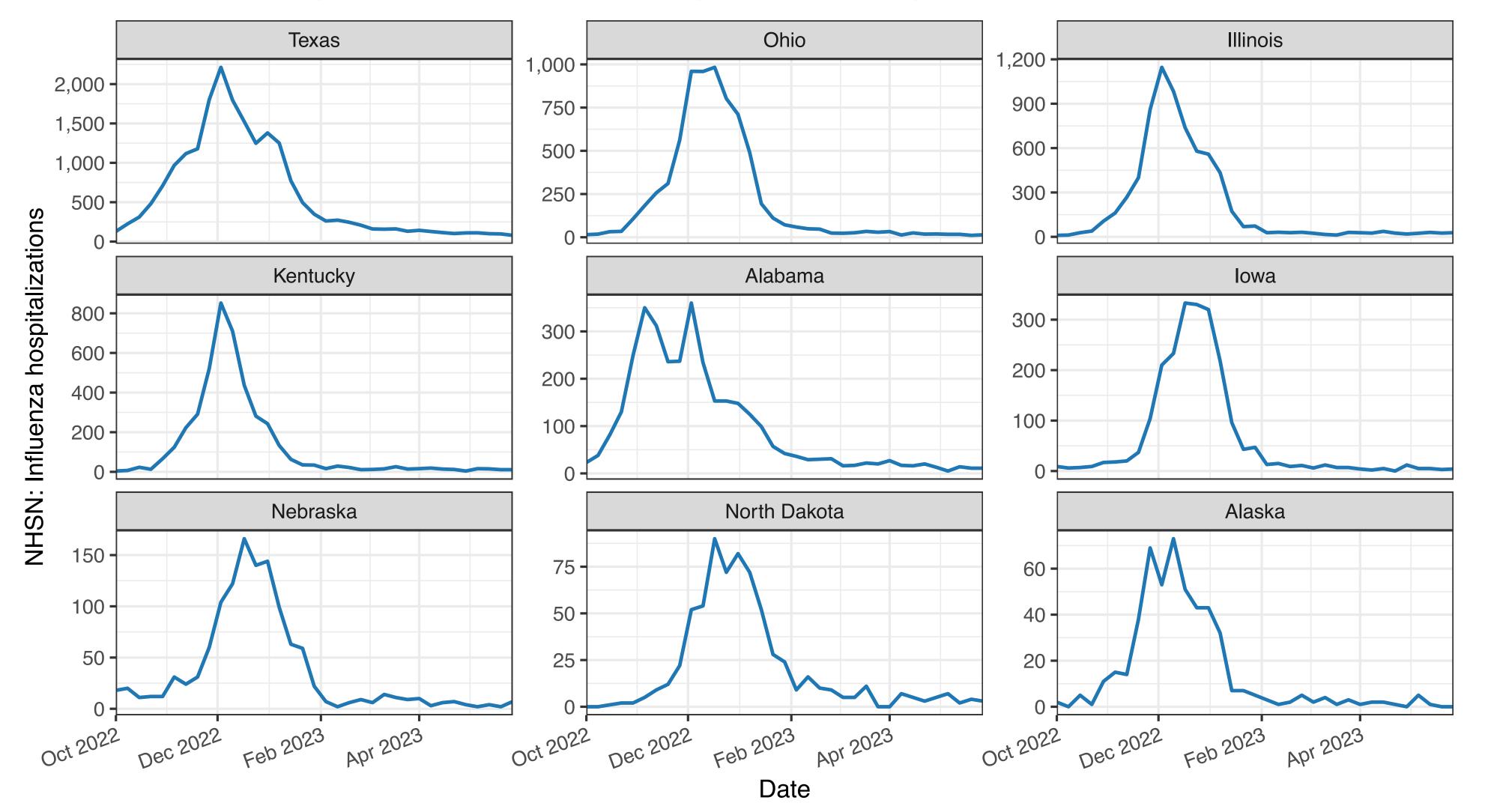
### A central data challenge

- Since the COVID-19 pandemic, FluSight is based on a new data stream:
- Hospitalizations with influenza as reported in National Healthcare Safety Network (NHSN)
- This surveillance signal came online during the COVID-19 pandemic
- At 2023/24 season start, only 1 past season of data with typical patterns of flu transmission



### What would you do?

- You have 1 season of available historical data for each of 52 states/jurisdictions (9 shown)
- What model would you reach for first? If you could try 1 extension, what would it be?



- Notation:  $Z_{l,t}$  is our modeled variable (hospitalizations\*) for location l and time t
- With a Bayesian treatment:

$$\begin{split} Z_{l,t} \mid z_{l,t-1}, \dots, z_{l,t-J}, \varepsilon_{l,t} &= \sum_{j=1}^{J} \alpha_j z_{l,t-j} + \varepsilon_{l,t} \\ \varepsilon_{l,t} &\sim \text{Normal}(0, \sigma_{\varepsilon,l}^2) \\ \alpha_j \mid \psi \sim \text{Normal}(0, \psi^2) \\ \psi, \sigma_{\varepsilon,l} &\sim \text{Half-Cauchy}(0,1) \end{split}$$

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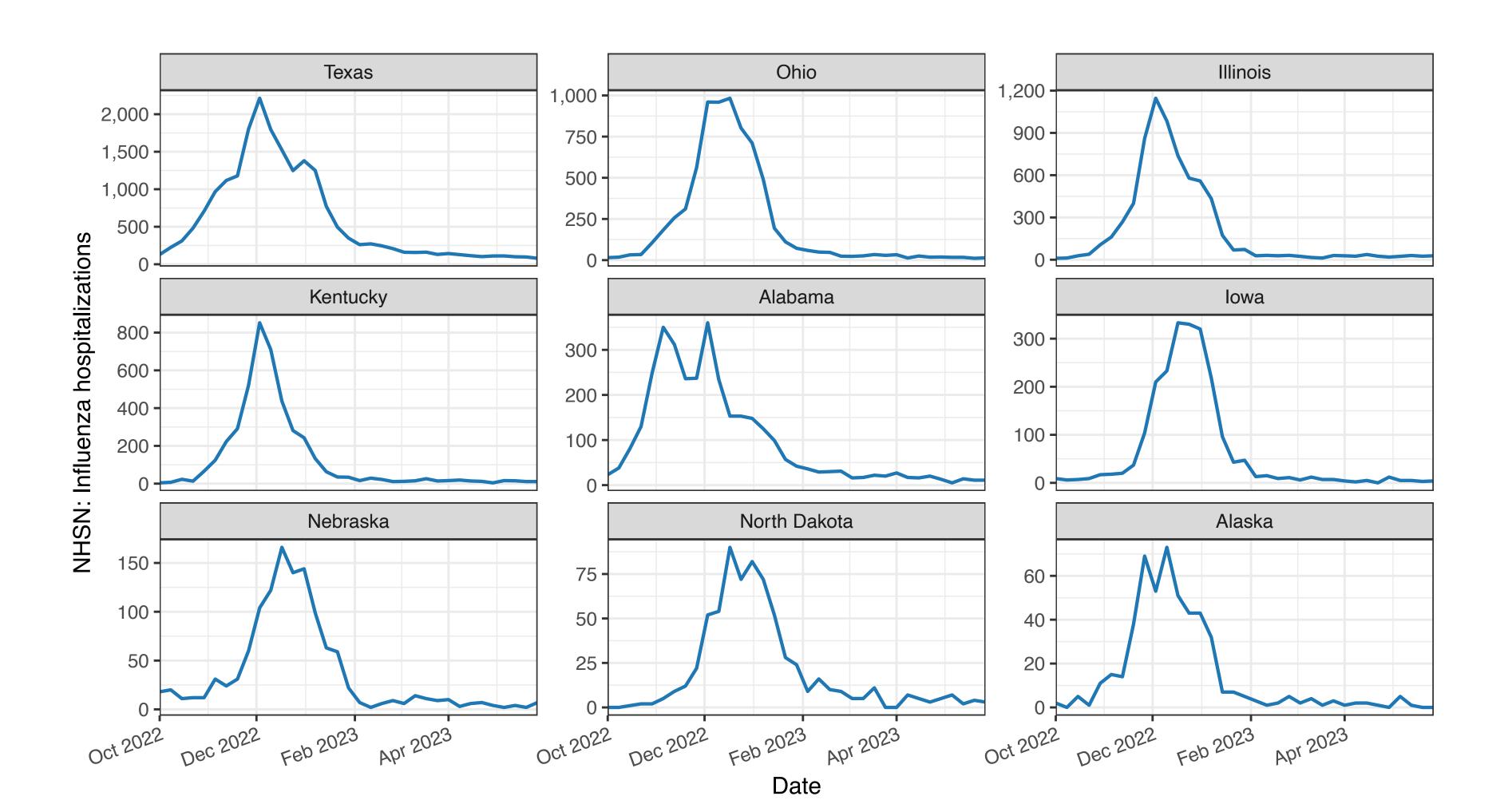
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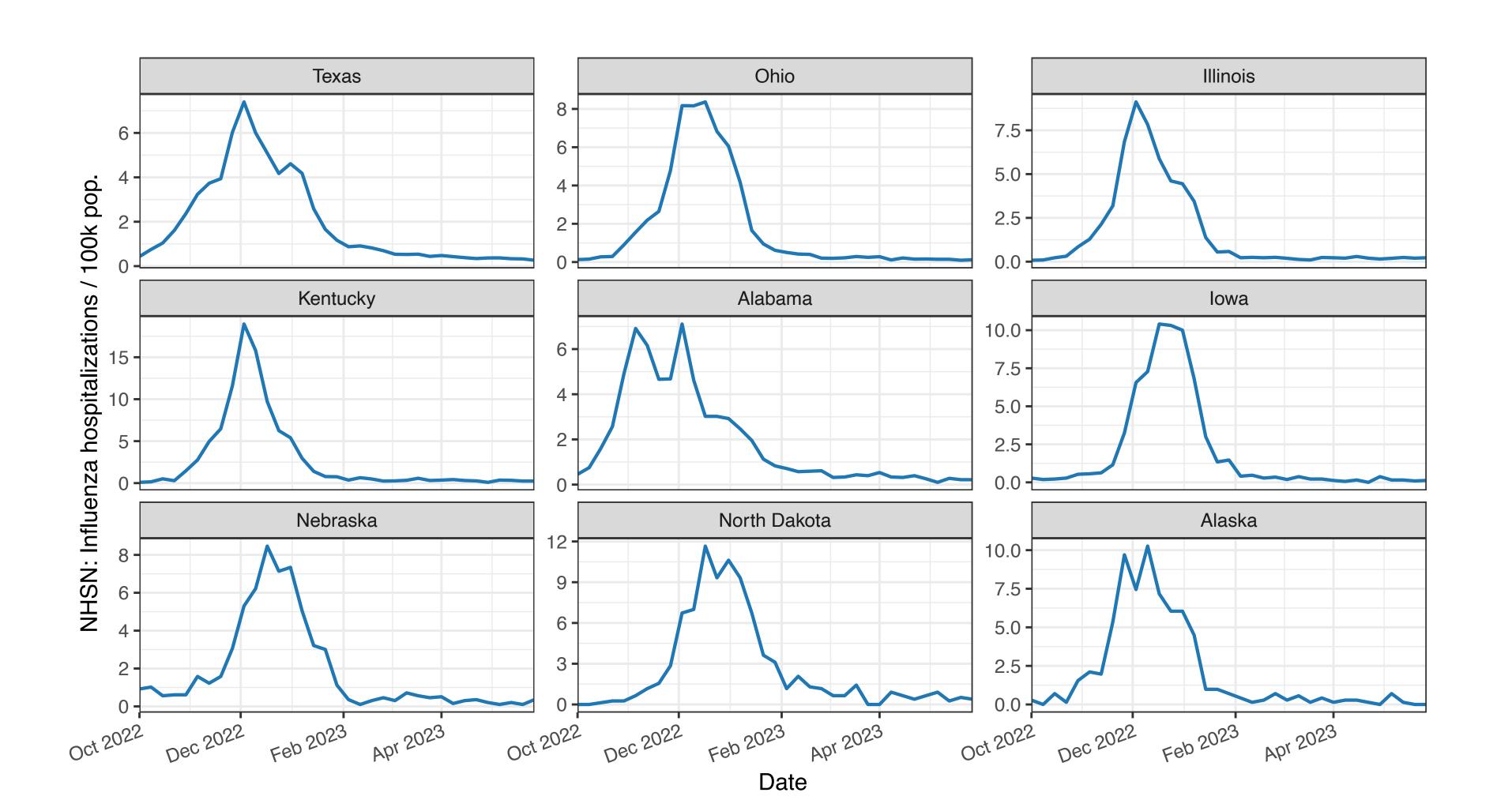
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- Chose J=8 based on intuition/a guess

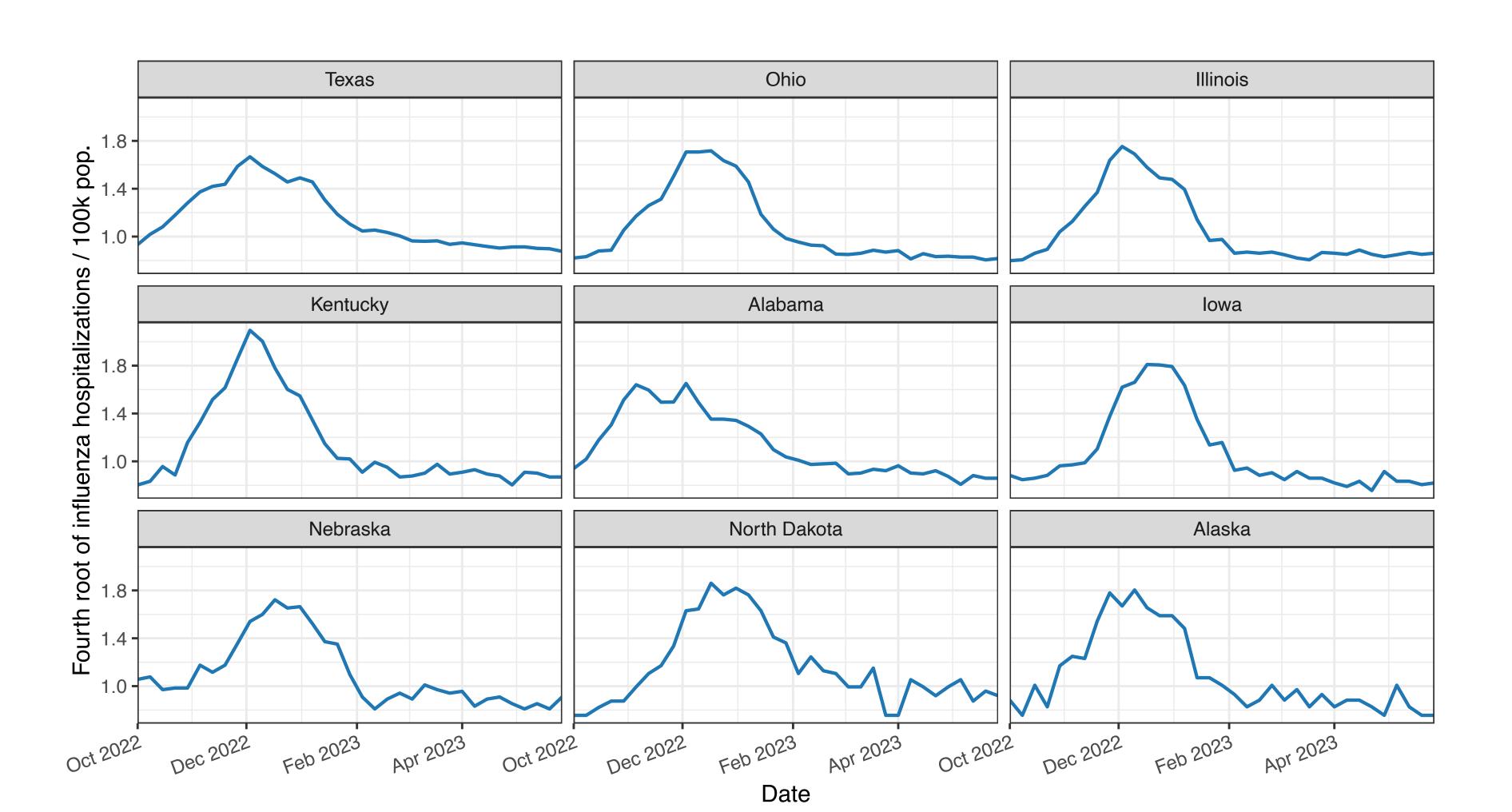
- Challenges:
  - Our target signal is hospital admissions, which varies in magnitude with state population
  - The signal has more variability around its trend near the peak than in the shoulders



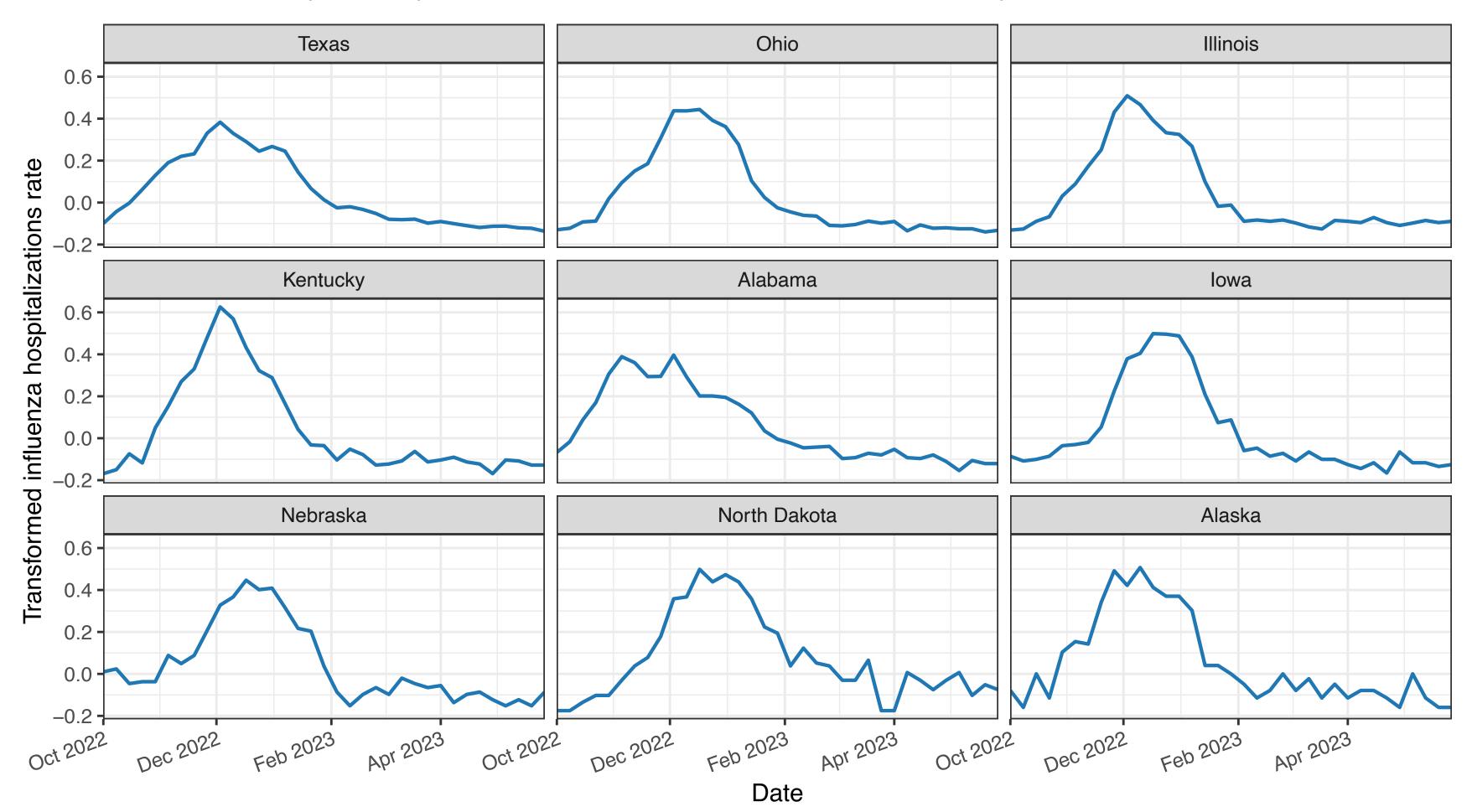
- What I did (I think this could be refined/simplified):
  - Convert to a hospitalization rate per 100k population



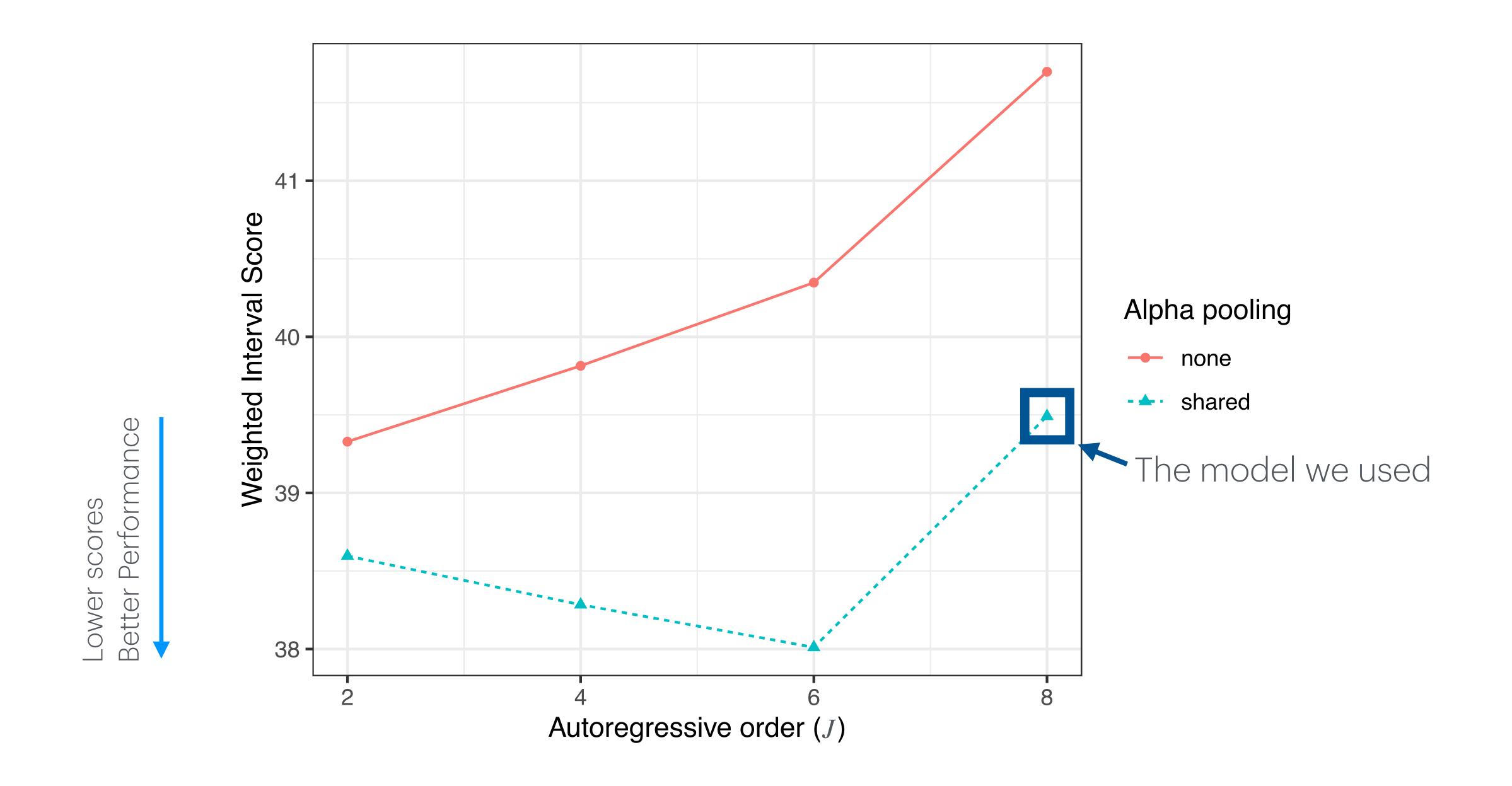
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  - Convert to a hospitalization rate per 100k population
  - Take the fourth root, with an offset of 0.325
  - Center and scale by the per-location mean and 95th percentile



### Post-hoc evaluation results for AR model



### AR performance in overall results

AR models with pooling;
AR models without
pooling, J=2 or J=4

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### Model 1 Conclusion

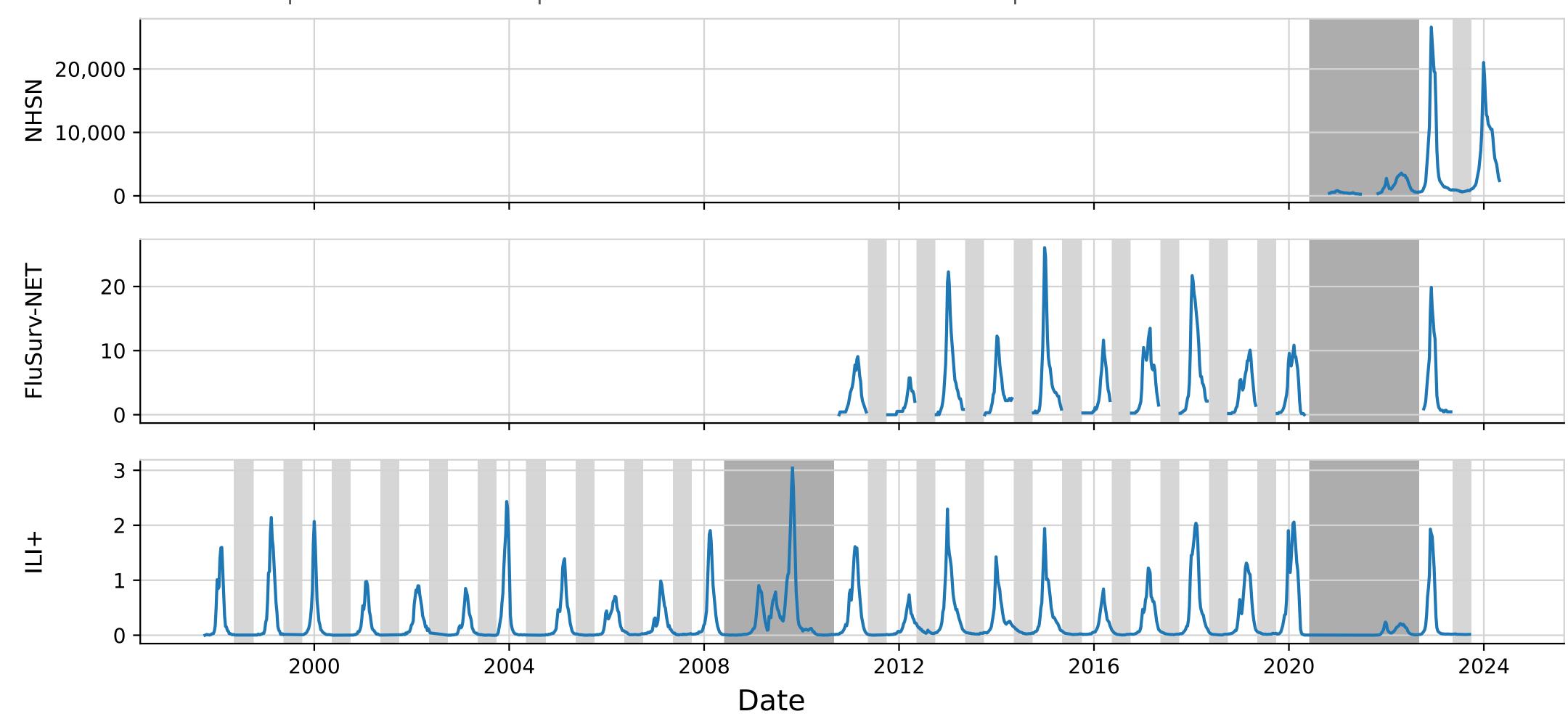
Sweating the details on a model from 1927 can generate some pretty decent forecasts

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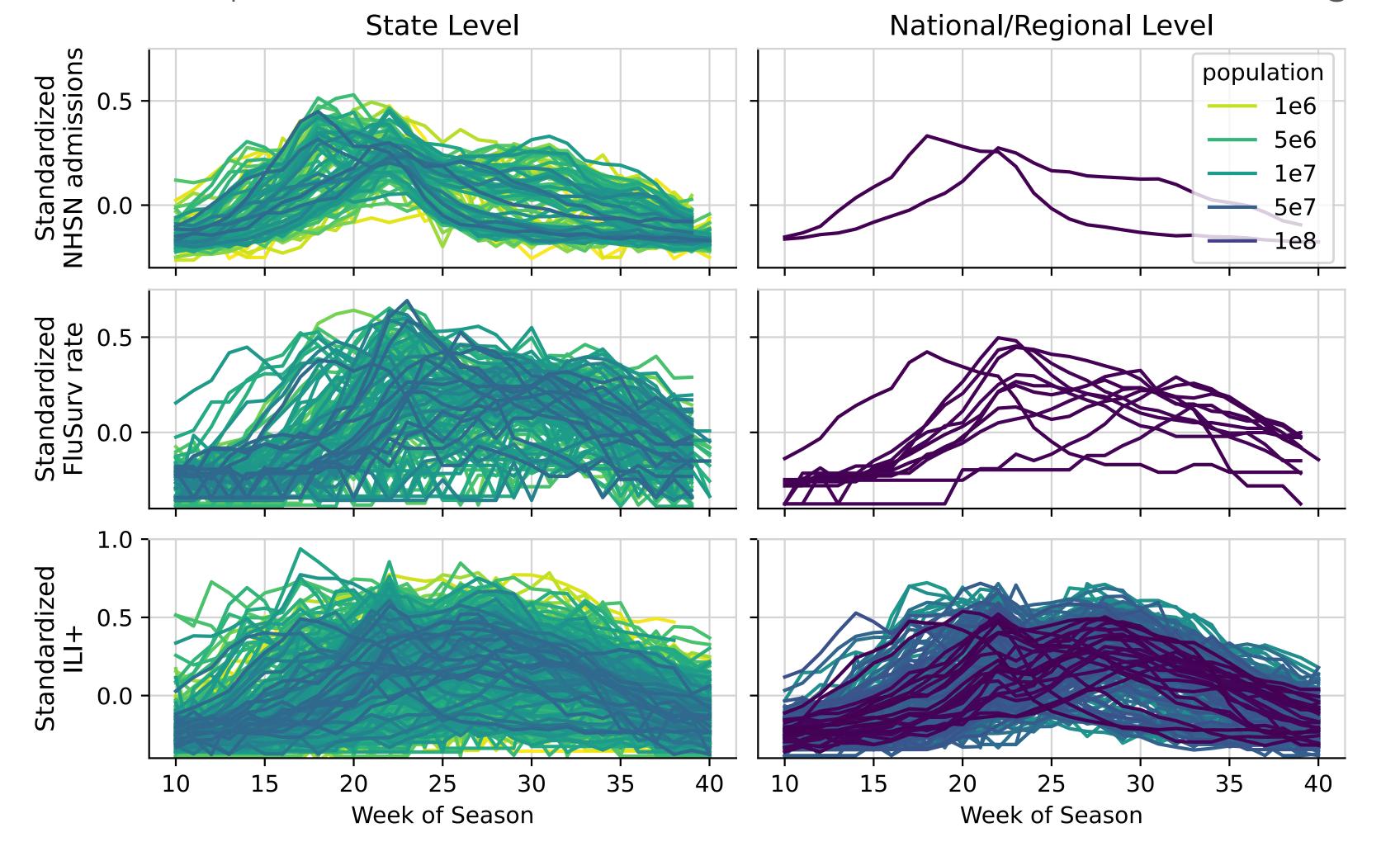
### Actually, we have more data!

- We augment the target NHSN data with 2 other signals with a longer history
  - FluSurv-NET: influenza hospitalizations in selected hospitals
  - ILI+: estimated percent of outpatient doctor visits where patient has influenza

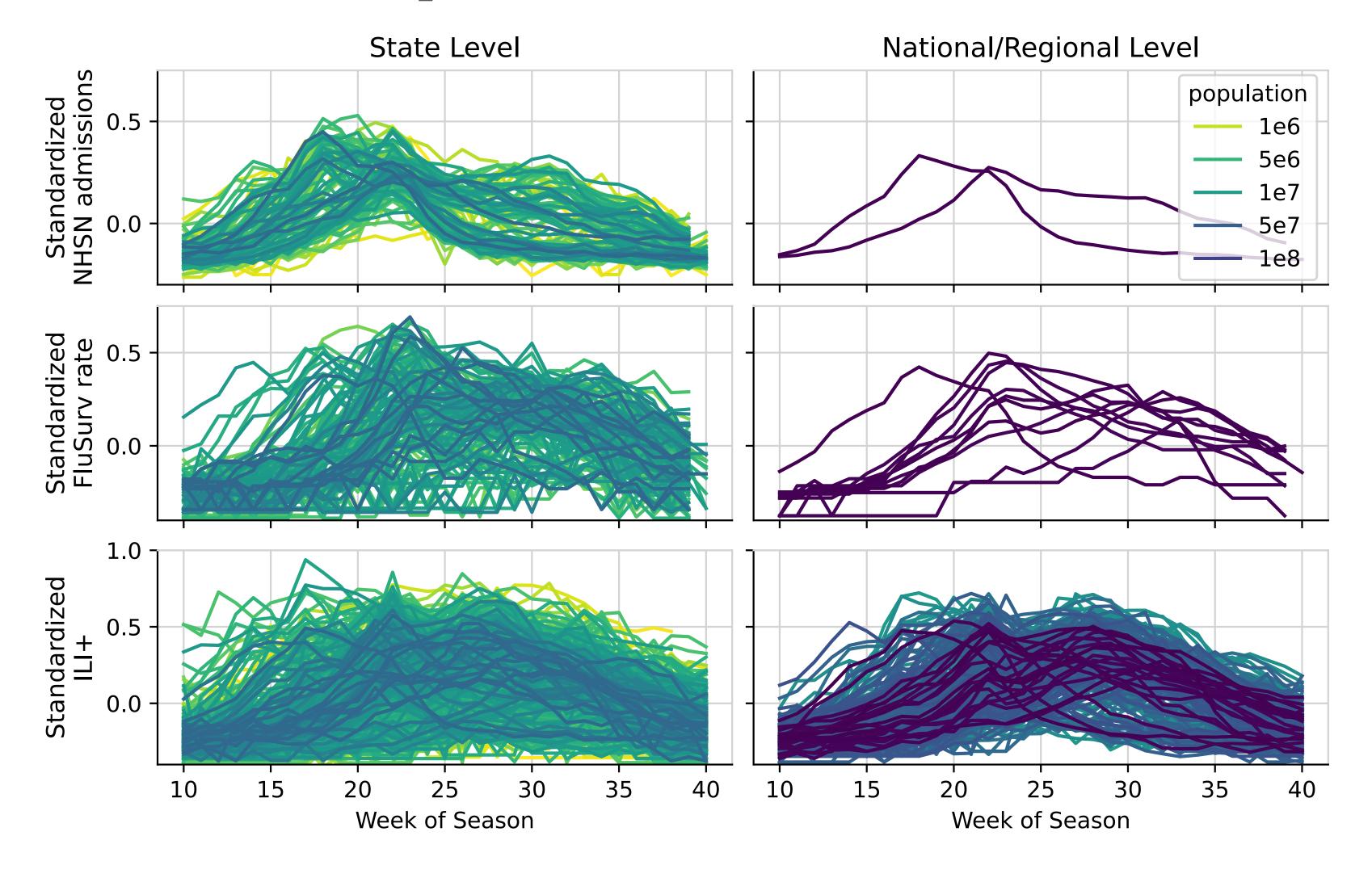


### Data preprocessing

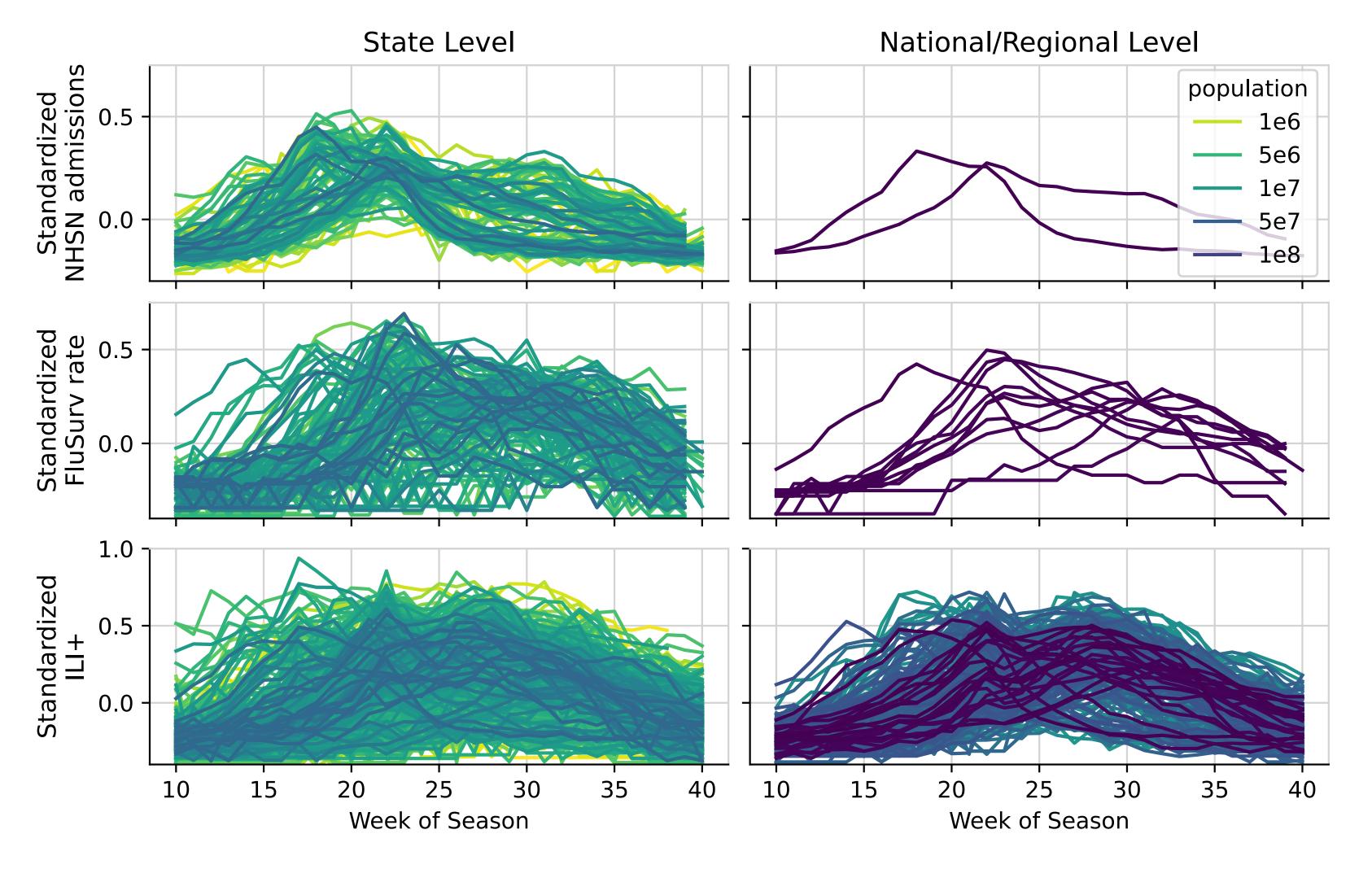
- · We apply the same transformations we discussed for the AR model
  - Fourth root: stabilize variance across different times
  - Center and scale: put the data on a similar scale for different locations, signals



# What would you do with all this data?



# What would you do with all this data?



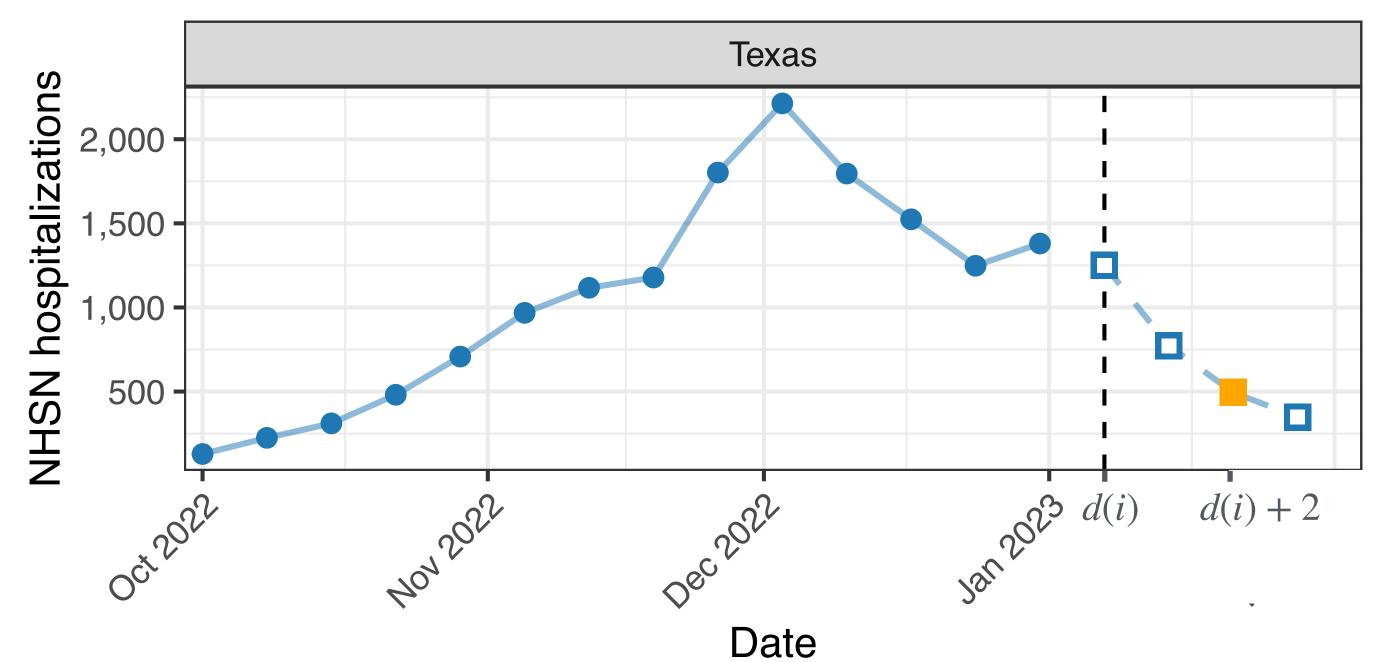
• My (first) answer: machine learn the hell out of it

#### Some notation

- Let i index **forecast tasks** defined by a combination of:
  - s(i): data source (NHSN, FluSurv, ILI+)
  - l(i): location (which state, region, or national level unit)
  - d(i): reference date, when we are making the forecast
  - h(i): forecast horizon: 0, 1, 2, or 3 weeks ahead
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- Example with s(i) = NHSN, l(i) = Texas, d(i) = Jan. 7, 2023, h(i) = 2



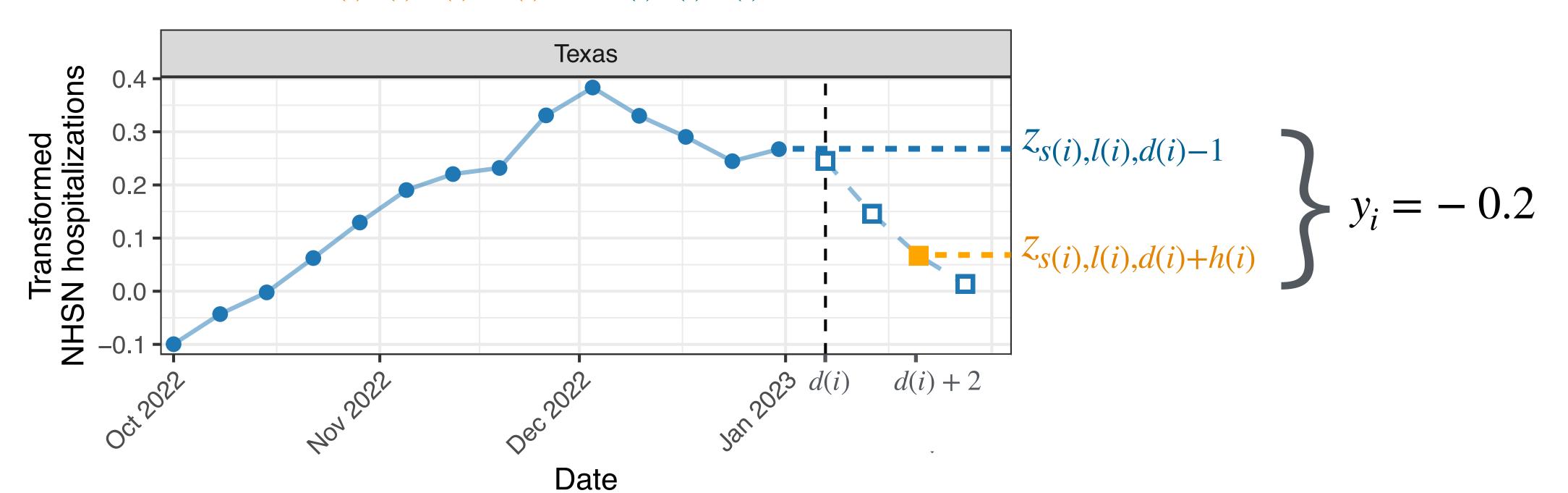
### Set up as a regression problem

- For each task i, we form the pair  $(x_i, y_i)$ :
  - $x_i$  is a vector of features measuring how the signal s(i) behaved in location l(i) near date d(i)
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  - $y_i$  is the prediction target
    - We set  $y_i$  = difference in transformed data between the target date and the last observation

$$= z_{s(i),l(i),d(i)+h(i)} - z_{s(i),l(i),d(i)-1}$$



### Features

• We used 114 features for each  $\boldsymbol{x}_i$ 

Group	Description	Count
1	A one-hot encoding of the data source.	3
2	A one-hot encoding of the location.	65
3	A one-hot encoding of the spatial scale of the location ("state", "region", or "national").	3
4	The population of the location.	1
5	The week of the season with the most recent reported data, $d(i) - 1$ .	1
6	The difference between the week of the season with the most recent reported data and Christmas week; for instance, a value of 3 means that the most recent data report is for the week three weeks after Christmas.	1
7	The forecast horizon.	1
8	The most recent reported value of the surveillance signal, for the time $d(i) - 1$ .	1
9	The coefficients of a degree 2 Taylor polynomial fit to the trailing $w$ weeks of data, where $w \in \{4,6\}$ , with the reference point for the polynomial set to the time $d(i)-1$ . These coefficients are estimates of the local level, first derivative, and second derivative of the signal at the time $d(i)-1$ .	6
10	The coefficients of a degree 1 Taylor polynomial fit to the trailing $w$ weeks of data, where $w \in \{3, 5\}$ . These coefficients are estimates of the local level and first derivative of the signal at the time $d(i) - 1$ .	4
11	The rolling mean of the signal over the last $w$ weeks, where $w \in \{2,4\}$ .	2
12	The values of all features from groups 8 through 11 at lags 1 and 2, representing estimates of the local level and first and second derivatives of the signal in each of the previous two weeks.	26

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- Note: when predicting a target signal and location, features measure information only about that signal and location
- Example: s(i) = NHSN, l(i) = Texas
  - $x_i$  does not contain any info. about FluSurv or ILI+
  - $x_i$  does not contain any info. about New Mexico or Oklahoma

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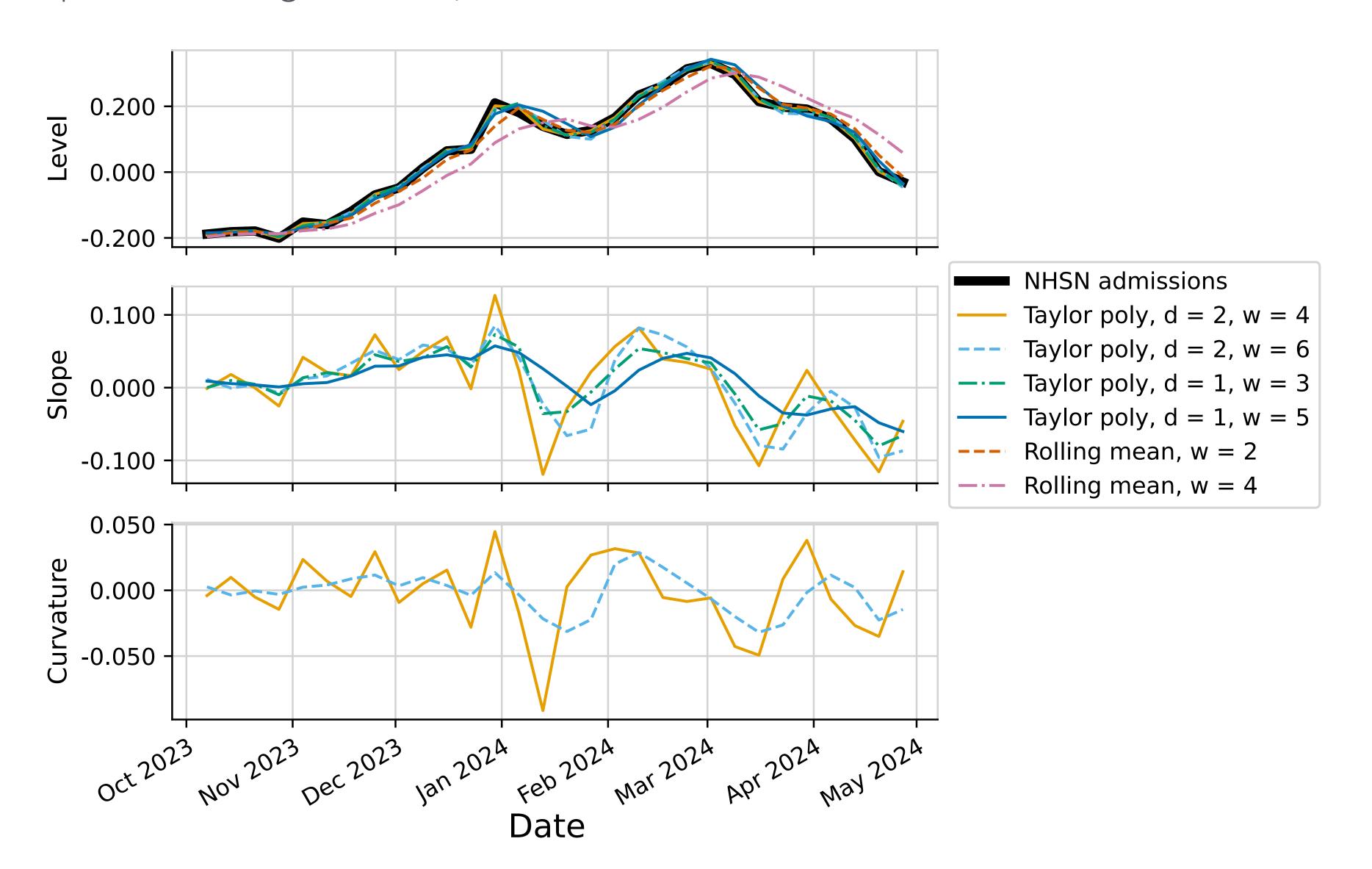
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- However, the model is trained on examples  $(x_i, y_i)$  from all data sources and locations!

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## Local level, slope, and curvature features

• Example for Michigan, 2023/24 season



# Gradient boosting quantile regression

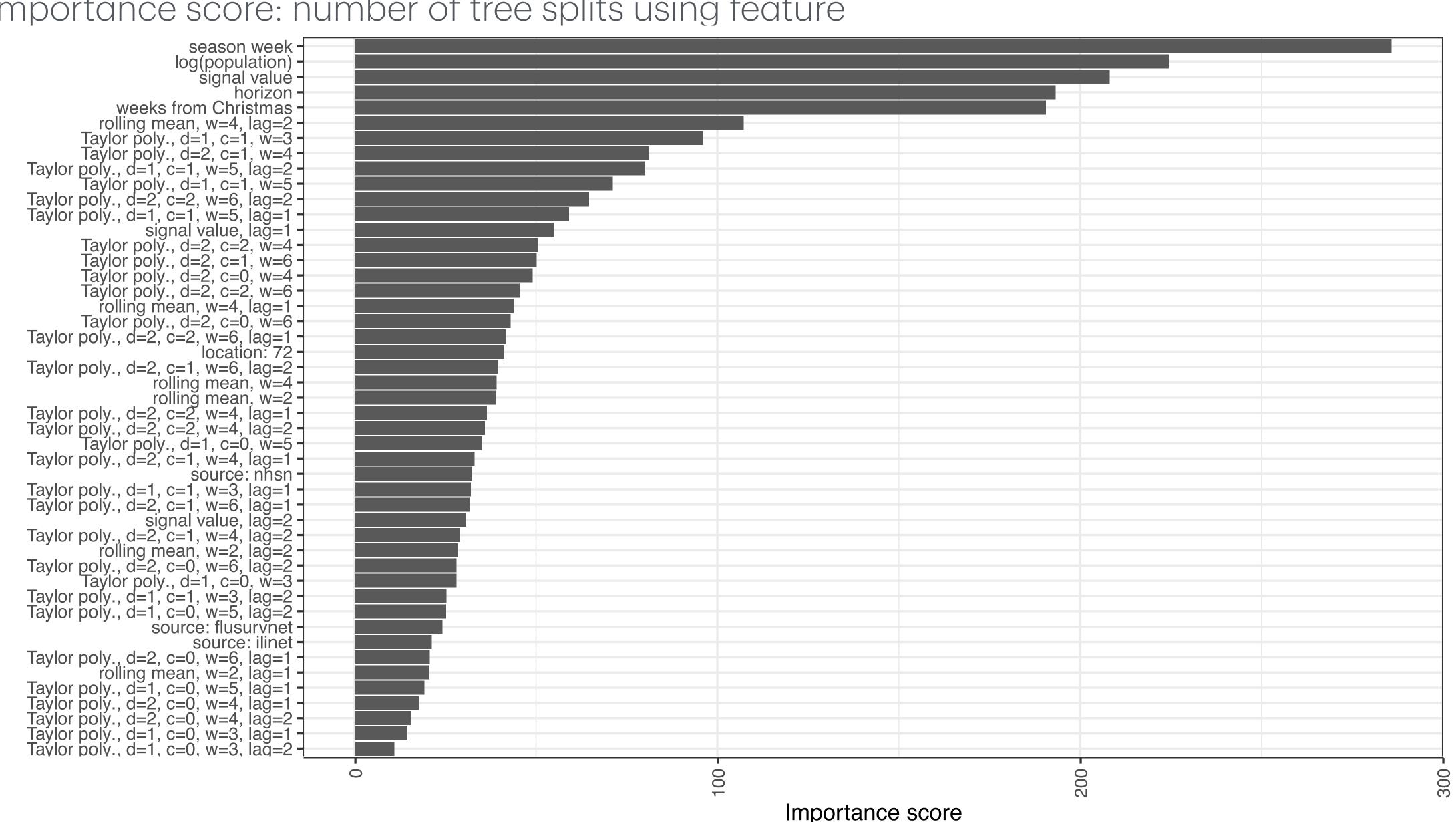
- We now have a bunch of training examples  $(x_i, y_i)$
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  - In particular, we want quantiles of that distribution at the levels  $\tau \in \{0.01, 0.025, ..., 0.99\}$
- We use gradient boosting quantile regression (GBQR)
  - For each  $\tau$ , learn a flexible mapping  $f_{\tau}(x)$  from features x to a predictive quantile at level  $\tau$
  - $f_{\tau}(x)$  takes the form of a sum of regression trees
  - Fit by targeting the quantile loss using the LightGBM package

## Feature Importance

• Importance score: number of tree splits using feature



### Two GBQR model variations

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- GBQR: the main model, trained on all 114 features
- GBQR-no-level: same model, not allowed to see features measuring local level of the signal
  - Introduced partway through the season
  - I got nervous: would a model that made its predictions based on the level of the signal always predict a decrease if recent incidence was large?
    - This would seem bad in a severe season

### Flusion: an ensemble of 3 models

- Three component models:
  - 1. GBQR: A gradient boosting quantile regression model, all 114 features
  - 2. GBQR-no-level: Same as GBQR, but not allowed to see measures of local level of signal
  - 3. ARX: Bayesian autoregressive model
    - This model also used 1 covariate: a spike function peaking at Christmas
    - This had essentially no impact on model performance
- Each model produces a set of predictive quantiles at 23 quantile levels from 0.01 to 0.99
- Flusion takes the average of these quantiles

## Overall Results: FluSight 2023/24 season

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Lower rank Worse Performan

Model	% Submitted	MWIS	m rMWIS	MAE	rMAE	50% Cov.	95% Cov.
Flusion	99.9	29.6	0.610	45.6	0.670	0.583	0.967
FluSight-ensemble	100.0	35.5	0.731	55.4	0.814	0.516	0.926
Other Model #1	100.0	35.6	0.731	54.0	0.792	0.558	0.940
Other Model #2	89.1	40.4	0.773	61.5	0.840	0.479	0.908
Other Model #3	97.8	39.9	0.806	59.3	0.857	0.363	0.793
Other Model #4	100.0	40.0	0.823	60.5	0.890	$\boldsymbol{0.497}$	0.884
Other Model #5	67.3	45.0	0.827	68.7	0.899	0.487	0.866
Other Model #6	100.0	41.5	0.851	64.4	0.945	0.466	0.903
Other Model #7	85.5	45.7	0.852	66.1	0.878	0.418	0.824
Other Model #8	100.0	41.6	0.856	60.7	0.893	0.460	0.855
Other Model #9	100.0	42.1	0.865	60.9	0.894	0.442	0.827
Other Model $#10$	98.8	44.3	0.901	67.7	0.986	0.456	0.939
Baseline-trend	99.9	43.9	0.906	67.0	0.990	0.618	0.922
Other Model $#11$	95.7	45.0	0.908	66.2	0.956	0.554	0.870
Other Model $#12$	87.0	45.0	0.936	70.7	1.050	0.449	0.929
Other Model #13	96.4	42.4	0.948	64.2	1.030	0.429	0.896
Other Model #14	93.6	48.7	0.980	70.8	1.020	0.473	0.838
Other Model #15	99.2	47.3	0.993	58.1	0.870	0.596	0.793
Baseline-flat	100.0	48.5	1.000	67.9	1.000	0.282	0.888

(Results for 11 lower-ranked models are suppressed for brevity)

## Experiment A: Component models

- Question: Which component model(s) drove Flusion's performance?
- Experiment: Scored individual components and ensembles of component model pairs
- Results:

Higher rank

Experiment	A:	Component	model	performance

Model	% Submitted	MWIS	rMWIS	MAE	rMAE	50% Cov.	95% Cov.
GBQR, ARX	100.0	29.9	0.618	45.3	0.668	0.570	0.958
Flusion	100.0	30.2	0.622	46.6	0.686	0.558	0.963
GBQR	100.0	30.3	0.625	46.3	0.682	0.529	$\boldsymbol{0.947}$
GBQR, GBQR-no-level	100.0	30.4	0.628	47.1	0.694	0.546	0.958
GBQR-no-level, ARX	100.0	33.2	0.685	52.2	0.769	0.528	0.958
$\operatorname{GBQR} ext{-no-level}$	100.0	33.9	0.698	52.6	0.775	0.523	0.944
ARX	100.0	39.5	0.815	60.0	0.884	$\boldsymbol{0.485}$	0.917
Baseline-flat	100.0	48.5	1.000	67.9	1.000	0.282	0.888

Top 4
Include
GBQR

• Primary driver was whether or not GBQR was included

# Experiment B: Reduced training data

- Question: was training jointly on multiple signals and locations helpful?
- Experiment: Fit 2 model variations:
  - GBQR-by-location: fit to each location separately, all 3 data sources
  - GBQR-only-NHSN: fit to all locations jointly, only data from NHSN

#### Results:

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Experiment B: Reduced training data

Model	% Submitted	MWIS	rMWIS	MAE	$\mathbf{rMAE}$	50% Cov.	95% Cov.
GBQR	100.0	30.3	0.625	46.3	0.682	0.529	0.947
GBQR-by-location	100.0	37.8	0.780	57.9	0.854	0.327	0.891
GBQR-only-NHSN	100.0	41.5	0.857	63.7	0.939	0.361	0.838
Baseline-flat	100.0	48.5	1.000	67.9	1.000	0.282	0.888

• Training jointly on data from all locations and data sources was key to strong performance

### Overview of this talk

- Motivation, preview of results
- Modeling approaches
  - Model 1
  - Model 2
- Conclusions

### Summary & conclusions

- Flusion had the top rank among all contributors to FluSight in the 2023/24 season
- Key drivers of its performance were:
  - The use of a gradient boosting model for forecasting
  - Joint training on all locations
  - Joint training on data for the target system and 2 other signals with a longer history
- Many model refinements are possible!
  - Use type or subtype-specific data to see multiple waves within 1 season
  - · Use vaccination uptake and efficacy data to inform estimates of season severity
  - Improve handling of holiday effects
  - Allow the model to see contemporaneous data:
    - Other signals
    - Other locations

•

## Summary & conclusions

- Simple methods like AR models can carry you a long way
- But modern methods and careful use of multiple data sources really are valuable!
- This approach indicates a way forward in a setting where public health data modernization initiatives may bring new surveillance systems online

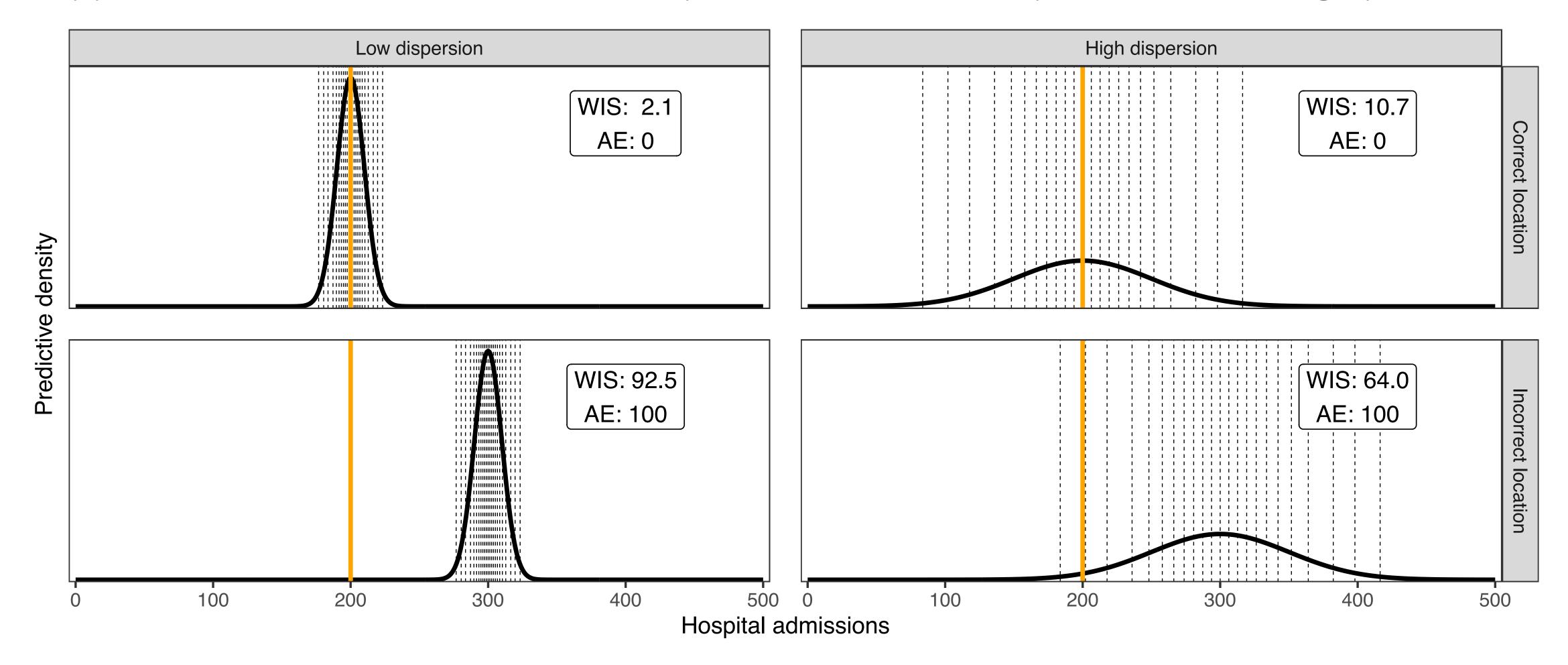
# Thanks for your attention!

- Questions?
- Acknowledgments to co-authors: Yijin Wang, Russel D. Wolfinger, Nicholas G. Reich
- Acknowledgments to funders:
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- Preprint available on arXiv: <a href="https://arxiv.org/abs/2407.19054">https://arxiv.org/abs/2407.19054</a>



# Evaluation: Weighted Interval Score (WIS)

- WIS can be interpreted as a generalization of absolute error to a set of predictive quantiles
  - Measures the distance of the distribution from the observed outcome
  - Lower is better
  - Approximates CRPS as the number of quantiles increases; equivalent to average pinball loss



#### Forecast evaluation

We use 6 metrics to evaluate forecast accuracy and calibration

- Mean absolute error (MAE)
  - |m-y|, where m is the predictive median and y is the observed value
- Mean weighted interval score (MWIS)

• Let 
$$\{q_k: k=1,\ldots,K\}$$
 denote a set of predictive quantiles at levels  $\tau_1,\ldots,\tau_K$ . 
$$WIS(\{q_k: k=1,\ldots,K\},y) = \frac{1}{K}\sum_k 2\cdot QS_{\tau_k}(q_k,y)$$

$$QS_{\tau_k}(q_k, zy) = \tau_k \max(y - q_k, 0) + (1 - \tau_k) \max(q_k - y, 0)$$

- Relative MAE (rMAE), Relative MWIS (rMWIS), see next slide
- 50% Interval Coverage, 95% Interval Coverage
  - What proportion of the time did central prediction intervals include the eventually observed value?

#### Relative score metrics

#### Challenge:

- different forecasters submit predictions for different locations and dates
- MAE and WIS are sensitive to the scale of the prediction target
- MAE and WIS values for forecasts in different locations and dates are not comparable

#### Our approach has 3 steps:

- 1. For each pair of models m and m', compute the MAE (or MWIS) on the subset of location/dates they have in common, denoted by  $MAE^m_{\mathcal{F}_{m,m'}}$  and  $MAE^{m'}_{\mathcal{F}_{m,m'}}$
- 2. For model m, compute the geometric mean of ratios of MAEs for m compared to all other models  $\frac{1}{(M-1)}$

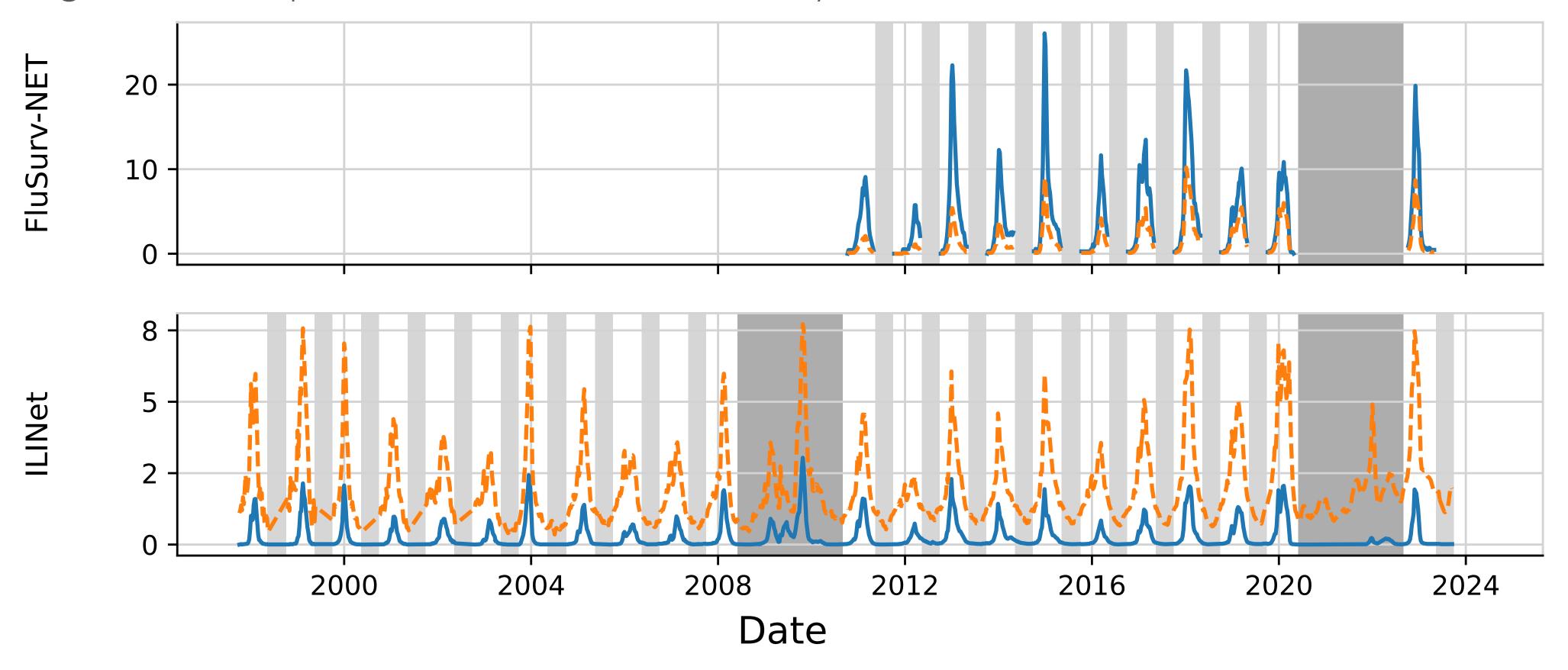
$$\theta^{m} = \left(\frac{1}{1} \frac{MAE_{\mathcal{J}_{m,m'}}^{m,m'}}{MAE_{\mathcal{J}_{m,m'}}^{m'}}\right)^{1/(M-1)}$$

3. Standardize relative to a baseline (in our case, Baseline-flat)

$$rMAE^{m} = \frac{\theta^{m}}{\theta^{baseline}}$$

## Data adjustments

- For both other signals, we employ adjustments (original in orange, adjusted in blue)
  - FluSurv-NET: adjust for different case capture rates from season to season due to changing testing rates and test sensitivity
  - ILI+: combine a measure of influenza-like illness (ILI) with influenza test positivity rates to get a more specific measure of flu activity



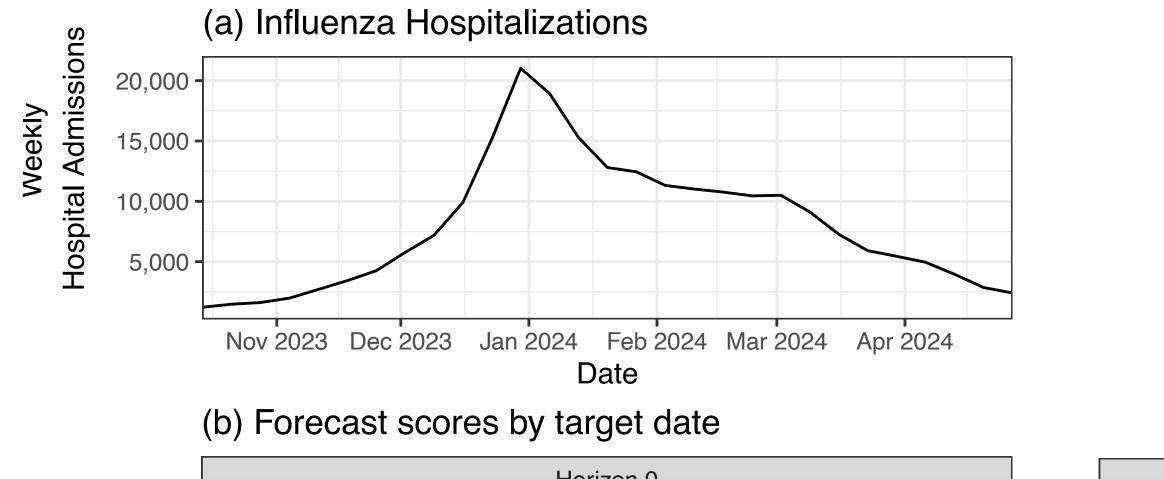
# Holiday effects in the ARX model

• We used a Bayesian specification of an autoregressive model (order J=8) with covariates

$$\begin{split} Y_{l,t} \mid y_{l,t-1}, \dots, y_{l,t-J}, x_{l,t-1}, \dots, x_{l,t-J}, \varepsilon_{l,t} &= \sum_{j=1}^{J} \alpha_j y_{l,t-j} + \sum_{j=1}^{J} \beta_j x_{l,t-j} + \varepsilon_{l,t} \\ X_{l,t} \mid x_{l,t-1}, \dots, x_{l,t-J}, \nu_{l,t} &= \sum_{j=1}^{J} \gamma_j x_{l,t-j} + \nu_{l,t} \\ \varepsilon_{l,t} &\sim \text{Normal}(0, \sigma_{\varepsilon,l}) \\ \nu_{l,t} &\sim \text{Normal}(0, \sigma_{\nu,l}) \end{split}$$

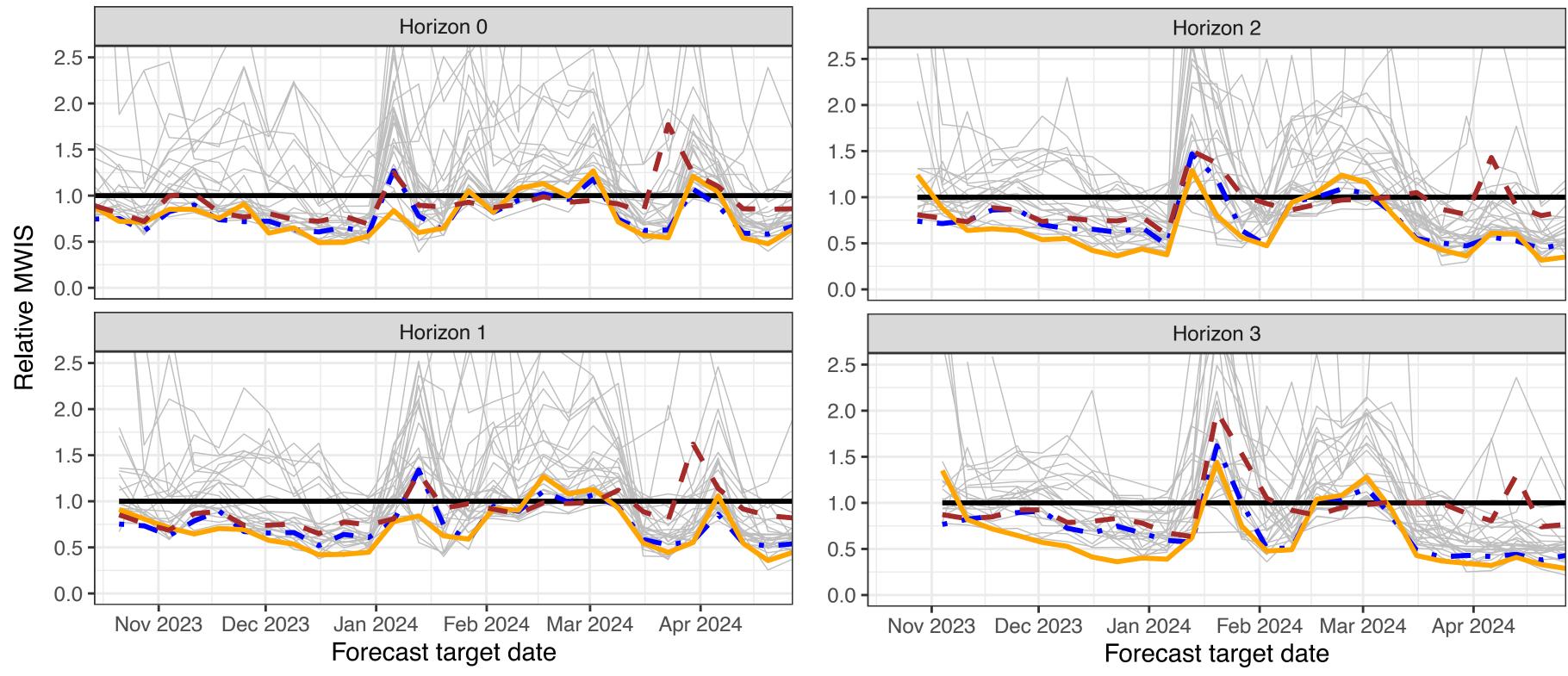
- Key idea for AR setup:
  - AR coefficients shared across locations (to avoid overfitting to limited data)
  - Separate variance innovation term per location (noise levels differ based on population)
- We used 1 covariate:
  - takes the value 3 on Christmas week
  - 2 one week before and one week after Christmas
  - 1 two weeks before and two weeks after Christmas
  - O otherwise

## MWIS by date and forecast horizon



#### Model

- Baseline-flat
- -- Baseline-trend
- -- FluSight-ensemble
- Flusion
- Other



### Quantile loss

- Suppose we have a set of observations  $y_i \sim \mathcal{D}, i=1,\ldots,n$
- We want to estimate the quantile q of the distribution  ${\mathscr D}$  at probability level  $\tau: P_{\mathscr D}(Y \le q) = \tau$
- $QS_{\tau}(q, y) = (1 \tau) \max(q y, 0) + \tau \max(y q, 0)$

• For a fixed value of y, the derivatives with respect to q are:

$$\frac{\partial}{\partial q} Q S_{\tau}(q,y) = -\tau \text{ if } y > q \qquad \text{and} \qquad \frac{\partial}{\partial q} Q S_{\tau}(q,y) = 1 - \tau \text{ if } y < q$$

# Optimizing quantile loss

• For a fixed  $y_i$ , the derivatives with respect to q are:

$$\frac{\partial}{\partial q}QS_{\tau}(q,y_i) = -\tau \text{ if } q < y_i \qquad \text{ and } \qquad \frac{\partial}{\partial q}QS_{\tau}(q,y_i) = 1 - \tau \text{ if } q > y_i$$

Averaging across all i:

$$\frac{\partial}{\partial q} \frac{1}{n} \sum_{i} QS_{\tau}(q, y_i) = \text{(proportion with } q < y_i) \cdot (1 - \tau) - \text{(proportion with } q > y_i) \cdot \tau$$

- Imagine applying gradient descent to find q:
  - The derivative w.r.t. q is 0 if the proportions are "balanced", with (proportion with  $y_i>q)=\tau$  and (proportion with  $y_i< q)=1-\tau$ 
    - In other words, q is a au-quantile of the sample  $y_i$ 's
  - The derivative is negative if

# Intro. to gradient boosting (formulas)

#### • Inputs:

- Training set with pairs  $(x_i, y_i)$ , i = 1, ..., n. Define  $\mathbf{y} = (y_1, ..., y_n)^\mathsf{T}$
- Loss function  $L(\hat{y}_i, y_i)$ : measures how well  $\hat{y}_i$  estimates  $y_i$  (lower loss is better)
- Method:
  - . We will construct the regression function  $f(x) = \sum_{b} f^{(b)}(x)$  iteratively
    - each  $f^{(b)}(x)$  will be a regression tree
  - . After step b-1, we have the predictions  $\hat{y}_i^{(b-1)} = \sum_{a=1}^{b-1} f^{(a)}(x_i)$ , collected in the vector  $\hat{\mathbf{y}}^{(b-1)}$
  - . After step b-1, the total loss is  $L_{tot}(\hat{\mathbf{y}}^{(b-1)}) = \sum_i L(\hat{y}_i^{(b-1)}, y)$
  - $\delta_i^{(b-1)} = -\frac{\partial}{\partial \hat{y}_i} L_{tot}(\hat{\mathbf{y}}) |_{\hat{\mathbf{y}} = \hat{\mathbf{y}}^{(b-1)}} \text{ indicates how to change } \hat{y}_i^{(b-1)} \text{ so as to reduce the total loss.}$
  - We fit the next regression tree  $f^{(b)}(x)$  to the pairs  $(x_i, \delta_i^{(b-1)})$