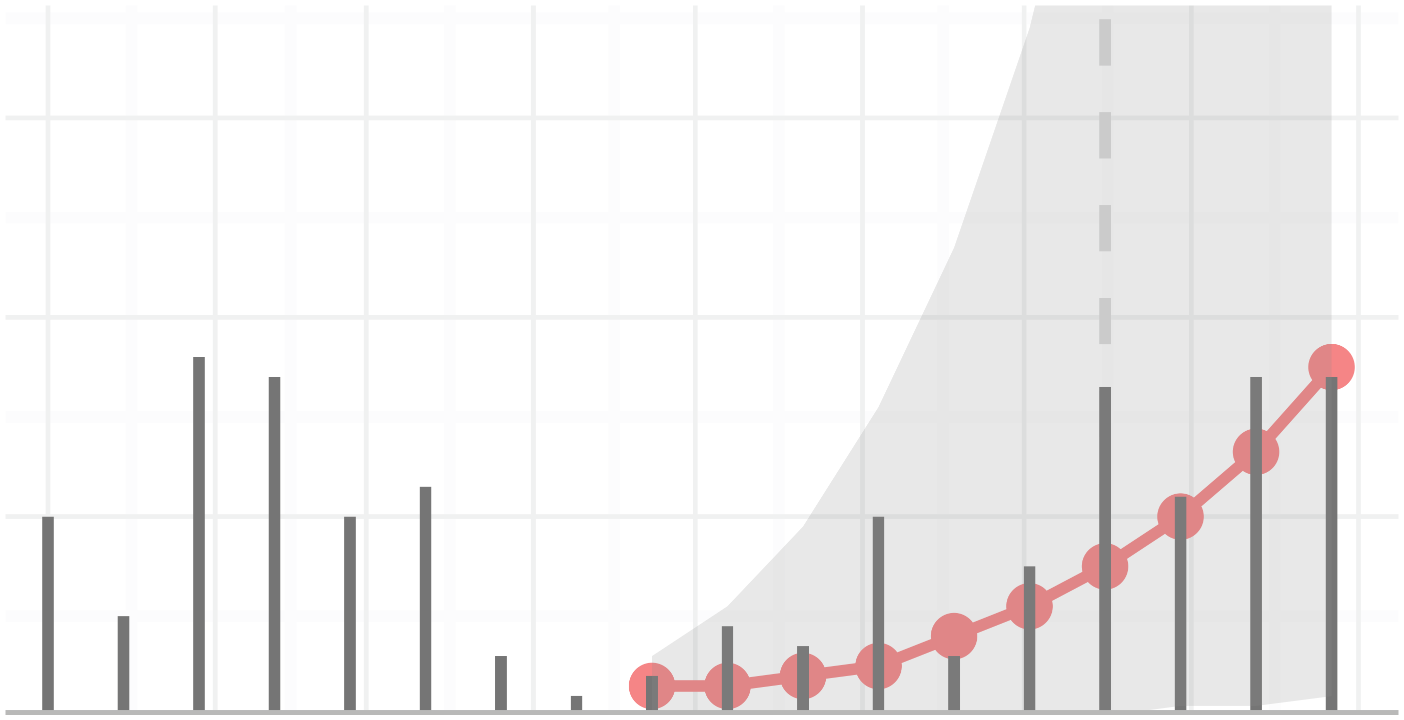
UMass Amherst



Statistical methods for real-time forecasts of infectious disease: dynamic time-series and machine learning approaches

Nicholas G. Reich

May 2017, MIDAS call

reichlab.io

Overview of the Reich Lab

Collaborative public health research at the intersection of biostatistics, data science, machine learning, and infectious disease epidemiology.

Methodological research: the science of learning from data.

Applied research: learning about disease systems.

Tools for public health: software, apps for decision support.

The work presented in these slides has been supported by
an NIGMS MIRA award (PI: Reich, R35GM119582),
a DARPA Young Faculty Award,
an NIAID R21 (PI: Reich, R21AI115173),
an NIAID R01 (PI: Lessler, R01AI102939)

1. Infectious disease forecasting
   - Ensemble forecasting of flu in U.S.
   - Forecasting dengue in Thailand

2. Modeling cost-effectiveness of active monitoring for Ebola

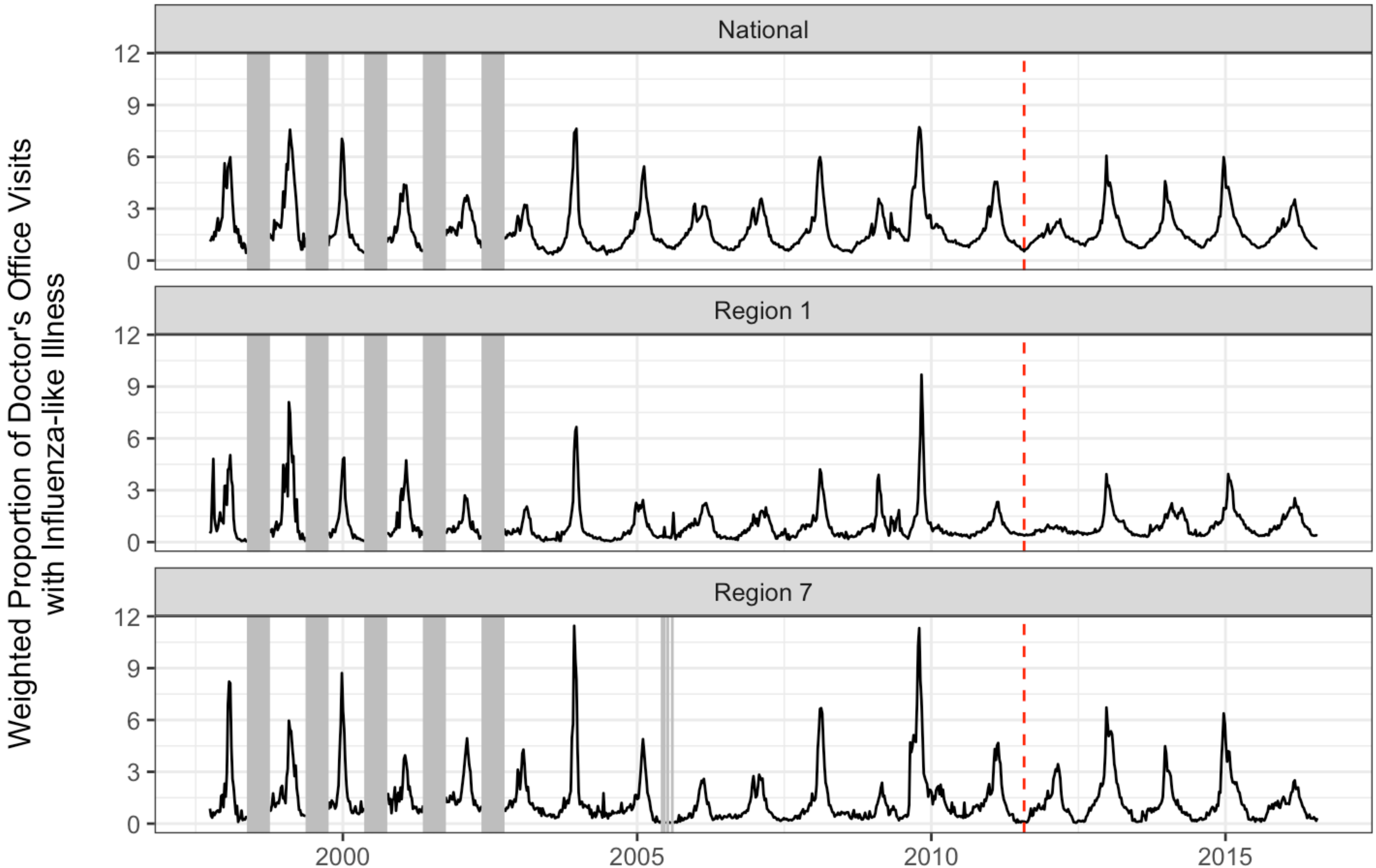
Ensemble forecasting

Ray and Reich, 2017 (under review)

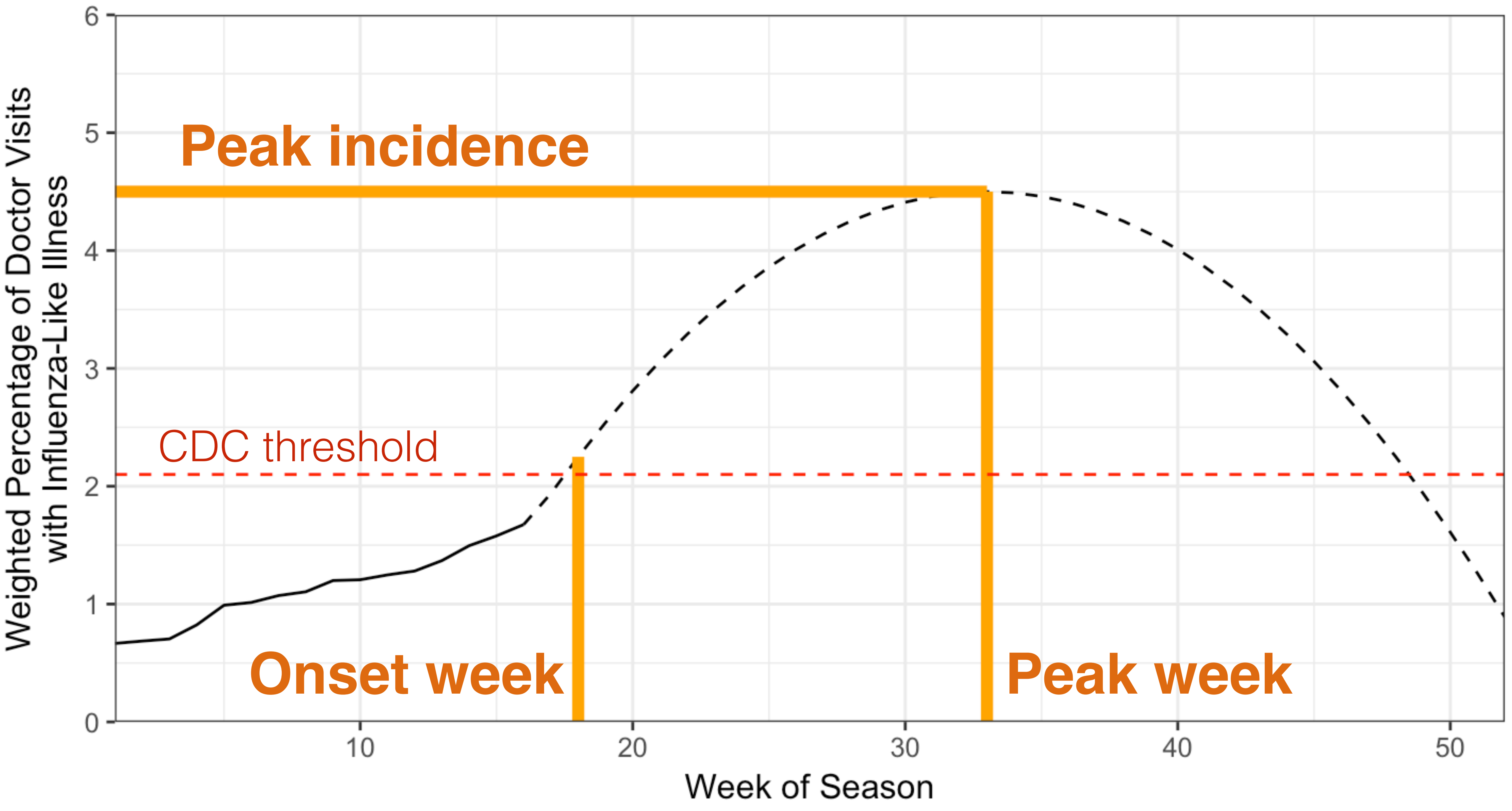
GitHub   arXiv

Motivating example

U.S. national and regional influenza data, from CDC



Defining seasonal prediction targets



Approach to forecasting

- Targets of interest driven by decision-makers.
- Probabilistic forecasts.
- "Real-time" data considerations.
- Pre-specified test phase predictions made once.

Ensemble overview

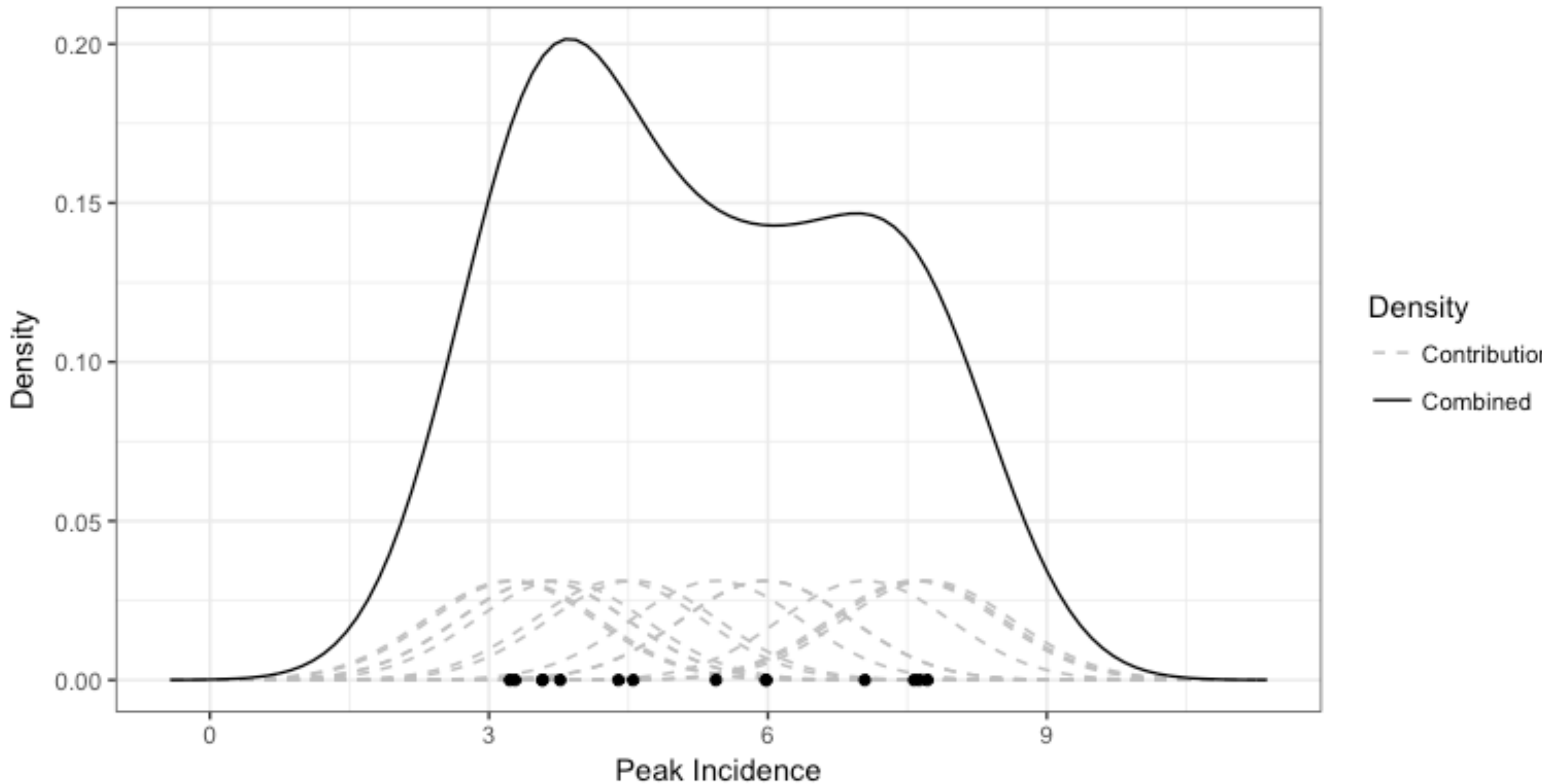
- An ensemble model fuses predictions from multiple models into a single combined prediction.

- Many different specific approaches; long seen as a powerful tool in predictive modeling.

- Recent work in the context of infectious disease: Yamana et al (2016), multiple teams participating in the influenza, dengue, chikungunya challenges.

Model 1

Kernel Density Estimation (KDE)

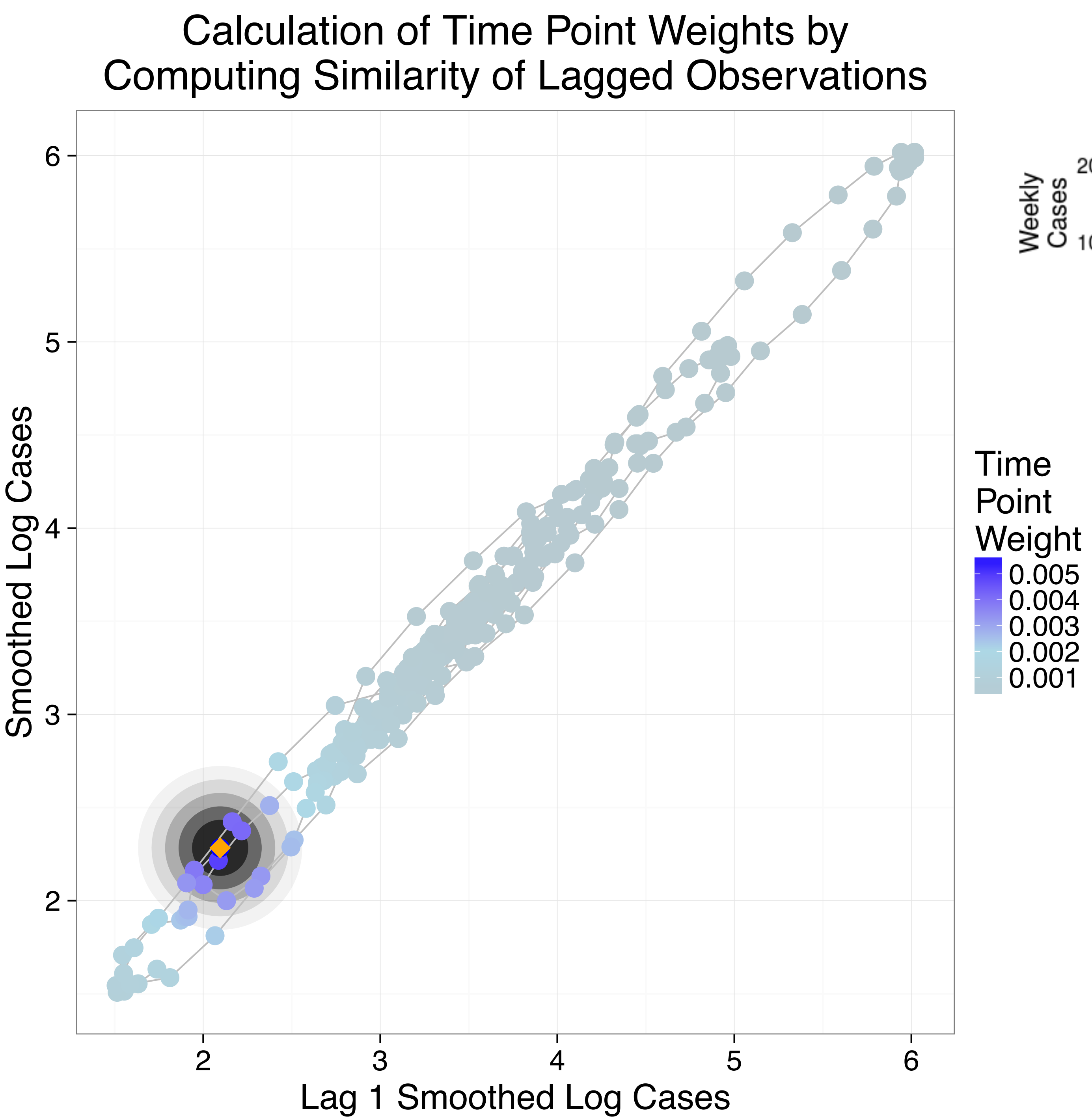


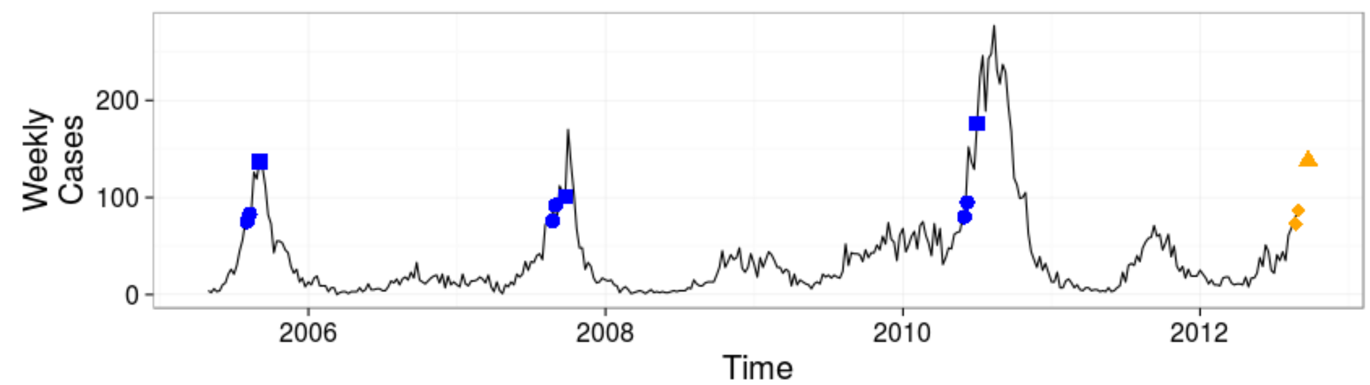
Estimated distribution, based on historical observations, of season peak incidence, peak week and onset week.

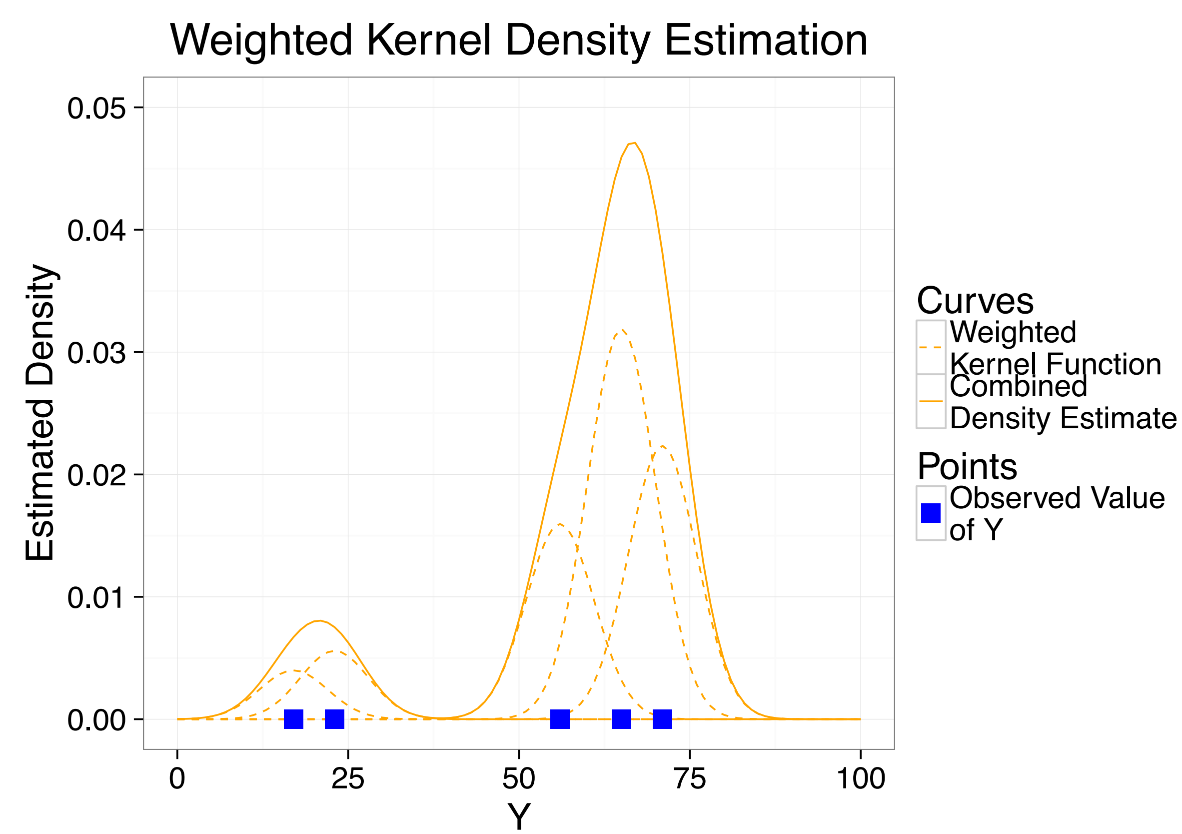
Distributions are not updated over the course of the season!

Model 2

Kernel Conditional Density Estimation (KCDE) + copulas



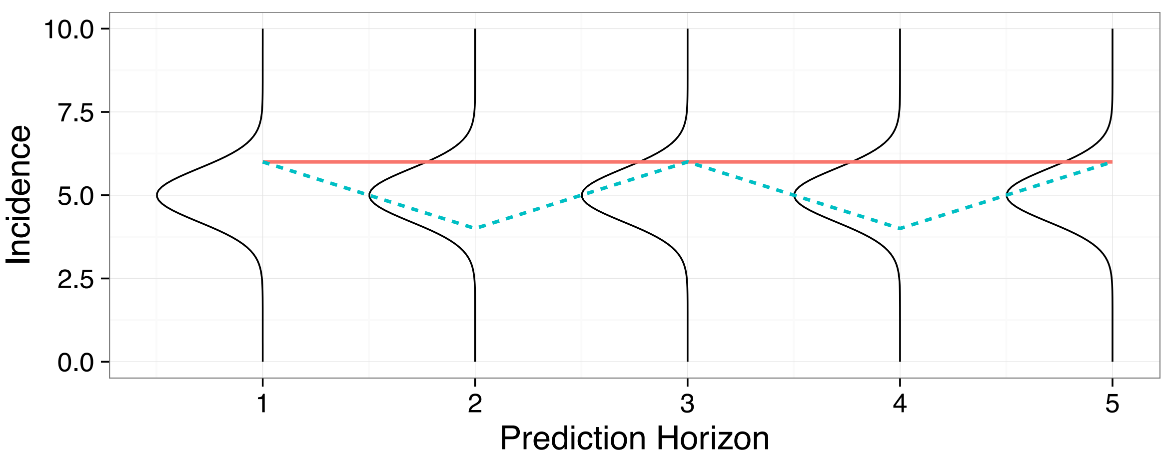




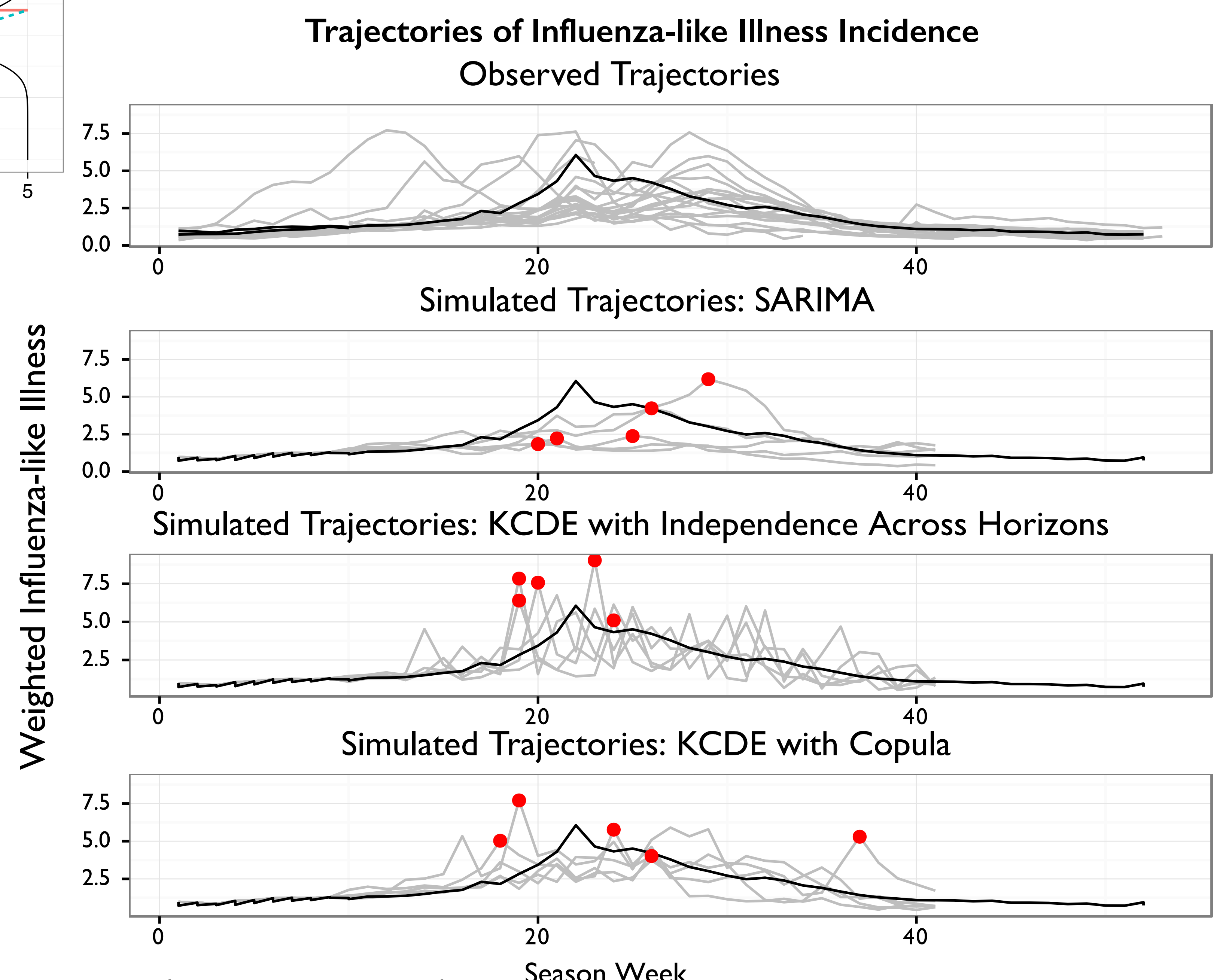
Ray et al. (under review)

Model 2 (con't)

Kernel Conditional Density Estimation (KCDE) + **copulas**



Copulas turn marginal distributions into trajectories by estimating a covariance structure between weeks.



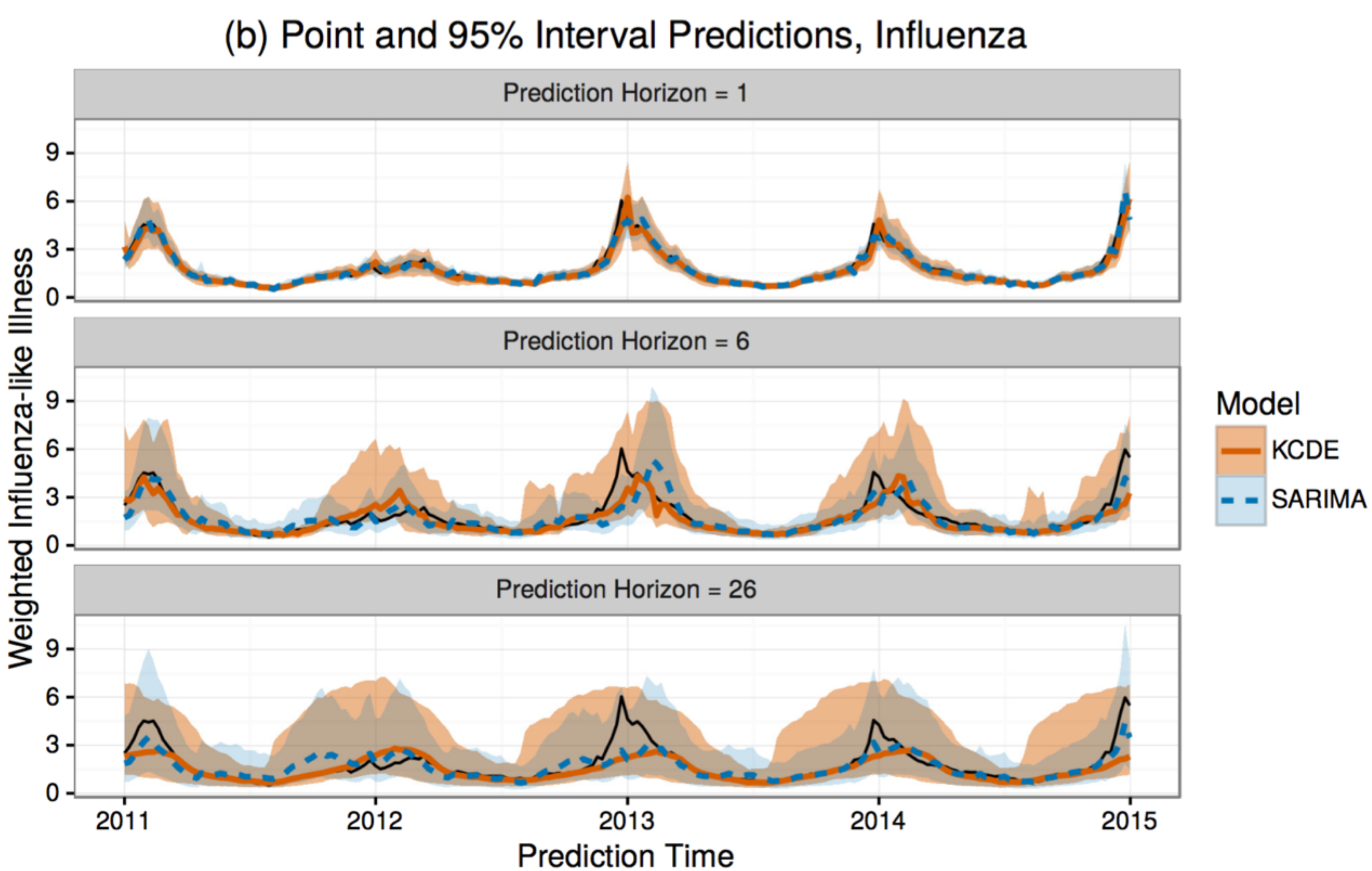
Ray et al. (under review)

Model 3

Seasonal Auto-Regressive Integrated Moving Average (SARIMA)

Equation for a SARIMA $(1,0,0)(2,1,0)_s$ model

$$X_t = X_{t-s} + \alpha_1(X_{t-1} - X_{t-s-1}) + \phi_1(X_{t-s} - X_{t-2s}) - \alpha_1 \cdot \phi_1(X_{t-s-1} - X_{t-2s-1}) + \phi_2(X_{t-2s} - X_{t-3s}) + \alpha_1 \cdot \phi_2(X_{t-2s-1} - X_{t-3s-1})$$



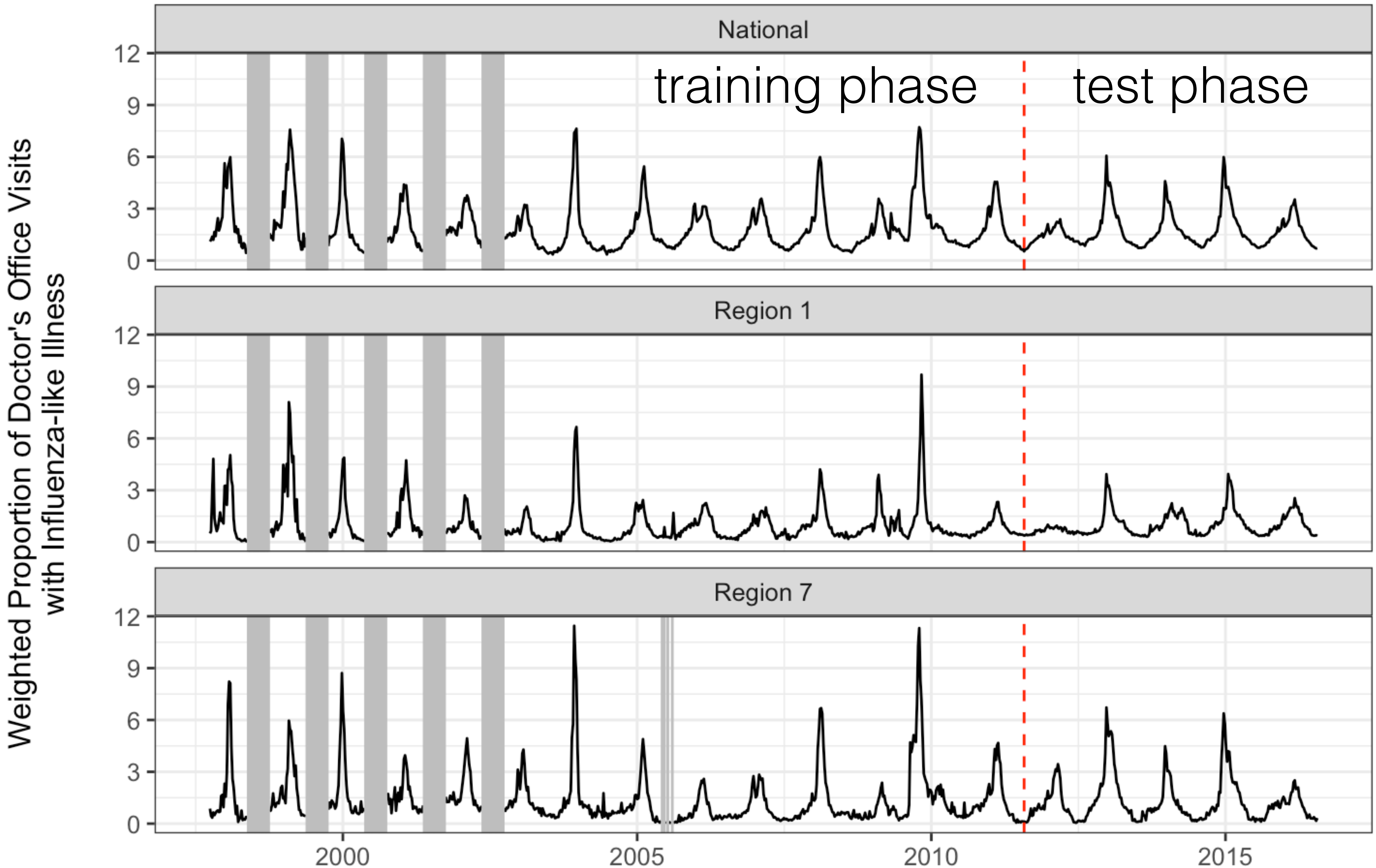
A classical statistical model for time-series.

Uses similar info as KCDE but makes more parametric assumptions.

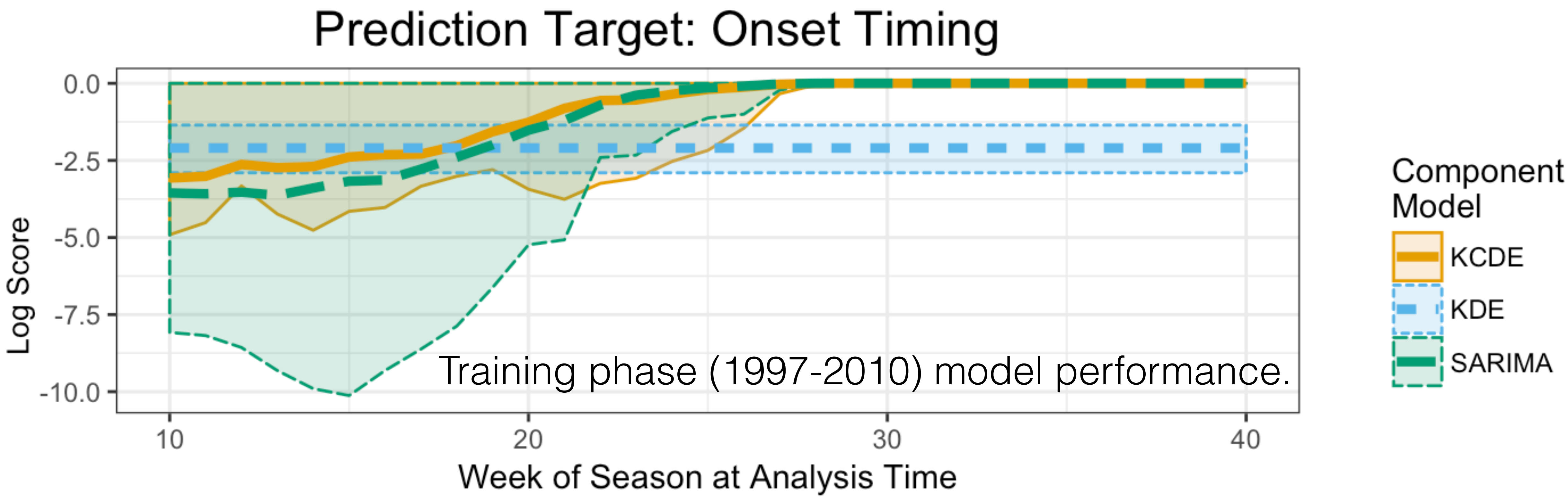
Figure from Ray et al. (under review)

Pre-specified evaluation

U.S. national and regional influenza data, from CDC

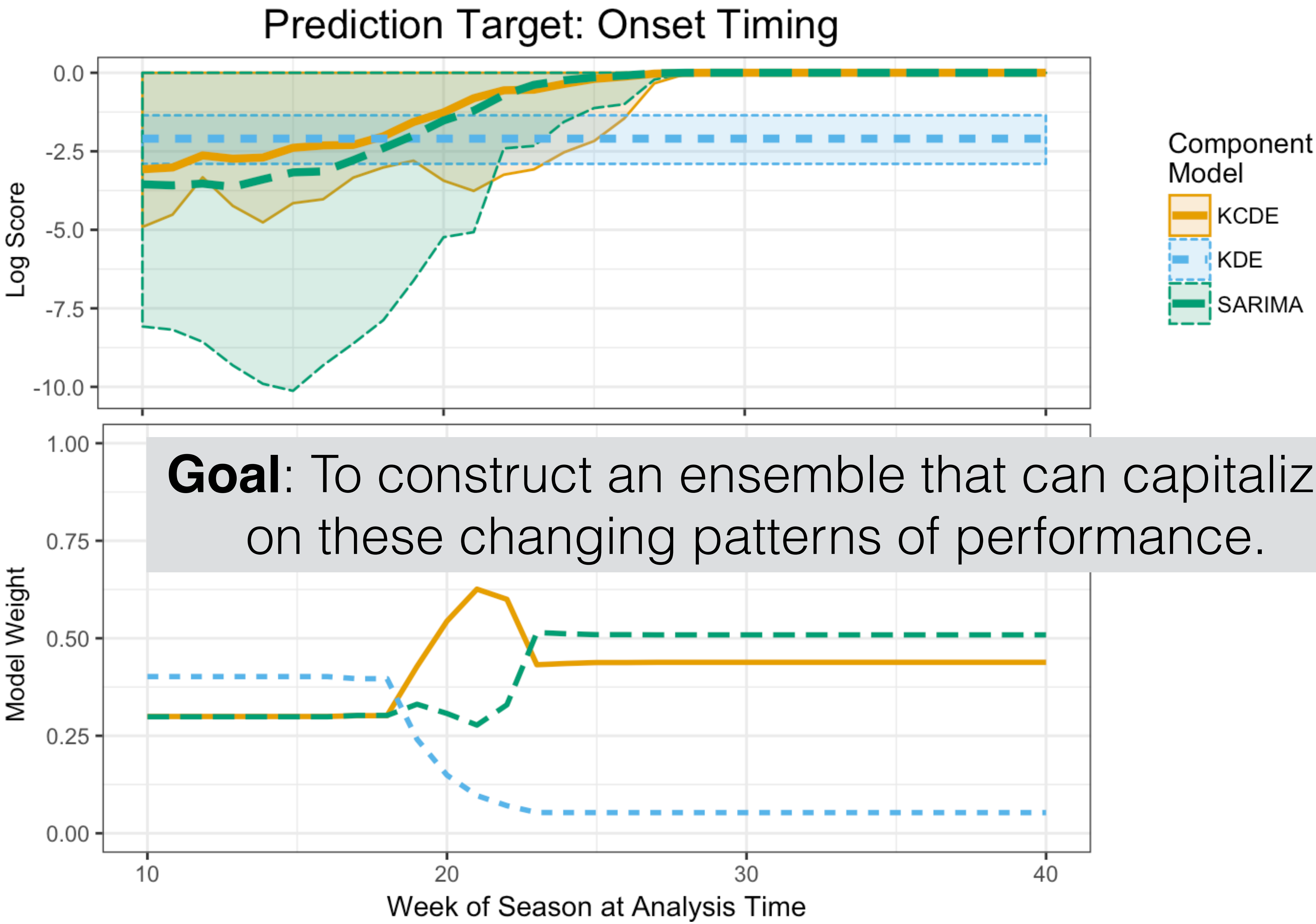


Model performance varies



Goal: To construct an ensemble that can capitalize on these changing patterns of performance.

Model performance varies



Goal: To construct an ensemble that can capitalize on these changing patterns of performance.

Model "stacking" framework

- We want a predictive distribution for $y|\mathbf{x}$.
  - y = e.g. season onset timing, peak timing, or peak incidence
  - $\mathbf{x}$ = time of year, recent incidence, weather, ...
- We have $M = 3$ predictive distributions $f_m(y|\mathbf{x})$ from different models
- Combine with covariate-dependent weights $\pi_m(\mathbf{x})$:

$$f(y|\mathbf{x}) = \sum_{m=1}^{M} \pi_m(\mathbf{x}) f_m(y|\mathbf{x})$$

- We require $\pi_m(\mathbf{x}) \geq 0$ and $\sum_{m=1}^{M} \pi_m(\mathbf{x}) = 1$ for each $\mathbf{x}$. One approach:

$$\pi_m(\mathbf{x}) = \frac{\exp\{\rho_m(\mathbf{x})\}}{\sum_{m'=1}^{M} \exp\{\rho_{m'}(\mathbf{x})\}}$$

- We estimate the functions $\rho_m(\mathbf{x})$ via Gradient Tree Boosting (GTB)

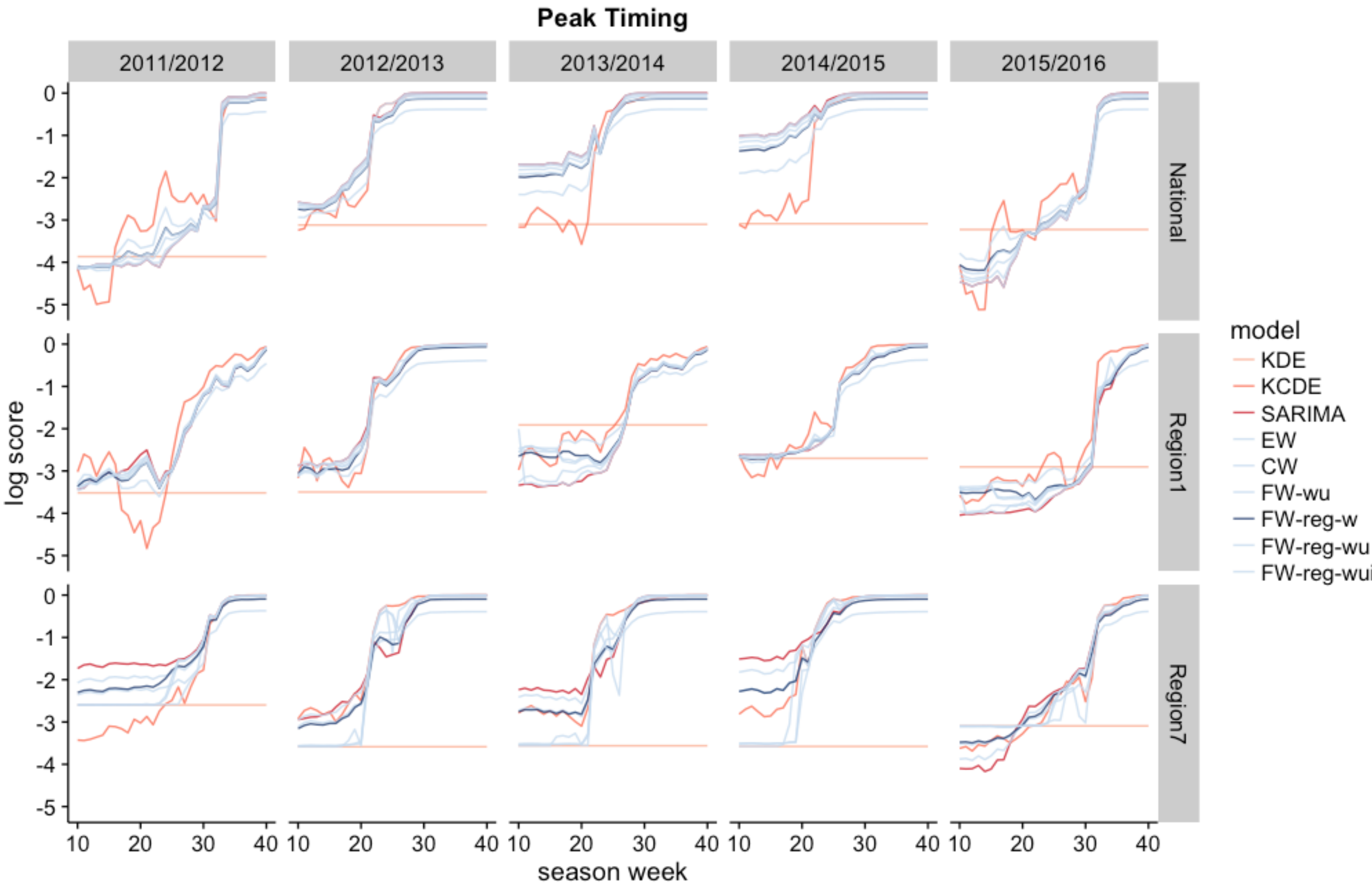
Weighting schemes

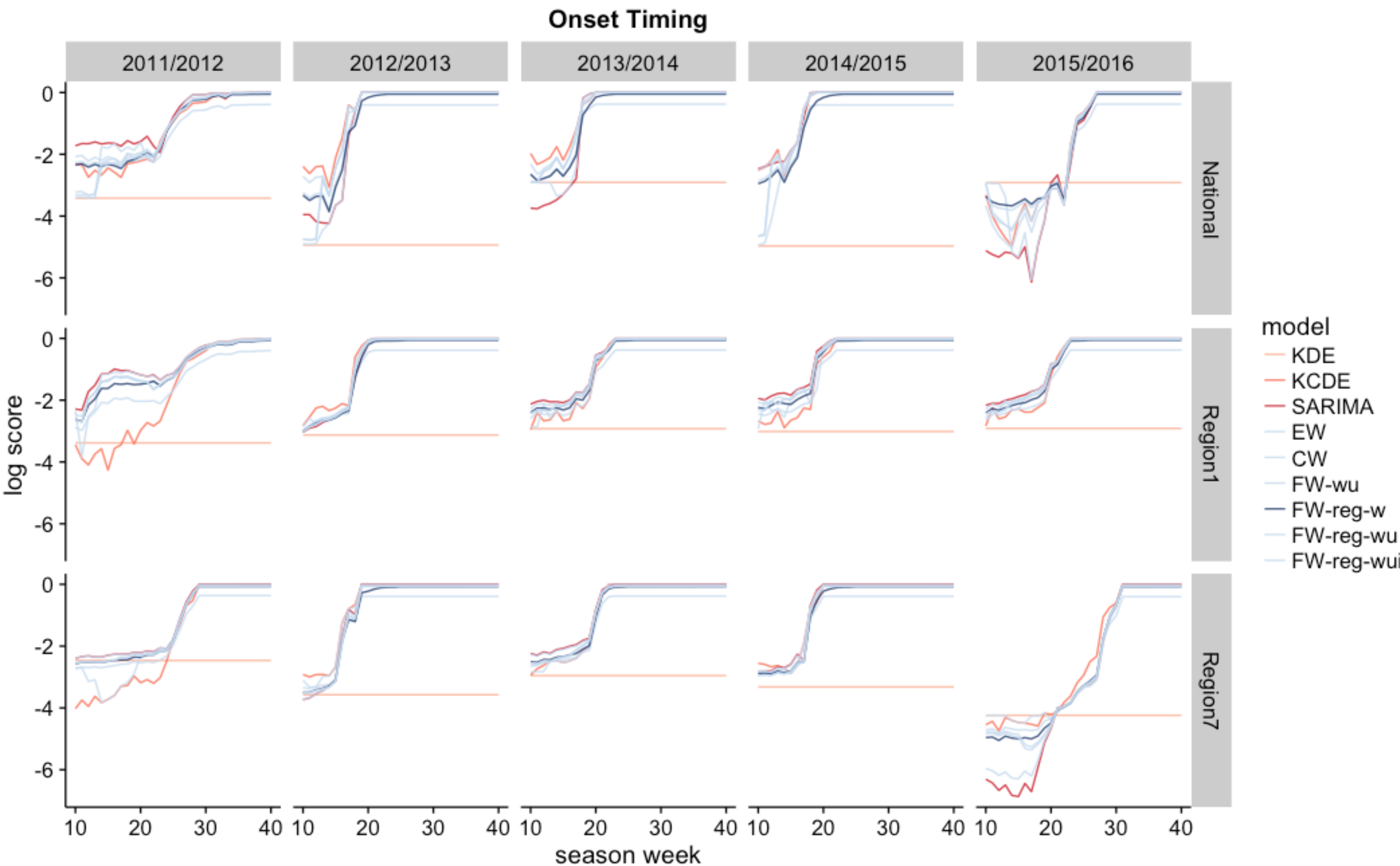
1. Equal Weights **(EW)**: $\pi_m(x) = 1/M$.
2. Constant Weights **(CW)**: $\pi_m(x) = \pi_m$.
3. Feature-weighted **(FW)**: $\pi_m(x)$ depends on features including week of the season and model uncertainty for the KCDE and SARIMA models.
4. Feature-weighted with regularization: $\pi_m(x)$ depends on features, but with regularization:
   1. (**FW-reg-w**) week of the season;
   2. (**FW-reg-wu**) week of the season and model uncertainty for the KCDE and SARIMA models;
   3. (**FW-reg-wui**) week of the season, model uncertainty for the KCDE and SARIMA models, and incidence in the most recent week.

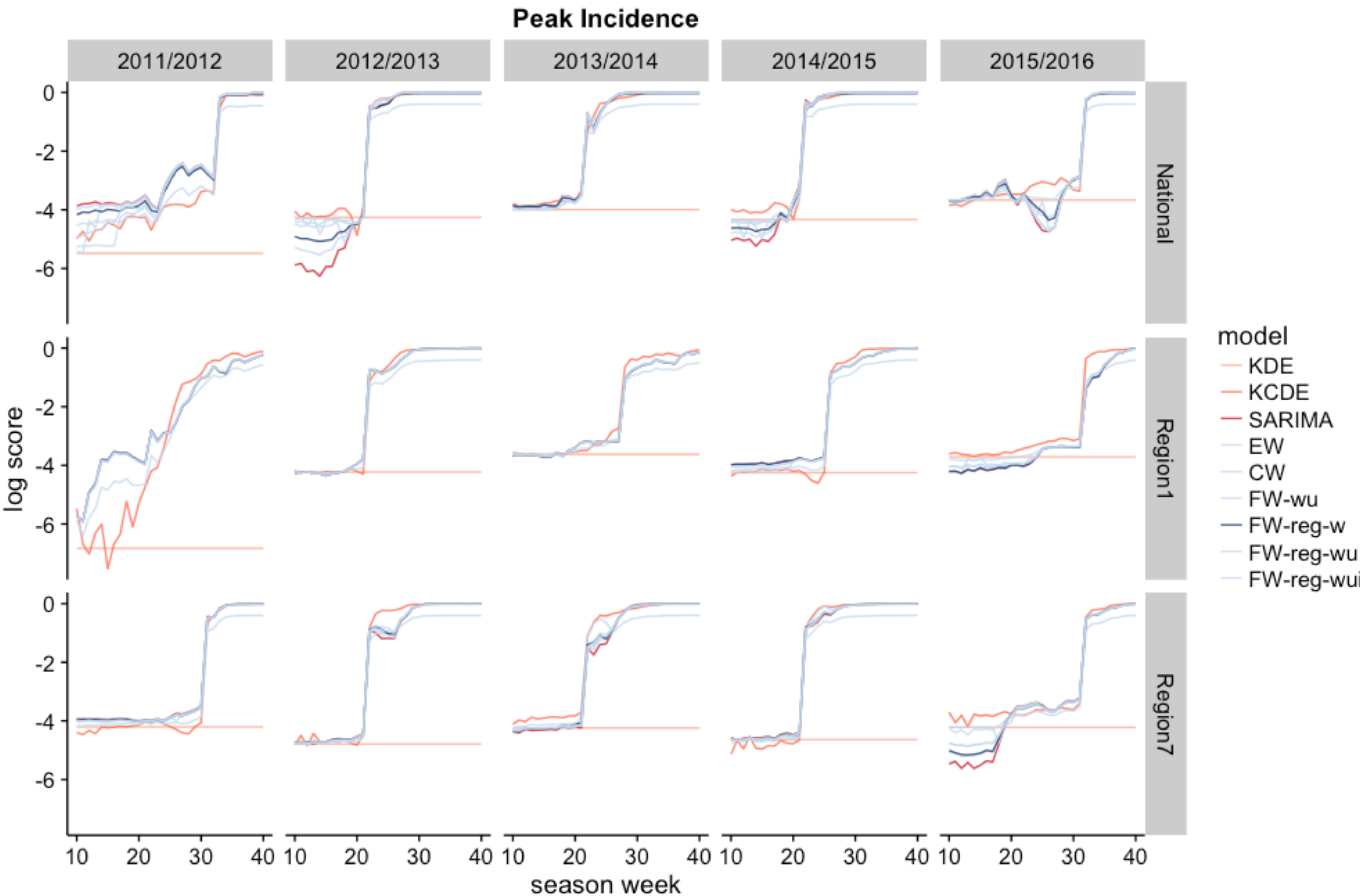
"Public health actions informed by forecasts that later prove to be inaccurate can have negative consequences, including the loss of credibility, wasted and misdirected resources, and, in the worst case, increases in morbidity or mortality. "

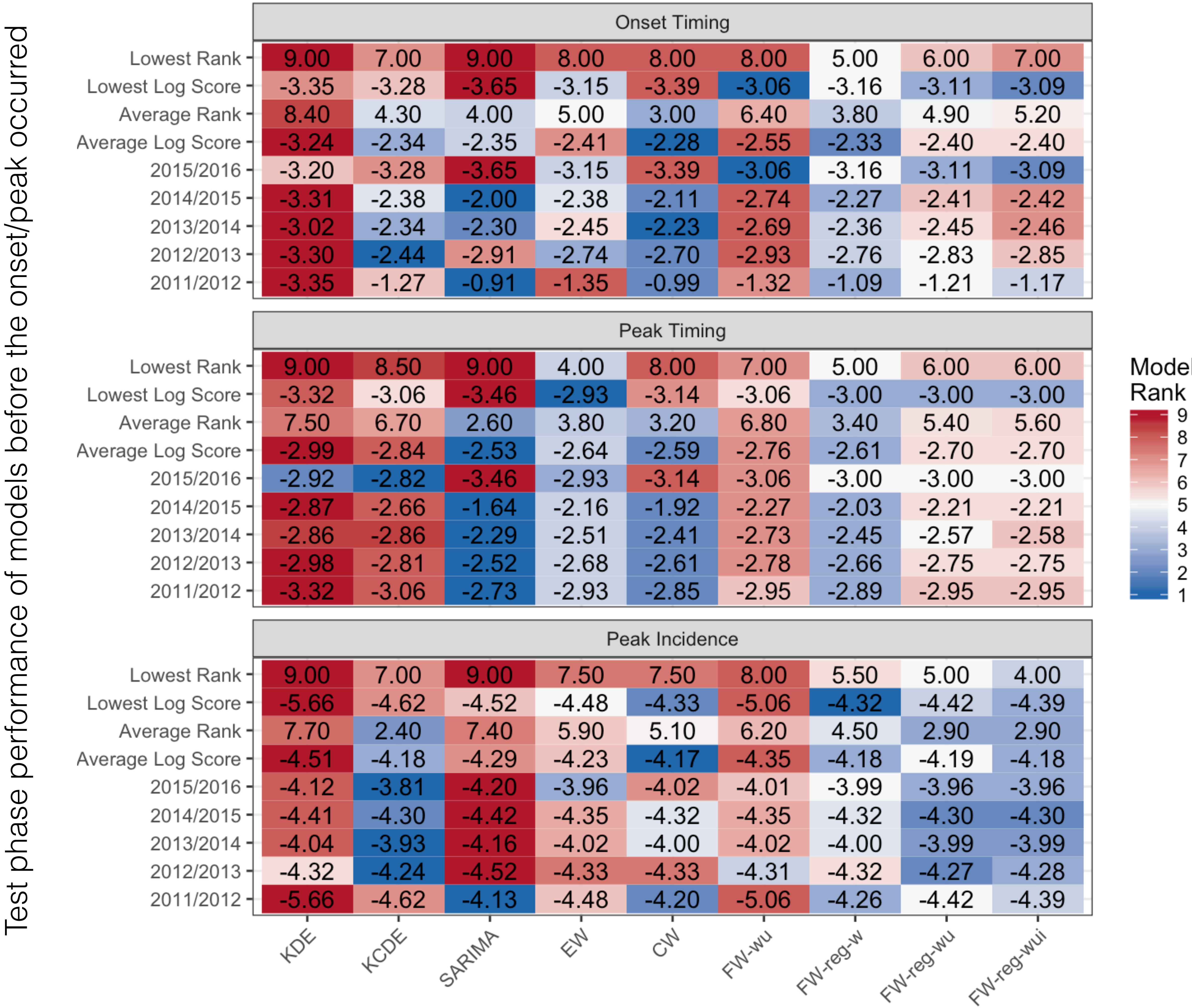
– Biggerstaff et al. BMC Infectious Diseases 2016.

Overall goal: create a model that shows
(1) good **overall** performance, and,
(2) consistent accuracy **every year.**


Peak Timing
2011/2012
2012/2013
2013/2014
2014/2015
2015/2016
National
Region1
Region7
log score
season week
0
-1
-2
-3
-4
-5
10
20
30
40
model
KDE
KCDE
SARIMA
EW
CW
FW-wu
FW-reg-w
FW-reg-wu
FW-reg-wui


Onset Timing
2011/2012
2012/2013
2013/2014
2014/2015
2015/2016
National
Region1
Region7
log score
season week
0
-2
-4
-6
10
20
30
40
model
KDE
KCDE
SARIMA
EW
CW
FW-wu
FW-reg-w
FW-reg-wu
FW-reg-wui


Peak Incidence
2011/2012
2012/2013
2013/2014
2014/2015
2015/2016
National
Region1
Region7
log score
season week
model
KDE
KCDE
SARIMA
EW
CW
FW-wu
FW-reg-w
FW-reg-wu
FW-reg-wui


Test phase performance of models before the onset/peak occurred
Onset Timing
Lowest Rank 9.00 7.00 9.00 8.00 8.00 8.00 5.00 6.00 7.00
Lowest Log Score -3.35 -3.28 -3.65 -3.15 -3.39 -3.06 -3.16 -3.11 -3.09
Average Rank 8.40 4.30 4.00 5.00 3.00 6.40 3.80 4.90 5.20
Average Log Score -3.24 -2.34 -2.35 -2.41 -2.28 -2.55 -2.33 -2.40 -2.40
2015/2016 -3.20 -3.28 -3.65 -3.15 -3.39 -3.06 -3.16 -3.11 -3.09
2014/2015 -3.31 -2.38 -2.00 -2.38 -2.11 -2.74 -2.27 -2.41 -2.42
2013/2014 -3.02 -2.34 -2.30 -2.45 -2.23 -2.69 -2.36 -2.45 -2.46
2012/2013 -3.30 -2.44 -2.91 -2.74 -2.70 -2.93 -2.76 -2.83 -2.85
2011/2012 -3.35 -1.27 -0.91 -1.35 -0.99 -1.32 -1.09 -1.21 -1.17
Peak Timing
Lowest Rank 9.00 8.50 9.00 4.00 8.00 7.00 5.00 6.00 6.00
Lowest Log Score -3.32 -3.06 -3.46 -2.93 -3.14 -3.06 -3.00 -3.00 -3.00
Average Rank 7.50 6.70 2.60 3.80 3.20 6.80 3.40 5.40 5.60
Average Log Score -2.99 -2.84 -2.53 -2.64 -2.59 -2.76 -2.61 -2.70 -2.70
2015/2016 -2.92 -2.82 -3.46 -2.93 -3.14 -3.06 -3.00 -3.00 -3.00
2014/2015 -2.87 -2.66 -1.64 -2.16 -1.92 -2.27 -2.03 -2.21 -2.21
2013/2014 -2.86 -2.86 -2.29 -2.51 -2.41 -2.73 -2.45 -2.57 -2.58
2012/2013 -2.98 -2.81 -2.52 -2.68 -2.61 -2.78 -2.66 -2.75 -2.75
2011/2012 -3.32 -3.06 -2.73 -2.93 -2.85 -2.95 -2.89 -2.95 -2.95
Peak Incidence
Lowest Rank 9.00 7.00 9.00 7.50 7.50 8.00 5.50 5.00 4.00
Lowest Log Score -5.66 -4.62 -4.52 -4.48 -4.33 -5.06 -4.32 -4.42 -4.39
Average Rank 7.70 2.40 7.40 5.90 5.10 6.20 4.50 2.90 2.90
Average Log Score -4.51 -4.18 -4.29 -4.23 -4.17 -4.35 -4.18 -4.19 -4.18
2015/2016 -4.12 -3.81 -4.20 -3.96 -4.02 -4.01 -3.99 -3.96 -3.96
2014/2015 -4.41 -4.30 -4.42 -4.35 -4.32 -4.35 -4.32 -4.30 -4.30
2013/2014 -4.04 -3.93 -4.16 -4.02 -4.00 -4.02 -4.00 -3.99 -3.99
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2011/2012 -5.66 -4.62 -4.13 -4.48 -4.20 -5.06 -4.26 -4.42 -4.39
KDE
KCDE
SARIMA
EW
CW
FW-wu
FW-reg-w
FW-reg-wu
FW-reg-wui
Model Rank
9
8
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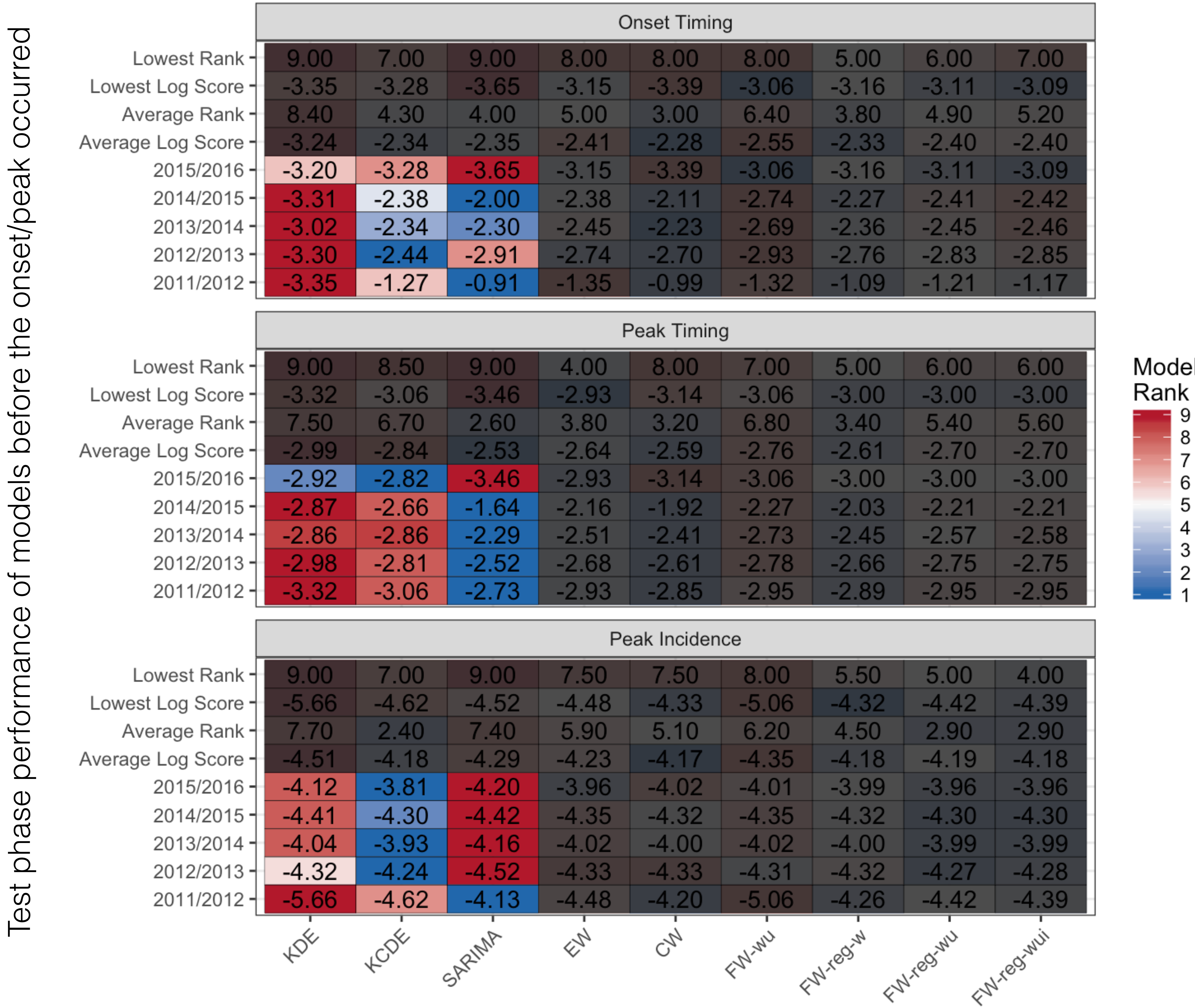
3
2
1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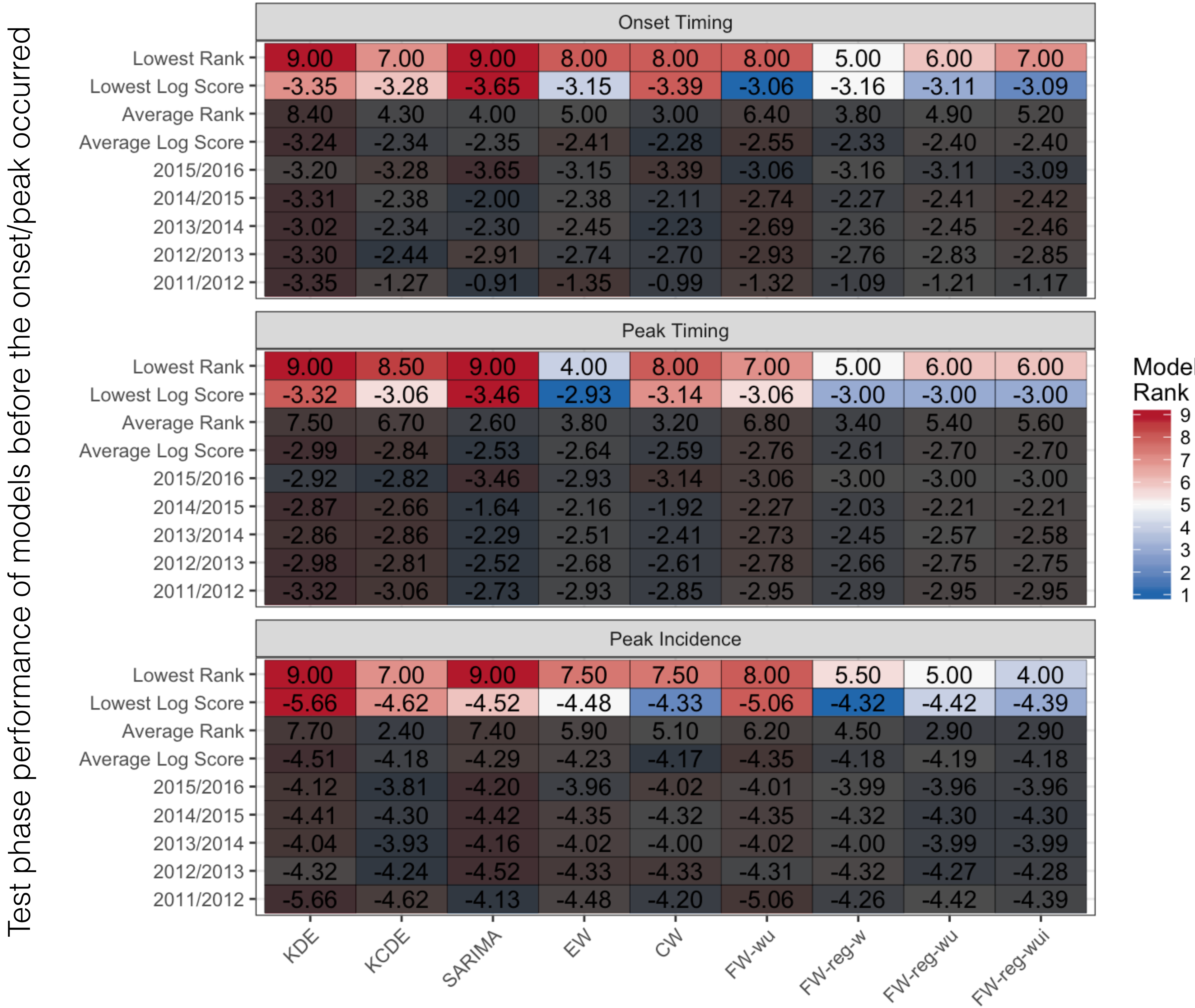
2012/2013 -4.32 -4.24 -4.52 -4.33 -4.33 -4.31 -4.32 -4.27 -4.28
2011/2012 -5.66 -4.62 -4.13 -4.48 -4.20 -5.06 -4.26 -4.42 -4.39
KDE KCDE SARIMA EW CW FW-wu FW-reg-w FW-reg-wu FW-reg-wui
Model Rank
9 8 7 6 5 4 3 2 1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2012/2013 -4.32 -4.24 -4.52 -4.33 -4.33 -4.31 -4.32 -4.27 -4.28
2011/2012 -5.66 -4.62 -4.13 -4.48 -4.20 -5.06 -4.26 -4.42 -4.39
KDE
KCDE
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EW
CW
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FW-reg-w
FW-reg-wu
FW-reg-wui
Model Rank
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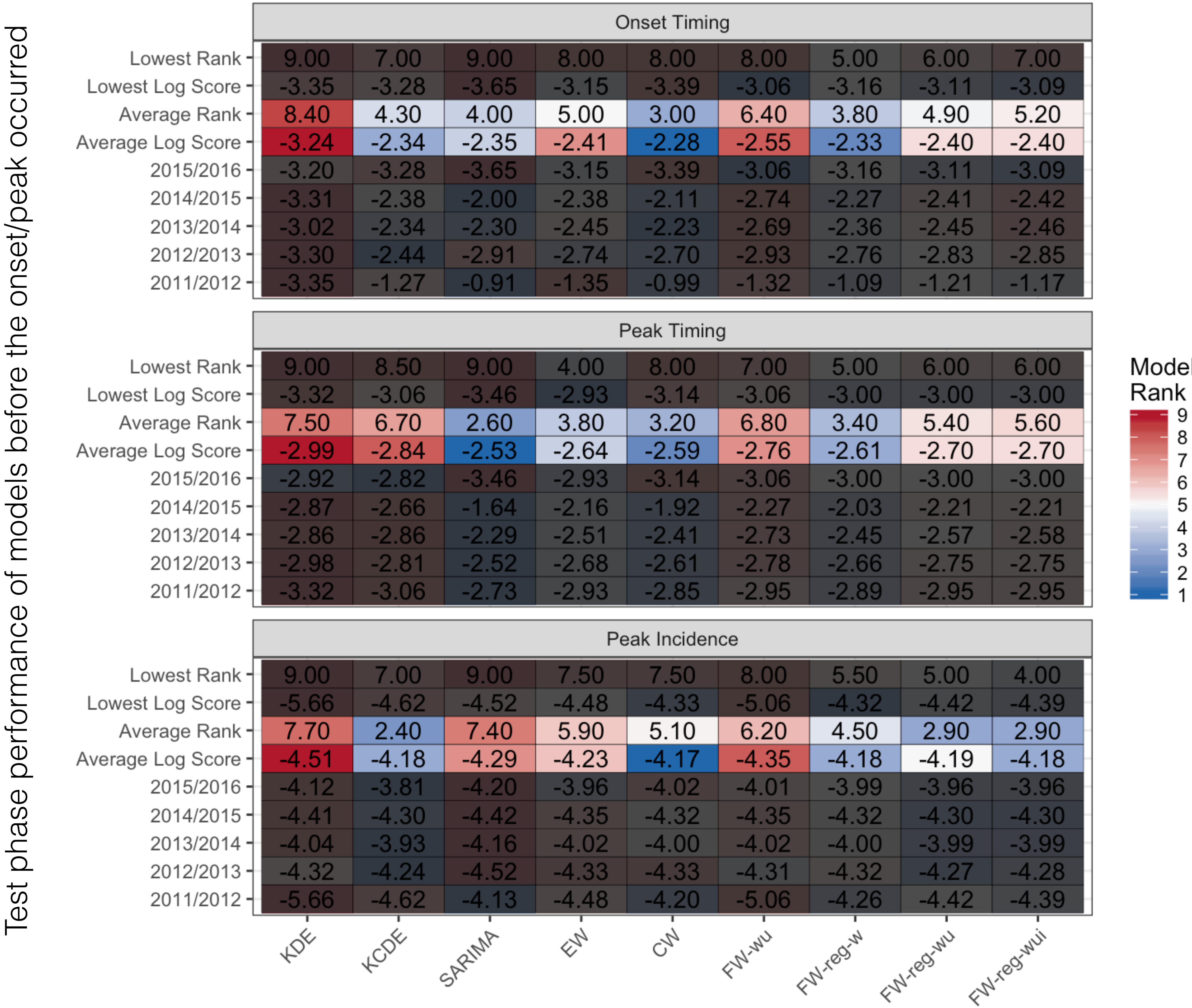
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2012/2013 -2.98 -2.81 -2.52 -2.68 -2.61 -2.78 -2.66 -2.75 -2.75
2011/2012 -3.32 -3.06 -2.73 -2.93 -2.85 -2.95 -2.89 -2.95 -2.95
Peak Incidence
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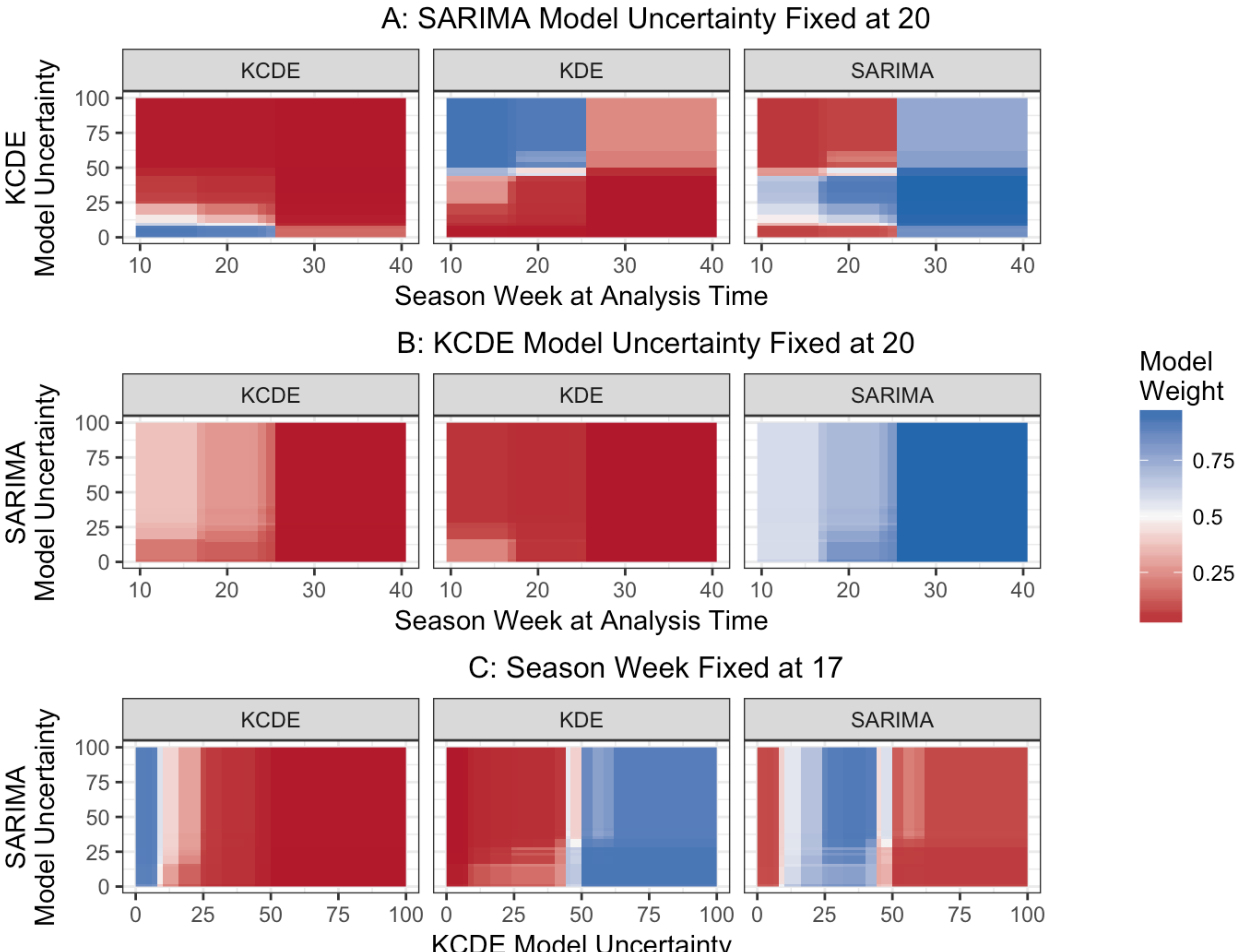
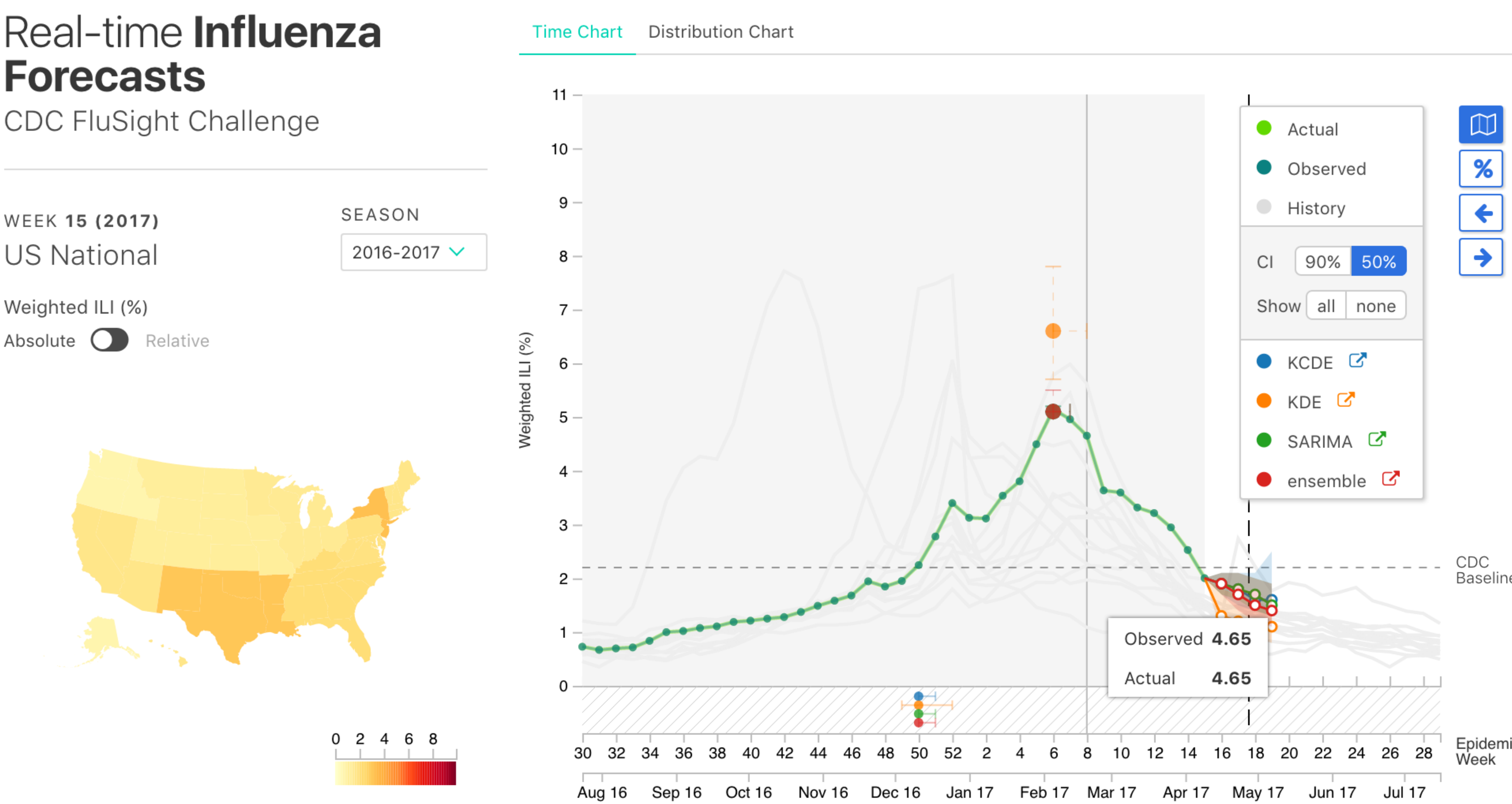
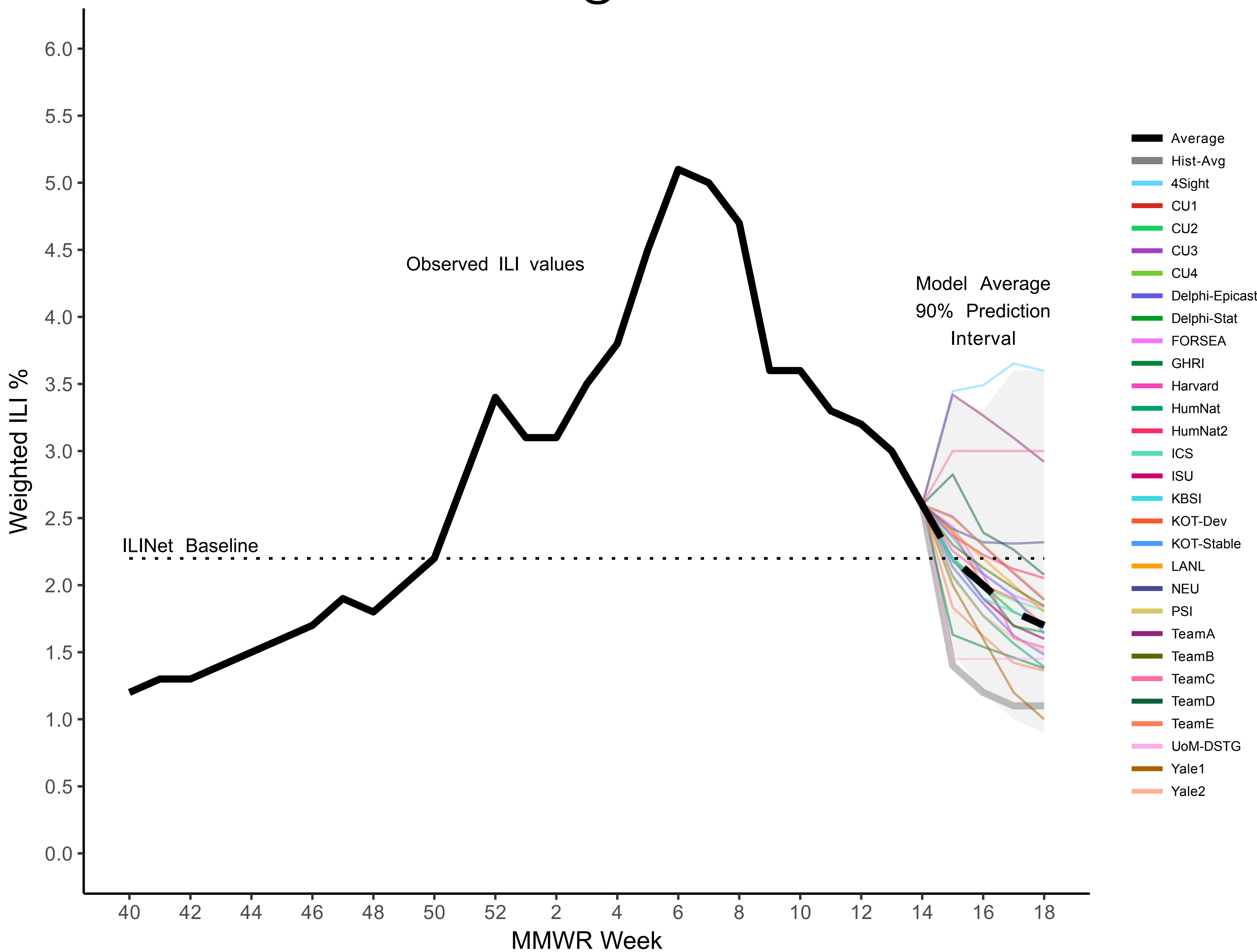
Lowest Log Score -5.66 -4.62 -4.52 -4.48 -4.33 -5.06 -4.32 -4.42 -4.39
Average Rank 7.70 2.40 7.40 5.90 5.10 6.20 4.50 2.90 2.90
Average Log Score -4.51 -4.18 -4.29 -4.23 -4.17 -4.35 -4.18 -4.19 -4.18
2015/2016 -4.12 -3.81 -4.20 -3.96 -4.02 -4.01 -3.99 -3.96 -3.96
2014/2015 -4.41 -4.30 -4.42 -4.35 -4.32 -4.35 -4.32 -4.30 -4.30
2013/2014 -4.04 -3.93 -4.16 -4.02 -4.00 -4.02 -4.00 -3.99 -3.99
2012/2013 -4.32 -4.24 -4.52 -4.33 -4.33 -4.31 -4.32 -4.27 -4.28
2011/2012 -5.66 -4.62 -4.13 -4.48 -4.20 -5.06 -4.26 -4.42 -4.39
KDE
KCDE
SARIMA
EW
CW
FW-wu
FW-reg-w
FW-reg-wu
FW-reg-wui
Model Rank
9
8
7
6
5
4
3
2
1


A: SARIMA Model Uncertainty Fixed at 20
KCDE
KDE
SARIMA
KCDE Model Uncertainty
Season Week at Analysis Time
B: KCDE Model Uncertainty Fixed at 20
SARIMA Model Uncertainty
Season Week at Analysis Time
C: Season Week Fixed at 17
SARIMA Model Uncertainty
KCDE Model Uncertainty
Model Weight
0.75
0.5
0.25

reichlab.io/flusight



CDC FluSight 2016-2017



A collaborative ensemble planned for the 2017-2018 season.

Guidelines (in progress) for collaborative ensemble:
https://github.com/FluSightNetwork/cdc-flusight-ensemble/

Ensemble summary

- Across all regions and targets, some ensemble model specifications provided **more consistent and reliable performance** than any baseline model, although differences are often small.

- Across all regions and targets, **simpler ensembles performed better**: equal-weight, constant-weight and feature-weighted by week (FW-reg-w).

- More locations, models, test phase seasons, disease settings are needed to better assess long-run performance.

Forecasting Dengue in Thailand

Reich et al. PLOS NTD, 2016.

impetus

from spatial surveillance *to disease dynamics*

September 2016

UMass Amherst

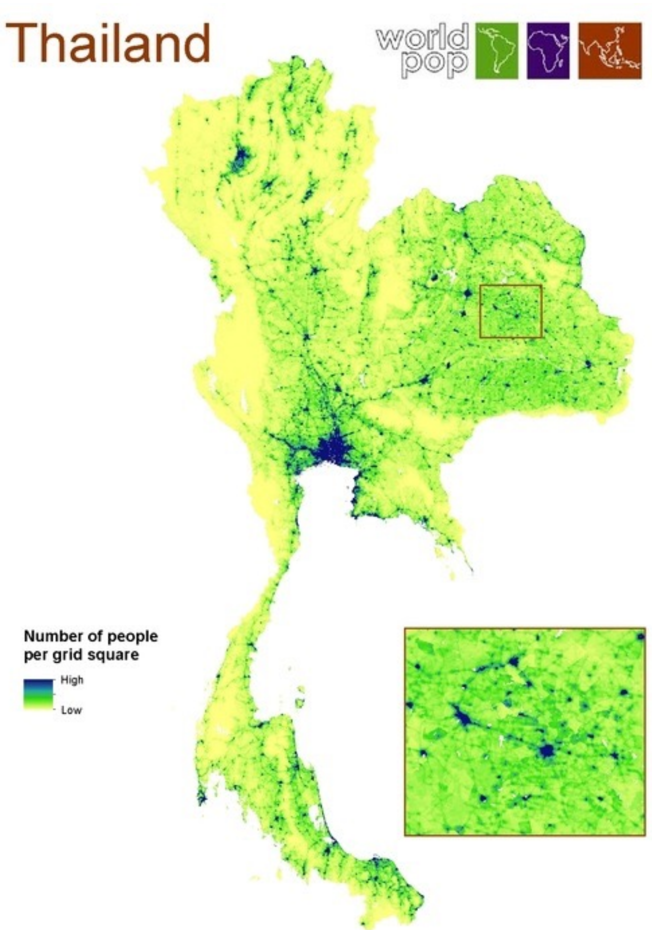
MINISTRY OF PUBLIC HEALTH

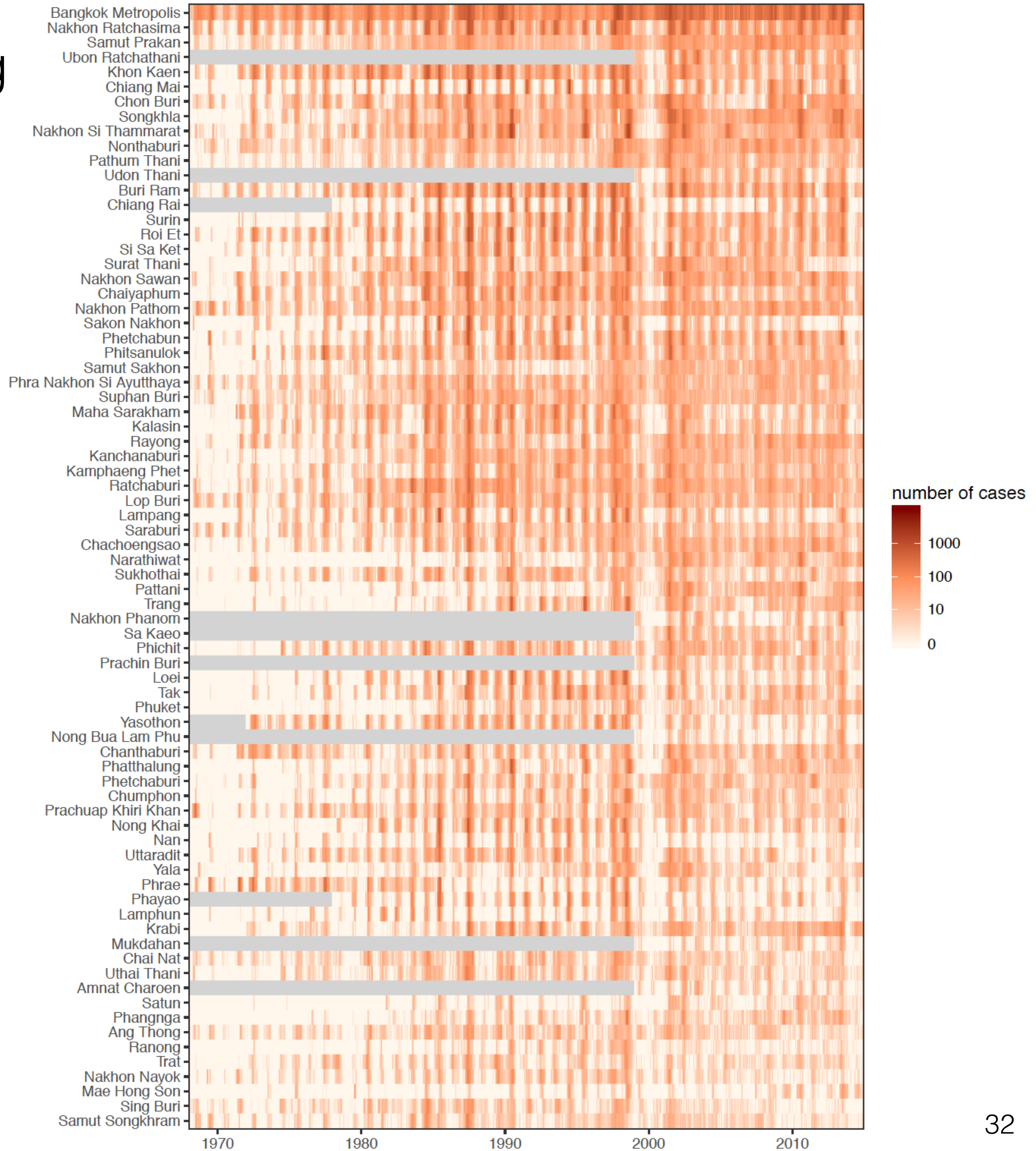
JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Methods for reducing spatial uncertainty and bias in disease surveillance

NIAID R01, PI: Dr. Justin Lessler, R01AI102939

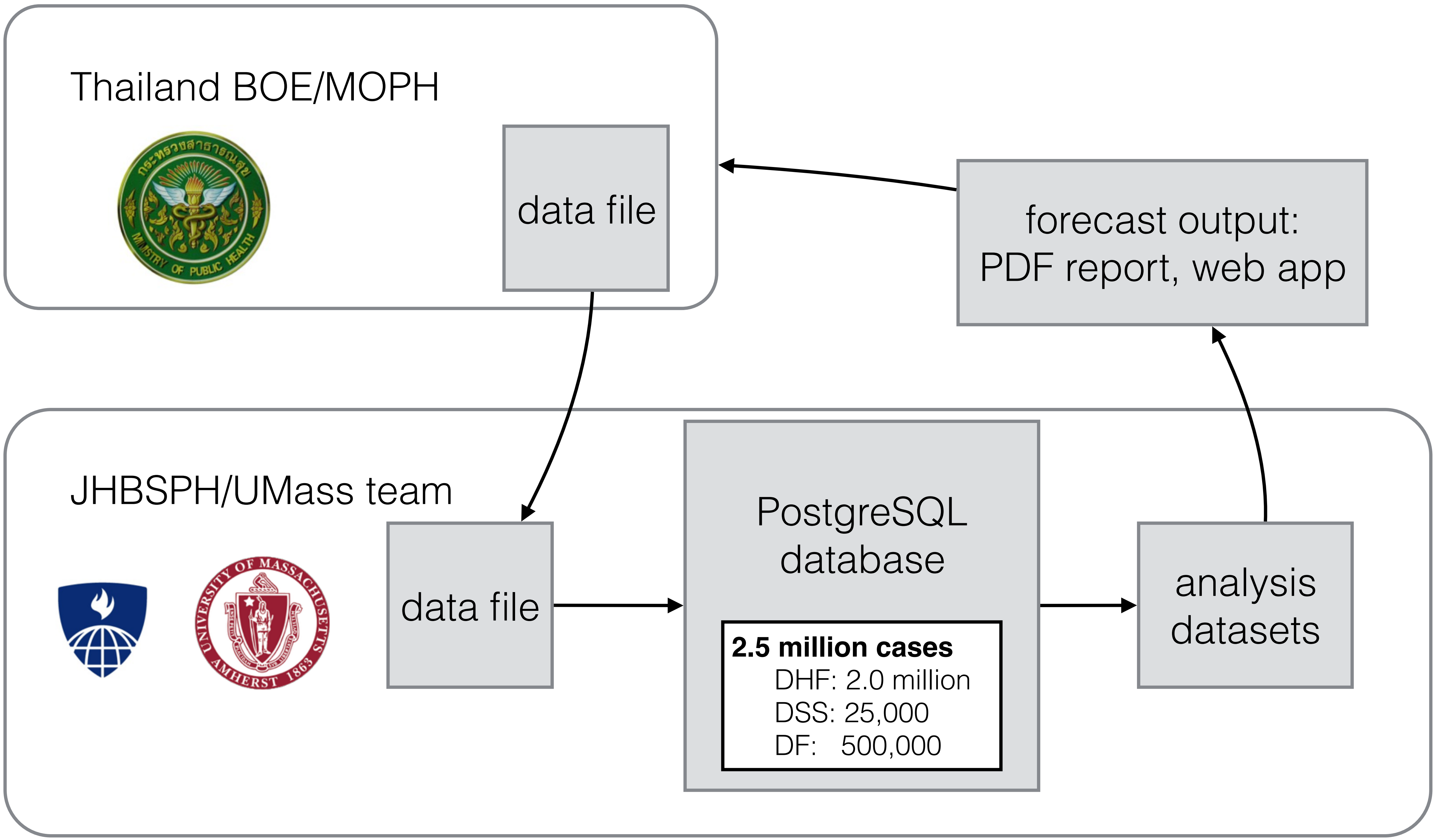
Real-time forecasting of dengue fever in Thailand



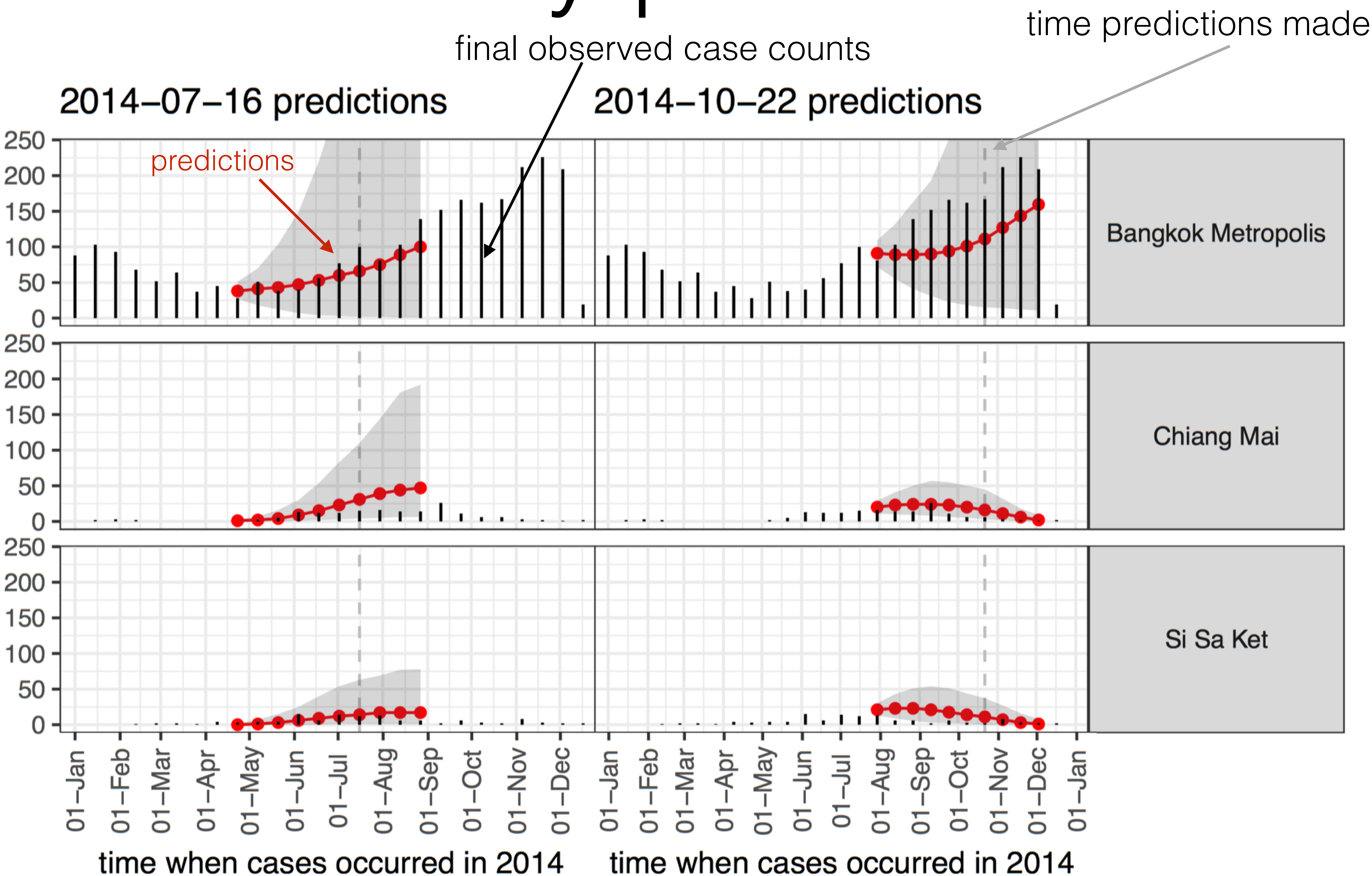


Integrating real-time infectious disease forecasts into public health practice.

Real-time forecast pipeline



Biweekly predictions



Reich et al. (2016)

Dengue prediction in Thailand

https://iddynamics.jhsph.edu/apps/shiny/dengue_forecasts/

Logged in as shiny-nick Logout

Dengue prediction in Thailand

Choose language

- ( ) ไทย
- (•) English

These forecasts should be considered preliminary drafts, pending model validation.

Select Date

2016-02-12

Previous | Next

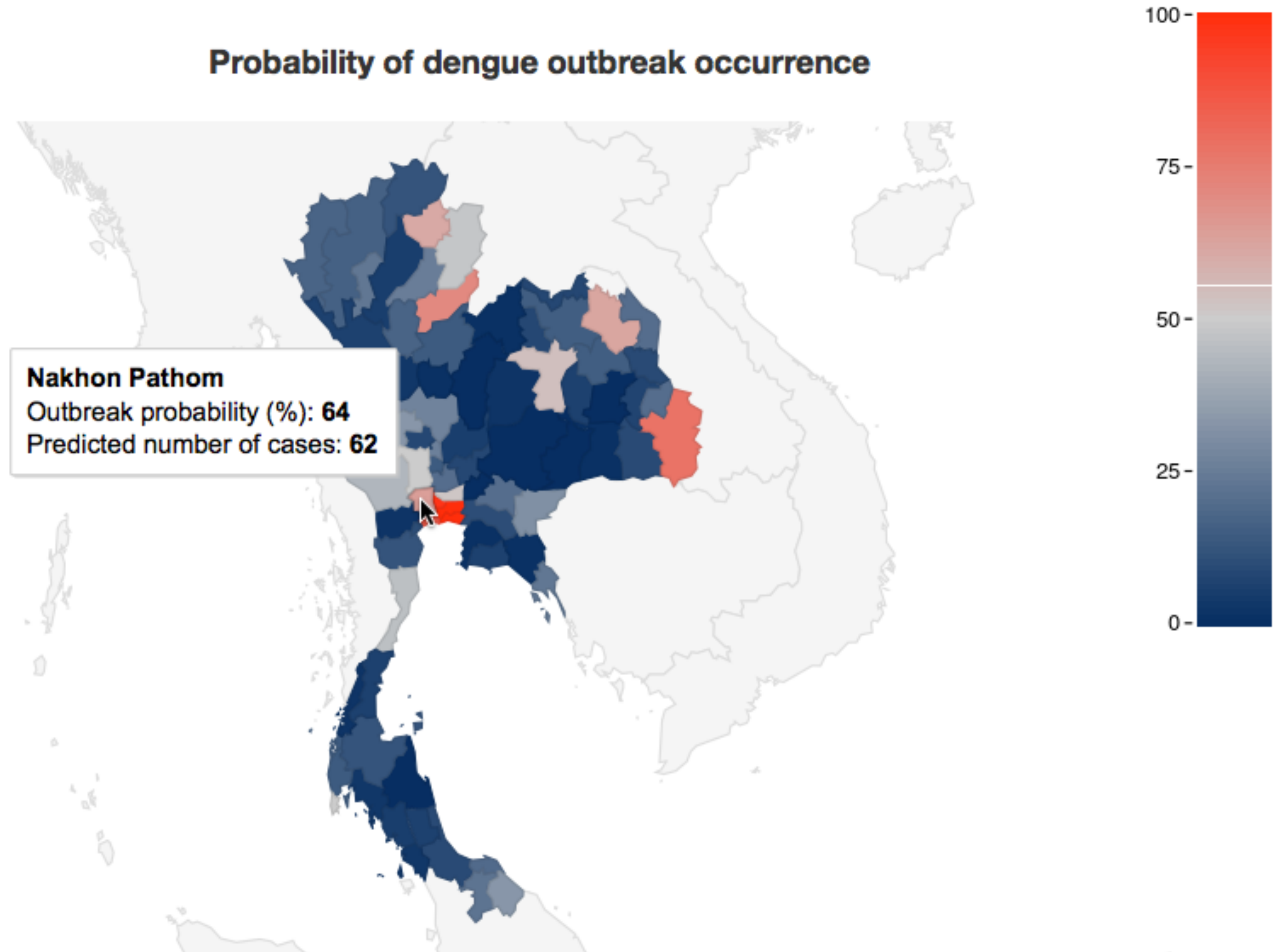
Select variable

Outbreak probability (%)

This app was created by Stephen A Lauer, Krzysztof Sakrejda, and Nicholas G Reich at the University of Massachusetts-Amherst, in collaboration with the Thai Ministry of Public Health and researchers at Johns Hopkins Bloomberg School of Public Health. This work was funded in part by the U.S. National Institutes of Health through the grant "Methods for Reducing Spatial Uncertainty and Bias in Disease Surveillance" (R01AI102939).

Map | Plot

Probability of dengue outbreak occurrence



Dengue prediction in Thailand

https://iddynamics.jhsph.edu/apps/shiny/dengue_forecasts/

Search

Logged in as shiny-nick Logout

Dengue prediction in Thailand

Choose language

- ( ) ไทย
- (•) English

These forecasts should be considered preliminary drafts, pending model validation.

Select MOPH region

1

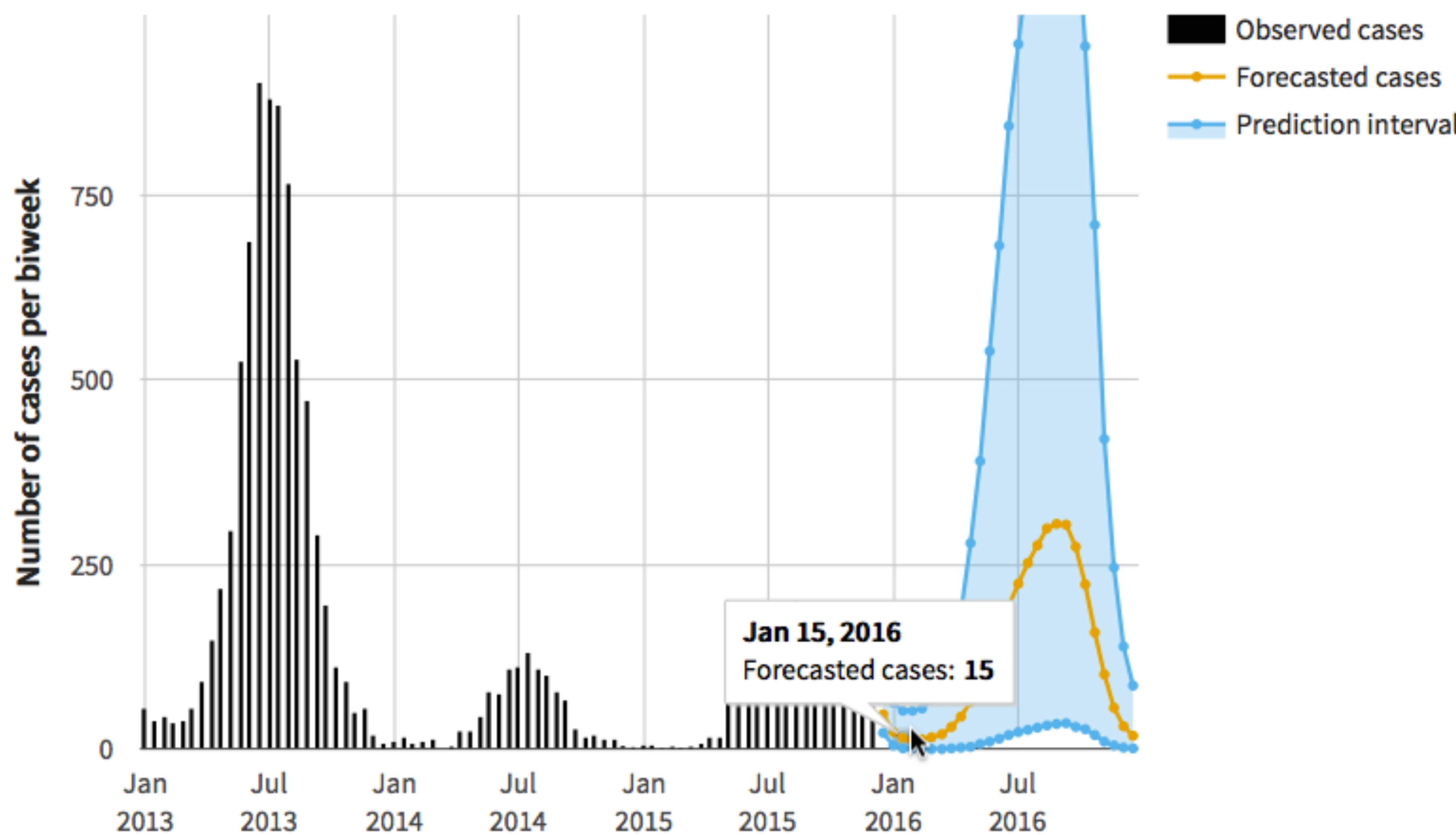
Select start year

2013

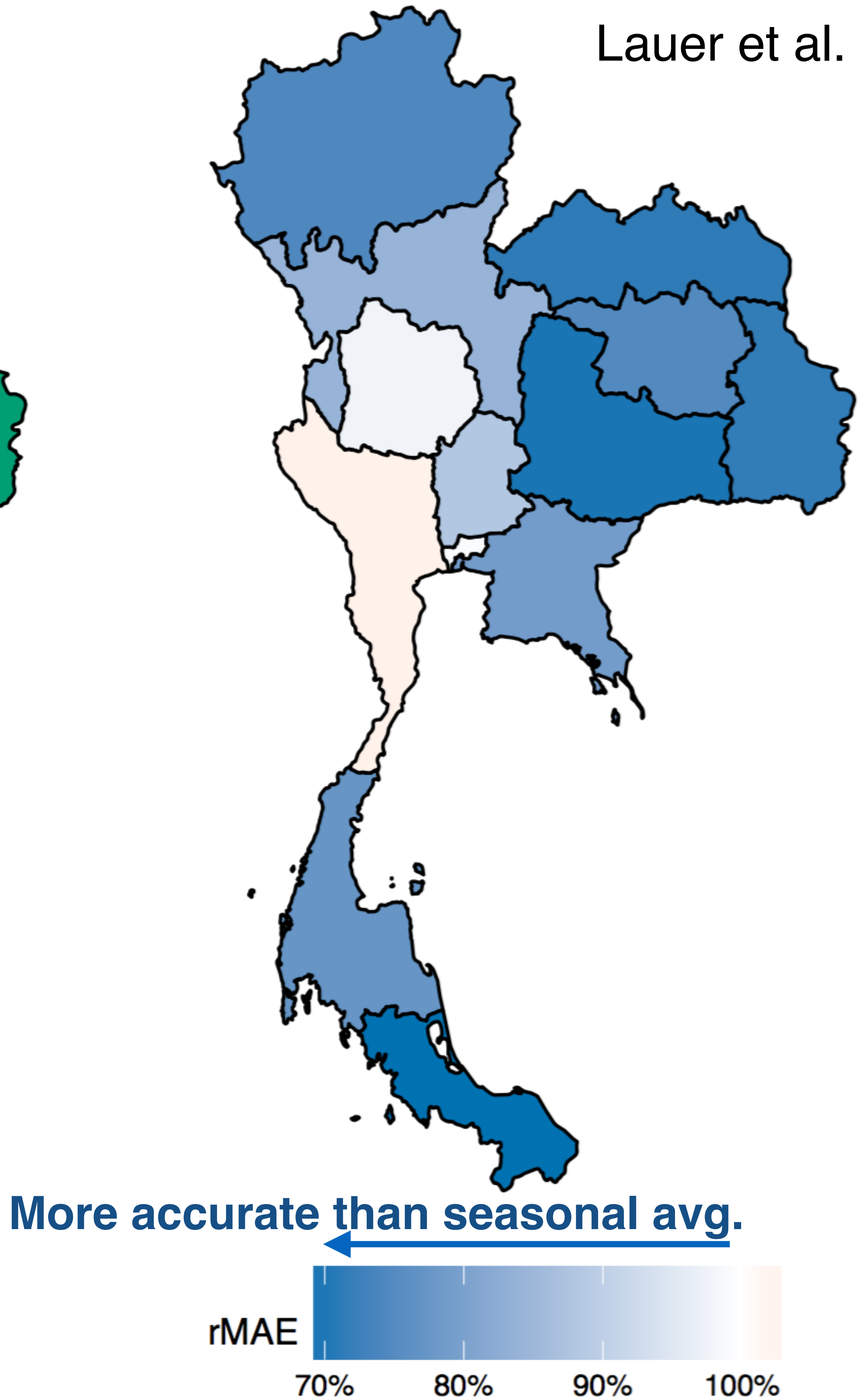
This app was created by Stephen A Lauer, Krzysztof Sakrejda, and Nicholas G Reich at the University of Massachusetts-Amherst, in collaboration with the Thai Ministry of Public Health and researchers at Johns Hopkins Bloomberg School of Public Health. This work was funded in part by the U.S. National Institutes of Health through the grant "Methods for Reducing Spatial Uncertainty and Bias in Disease Surveillance" (R01AI102939).

Map | Plot

Observed and forecasted cases of dengue fever in MOPH Region 1



Annual incidence predictions



Overall findings

- Even with reporting delays, a simple spatial model provides now-casts that are more accurate than seasonal average models in over 50% of the 77 Thai provinces at up to a 3-month horizon.
- Accuracy and utility of real-time predictions are impacted by case reporting delays, but can be improved with location-specific delay adjustments (ongoing work).
- The benefits of including climate, spatial effects, seasonality, vary by location and forecast horizon.

Integration with Public Health Practice

- Thai MOPH is eager to use forecasts to allocate resources, target interventions.
- We engage in an ongoing dialogue about best temporal and spatial scale of forecasts, and forecast “deadlines” to be considered in decision-making.
- Our forecasts are being disseminated to national and regional decision-makers.
- In practice, lists of locations ranked by predicted dengue incidence are starting to be used to target interventions.

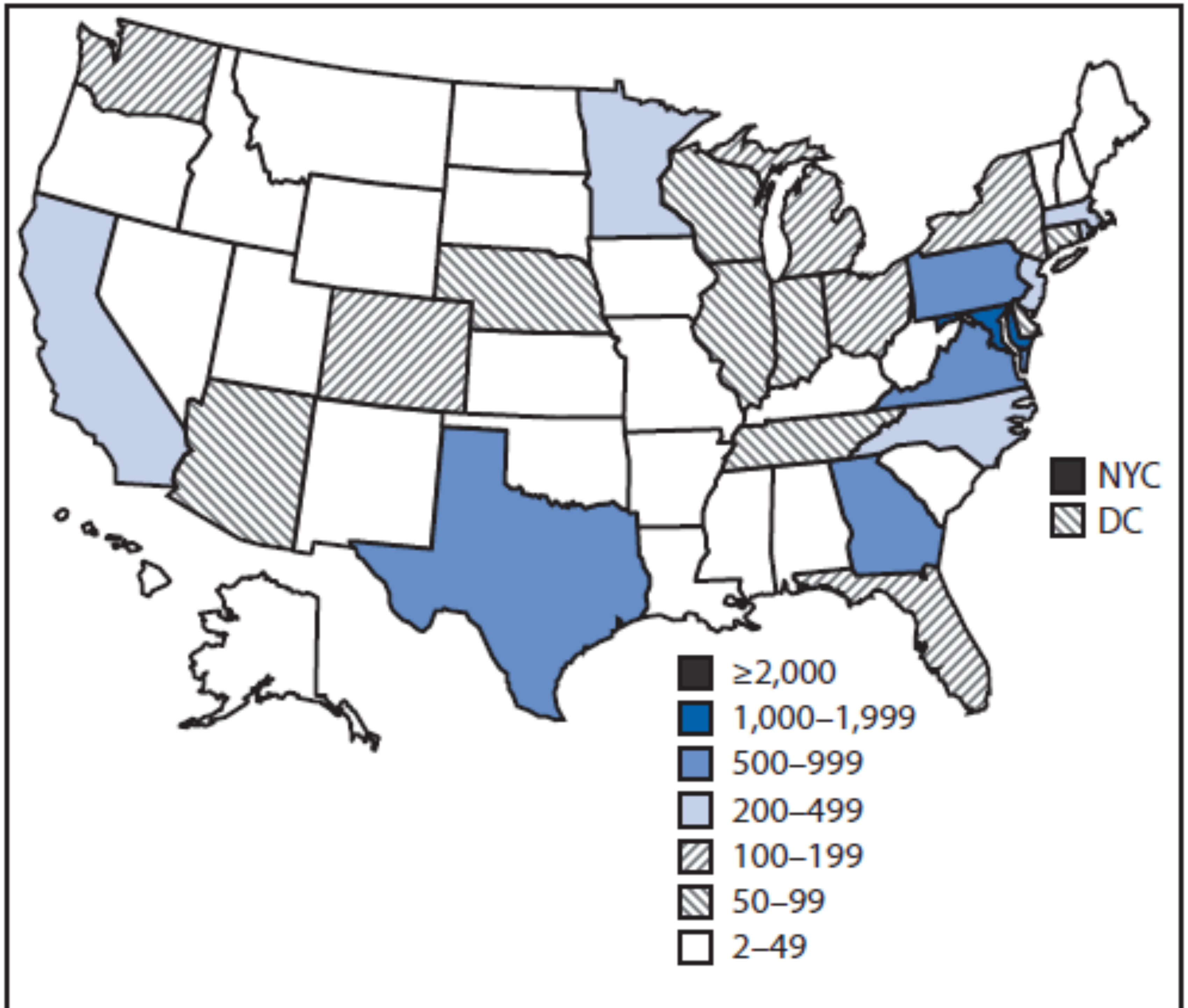
Modeling cost-effectiveness of active monitoring for Ebola

Reich et al. (under review)

To improve rapid identification and evaluation of individuals infected with Ebola, on October 27, 2014, the U.S. Centers for Disease Control and Prevention (CDC) recommended active monitoring of individuals potentially exposed to Ebola virus.

Individuals under active monitoring were asked to contact local health authorities to report their health status every day for 21 days after their last potential exposure

Number of persons with potential Ebola exposure monitored in 50 states, New York City, and the District of Columbia — November 3, 2014–March 8, 2015

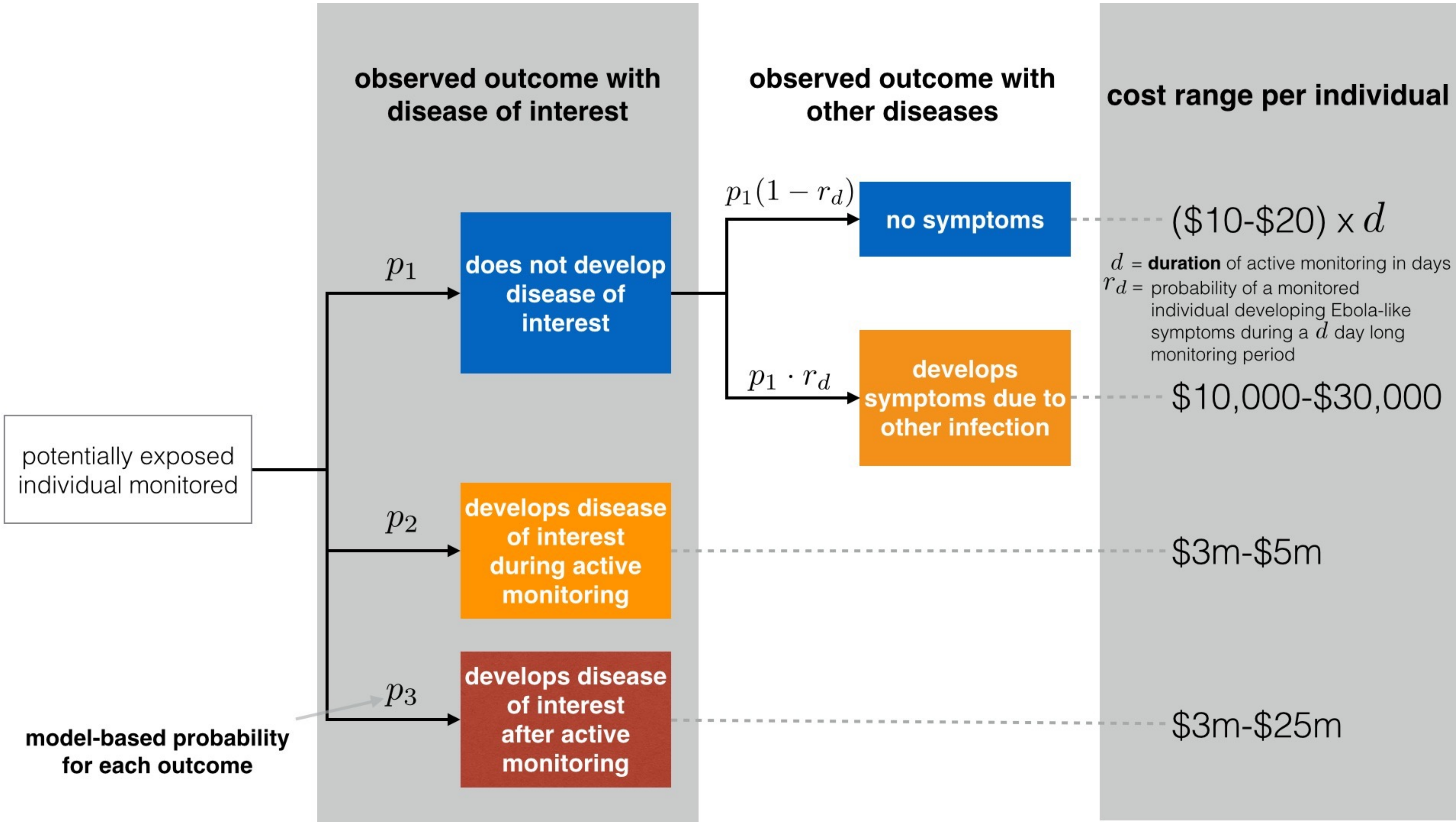


Stehling-Ariza et al., MMWR, 2015.

Overall goals

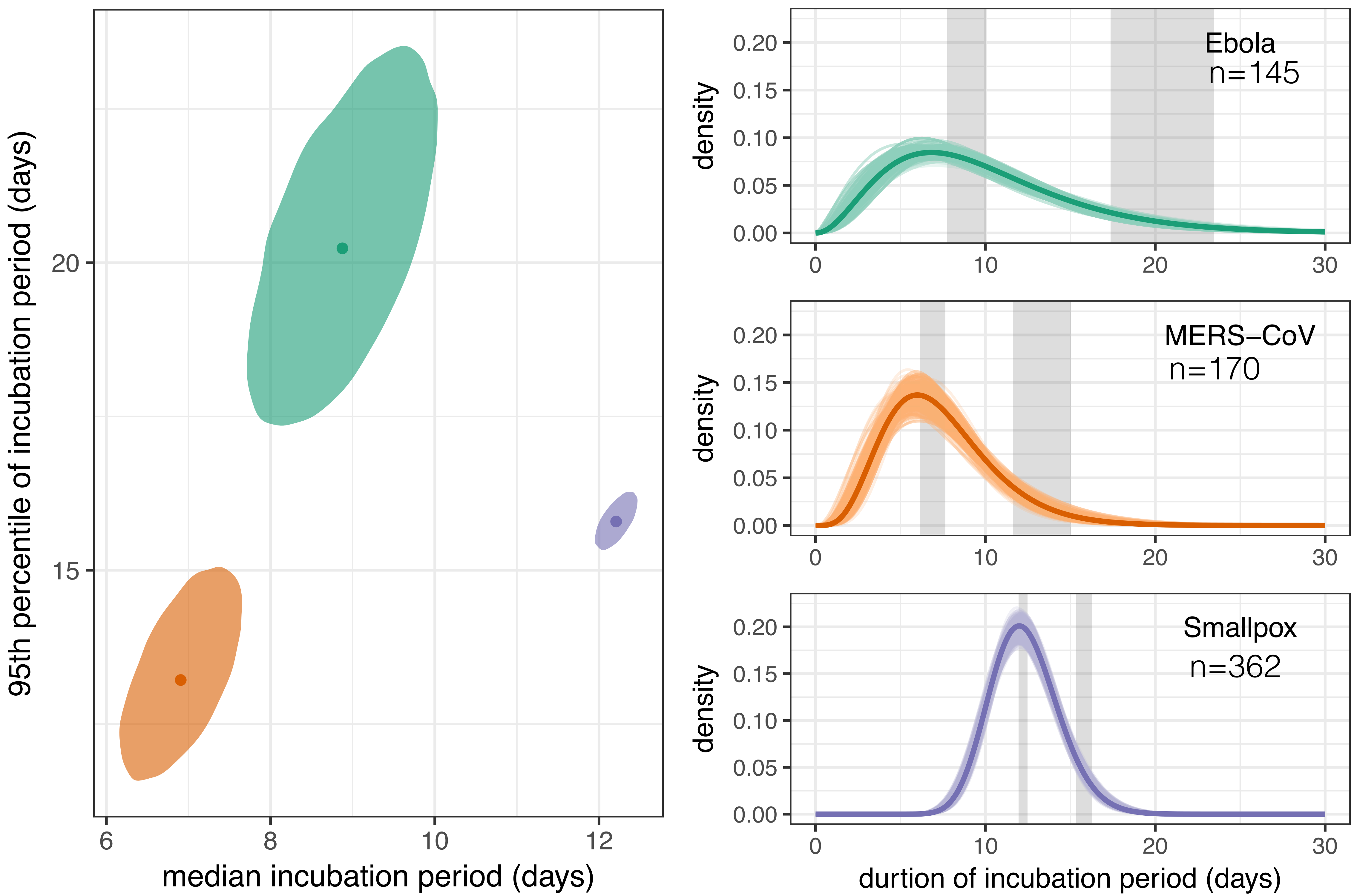
- To quantify (with uncertainty) the risk and costs associated with specific durations of active monitoring.
- To develop a framework that could be used to provide empirical evidence for public health policies in future outbreaks.
- To provide full case-study for Ebola in NYC, with additional analyses related to smallpox and MERS.

Model framework



p_2 and p_3 depend on the incubation period distribution.
Costs are based on data from the NYC DOHMH Ebola experience.

Incubation period distributions



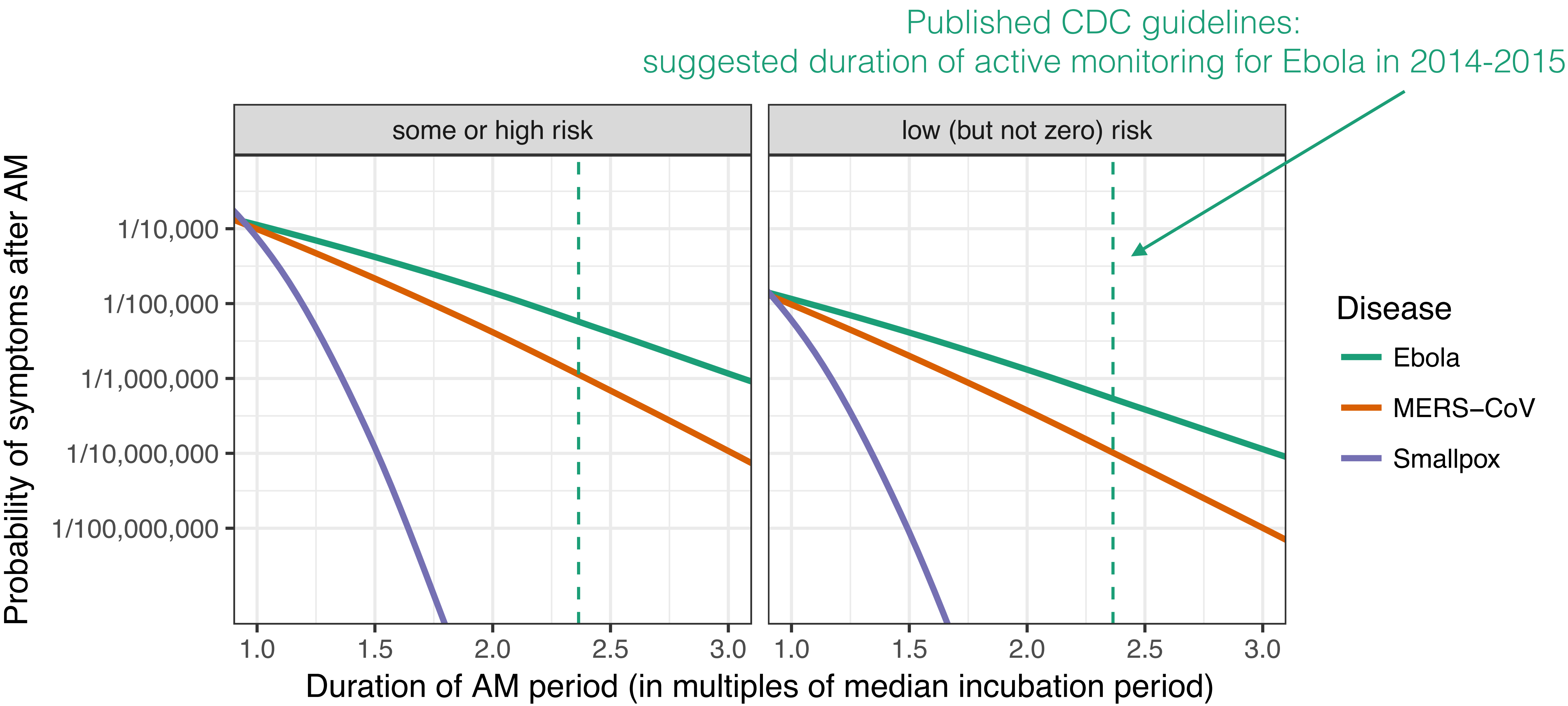
Ebola data: Faye et al, 2015. **MERS data**: Virlogeux et al, 2016. **Smallpox data**: Litvinjenko et al, 1972; Mack, 1972; Nishiura, 2009.

Estimated risks of monitored individuals

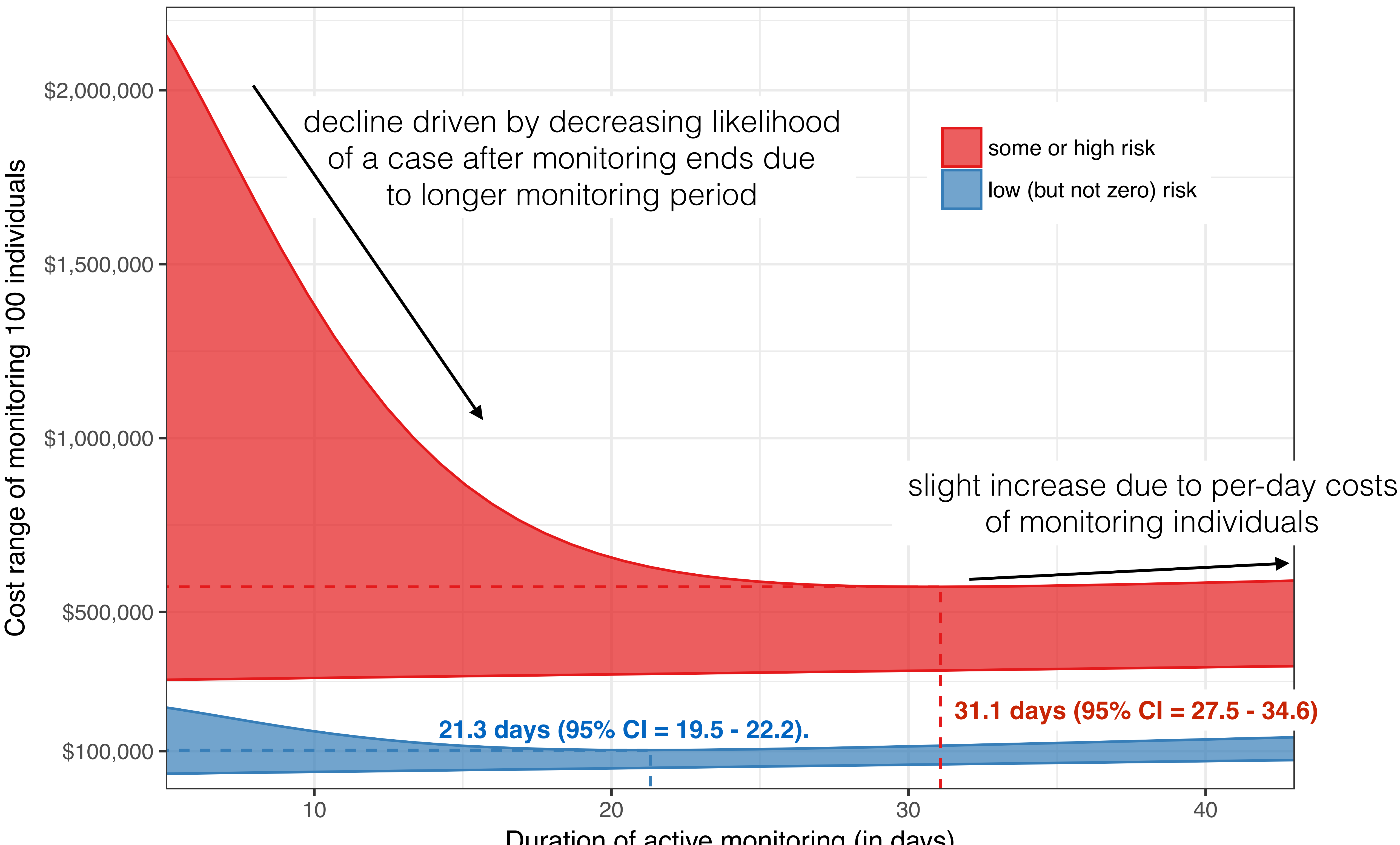
CDC Risk level	Number of cases reported in the U.S.	Estimated number of monitored individuals in U.S.*	Estimated probability of developing Ebola
"Low (but not zero) risk"	3	26,000	1/10,000
"Some or high risk"	1	1,000	1/1,000

*Extrapolated based on published data on monitored individuals from Nov 2014 - Mar 2015.

Risks vs. duration of monitoring



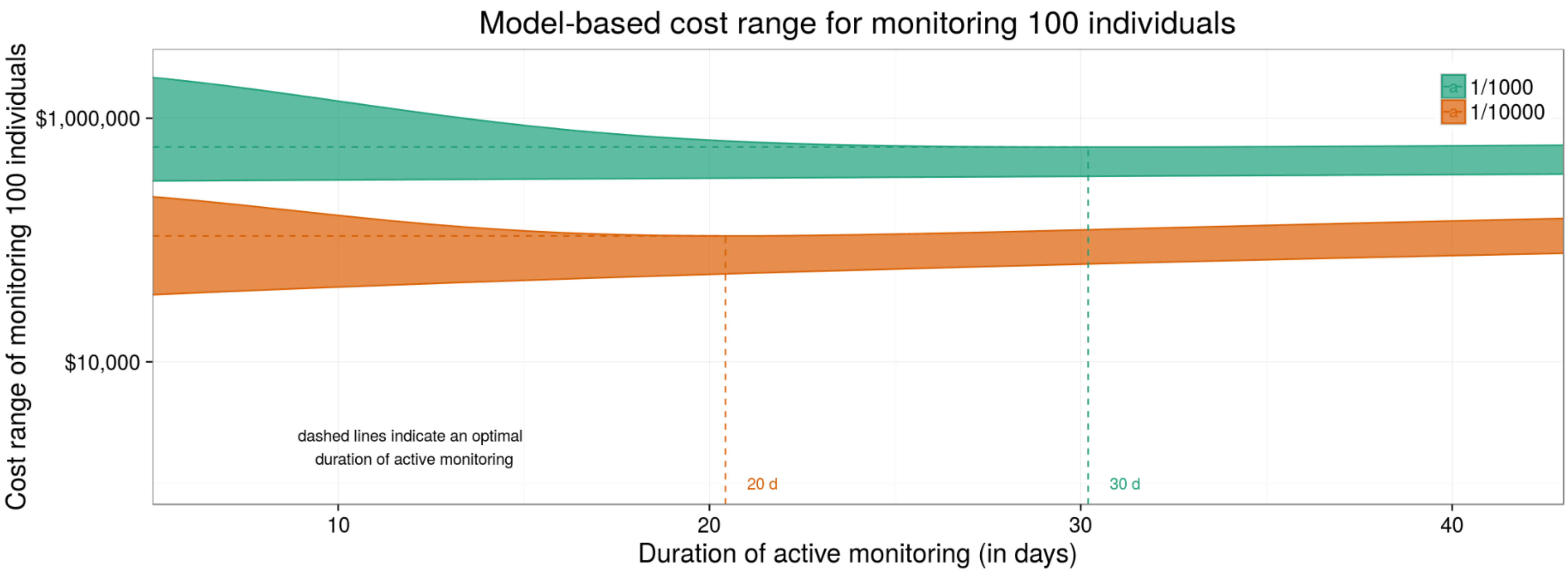
Costs vs. duration of monitoring



iddynamics.jhsph.edu

Determining Durations for Active Monitoring

Model Overview | **Costs of Active Monitoring Programs** | Incubation Period Estimates



Pathogen

- (•) Ebola
- ( ) MERS-CoV
- ( ) Smallpox

Probability a monitored individual develops symptoms

- [ ] 1/10
- [ ] 1/100
- [x] 1/1,000
- [x] 1/10,000

Number of secondary cases

0 4 25

Cost per case ($000,000s)

0 3 5 20

Cost per monitored person-day ($)

0 10 20 100

Cost of a false positive ($000s)

0 10 30 100

Expected number of monitored-person-days needed to have 1 hospitalized false positive

1,000 10,000

http://iddynamics.jhsph.edu/apps/shiny/activemonitr/

Overall findings

- While data from New York City's active monitoring program suggests that the per-individual cost of monitoring is "low" (about $10–$20 per day), the total program cost can be substantial ($1.9m in NYC).

- Cost-efficiency may be achieved by using exposure-risk categories to modify the duration or intensity of active monitoring.

- This framework could be adapted to develop empirically based public health policies in future outbreaks.

Thank you!

with acknowledgments to…

Current Trainees:
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