

A Real-Time Early Warning System to Anticipate Respiratory Disease Outbreaks Using Transfer Learning

Raul Garrido-Garcia MS^{1,2,3}, Leonardo Clemente MS^{1,3,4}, Austin G. Meyer MD, PhD, MS, MPH^{1,5}, George Dewey PhD, MPH^{1,3}, Shihao Yang PhD^{1,6}, Mauricio Santillana MS, PhD^{1,2,3,7*}

¹Machine Intelligence Group for the betterment of Health and the Environment, Northeastern University, Boston, 02115, MA, United States.

²Department of Physics, Northeastern University, Boston, 02115, MA, United States.

³Network Science Institute, Northeastern University, Boston, 02115, MA, United States.

⁴Instituto Tecnológico y de Estudios Superiores de Monterrey, Oaxaca, Nuevo León, Mexico.

⁵Baylor Scott and White Health, Temple, 76502, TX, United States.

⁶H. Milton Stewart School of Industrial and Systems Engineering, Georgia Institute of Technology, Atlanta, 30332, GA, United States.

⁷Department of Epidemiology, Harvard T.H. Chan School of Public Health,, Boston, 02115, MA, United States.

*Corresponding author(s). E-mail(s): m.santill@g.harvard.edu;

Contributing authors: garridogarcia.r@northeastern.edu; clemclem1991@gmail.com; austin.g.meyer@gmail.com; g.dewey@northeastern.edu; shihao.yang@isye.gatech.edu;

Contents

1	Variability of Onsets and Peaks	3
2	Illustrative Performance of Flusight Forecasting Models	4
3	Google Trends Used	7
4	Retrospective EWS Results	8
5	Results Comparison with and without Google Trends	13
6	Comparison Onsets between classic ILI Definition and our definition	14
7	Onset Examples 2024-2025 Real-Time Predictions	15
8	Peak Examples 2024-2025 Real-Time Predictions	39
9	Granger Causality Analysis	66
10	Onset Detection Methodology	68
11	Formal Definition of the Early Warning Algorithm	68
12	Sensitivity of Onset Detection to Exponential Growth Duration	69
13	Sensitivity of Correlation Threshold	104

1 Variability of Onsets and Peaks

Using historical state-level ILI onset weeks, we clustered states by timing variability (Supplementary Fig. 5). Low variability states (13 states) show onset ranges of 3–7 weeks with a median of 5 weeks, moderate variability states (22 states) exhibit ranges of 8–13 weeks with a median of 10 weeks, and high variability states (14 states) demonstrate ranges of 14–20 weeks with a median of 16.5 weeks. This means that while some states begin flu season within approximately one month most years, the majority experience 2–4 months of temporal spread in onset timing.

Peak timing uncertainty presents an even greater challenge (Supplementary Fig. 6). Low variability states (12 states) show peak ranges of 5–6 weeks, moderate variability states (22 states) exhibit ranges of 7–12 weeks, and high variability states (15 states) demonstrate ranges of 13–20 weeks. The dispersion in peak timing significantly exceeds that of onsets (mean range 14.39 vs. 10.67 weeks across states), underscoring that identifying peaks in real-time presents a greater challenge than onset detection. This substantial historical uncertainty makes traditional forecasting approaches unreliable and highlights the critical need for data-driven early warning systems that can operate independently of historical timing patterns.

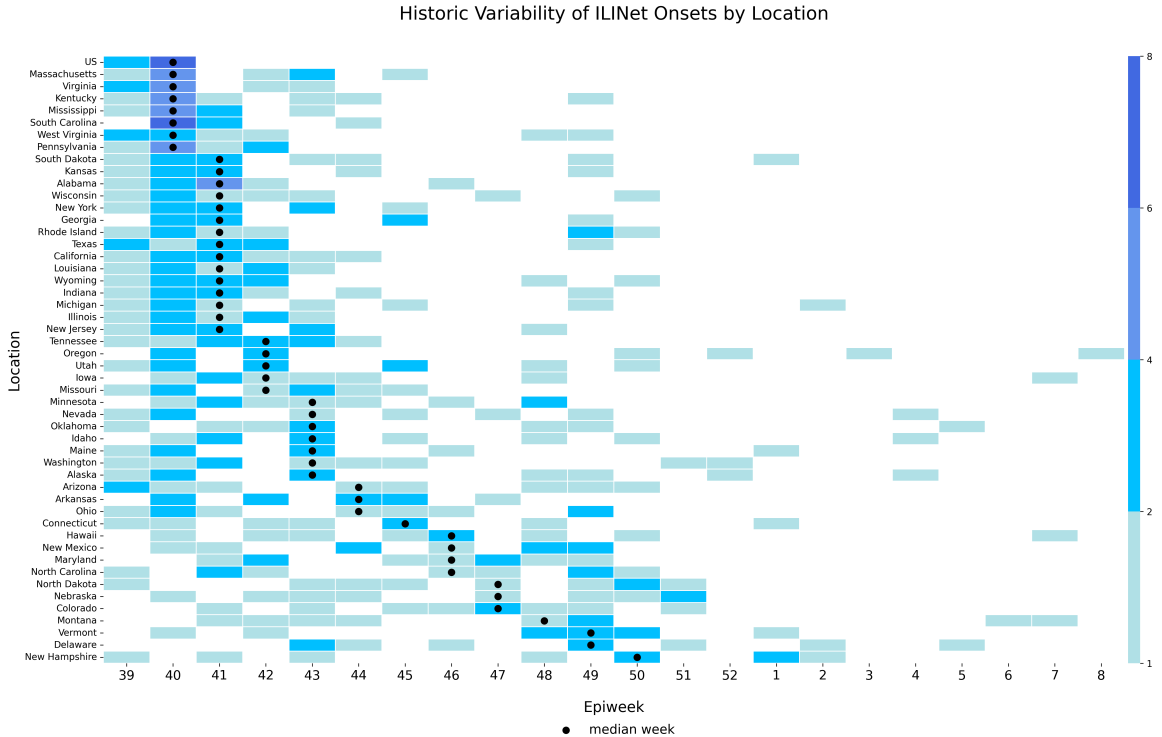


Fig. S1: Variability of ILI Onsets at state and national levels in the U.S. from 2010-2020. Each cell indicates the number of seasons in which a given location experienced onset during a particular epidemiological week. Darker shades represent higher frequencies, while black dots mark the median onset week for each location. This figure highlights substantial spatiotemporal heterogeneity in onset timing, illustrating both early and late season dynamics across states.

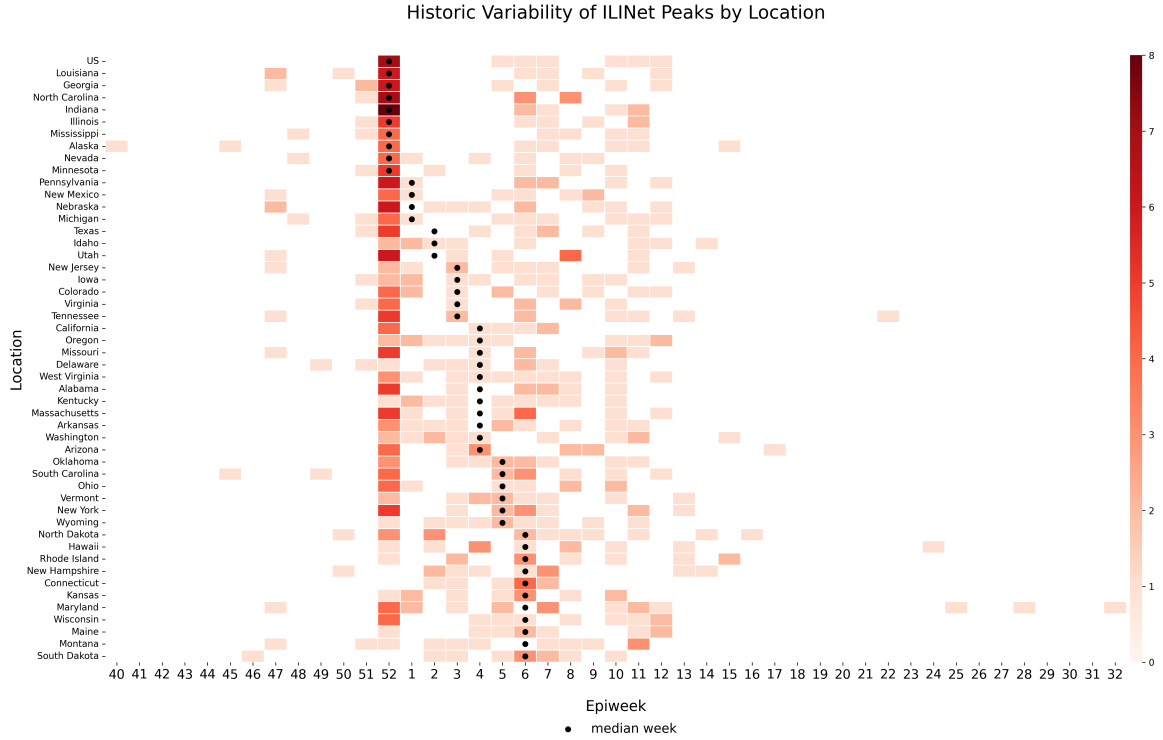


Fig. S2: Variability of ILI Peaks at state and national levels in the U.S. from 2010-2020. Each cell indicates the number of seasons in which a given location experienced peaks during a particular epidemiological week. Darker shades represent higher frequencies, while black dots mark the median peak week for each location. This figure highlights substantial spatiotemporal heterogeneity in peak timing, illustrating both early and late season dynamics across states.

2 Illustrative Performance of Flusight Forecasting Models

Together, the following examples illustrate a fundamental limitation of point-forecasting-oriented epidemic models for early warning applications. Across multiple seasons and forecast issuance times, the FluSight ensemble—an ensemble of all models submitted to the FluSight Challenge—and related forecasting approaches struggle to anticipate sharp regime changes, such as outbreak onsets and rapid epidemic accelerations, in advance. In many instances, meaningful deviations from baseline in the forecasts emerge only after the outbreak onset has already occurred, indicating that predictions are initiated too late to provide actionable early warning. In many cases, forecasts only adjust meaningfully after the onset or peak has already occurred, effectively reacting to rather than anticipating the transition. This limitation is particularly pronounced for peak prediction: forecasts issued six weeks before the peak exhibit substantial uncertainty in both timing and magnitude, with wide predictive intervals and inconsistent alignment with the realized peak week. These observations suggest that while such models can provide useful short-term forecasts under smooth dynamics, they are less suited for the early detection of discrete epidemiological events—motivating complementary early warning systems designed specifically to detect onsets and peaks under abrupt, non-stationary dynamics.

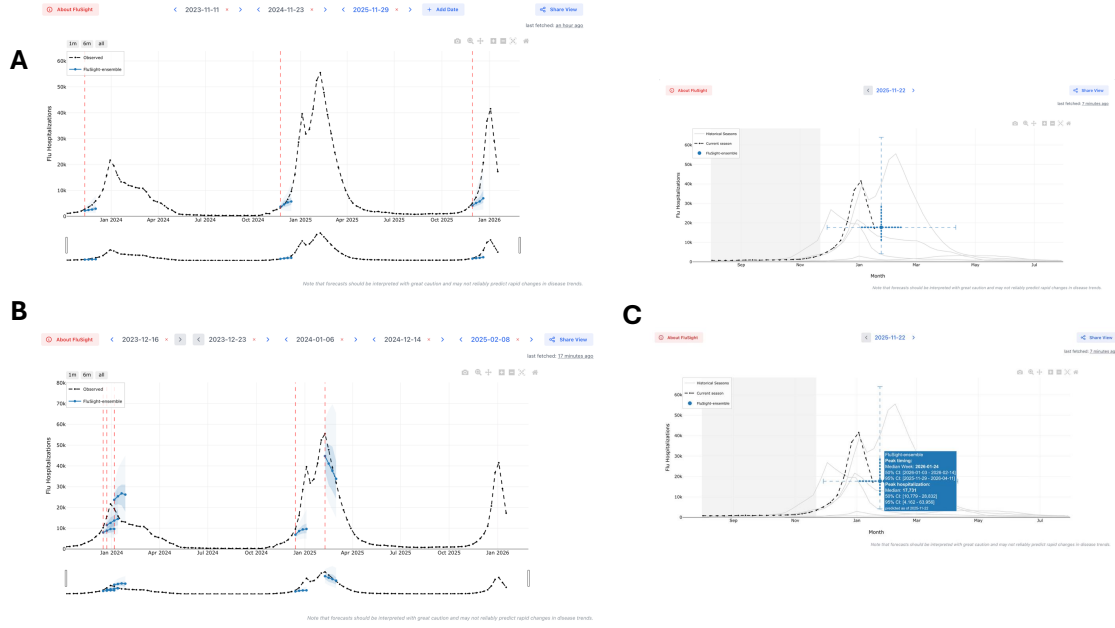


Fig. S3: Example of Flusight ensemble forecast for Influenza Hospitalizations in the U.S. Across all panels, the dashed black curve shows observed hospitalizations, blue points and intervals denote ensemble forecasts, and vertical red dashed lines indicate forecast issuance dates. **A)** Example of FluSight ensemble forecasts of U.S. influenza hospitalizations across multiple forecast issuance dates. **B)** FluSight ensemble forecasts of U.S. influenza hospitalizations centered around outbreak onset. **C)** Seasonal peak-timing forecasts issued approximately six weeks prior to the observed peak.

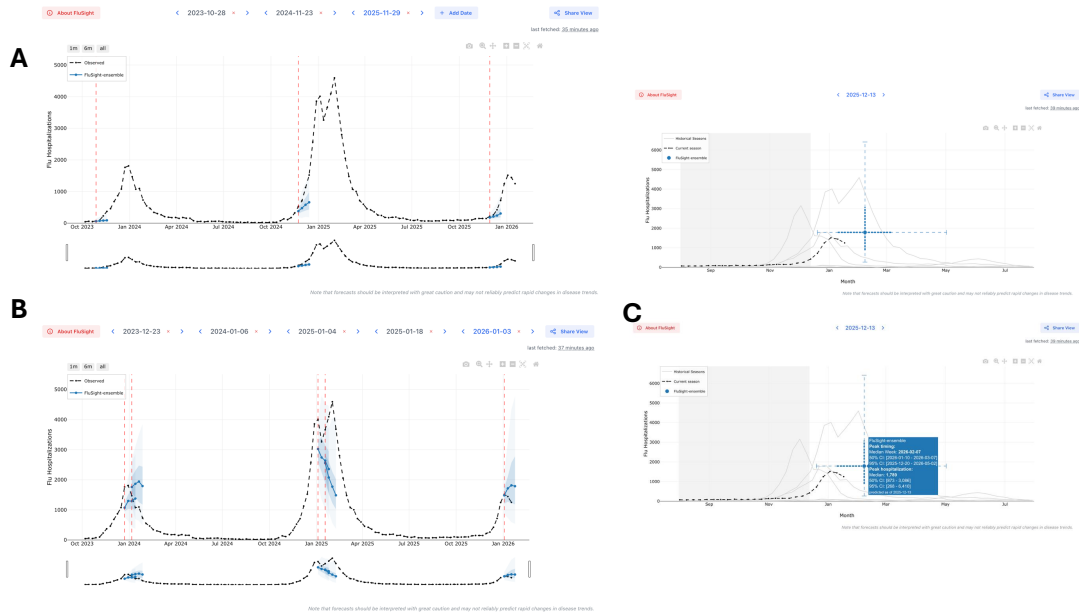


Fig. S4: Example of Flusight ensemble forecast for Influenza Hospitalizations in California Across all panels, the dashed black curve shows observed hospitalizations, blue points and intervals denote ensemble forecasts, and vertical red dashed lines indicate forecast issuance dates. **A)** Example of FluSight ensemble forecasts of California influenza hospitalizations across multiple forecast issuance dates. **B)** FluSight ensemble forecasts of California influenza hospitalizations centered around outbreak onset. **C)** Seasonal peak-timing forecasts issued approximately six weeks prior to the observed peak.

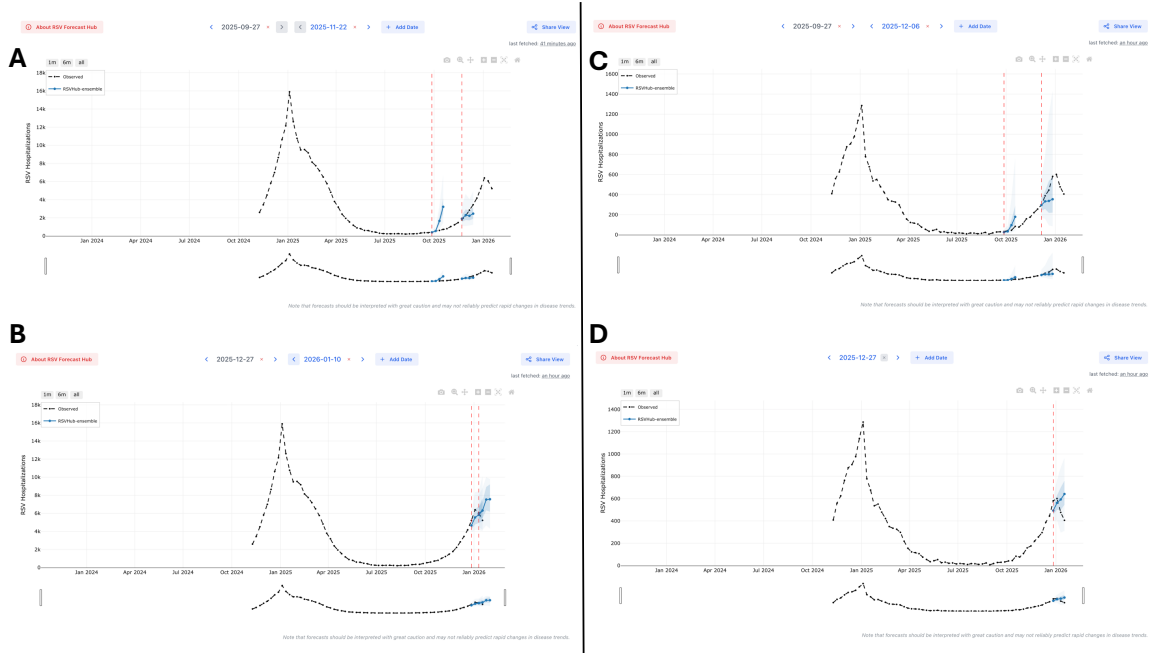


Fig. S5: Example of FluSight ensemble forecast for RSV Hospitalizations Across all panels, the dashed black curve shows observed hospitalizations, blue points and intervals denote ensemble forecasts, and vertical red dashed lines indicate forecast issuance dates. **A)** Example of FluSight ensemble forecasts of U.S. RSV hospitalizations across multiple forecast issuance dates. **B)** FluSight ensemble forecasts of U.S. RSV hospitalizations centered around outbreak onset. **C)** Example of FluSight ensemble forecasts of Texas RSV hospitalizations across multiple forecast issuance dates. **D)** FluSight ensemble forecasts of Texas RSV hospitalizations centered around outbreak onset.

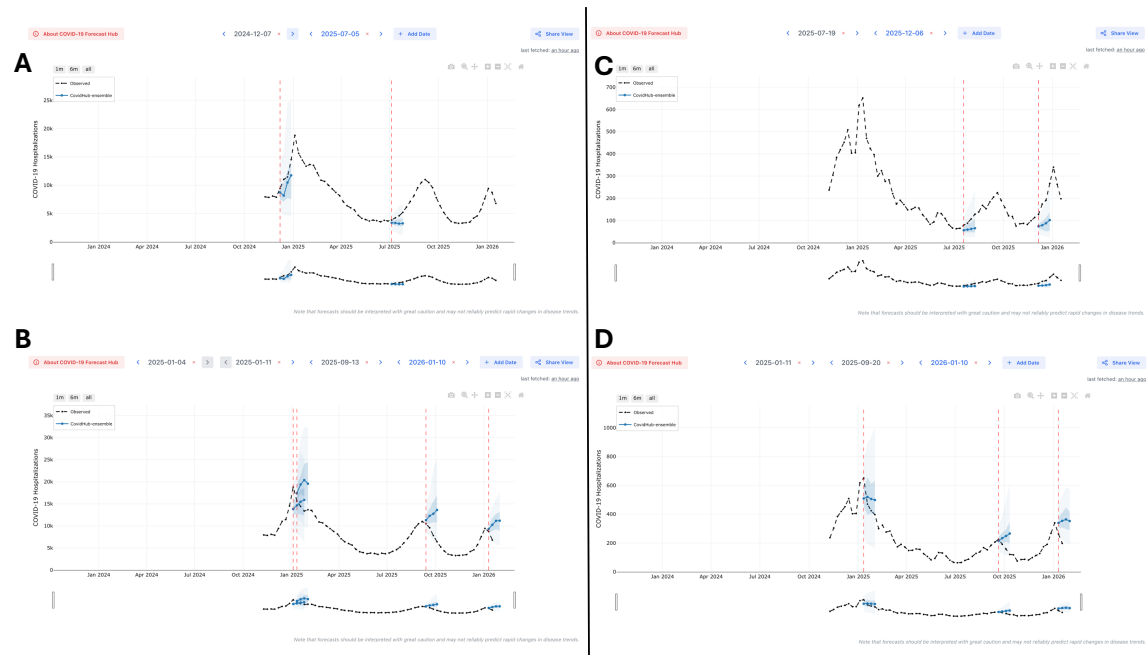


Fig. S6: Example of Flusight ensemble forecast for COVID-19 Hospitalizations Across all panels, the dashed black curve shows observed hospitalizations, blue points and intervals denote ensemble forecasts, and vertical red dashed lines indicate forecast issuance dates. **A)** Example of FluSight ensemble forecasts of U.S. COVID-19 hospitalizations across multiple forecast issuance dates. **B)** FluSight ensemble forecasts of U.S. COVID-19 hospitalizations centered around outbreak onset. **C)** Example of FluSight ensemble forecasts of Massachusetts COVID-19 hospitalizations across multiple forecast issuance dates. **D)** FluSight ensemble forecasts of Massachusetts COVID-19 hospitalizations centered around outbreak onset.

3 Google Trends Used

Box 1: Google Search Terms

anosmia, chest pain, chest tightness, cold, cold symptoms, cold with fever, contagious flu, cough, cough and fever, cough fever, covid, covid nhs, covid symptoms, covid-19, covid-19 who, dry cough, feeling exhausted, feeling tired, fever, fever cough, flu and bronchitis, flu complications, how long are you contagious, how long does covid last, how to get over the flu, how to get rid of flu, how to get rid of the flu, how to reduce fever, influenza, influenza b symptoms, isolation, joints aching, loss of smell, loss taste, nose bleed, oseltamivir, painful cough, pneumonia, pneumonia and have the flu, quarantine, remedies for the flu, respiratory flu, robitussin, robitussin cf., robitussin cough, rsv, runny nose, sars-cov 2, sars-cov-2, sore throat, stay home, strep, strep throat, symptoms of bronchitis, symptoms of flu, symptoms of influenza, symptoms of influenza b, symptoms of pneumonia, symptoms of rsv, tamiflu dosage, tamiflu dose, tamiflu drug, tamiflu generic, tamiflu side effects, tamiflu suspension, tamiflu while pregnant, tamiflu wiki, tessalon

4 Retrospective EWS Results



Fig. S7: Onset Detection Performance During Retrospective Validation and Retrospective Experiment. Top Row: Validation Period (2014-2020 Seasons). **A)** Left: Summary of onset detection outcomes across U.S. states using the Early Warning System (EWS). Most onsets were detected early (94.9%), with minimal synchronous (1.2%) and late warnings (1.6%). Only 0.3% of outbreaks were missed. Right: State-level quality of detection alarms, showing the proportion of true detections and false alarms. While early detections dominate, a small number of false alarms (5.9%) are also observed. **B)** Distribution of onset detection earliness during the validation period. The majority of detections occurred 3 to 6 weeks prior to the onset, peaking at 6 weeks in advance, indicating strong predictive lead time. **Bottom Row: Retrospective Out-of Sample Experiment (2022-2023 and 2023-2024 Seasons).** **C)** Left: Summary of onset detection performance during the two most recent seasons. Early detections remain high (86.8%), with small increases in synchronous (6.1%) and late warnings (3.7%). Only one outbreak was missed. Right: Alarm characterization highlights continued accuracy, with early warnings leading (89.5%) and a false alarm rate of 3.7%. **D)** Distribution of detection earliness in the retrospective test phase. Most detections occurred 3 to 6 weeks before onset, with a strong peak at 6 weeks. While performance is slightly more variable than the validation period, early warning capacity remains robust.

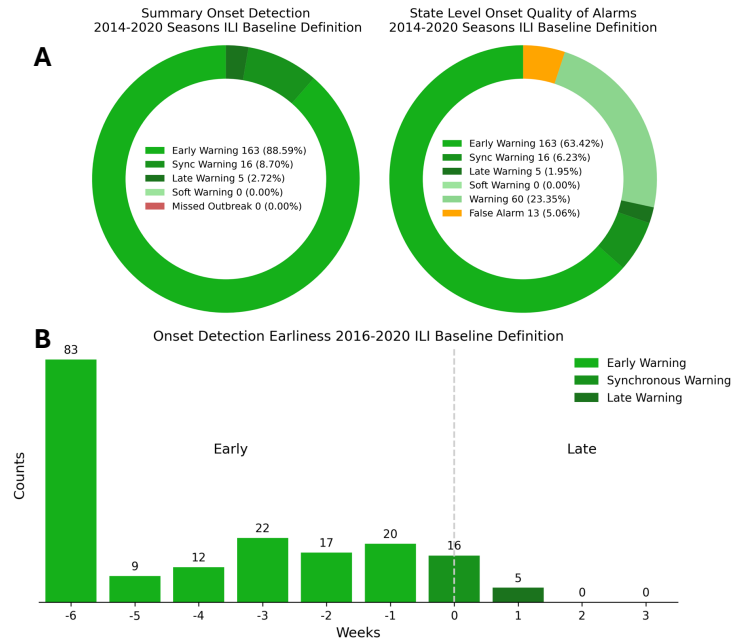


Fig. S8: Onset Detection Performance During Retrospective Validation and Retrospective Experiment Using baseline definition for ILI onset. **A)** Left: Summary of onset detection outcomes across U.S. states using the Early Warning System (EWS). Most onsets were detected early (88.59%), with minimal synchronous (8.70%) and late warnings (2.72%). No outbreaks were missed. Right: State-level quality of detection alarms, showing the proportion of true detections and false alarms. While early detections dominate, a small number of false alarms (5.06%) are also observed. **B)** Distribution of onset detection earliness during the validation period. The majority of detections occurred 6 weeks prior to the onset, indicating strong predictive lead time.



Fig. S9: Onset Detection Performance During Retrospective Validation and Retrospective Experiment. Top Row: Validation Period (2014–2020 Seasons). **A)** Left: Summary of peak detection outcomes across U.S. states using the Early Warning System (EWS). The majority of peaks were detected early (76.6%), with smaller proportions of synchronous (4.7%), late (4.3%), and early-late warnings (12.4%). A small number of outbreaks were missed (0.7%). Right: State-level quality of detection alarms, showing a high rate of early warnings (85.4%) and a false alarm rate of 6.3%. This indicates a strong balance between sensitivity and precision during the validation period. **B)** Distribution of peak detection earliness. Most detections occurred 3 to 6 weeks prior to the peak, with a pronounced concentration at 6 weeks. The early warning system consistently offered substantial lead time. **Bottom Row: Retrospective Out-of-sample Experiment (2022–2023 and 2023–2024 Seasons).** **C)** Left: Summary of peak detection performance during the two most recent seasons. Early warnings remained high (76.4%), while synchronous, late, and early-late warnings comprised 5.4%, 11.4%, and 4.5% respectively. Three outbreaks were missed (3.6%). Right: Alarm classification continues to show high early-warning effectiveness (82.6%) with a slight reduction in precision, as indicated by a false alarm rate of 4.3%. **D)** Distribution of detection earliness in the retrospective test phase. While most detections still occurred early, the distribution was more spread, with notable counts even in the late warning range (1–3 weeks post-peak). Despite this variability, the early detection lead time was largely preserved.

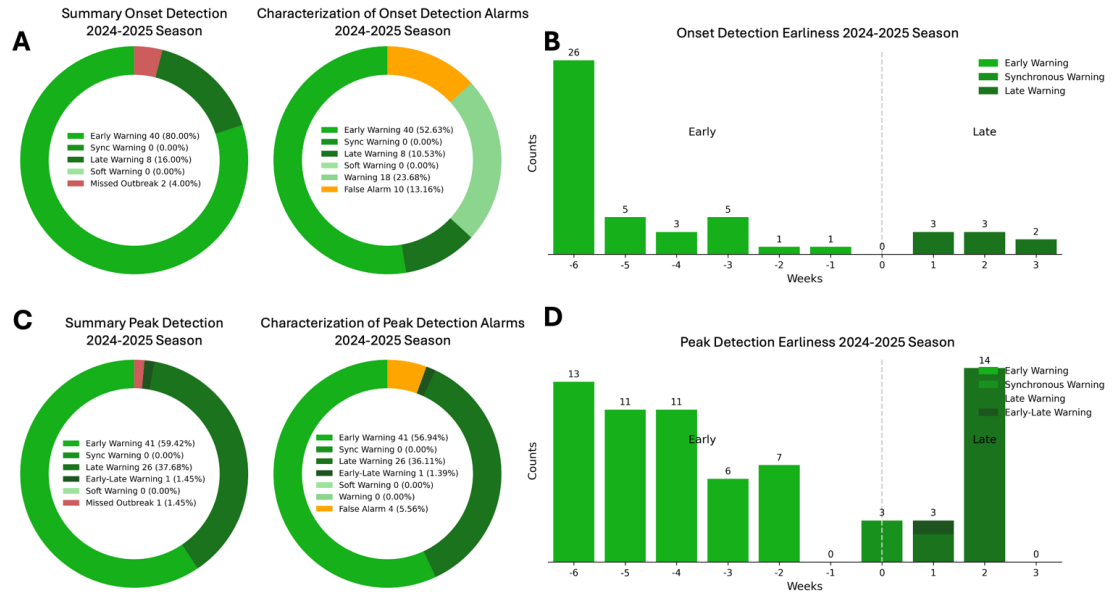


Fig. S10: Performance of Influenza Early Warning System for the 2024–2025 Season. Top Row: Onset Detection. A) Left: Summary of onset detection outcomes across U.S. states using the Early Warning System (EWS). Most onsets were detected early (80%), followed by late (16%) and missed outbreaks (4%). Only 2 onsets were missed. Right: Alarm classification based on onset detection, showing that early warnings comprised the majority (52.63%), followed by late warnings (10.53%), and false alarms (13.16%). **B)** Distribution of onset detection earliness. The majority of early detections occurred 3 to 6 weeks before onset, with a peak at 6 weeks prior. There were not many late warnings supporting the system’s ability to provide timely alerts despite variability in signal dynamics. **Bottom Row: Peak Detection. C)** Left: Summary of peak detection outcomes, showing that over half of peaks were detected early (59.42%), followed by late warnings (37.68%), and early-late warnings (1.45%). Only one peak was missed. **D)** Right: Distribution of detection earliness for peak events. Most early warnings occurred 3 to 6 weeks in advance of the peak, with late warnings concentrated around 2 weeks post-peak.

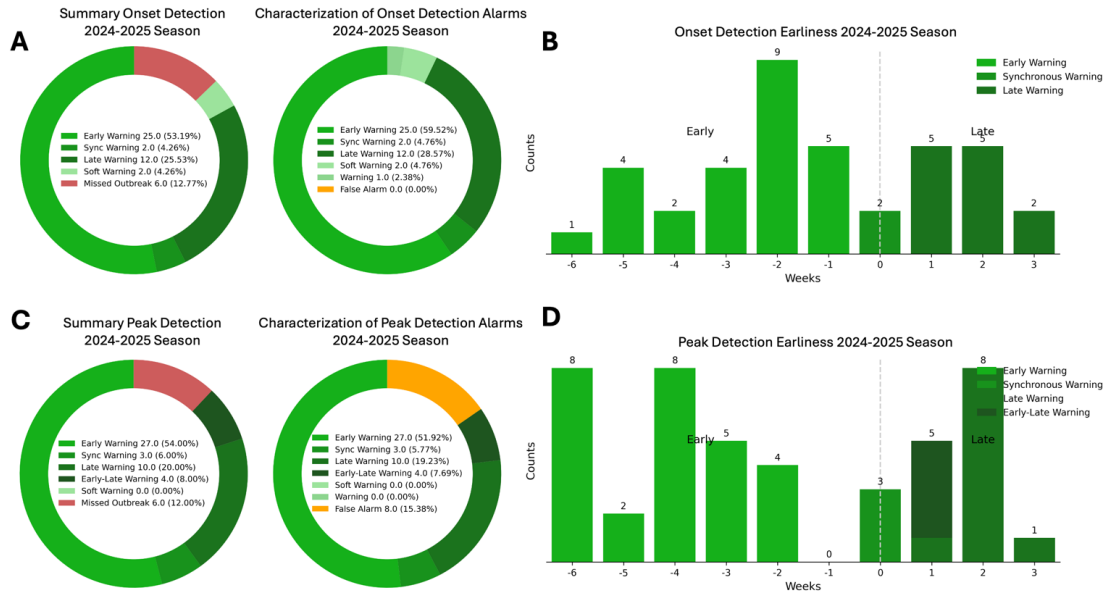


Fig. S11: Performance of RSV Early Warning System for the 2024–2025 Season. **Top Row: Onset Detection.** **A)** Left: Summary of onset detection outcomes across U.S. states using the Early Warning System (EWS). Most onsets were detected early (53.2%), followed by late (25.5%) and missed outbreaks (12.8%). Synchronous and soft warnings accounted for a smaller proportion (4.3% each). Right: Alarm classification based on onset detection, showing that early warnings comprised the majority (59.5%). No false alarms were recorded during this period. **B)** Distribution of onset detection earliness. The majority of early detections occurred 1–3 weeks before onset, with a peak at 2 weeks prior. Late warnings were most frequent 1–2 weeks after onset, supporting the system’s ability to provide timely alerts despite variability in signal dynamics. **Bottom Row: Peak Detection.** **C)** Left: Summary of peak detection outcomes, showing that over half of peaks were detected early (54%), with smaller shares of synchronous (6%), late (20%), and early-late warnings (8%). A small number of peaks were missed (12%), with no soft warnings recorded. **D)** Right: Distribution of detection earliness for peak events. Most early warnings occurred 3–6 weeks in advance of the peak, with late warnings concentrated around 1–2 weeks post-peak.

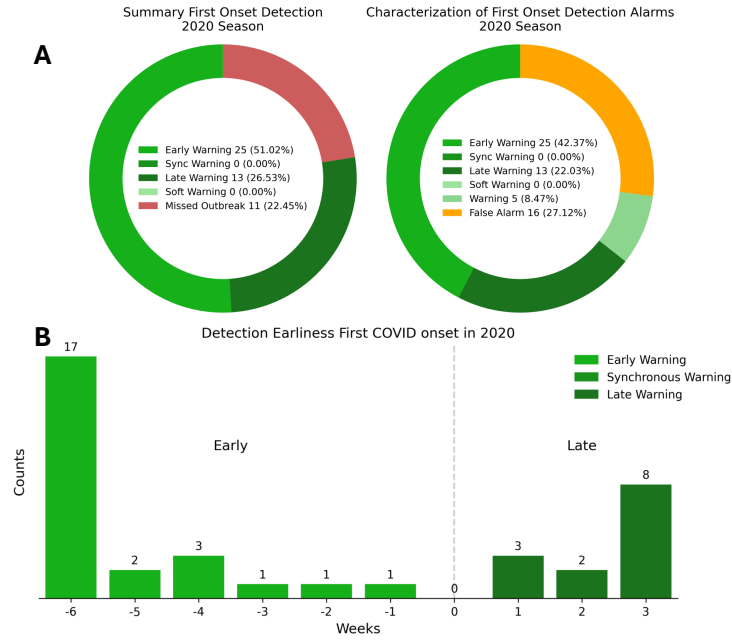


Fig. S12: Performance of COVID-19 Early Warning System for the First Onset of the Pandemic of 2020. **A)** Left: Summary of onset detection outcomes across U.S. states using the Early Warning System (EWS). 25 onsets were detected in advance, while an additional 13 were detected within three days after the epidemiological onset, corresponding to near-synchronous warnings. Right: State-level quality of detection alarms, showing the proportion of true detections and false alarms. While early detections dominate, a small number of false alarms (27.1%) are also observed. **B)** Distribution of onset detection earliness during the validation period. The majority of detections occurred 6 weeks prior to the onset, indicating strong predictive lead time.

5 Results Comparison with and without Google Trends

Performance of the early warning system across target diseases and validation phases, comparing surveillance-only signals with surveillance augmented by Google Trends (Table S1) and only Google Trends (Table S2). Detection rate, mean lead time, and positive predictive value (PPV) are reported for outbreak onset and peak detection.

Table S1: Performance of the early warning system across different target diseases and validation phases.

Signals Used	Validation phase	Disease	Onset			Peak		
			Det. (%)	Lead (wk)	PPV (%)	Det. (%)	Lead (wk)	PPV (%)
Surveillance Data	Retrospective (2014–2020)	ILI	99.3	3.2	93.0	81.3	3.2	82.3
Surveillance Data + GT	Retrospective (2014–2020)	ILI	99.3	3.4	93.0	84.2	3.9	69.3
Surveillance Data	Out-of-sample (2022–2024)	ILI	99.0	4.3	96.0	92.9	2.5	96.9
Surveillance Data + GT	Out-of-sample (2022–2024)	ILI	99.0	4.2	96.0	96.1	3.1	82.7
Surveillance Data	Out-of-sample (2024–2025)	Influenza	94.0	4.0	83.9	68.1	1.5	97.1
Surveillance Data + GT	Out-of-sample (2024–2025)	Influenza	96.0	4.0	82.8	60.8	2.6	94.4
Surveillance Data	Out-of-sample (2024–2025)	RSV	95.7	1.7	100.0	40.0	0.5	100.0
Surveillance Data + GT	Out-of-sample (2024–2025)	RSV	87.2	1.2	100.0	68.0	2.0	84.6

Note: Det. = Detection rate; GT = Google Terms; PPV indicates positive predictive value.

Table S2: Performance of the early warning system using only Google Searches for ILI in retrospective experiments.

Validation phase	Onset			Peak		
	Det. (%)	Lead (wk)	PPV (%)	Det. (%)	Lead (wk)	PPV (%)
2014–2015	76.8	3.3	91.4	97.6	4.1	61.5
2016–2017	82.4	2.4	98.1	91.1	4.5	59.0
2018–2019	92.0	2.0	97.2	98.5	4.9	61.7
Total 2014–2019	84.1	2.5	95.4	96.1	4.5	60.6

Note: Det. = Detection rate; GT = Google Terms; PPV indicates positive predictive value.

6 Comparison Onsets between classic ILI Definition and our definition

The CDC defines ILI onset as three consecutive weeks of activity above a baseline threshold (mean plus two standard deviations of non-influenza weeks from the previous three seasons), while our approach identifies onset based on sustained exponential growth patterns. Figure S13 presents the temporal alignment between these two definitions across all state-season pairs in our retrospective validation dataset, revealing that our growth-based definition typically identifies onset at similar or slightly earlier times relative to the CDC criterion, rather than systematically later as might be initially hypothesized.

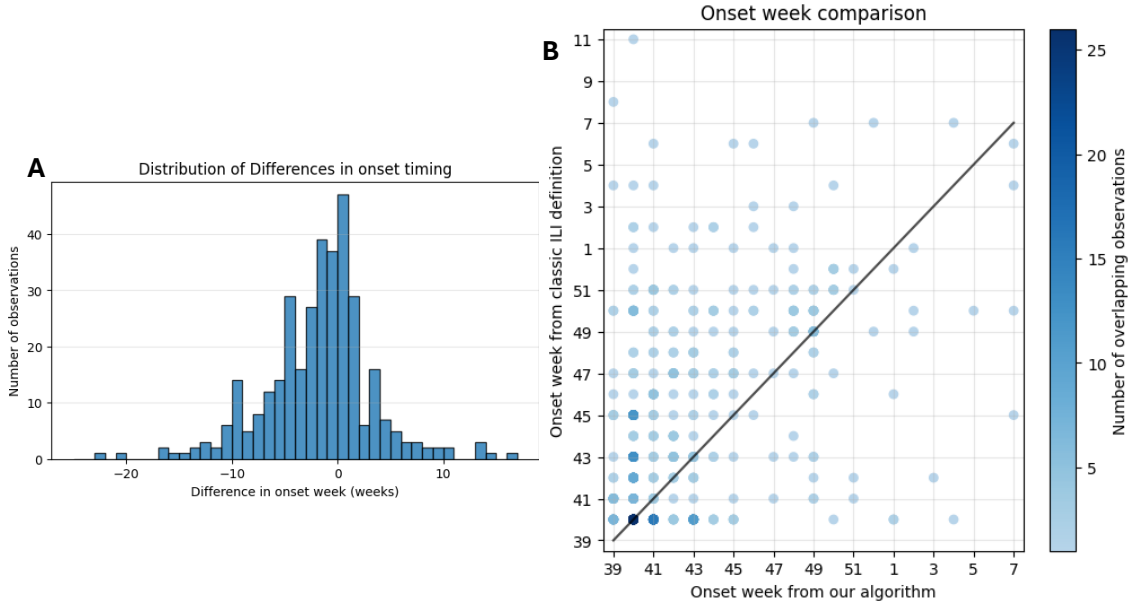


Fig. S13: Comparison between CDC-defined ILI onset and the onset definition used in this study. **A)** Distribution of differences in onset timing between the growth-based onset definition used in this study and the standard CDC ILI onset definition, expressed in weeks. Differences are computed as (onset week from our algorithm minus onset week from the CDC definition), such that negative values indicate earlier detection by the proposed method. The distribution is centered near zero with a slight skew toward negative values, indicating that the growth-based definition typically identifies onset at similar or earlier times relative to the CDC criterion. **B)** Scatter plot comparing onset weeks identified by the proposed algorithm (x-axis) and those identified using the classic CDC ILI definition (y-axis). Each point represents a state–season pair, with color intensity indicating the number of overlapping observations at that coordinate. The diagonal line denotes perfect agreement between the two definitions. Points lying above the diagonal correspond to cases where the proposed method detects onset earlier than the CDC definition, while points below indicate later detection. The predominance of points above the diagonal demonstrates that the growth-based onset definition tends to trigger earlier or at comparable times, rather than systematically later.

7 Onset Examples 2024-2025 Real-Time Predictions

To demonstrate the operational performance of our early warning system during real-time deployment, we present representative examples of onset detection across multiple U.S. states during the 2024–2025 ILI season. These examples illustrate how individual proxy signals—including Google Trends search queries and neighboring state surveillance data—aggregate through the ensemble voting mechanism to trigger early warning alarms several weeks before confirmed outbreak onsets. The figures show the complete temporal evolution of proxy activations, the voting threshold crossings, and the alignment between system predictions and observed ILI activity, providing transparent documentation of the system’s prospective performance across diverse geographic contexts and outbreak dynamics. Representative onset detection examples for all 50 states are provided in Figures S14–S63.

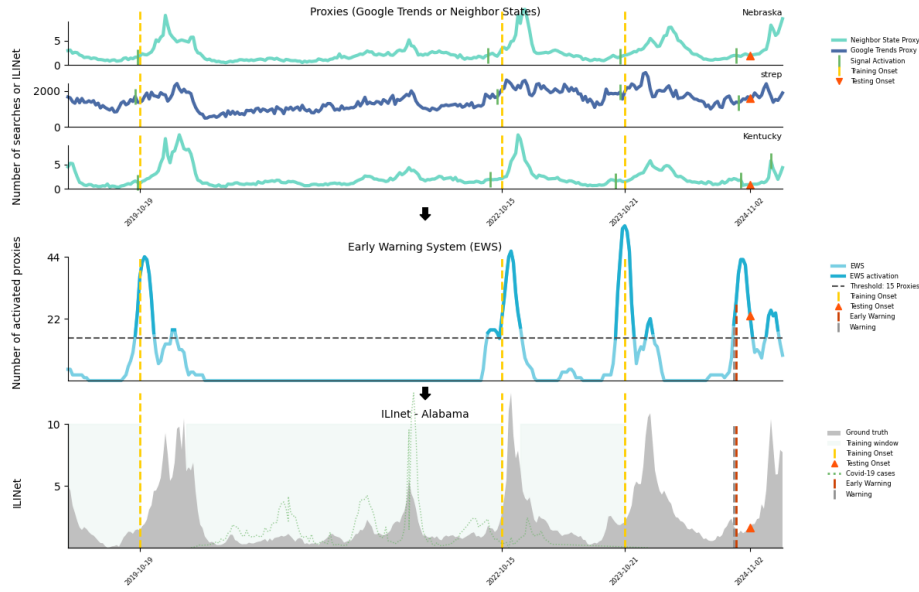


Fig. S14: Onset detection for Alabama during the 2024-2025 season

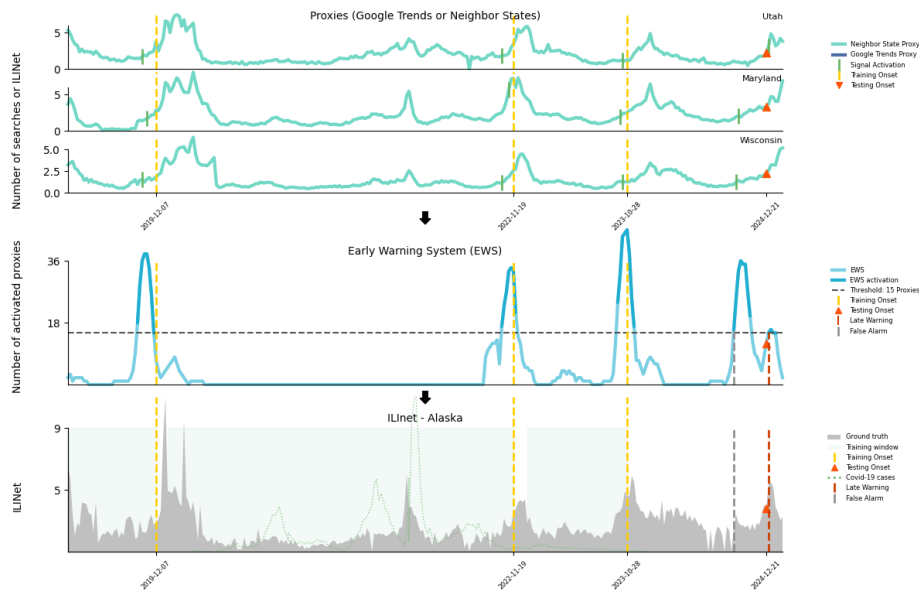


Fig. S15: Onset detection for Alaska during the 2024-2025 season

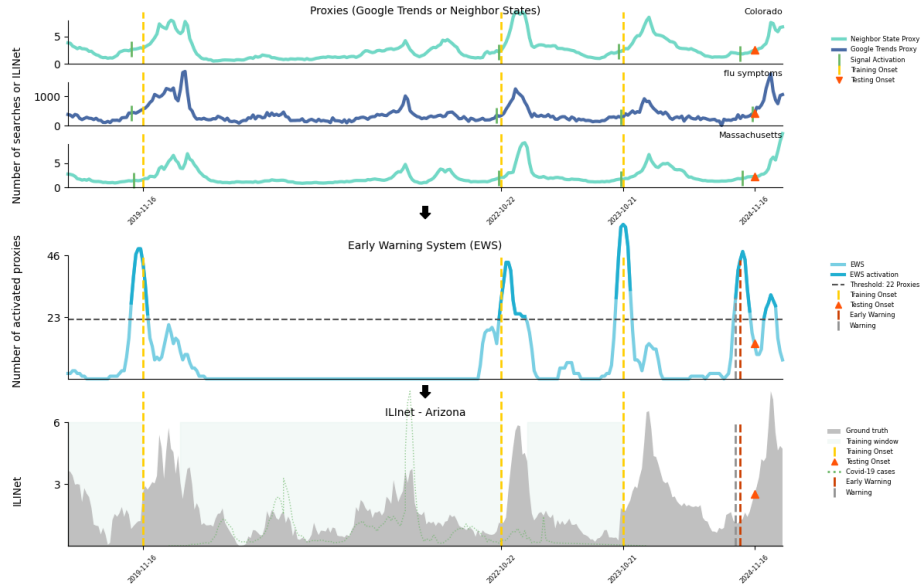


Fig. S16: Onset detection for Arizona during the 2024-2025 season

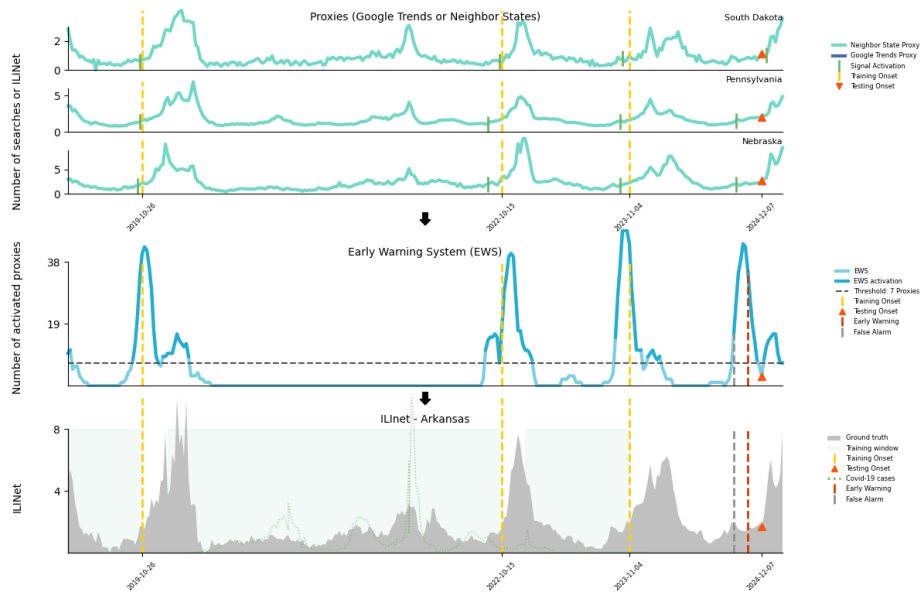


Fig. S17: Onset detection for Arkansas during the 2024-2025 season

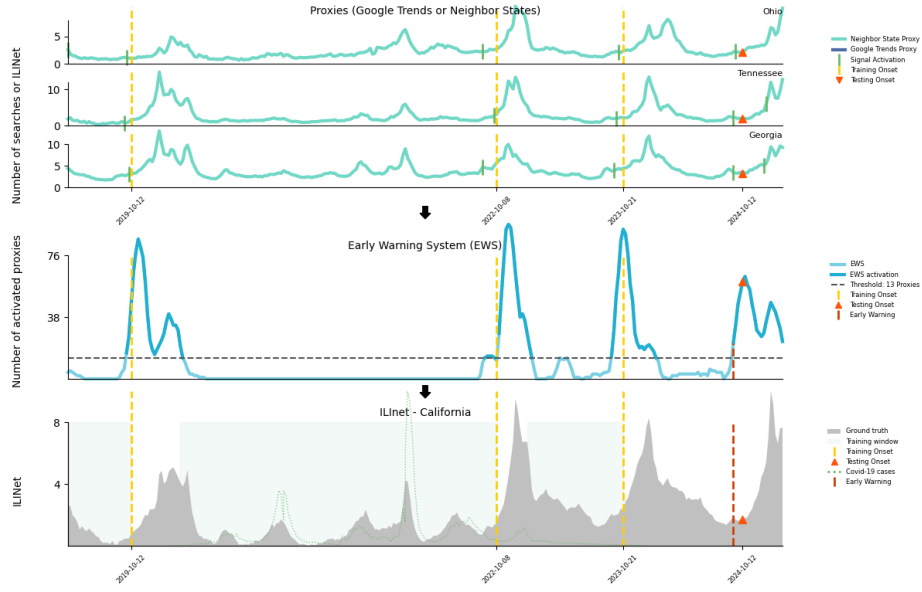


Fig. S18: Onset detection for California during the 2024-2025 season

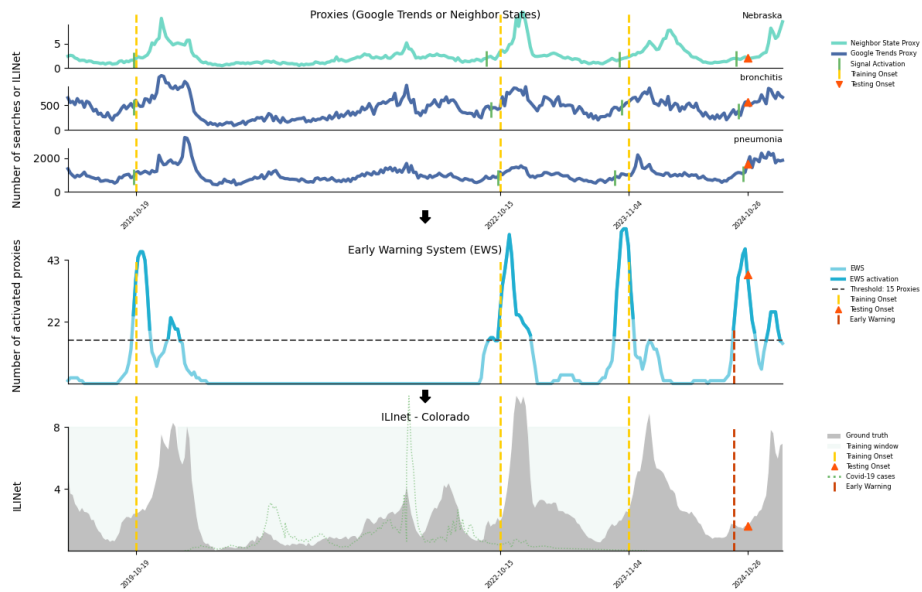


Fig. S19: Onset detection for Colorado during the 2024-2025 season

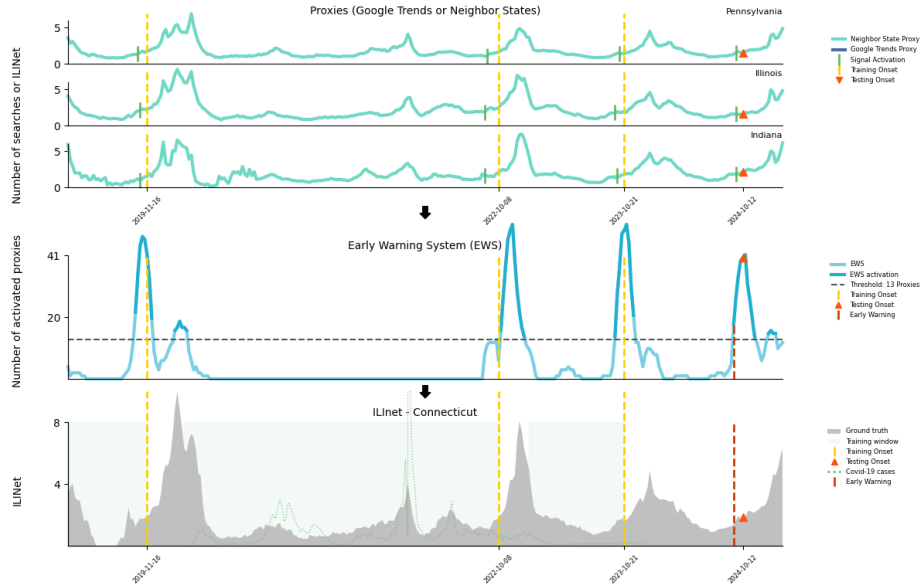


Fig. S20: Onset detection for Connecticut during the 2024-2025 season

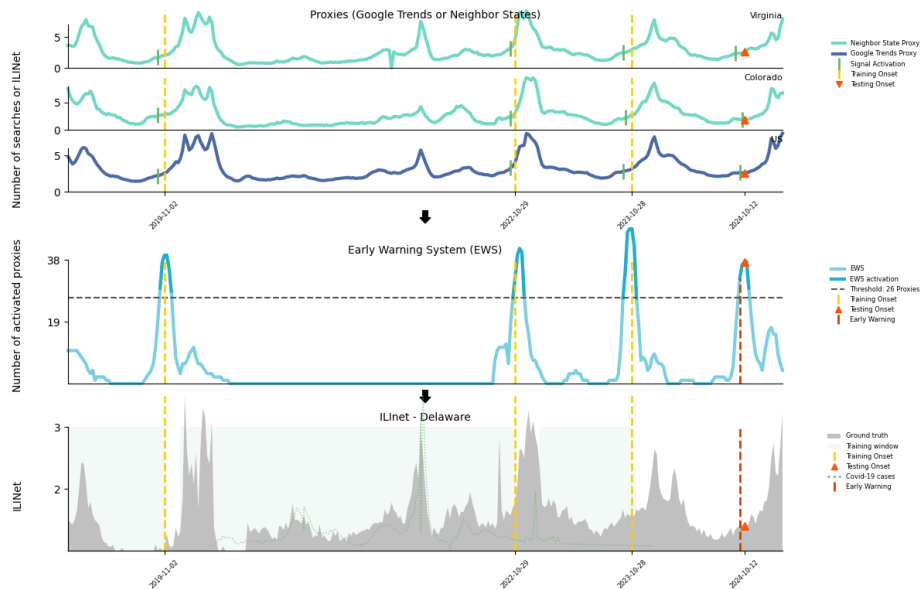


Fig. S21: Onset detection for Delaware during the 2024-2025 season

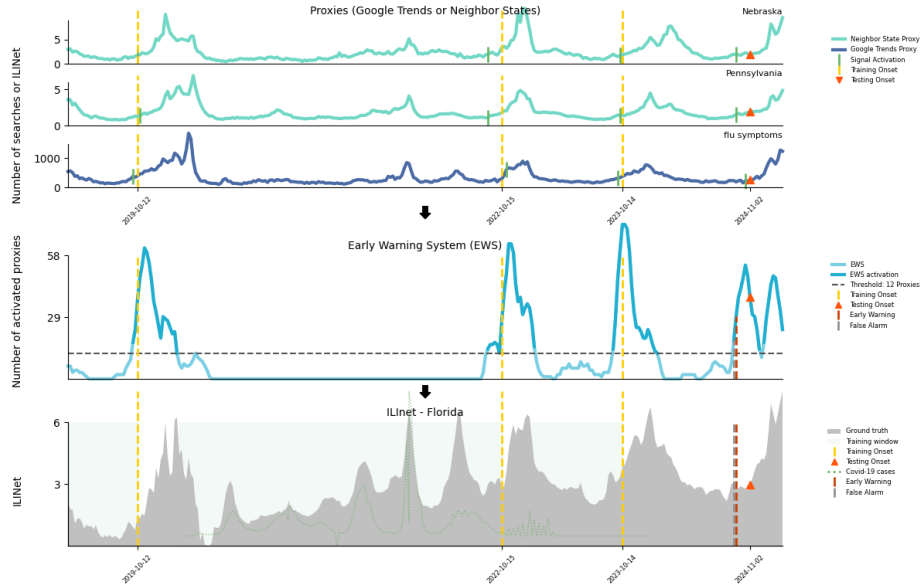


Fig. S22: Onset detection for Florida during the 2024-2025 season

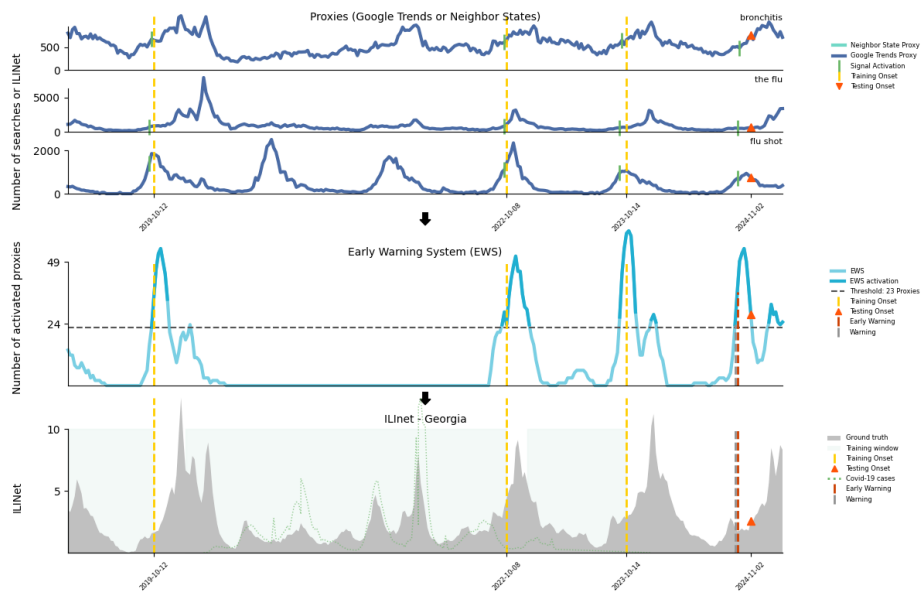


Fig. S23: Onset detection for Georgia during the 2024-2025 season

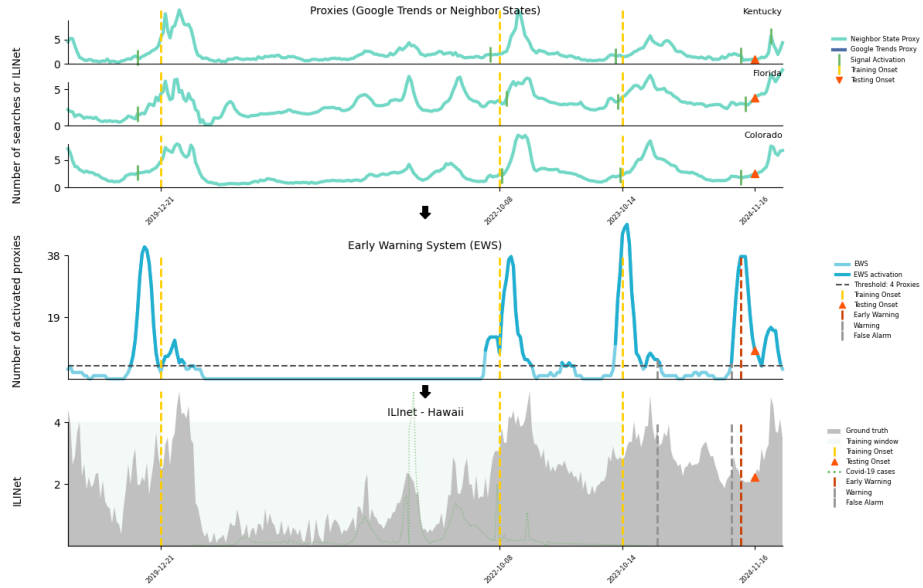


Fig. S24: Onset detection for Hawaii during the 2024-2025 season

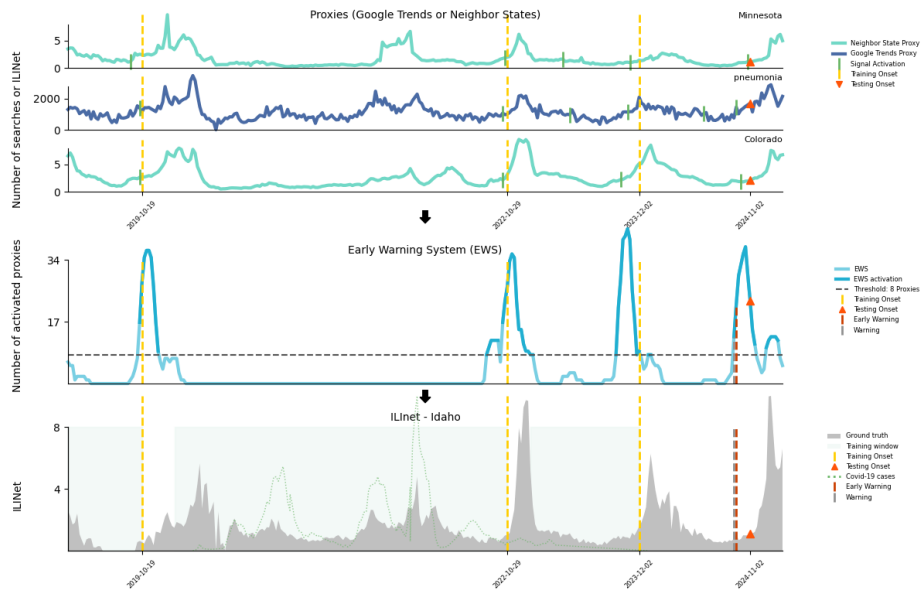


Fig. S25: Onset detection for Idaho during the 2024-2025 season

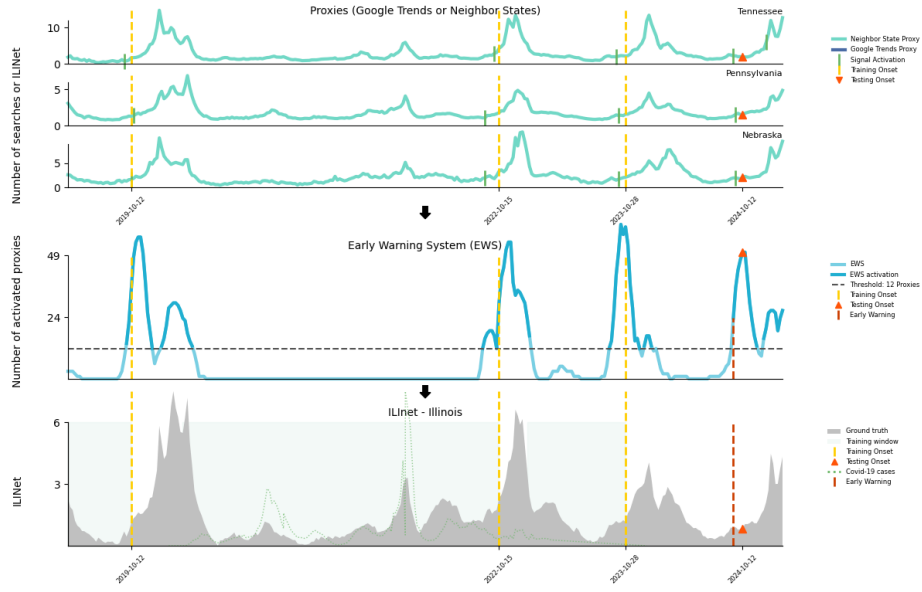


Fig. S26: Onset detection for Illinois during the 2024-2025 season

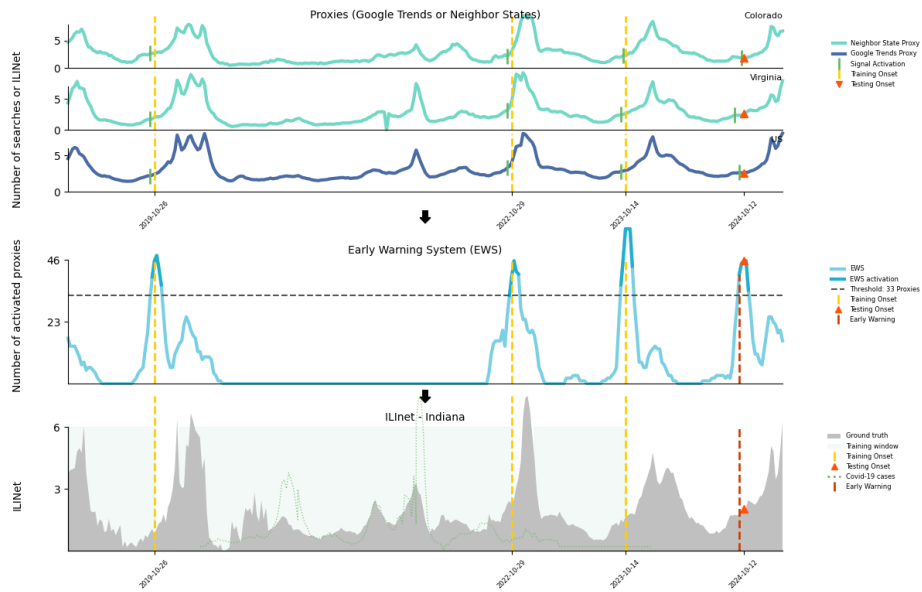


Fig. S27: Onset detection for Indiana during the 2024-2025 season

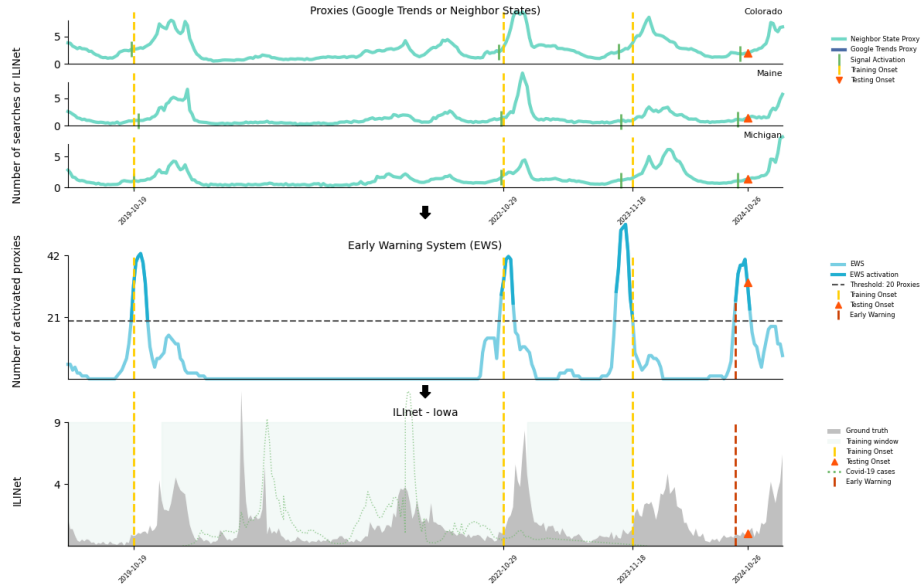


Fig. S28: Onset detection for Iowa during the 2024-2025 season

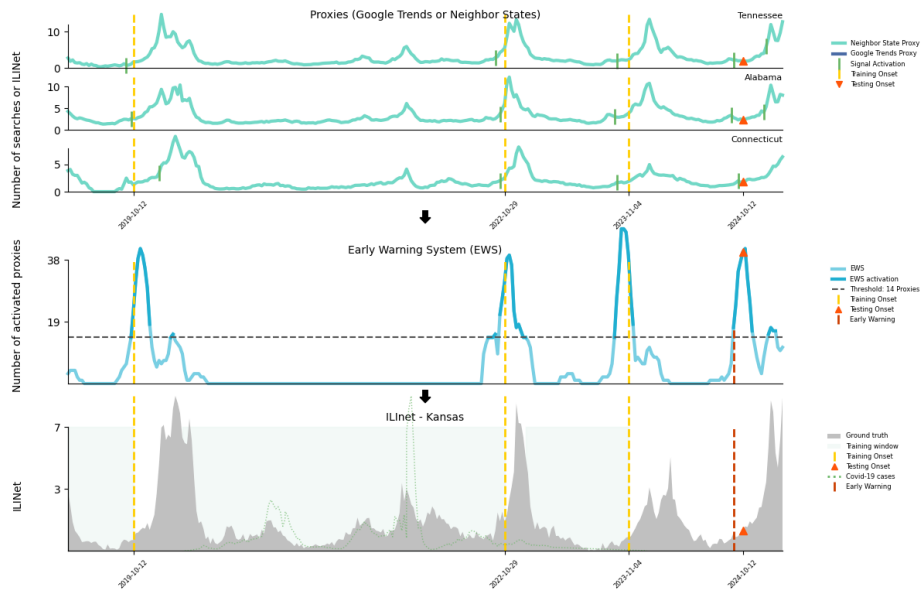


Fig. S29: Onset detection for Kansas during the 2024-2025 season

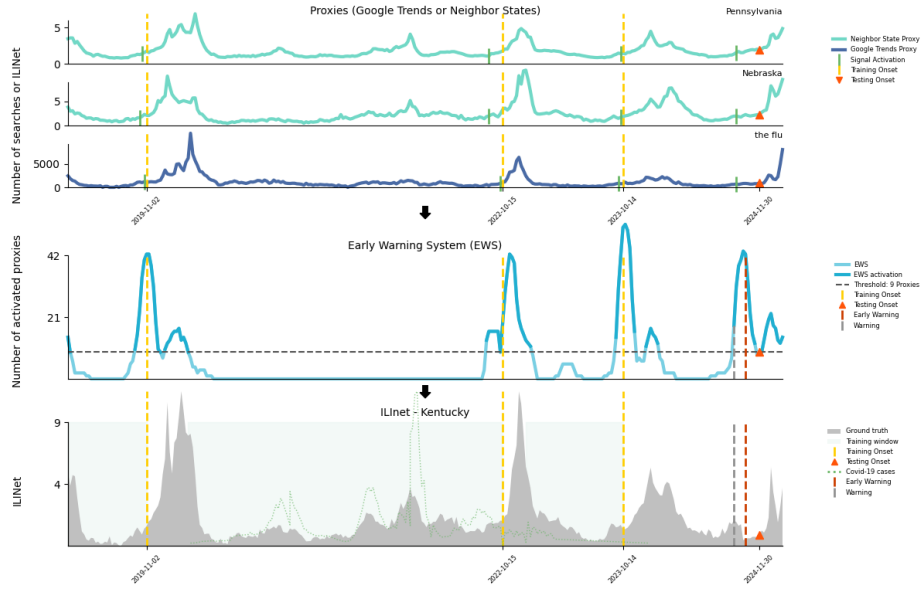


Fig. S30: Onset detection for Kentucky during the 2024-2025 season

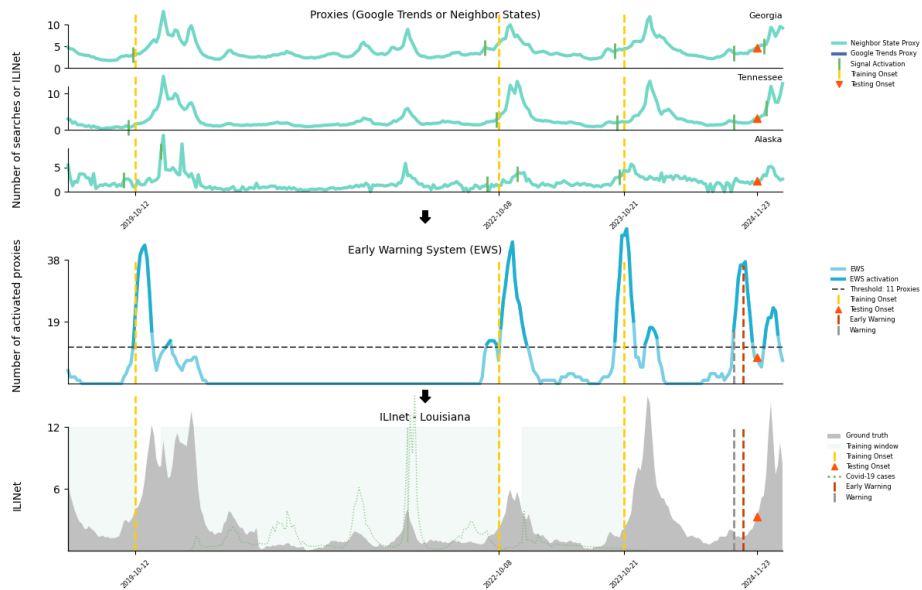


Fig. S31: Onset detection for Louisiana during the 2024-2025 season

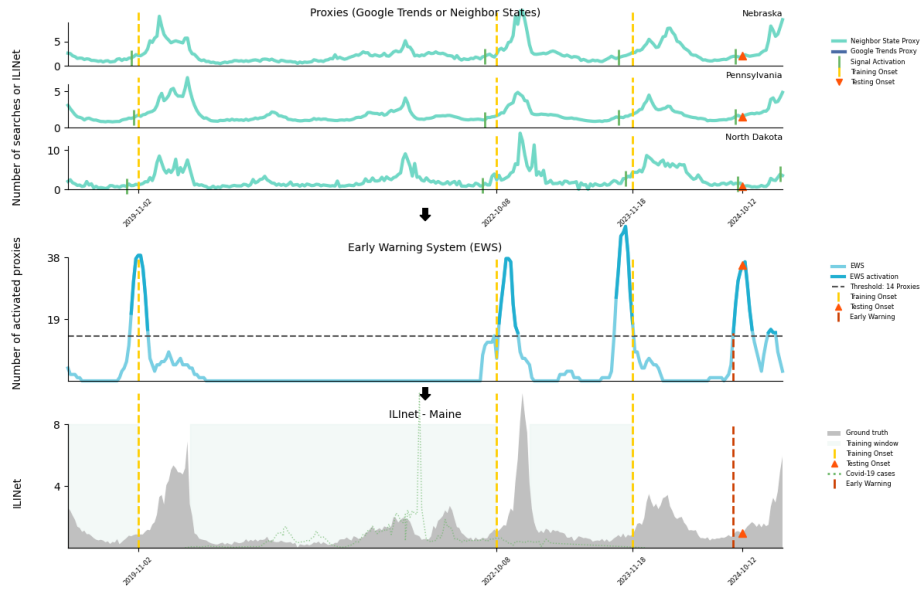


Fig. S32: Onset detection for Maine during the 2024-2025 season

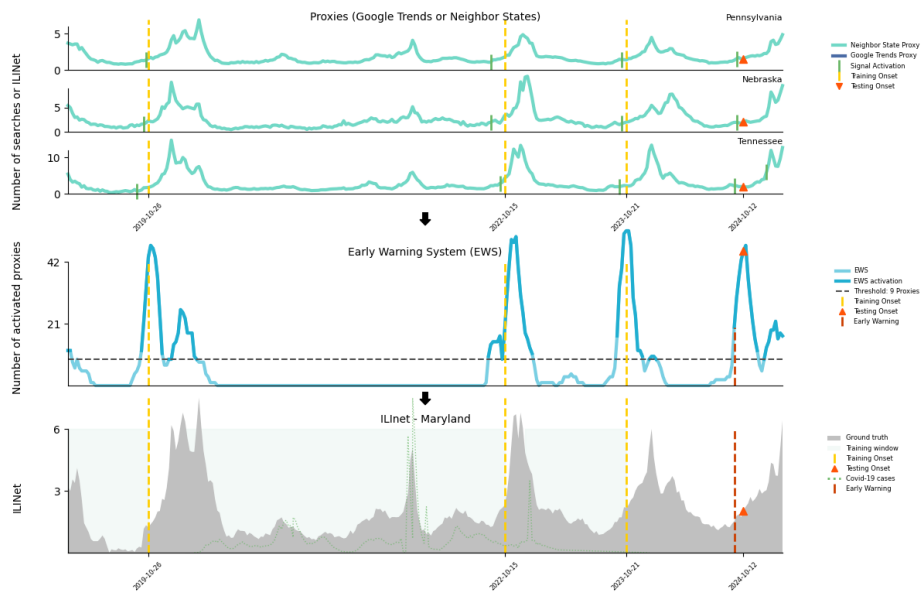


Fig. S33: Onset detection for Maryland during the 2024-2025 season

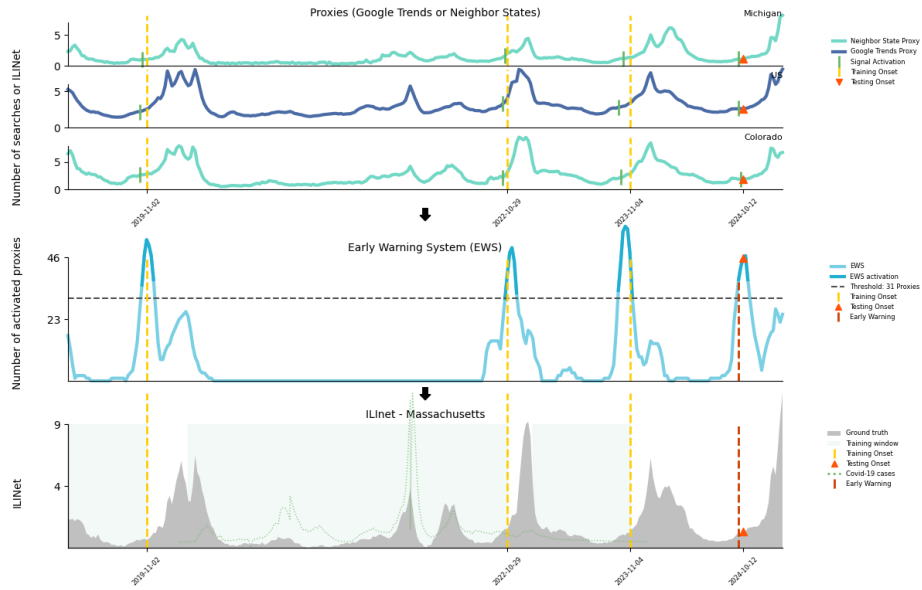


Fig. S34: Onset detection for Massachusetts during the 2024-2025 season

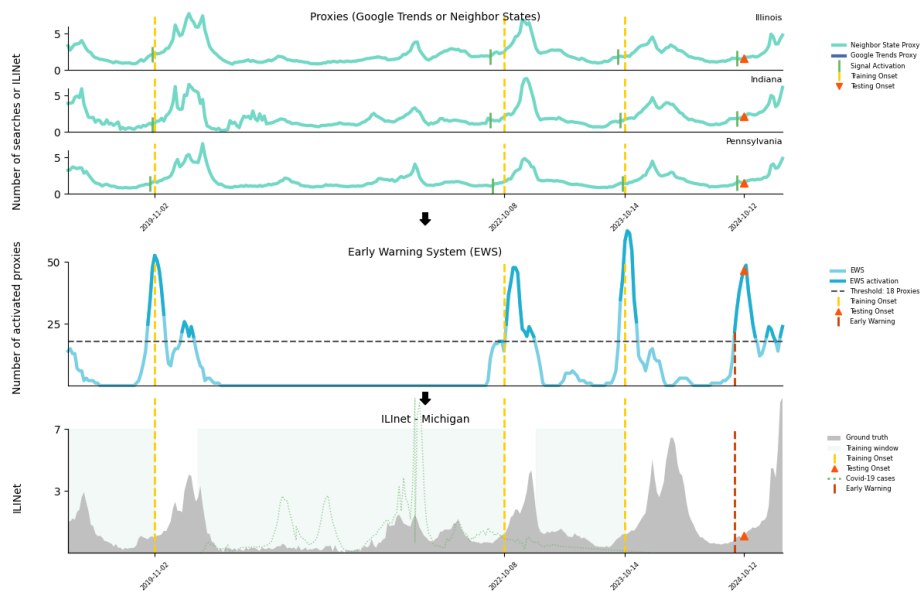


Fig. S35: Onset detection for Michigan during the 2024-2025 season

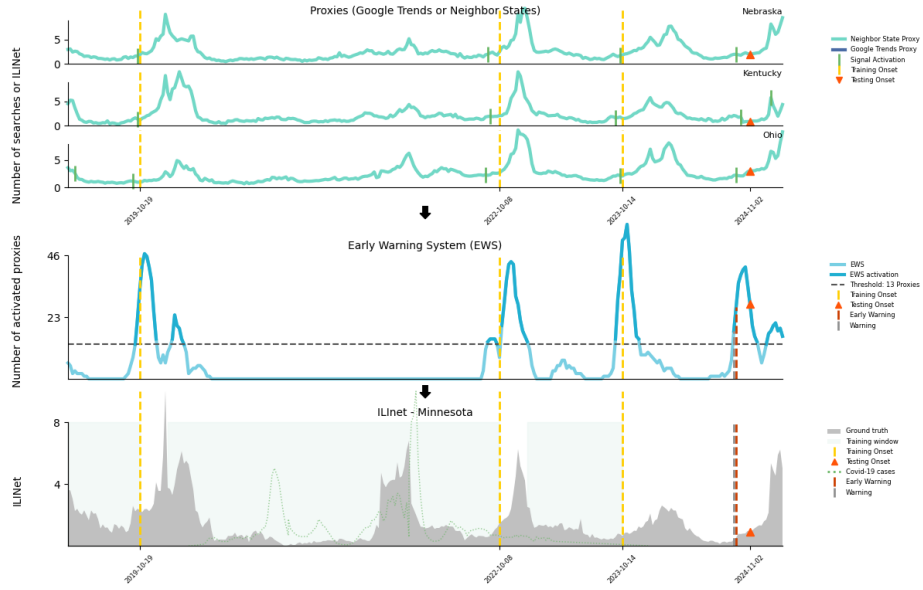


Fig. S36: Onset detection for Minnesota during the 2024-2025 season

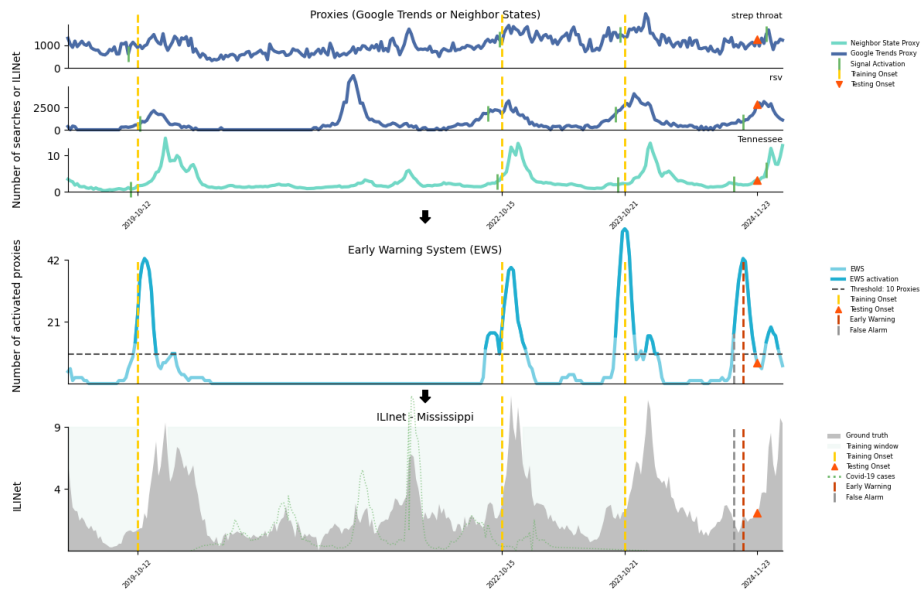


Fig. S37: Onset detection for Mississippi during the 2024-2025 season

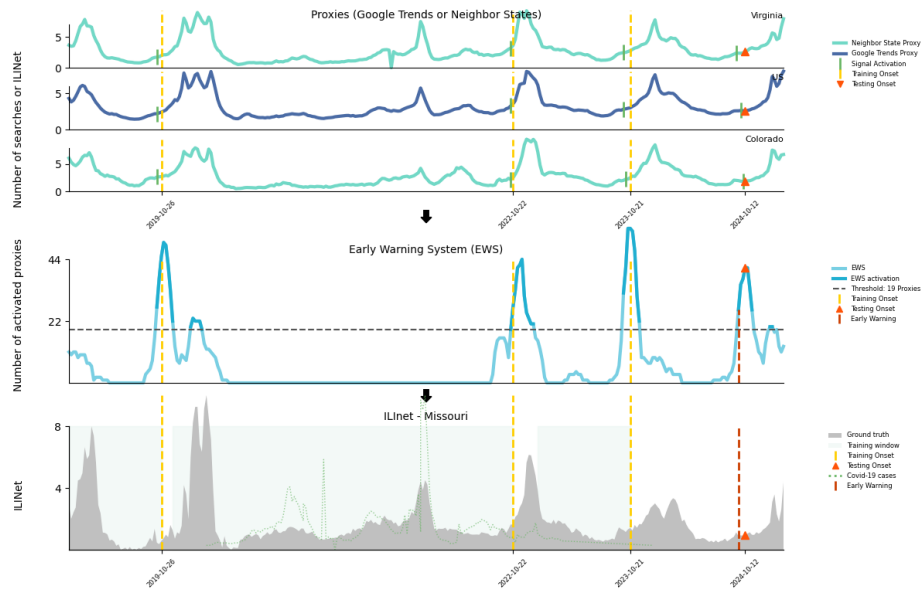


Fig. S38: Onset detection for Missouri during the 2024-2025 season

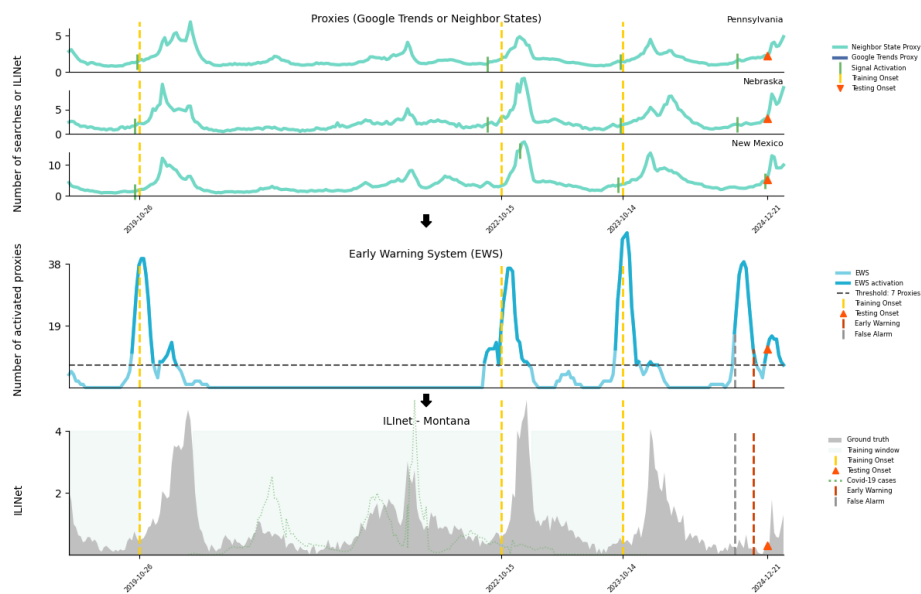


Fig. S39: Onset detection for Montana during the 2024-2025 season

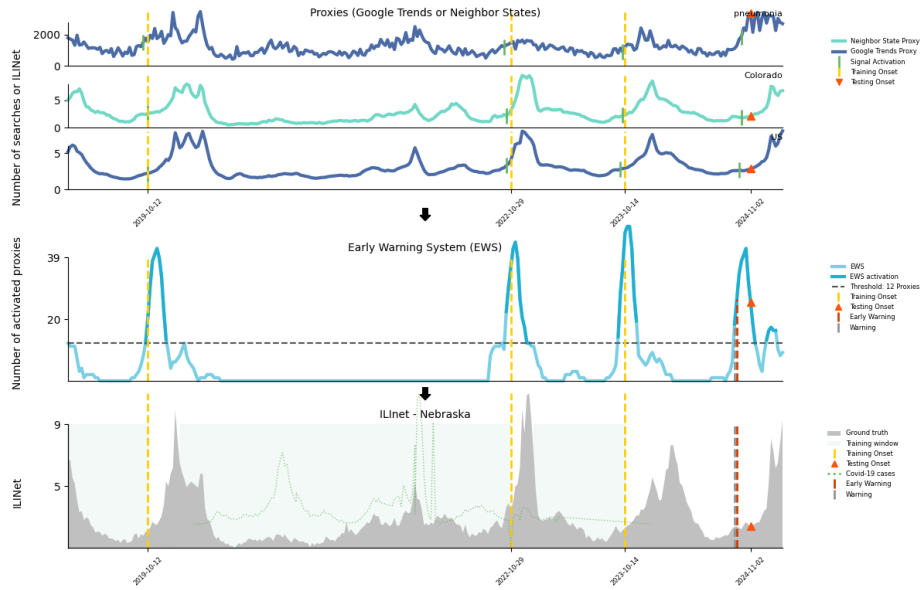


Fig. S40: Onset detection for Nebraska during the 2024-2025 season

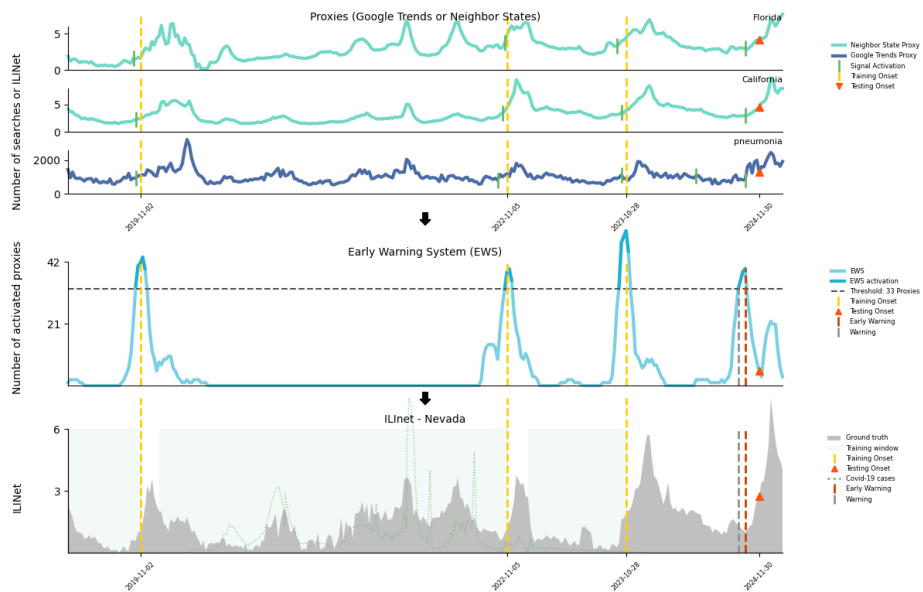


Fig. S41: Onset detection for Nevada during the 2024-2025 season

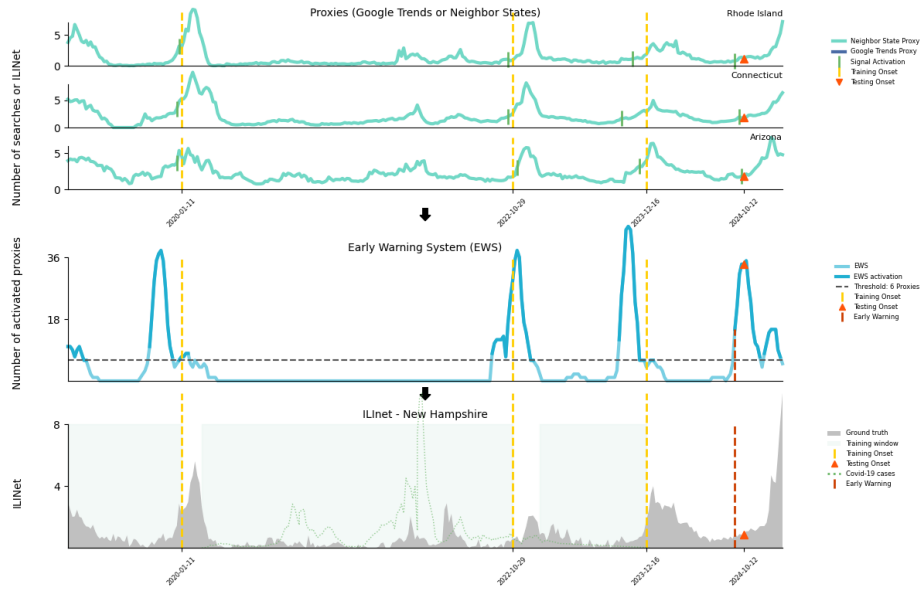


Fig. S42: Onset detection for New Hampshire during the 2024-2025 season

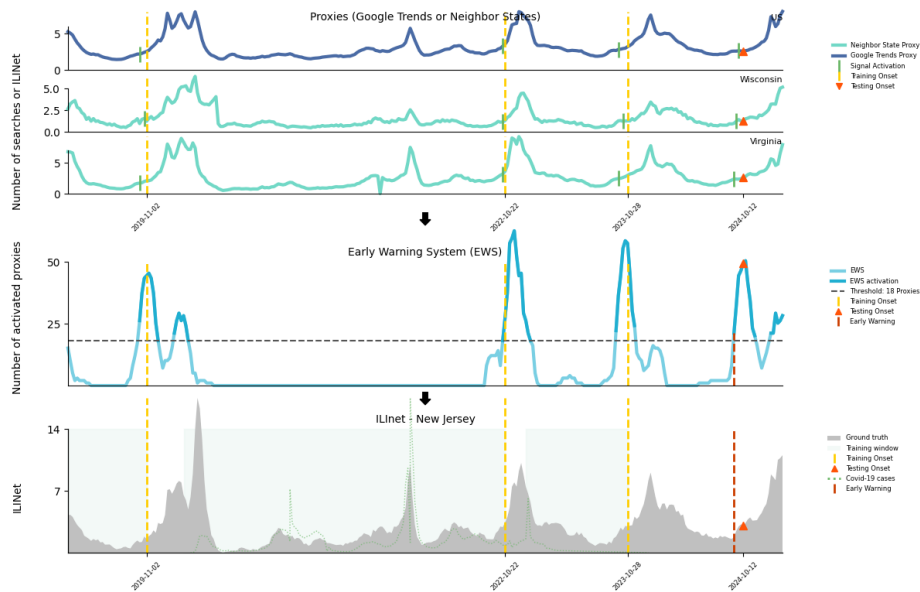


Fig. S43: Onset detection for New Jersey during the 2024-2025 season

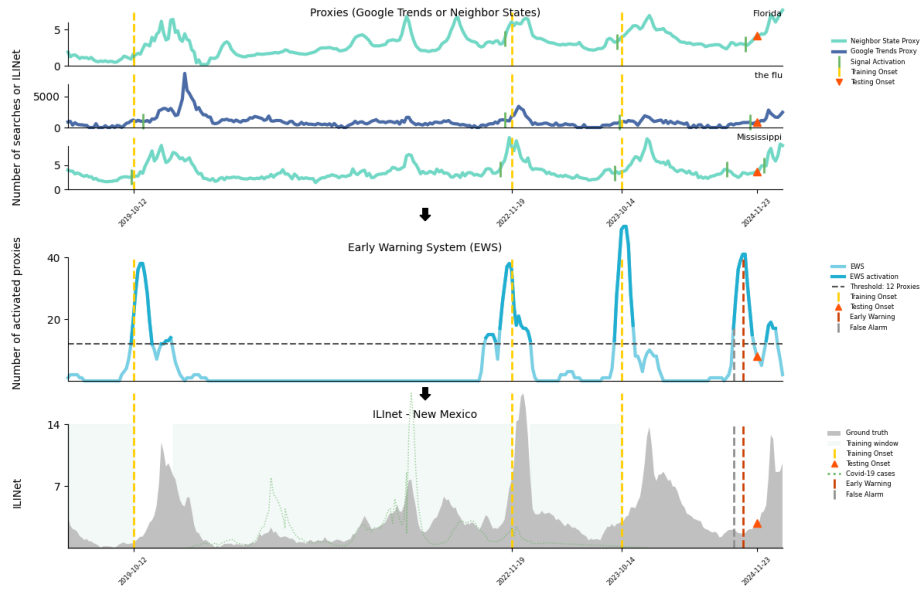


Fig. S44: Onset detection for New Mexico during the 2024-2025 season

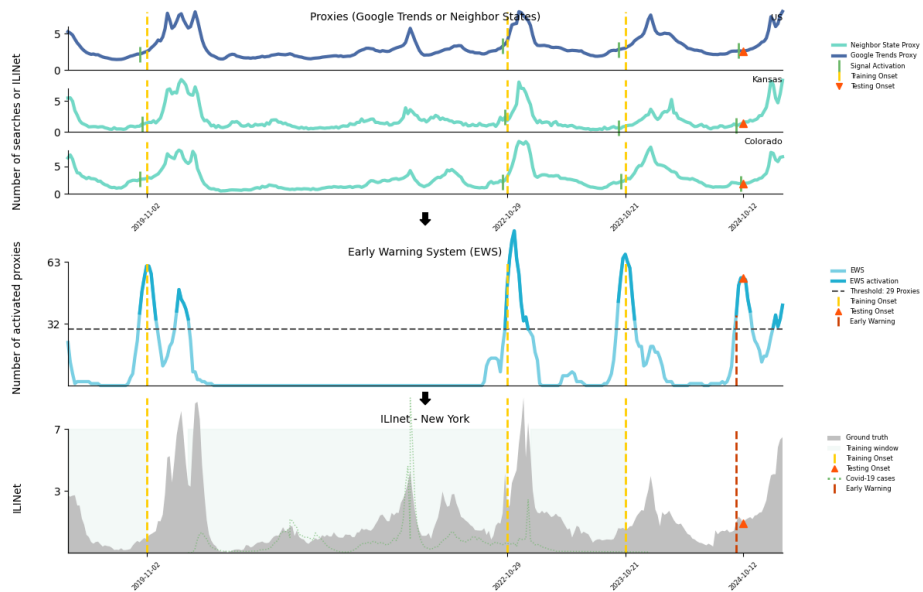


Fig. S45: Onset detection for New York during the 2024-2025 season

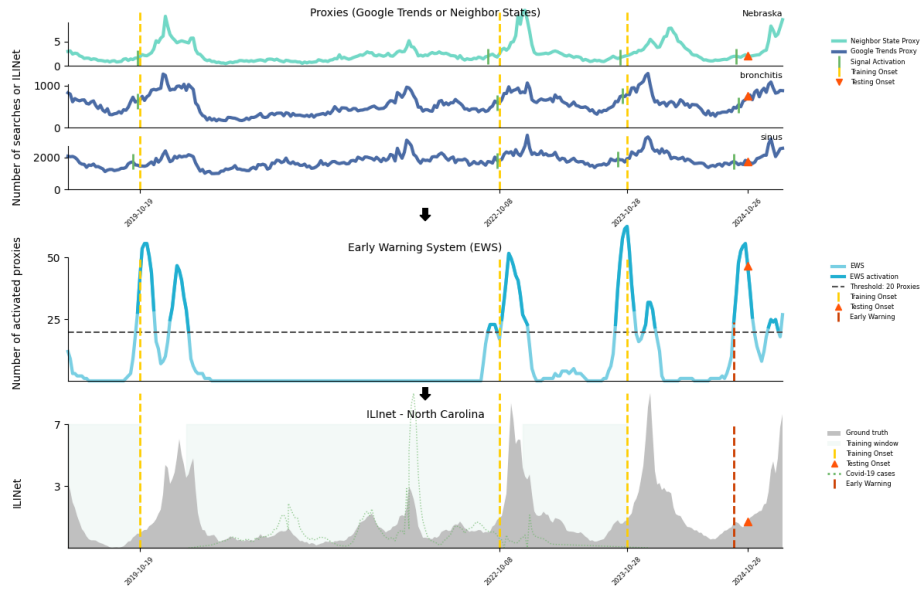


Fig. S46: Onset detection for North Carolina during the 2024-2025 season

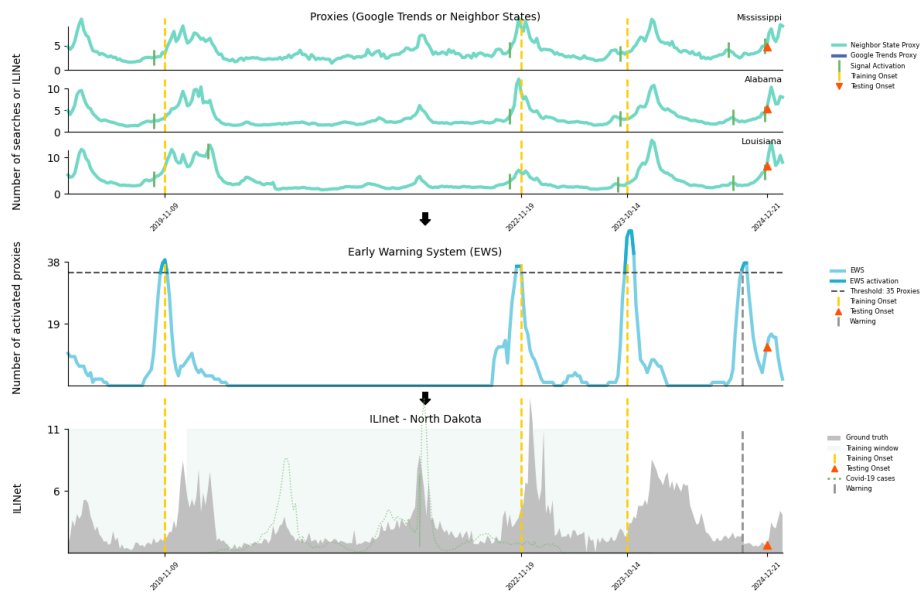


Fig. S47: Onset detection for North Dakota during the 2024-2025 season

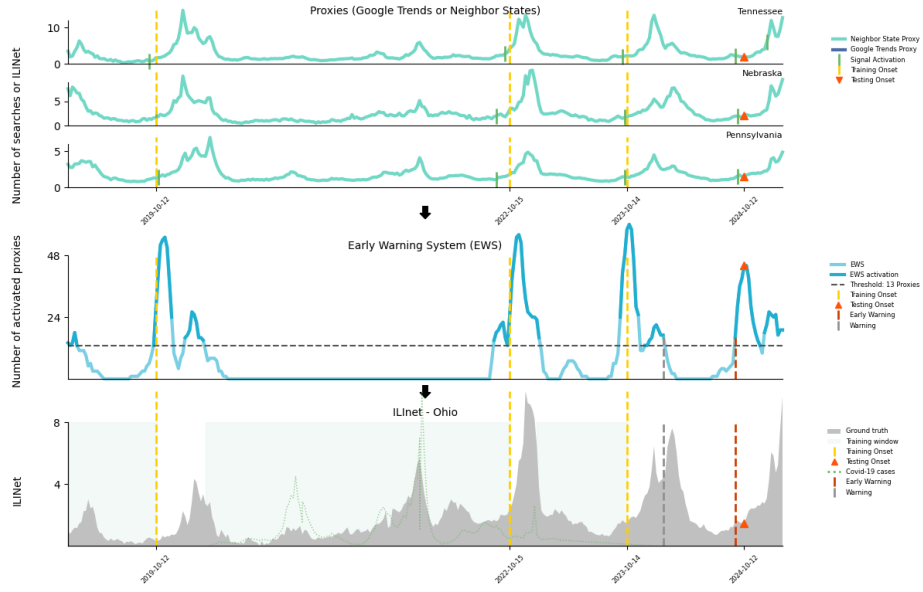


Fig. S48: Onset detection for Ohio during the 2024-2025 season

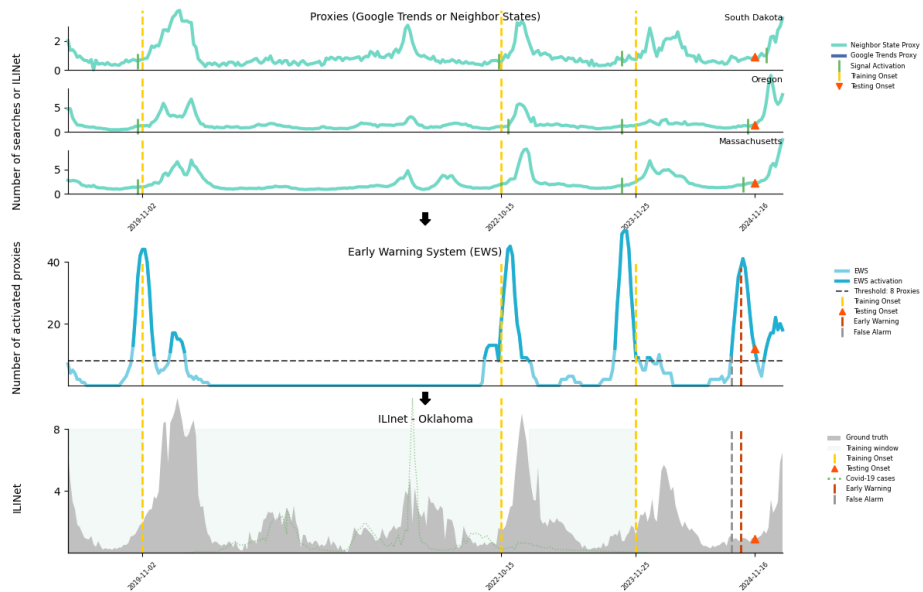


Fig. S49: Onset detection for Oklahoma during the 2024-2025 season

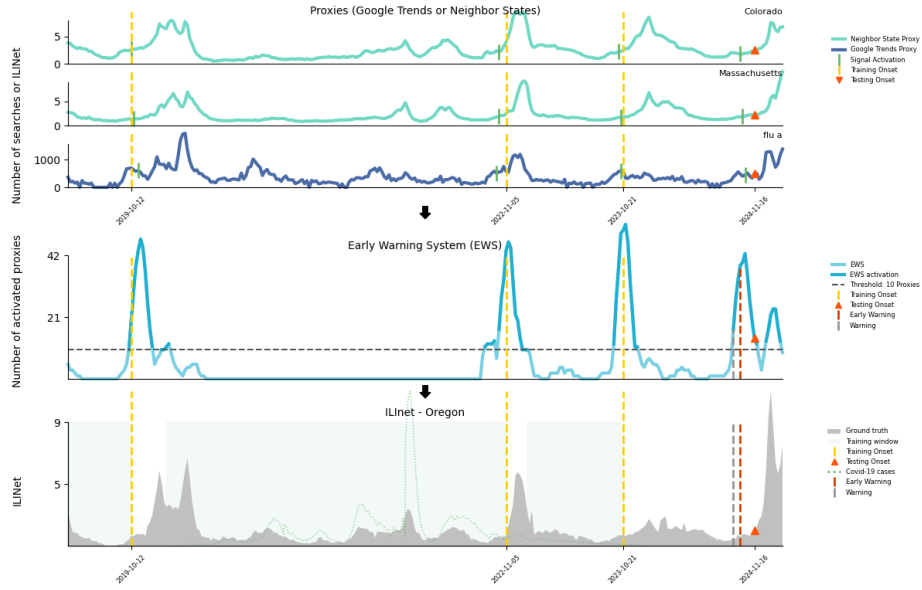


Fig. S50: Onset detection for Oregon during the 2024-2025 season

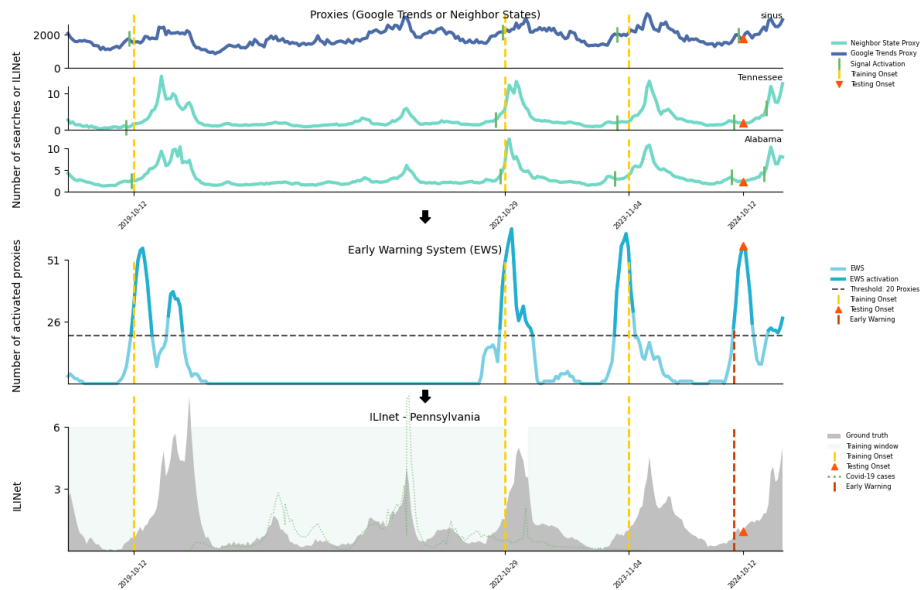


Fig. S51: Onset detection for Pennsylvania during the 2024-2025 season

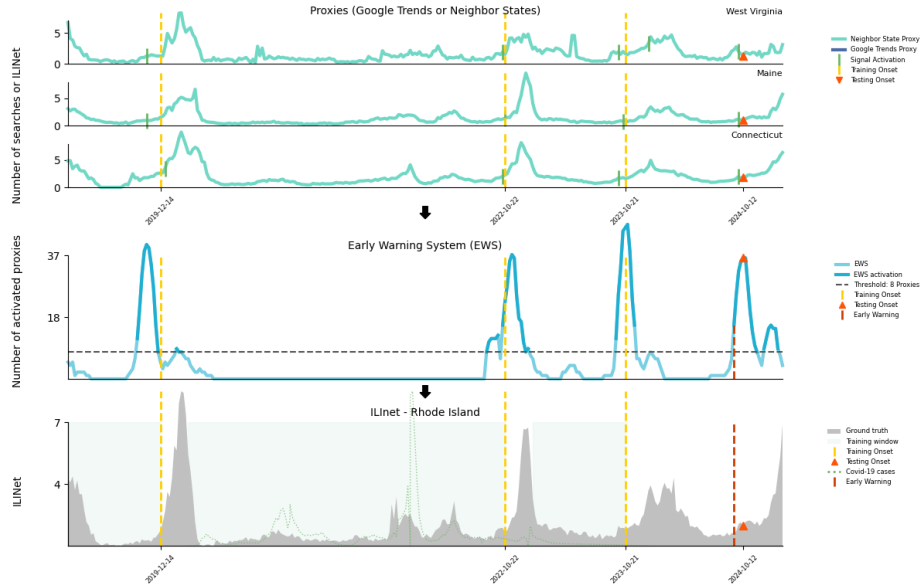


Fig. S52: Onset detection for Rhode Island during the 2024-2025 season

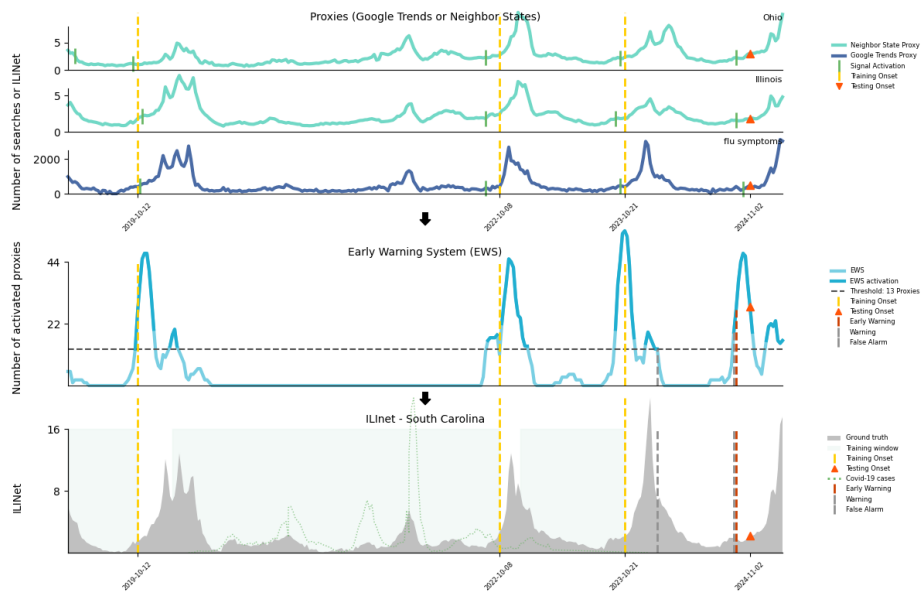


Fig. S53: Onset detection for South Carolina during the 2024-2025 season

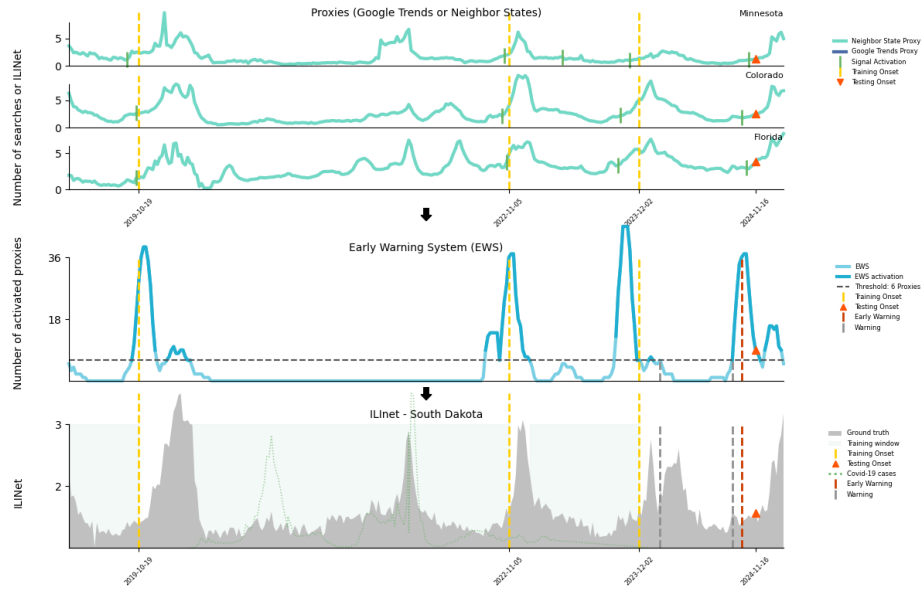


Fig. S54: Onset detection for South Dakota during the 2024-2025 season

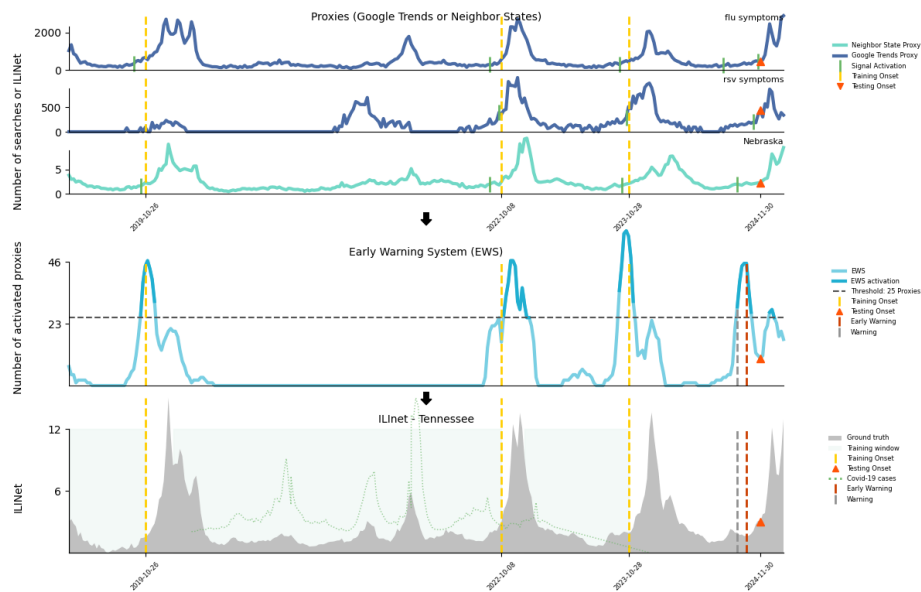


Fig. S55: Onset detection for Tennessee during the 2024-2025 season

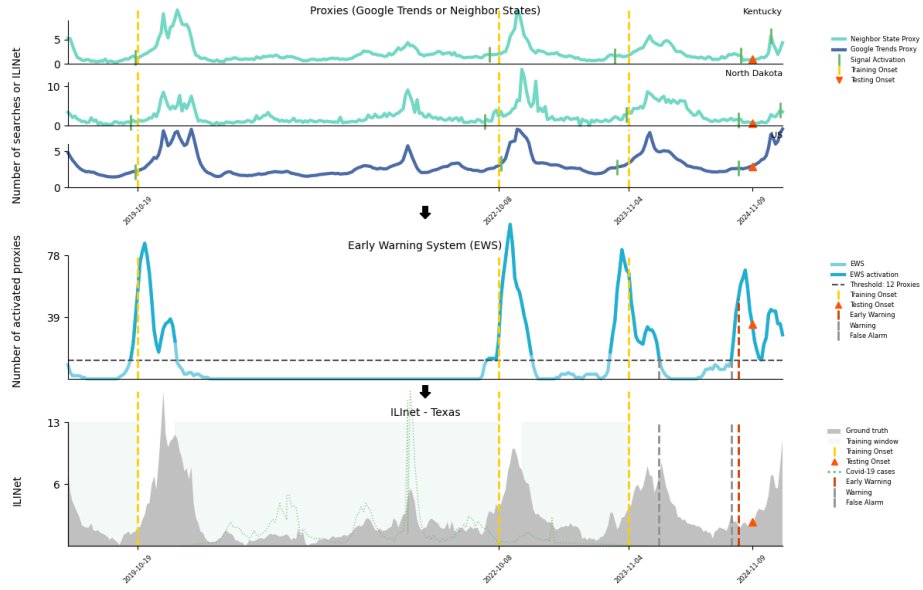


Fig. S56: Onset detection for Texas during the 2024-2025 season

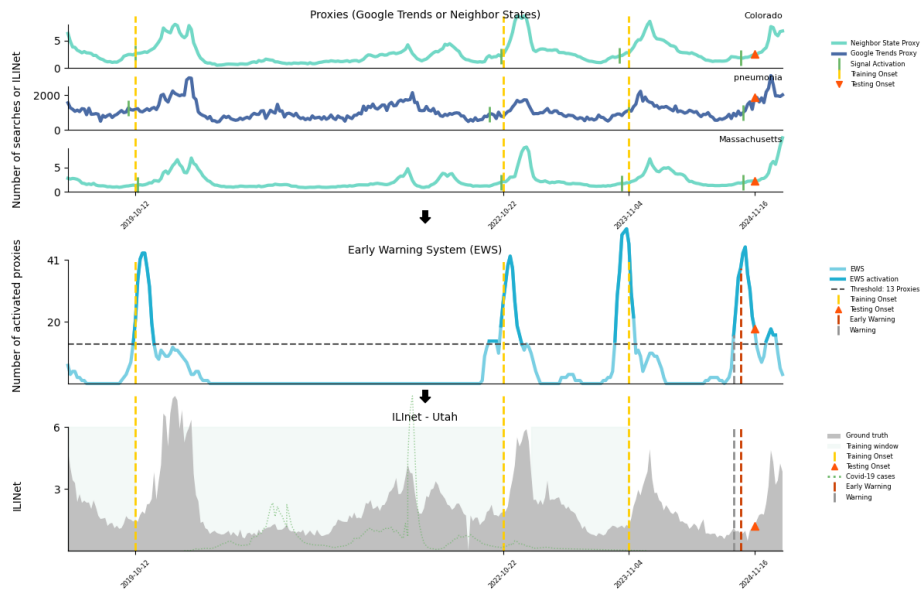


Fig. S57: Onset detection for Utah during the 2024-2025 season

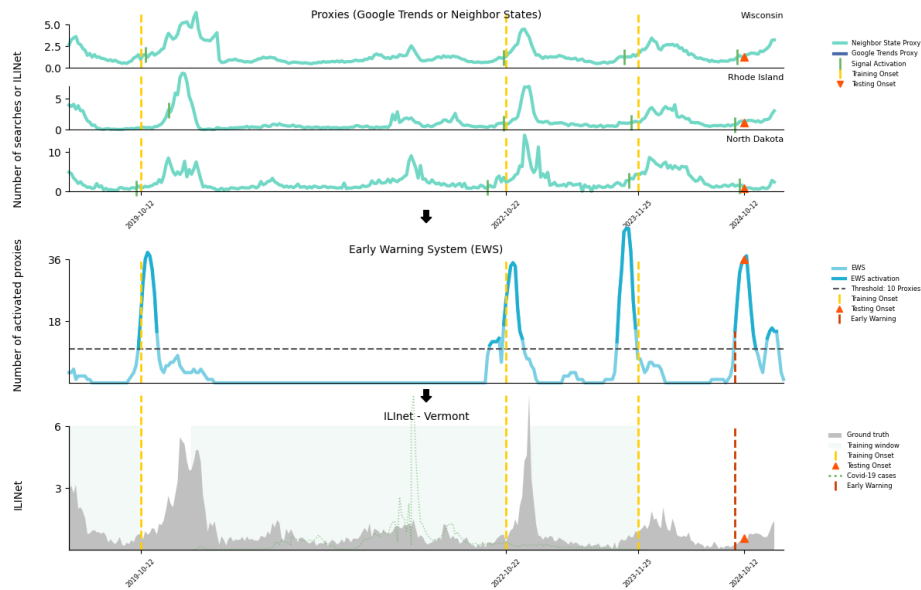


Fig. S58: Onset detection for Vermont during the 2024-2025 season

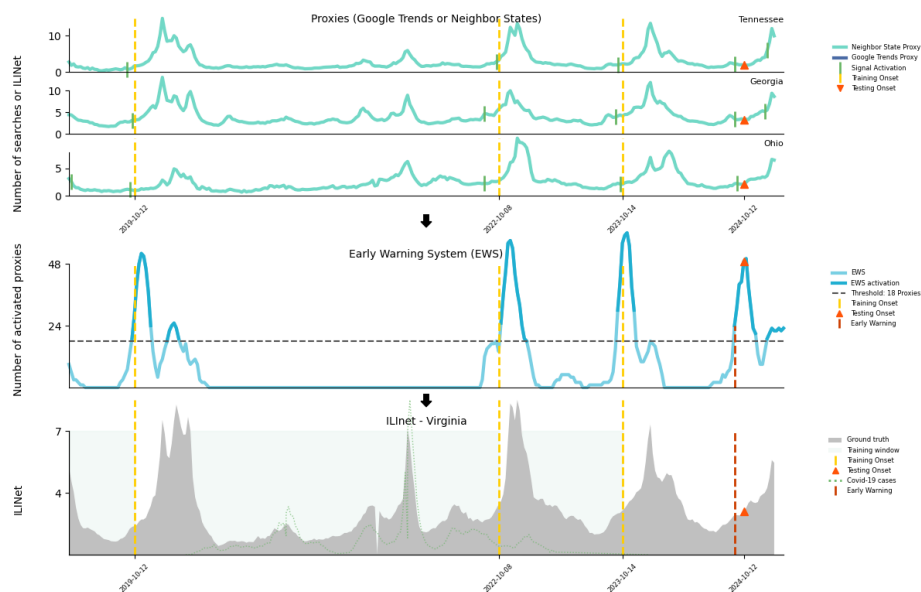


Fig. S59: Onset detection for Virginia during the 2024-2025 season

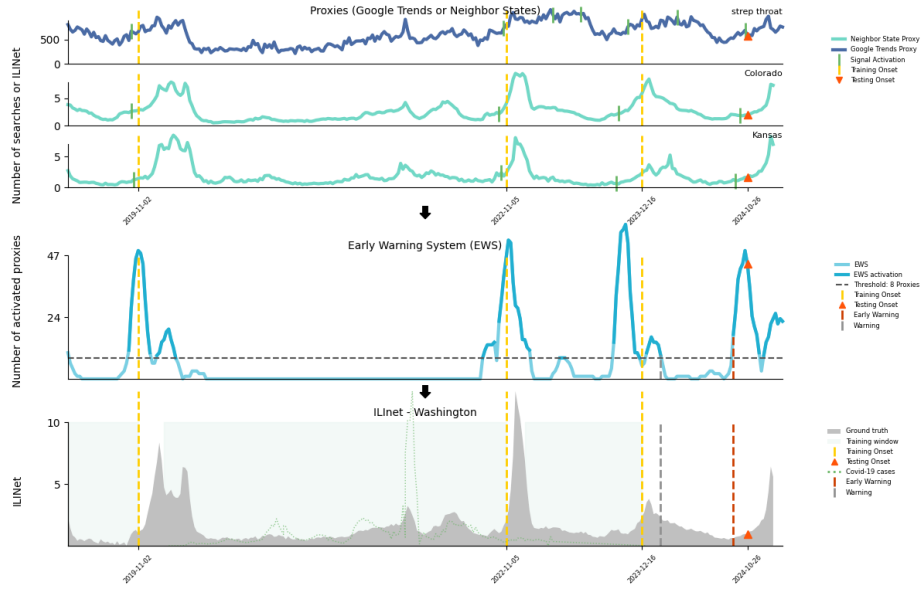


Fig. S60: Onset detection for Washington during the 2024-2025 season

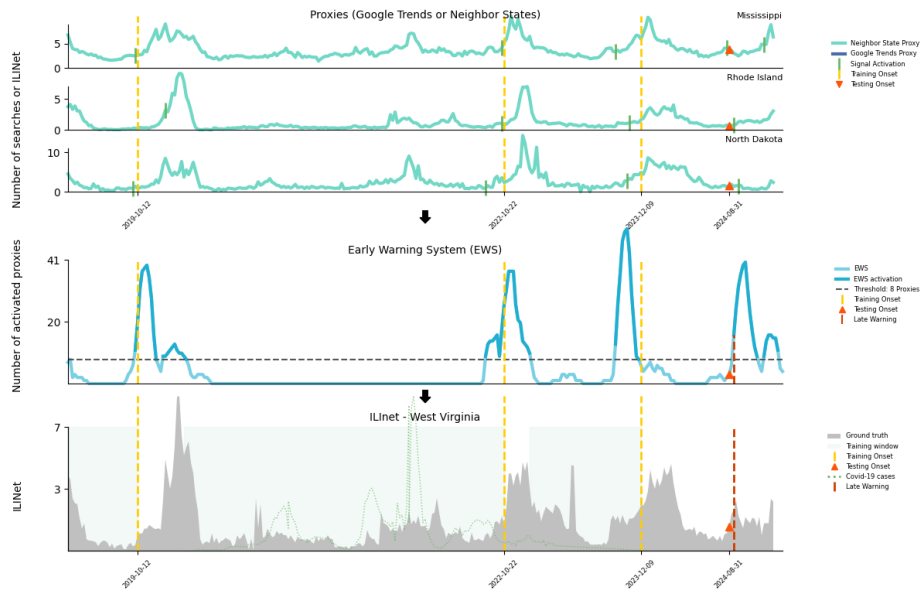


Fig. S61: Onset detection for West Virginia during the 2024-2025 season

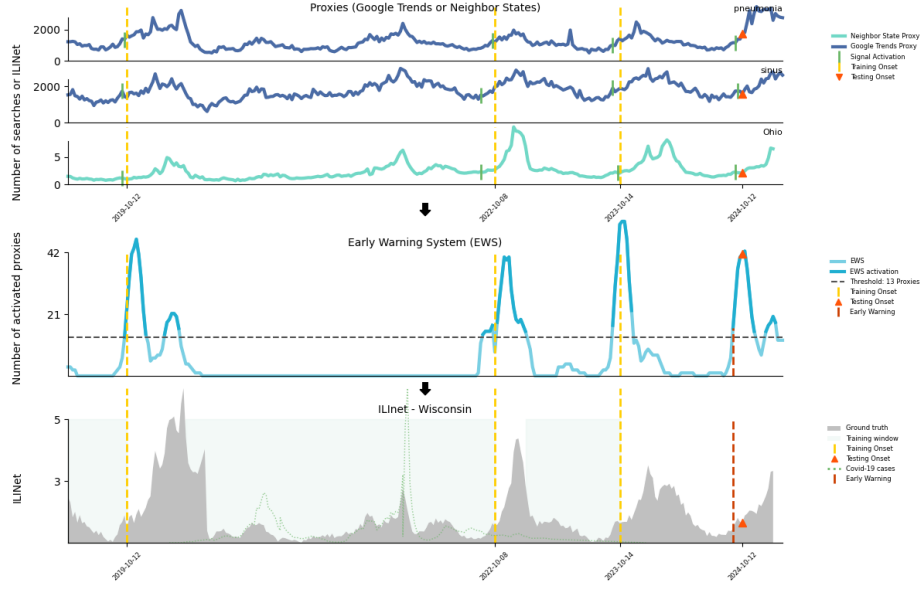


Fig. S62: Onset detection for Wisconsin during the 2024-2025 season

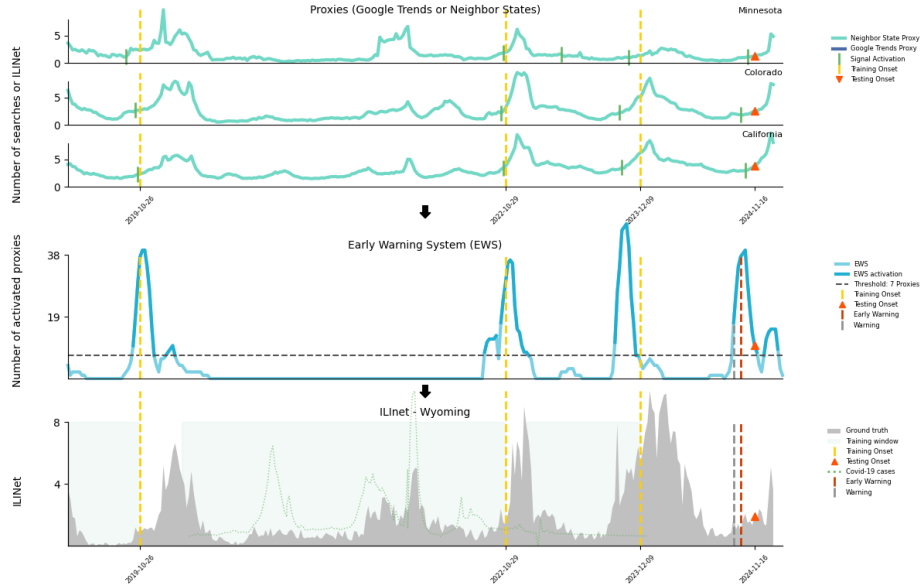


Fig. S63: Onset detection for Wyoming during the 2024-2025 season

8 Peak Examples 2024-2025 Real-Time Predictions

Complementing the onset detection examples, we present representative cases of peak detection during the 2024–2025 real-time deployment to demonstrate the system’s ability to anticipate epidemic maxima before the full outbreak trajectory unfolds. Peak detection is inherently more challenging than onset detection, as it requires identifying when disease activity has reached its maximum while operating under noisy surveillance signals and without access to future incidence data. These examples show how the ensemble voting mechanism integrates multiple proxy signals—including Google Trends queries and neighboring state patterns—to trigger peak warnings several weeks in advance or during the peak week itself. The temporal dynamics of proxy activations, threshold crossings, and

alignment with observed peak timing illustrate the operational performance of the system across geographically diverse contexts. Representative peak detection examples for all 50 states are provided in Figures S64–S113.

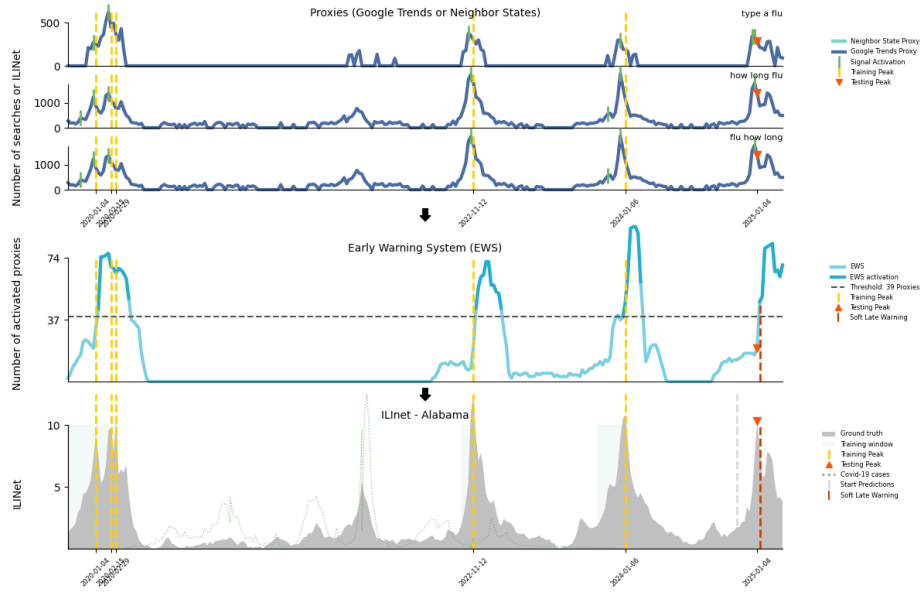


Fig. S64: Peak detection for Alabama during the 2024-2025 season

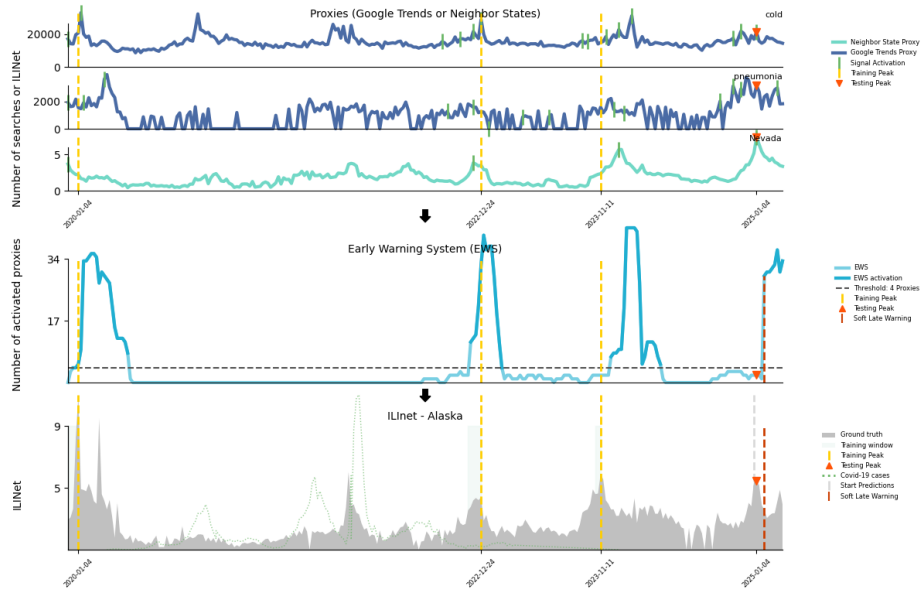


Fig. S65: Peak detection for Alaska during the 2024-2025 season

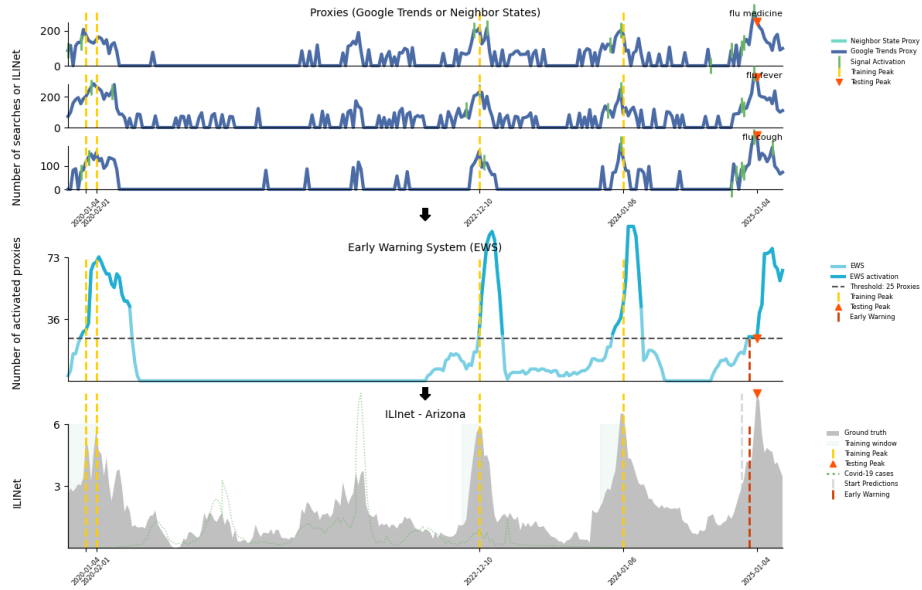


Fig. S66: Peak detection for Arizona during the 2024-2025 season

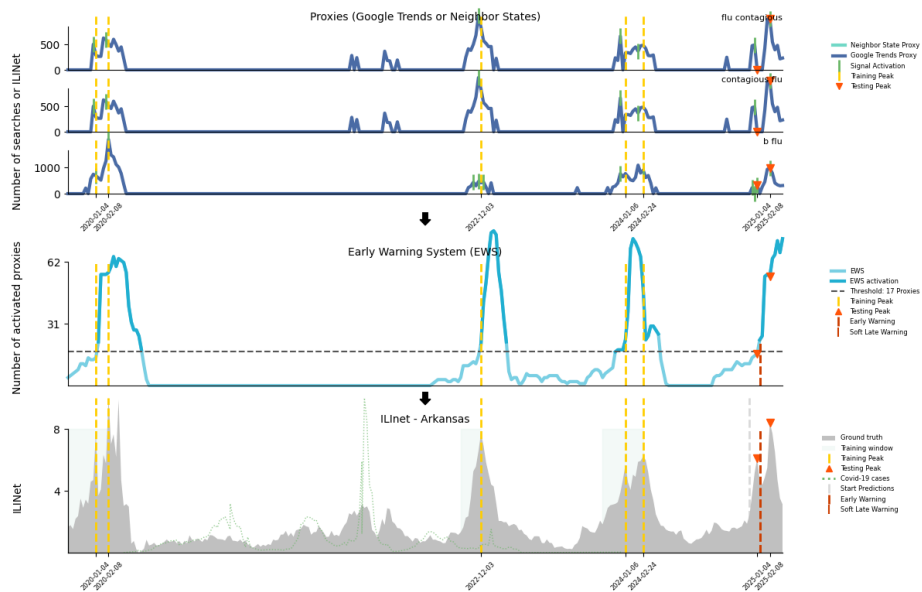


Fig. S67: Peak detection for Arkansas during the 2024-2025 season

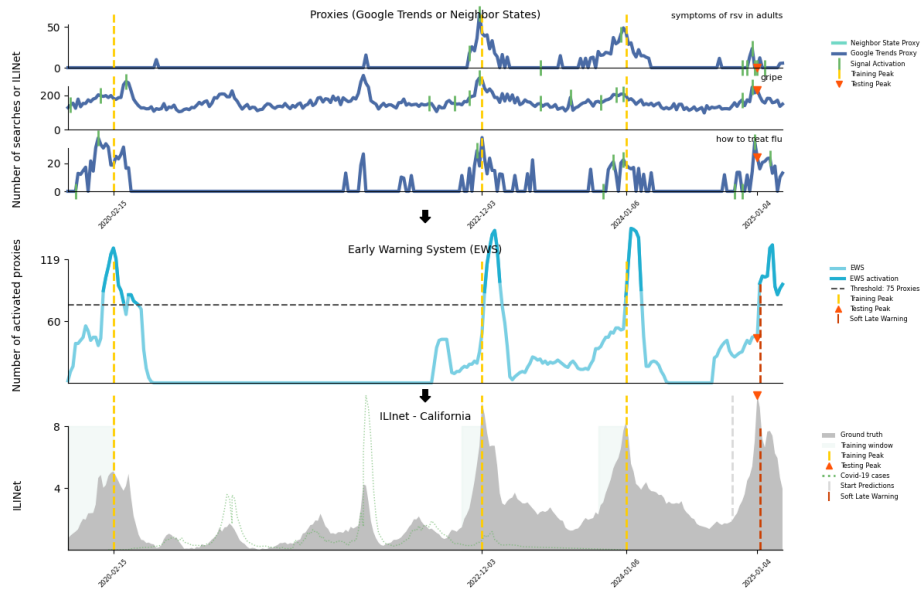


Fig. S68: Peak detection for California during the 2024-2025 season

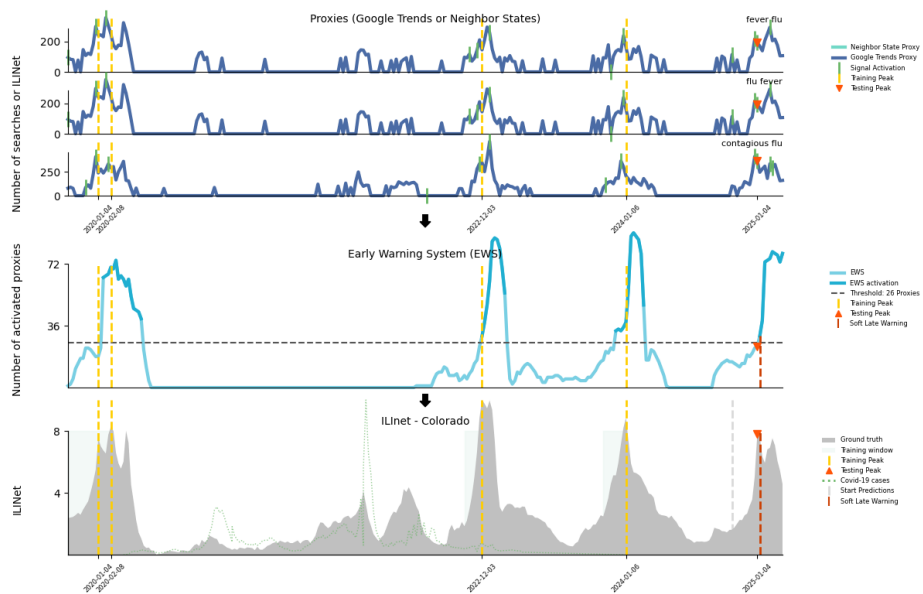


Fig. S69: Peak detection for Colorado during the 2024-2025 season

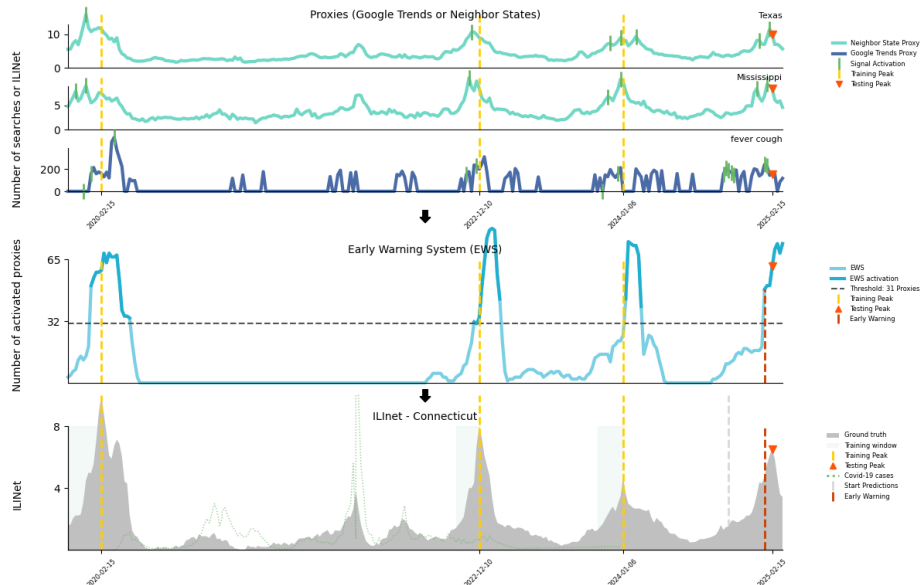


Fig. S70: Peak detection for Connecticut during the 2024-2025 season

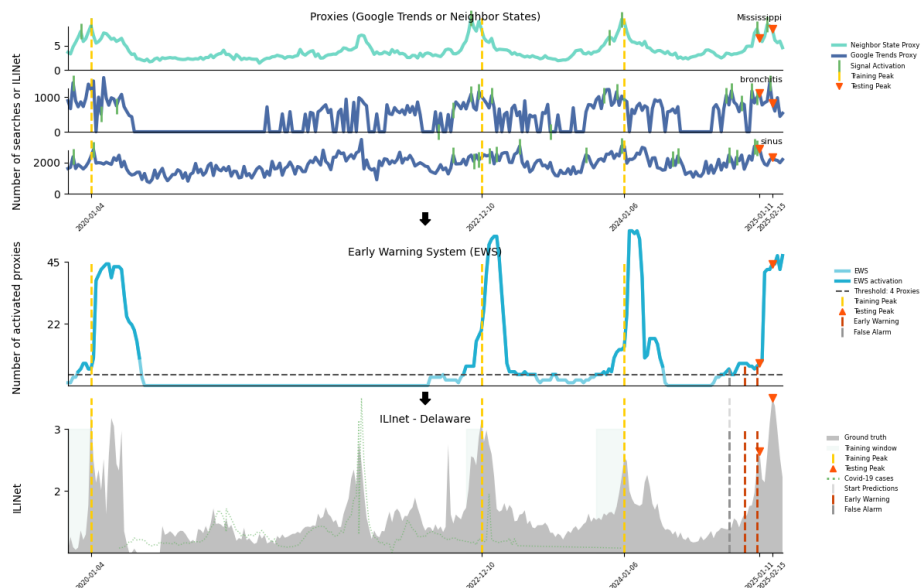


Fig. S71: Peak detection for Delaware during the 2024-2025 season

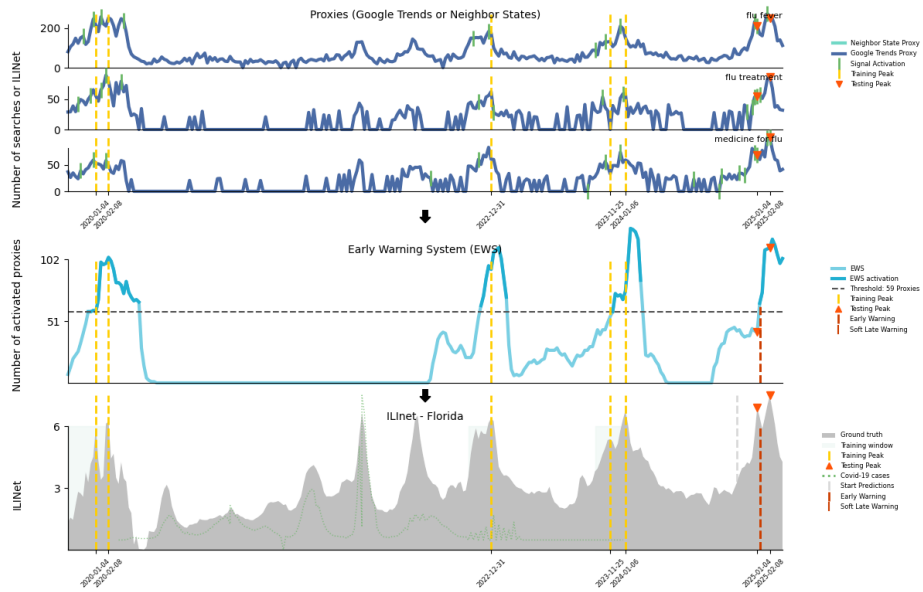


Fig. S72: Peak detection for Florida during the 2024-2025 season

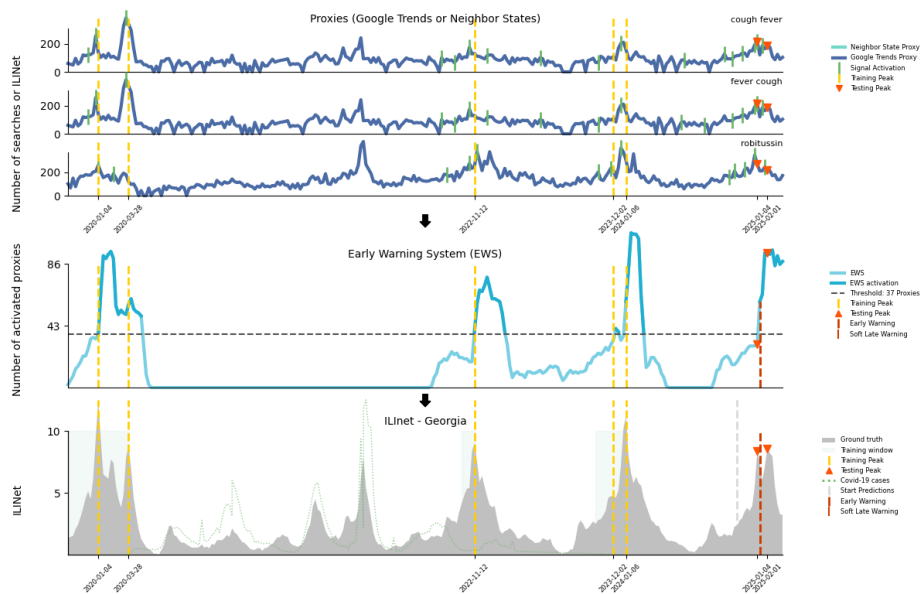


Fig. S73: Peak detection for Georgia during the 2024-2025 season

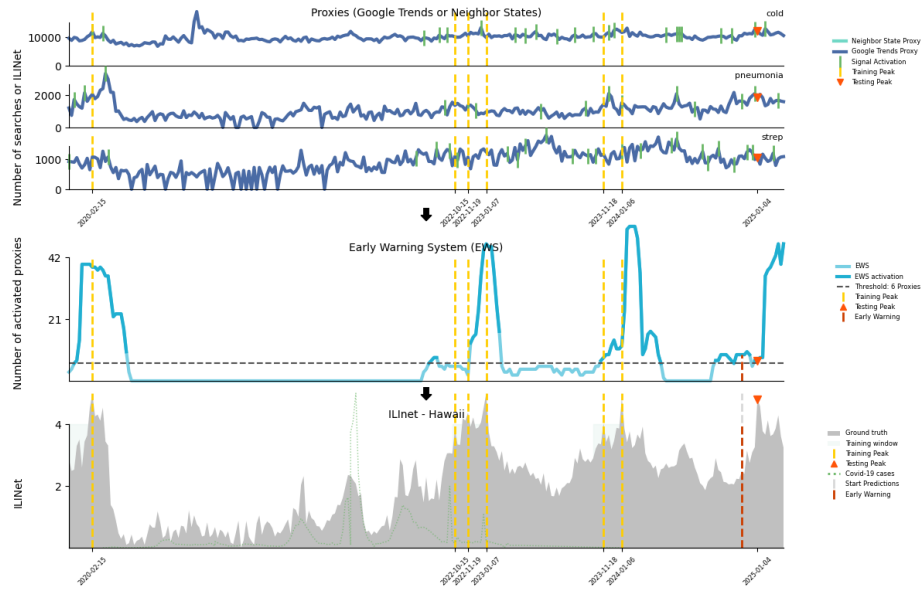


Fig. S74: Peak detection for Hawaii during the 2024-2025 season

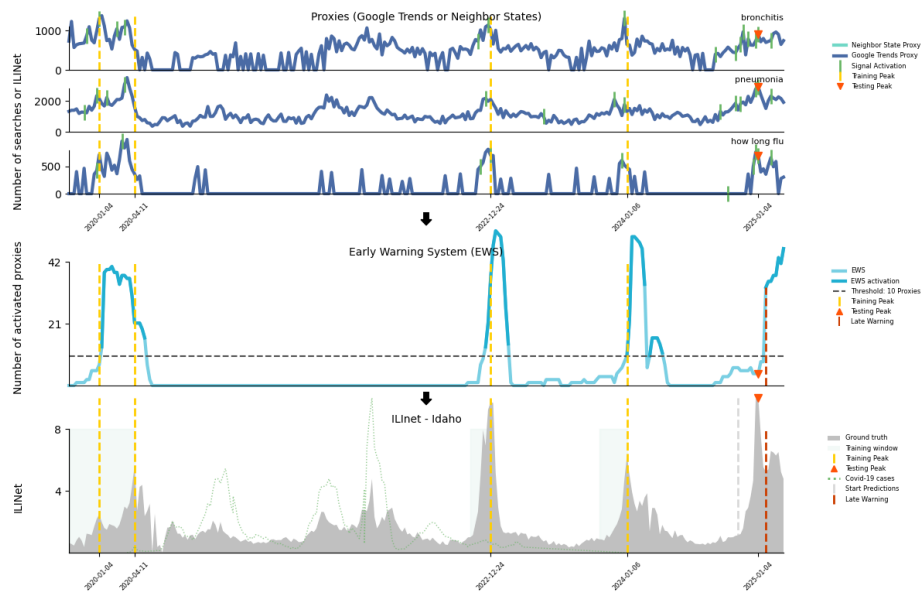


Fig. S75: Peak detection for Idaho during the 2024-2025 season

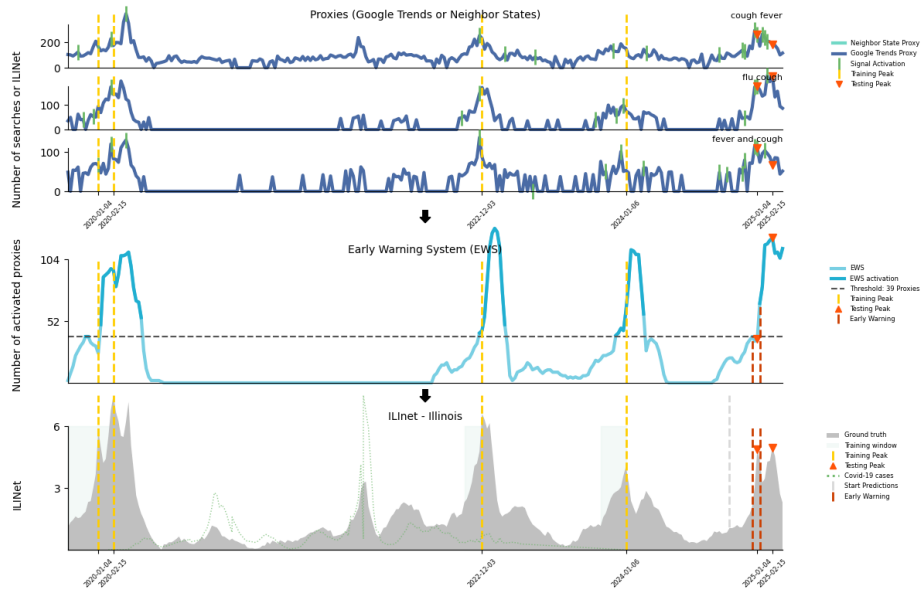


Fig. S76: Peak detection for Illinois during the 2024-2025 season

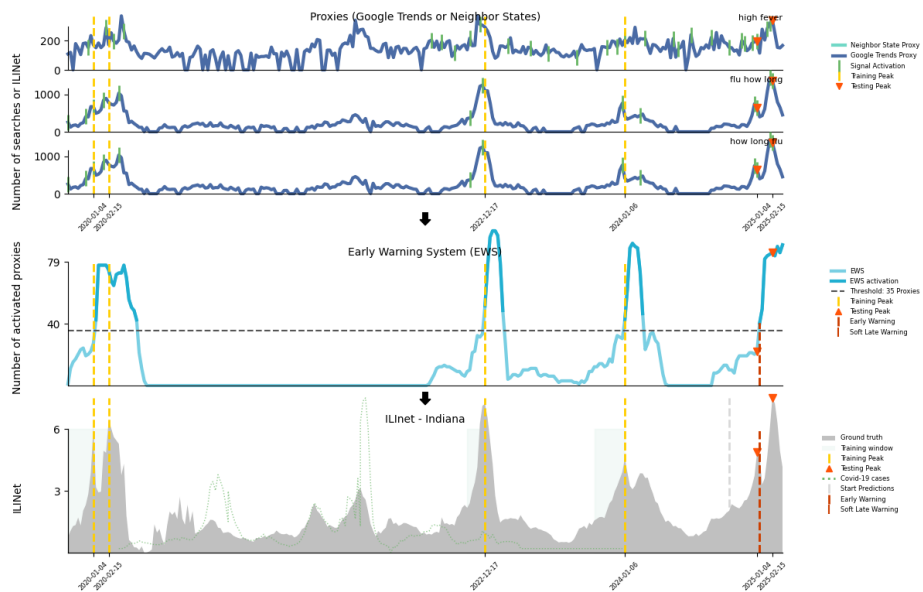


Fig. S77: Peak detection for Indiana during the 2024-2025 season

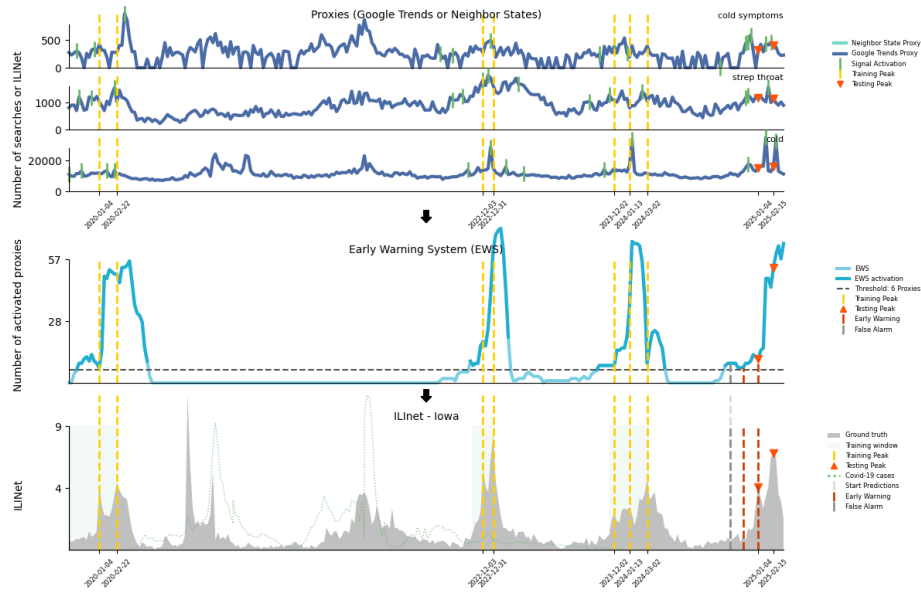


Fig. S78: Peak detection for Iowa during the 2024-2025 season

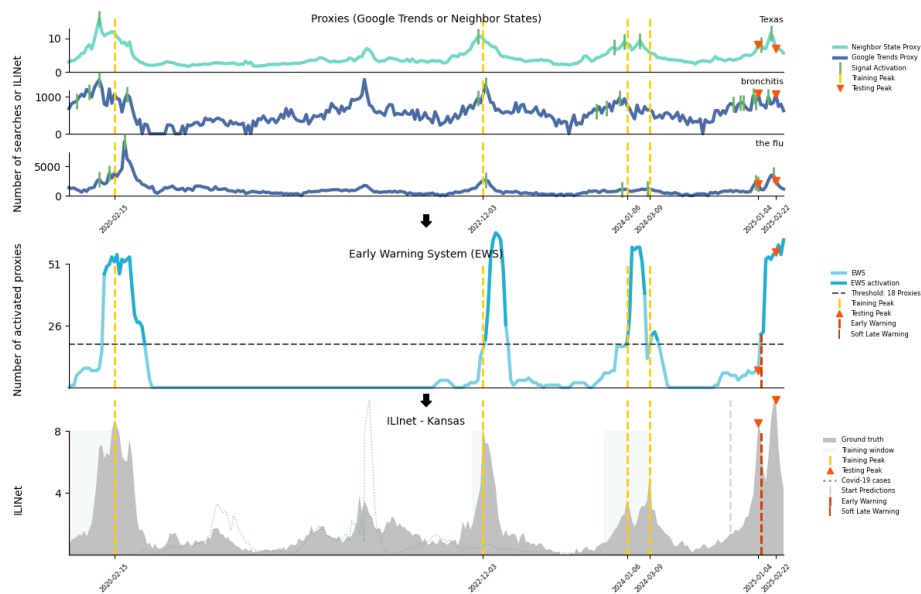


Fig. S79: Peak detection for Kansas during the 2024-2025 season

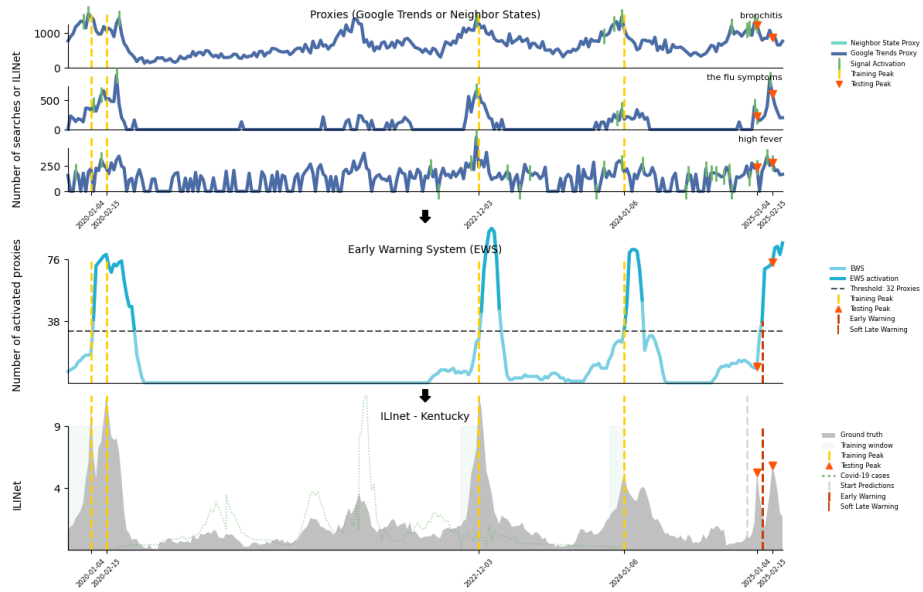


Fig. S80: Peak detection for Kentucky during the 2024-2025 season

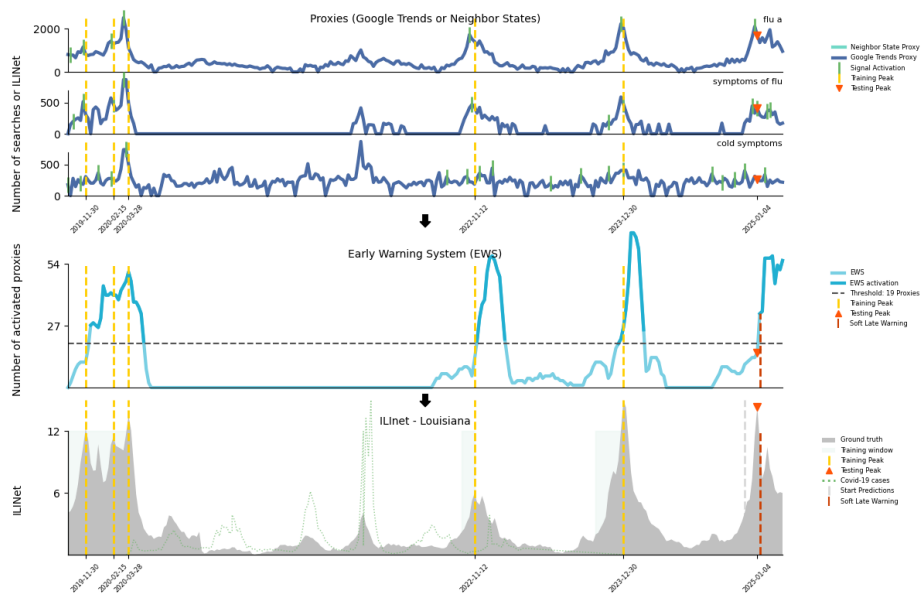


Fig. S81: Peak detection for Louisiana during the 2024-2025 season

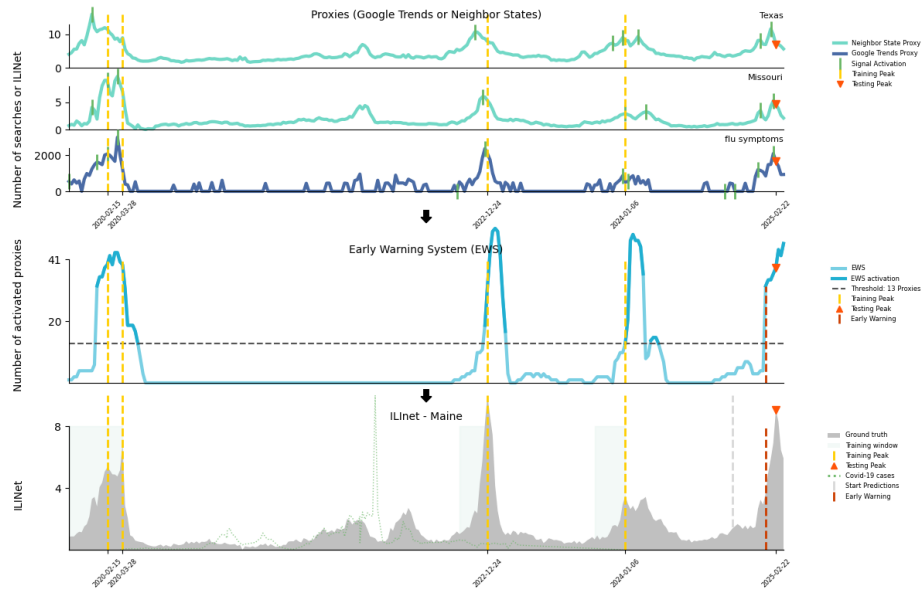


Fig. S82: Peak detection for Maine during the 2024-2025 season

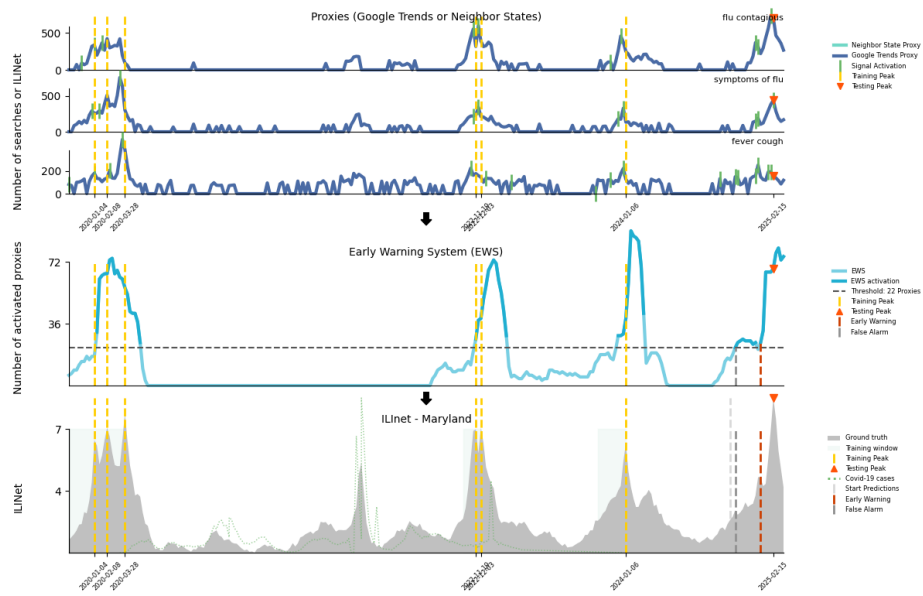


Fig. S83: Peak detection for Maryland during the 2024-2025 season

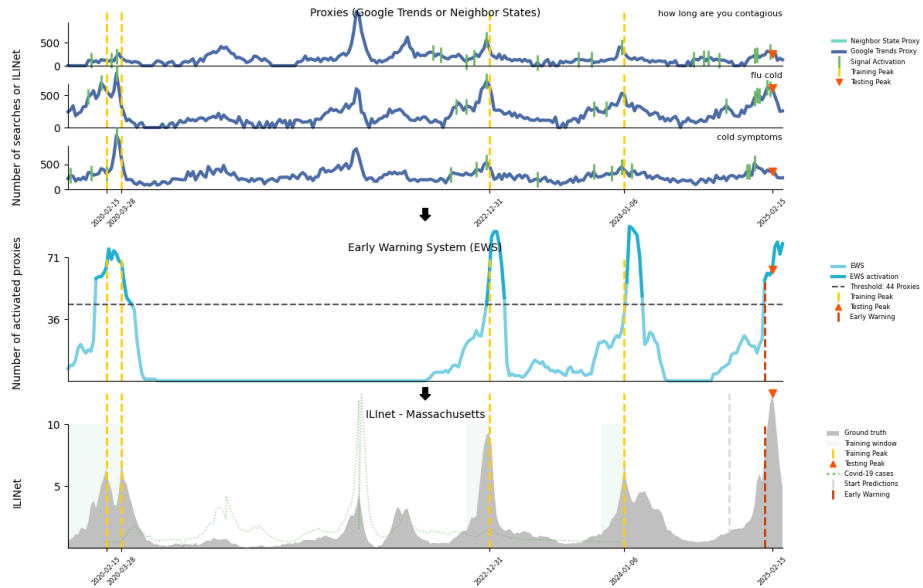


Fig. S84: Peak detection for Massachusetts during the 2024-2025 season

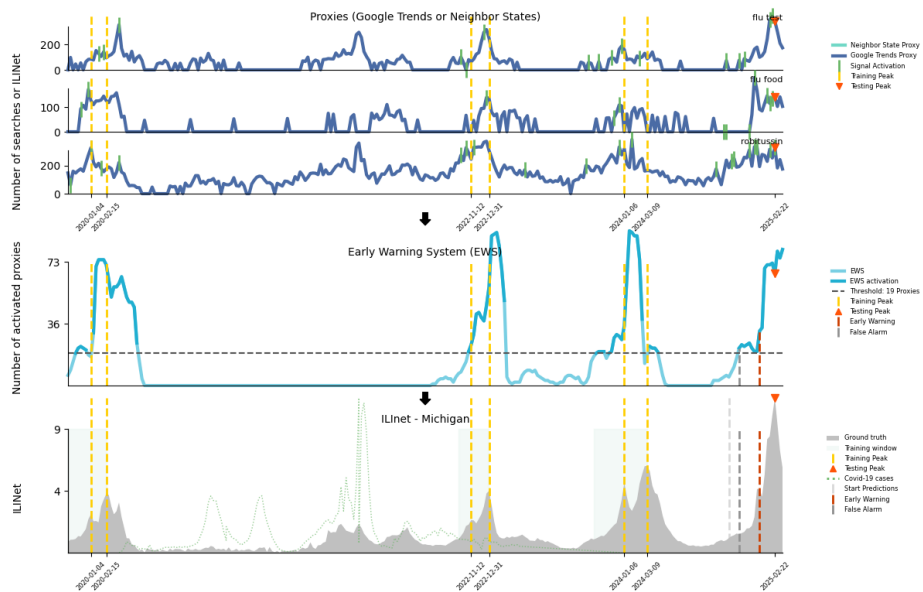


Fig. S85: Peak detection for Michigan during the 2024-2025 season

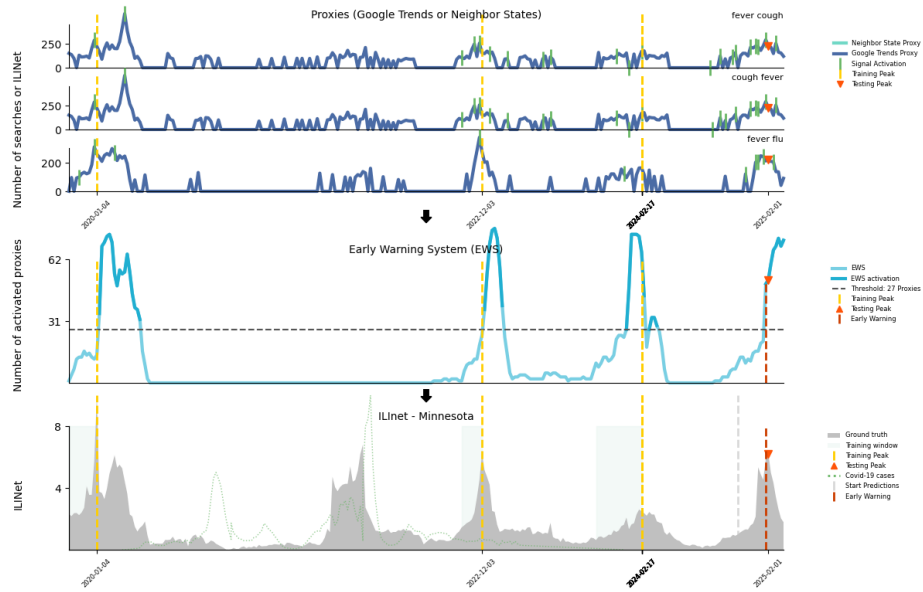


Fig. S86: Peak detection for Minnesota during the 2024-2025 season

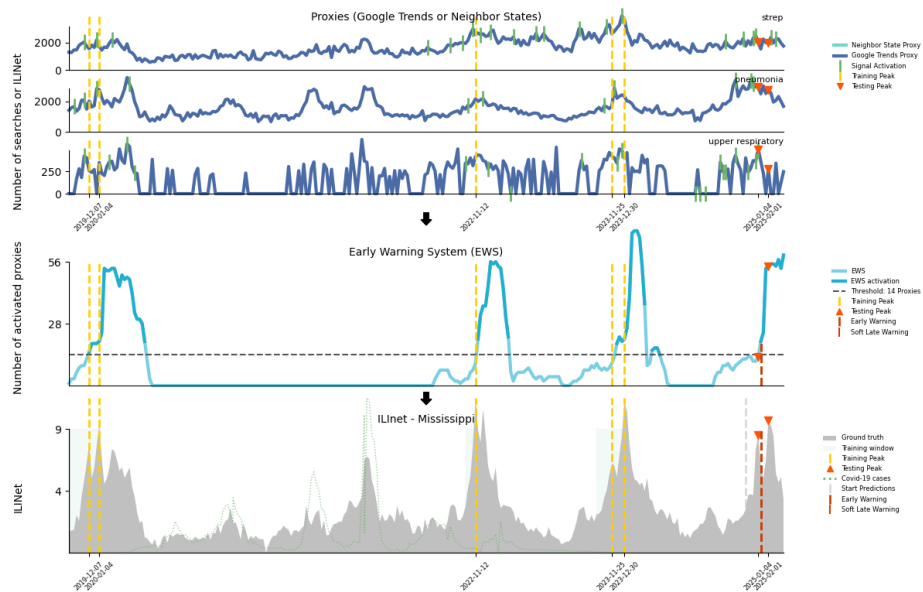


Fig. S87: Peak detection for Mississippi during the 2024-2025 season

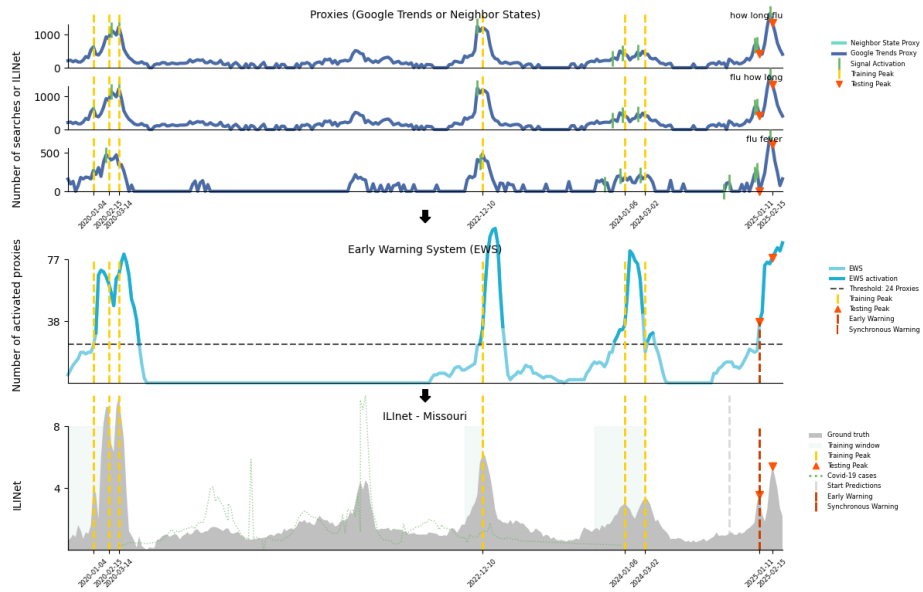


Fig. S88: Peak detection for Missouri during the 2024-2025 season

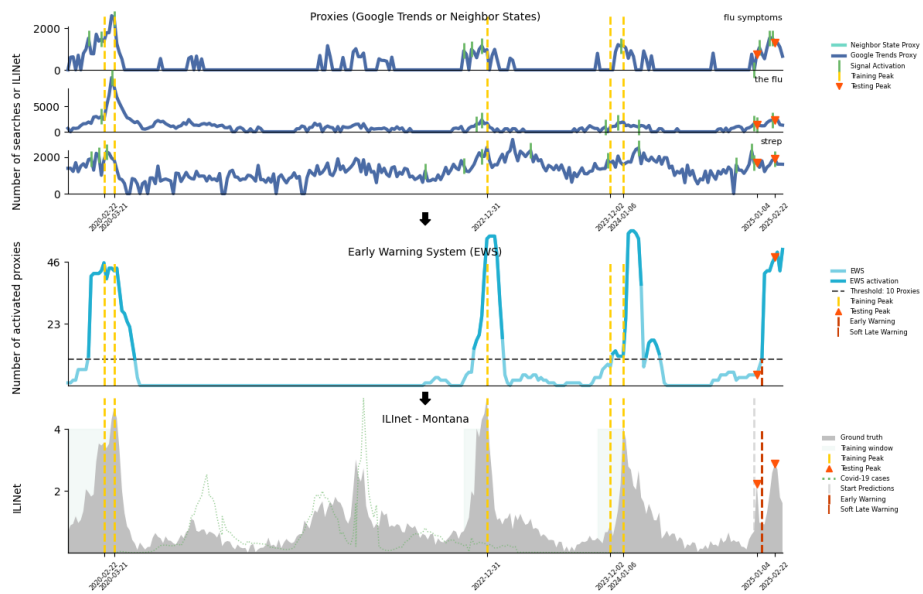


Fig. S89: Peak detection for Montana during the 2024-2025 season

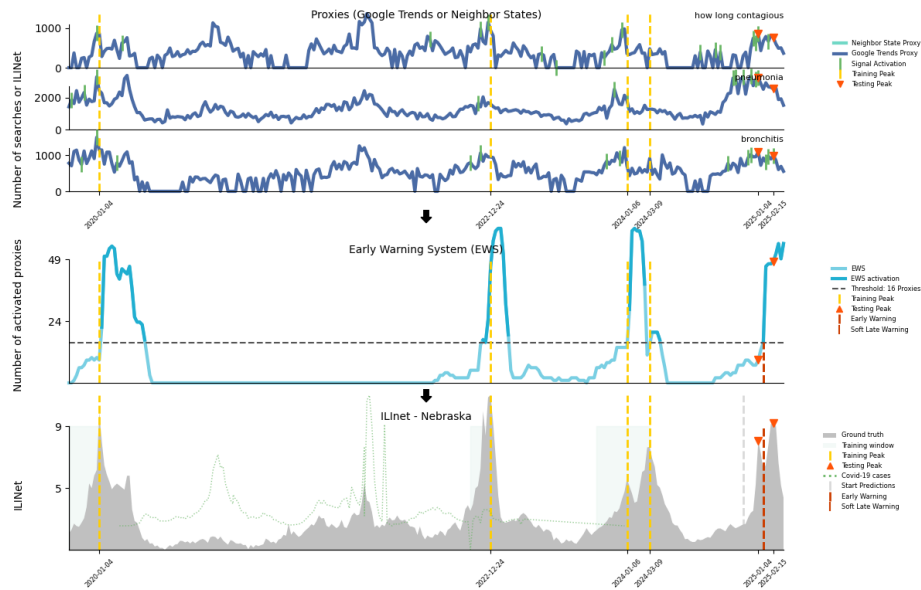


Fig. S90: Peak detection for Nebraska during the 2024-2025 season

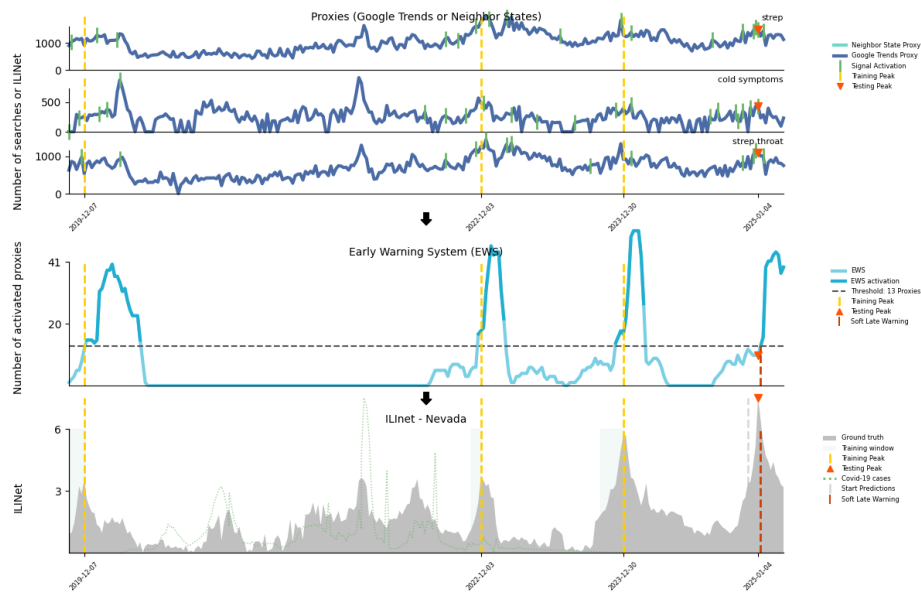


Fig. S91: Peak detection for Nevada during the 2024-2025 season

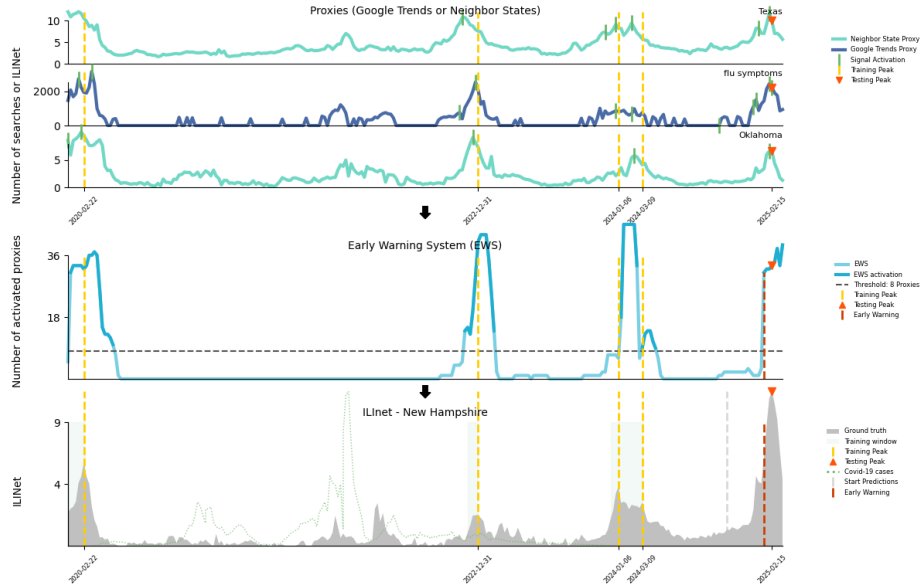


Fig. S92: Peak detection for New Hampshire during the 2024-2025 season

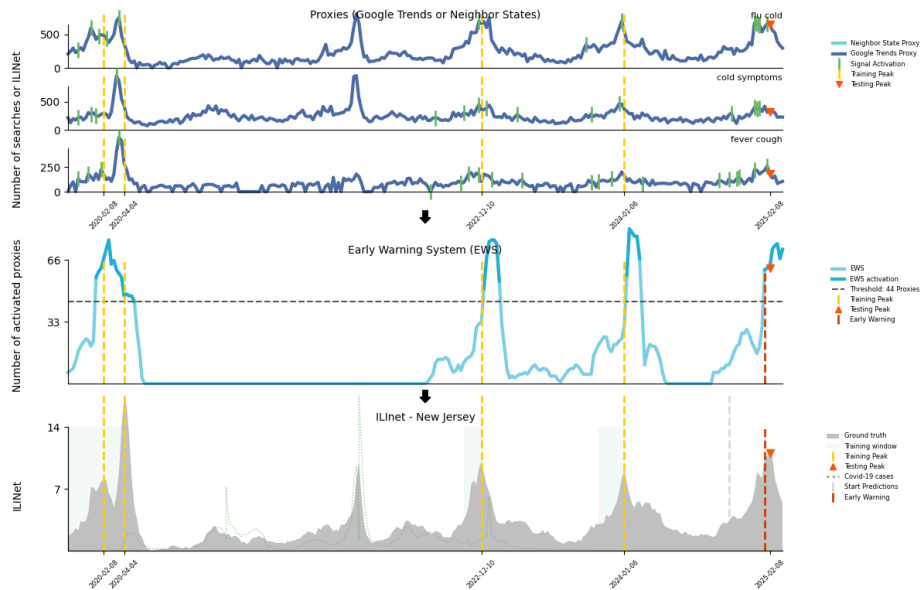


Fig. S93: Peak detection for New Jersey during the 2024-2025 season

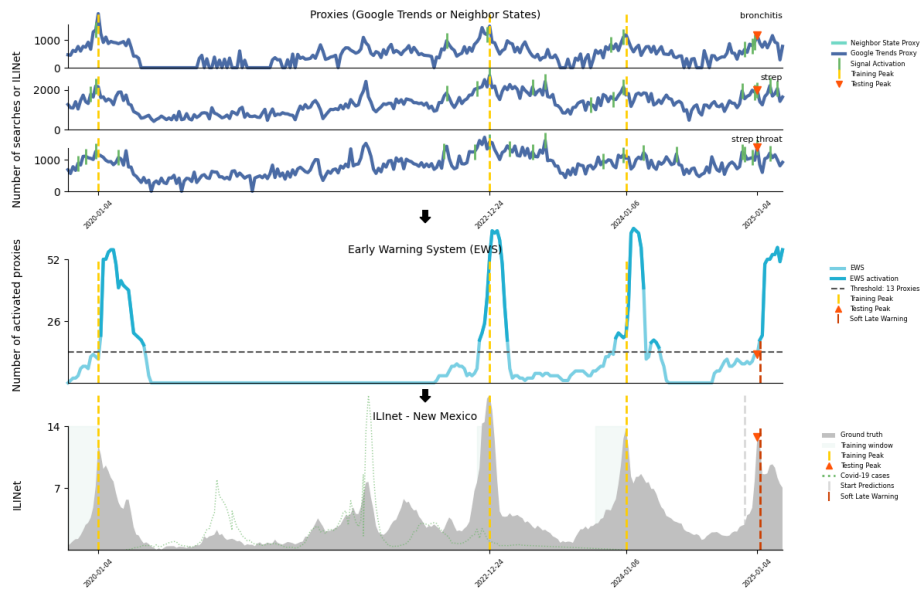


Fig. S94: Peak detection for New Mexico during the 2024-2025 season

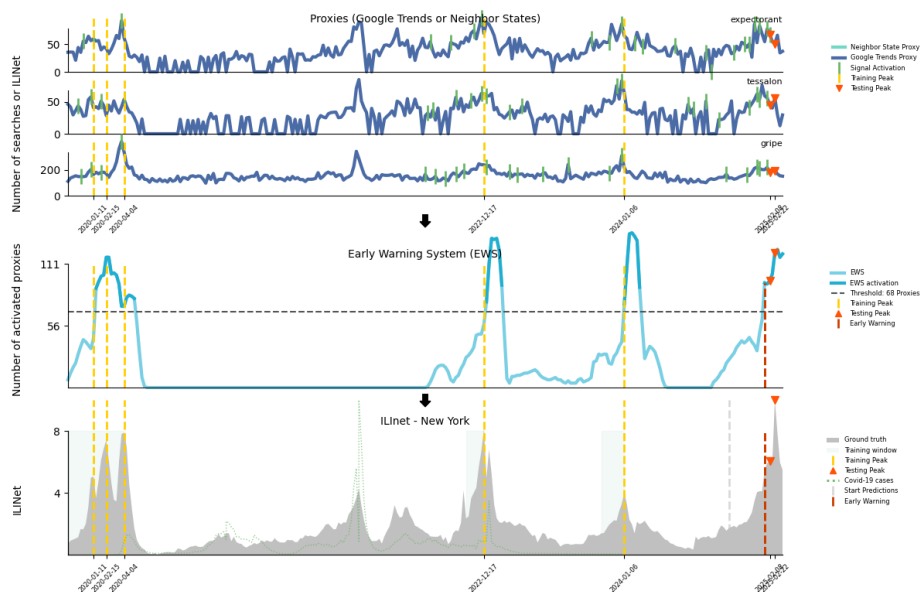


Fig. S95: Peak detection for New York during the 2024-2025 season

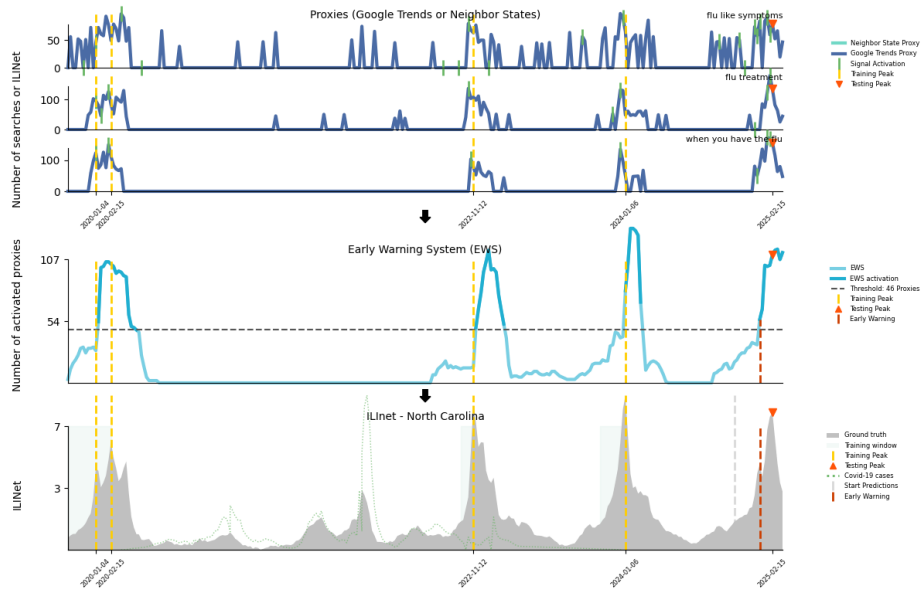


Fig. S96: Peak detection for North Carolina during the 2024-2025 season

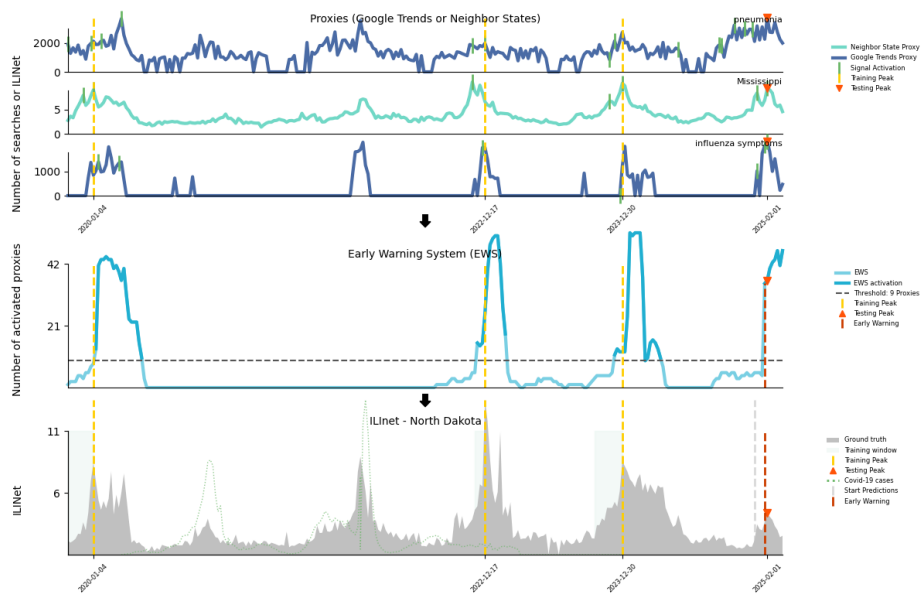


Fig. S97: Peak detection for North Dakota during the 2024-2025 season

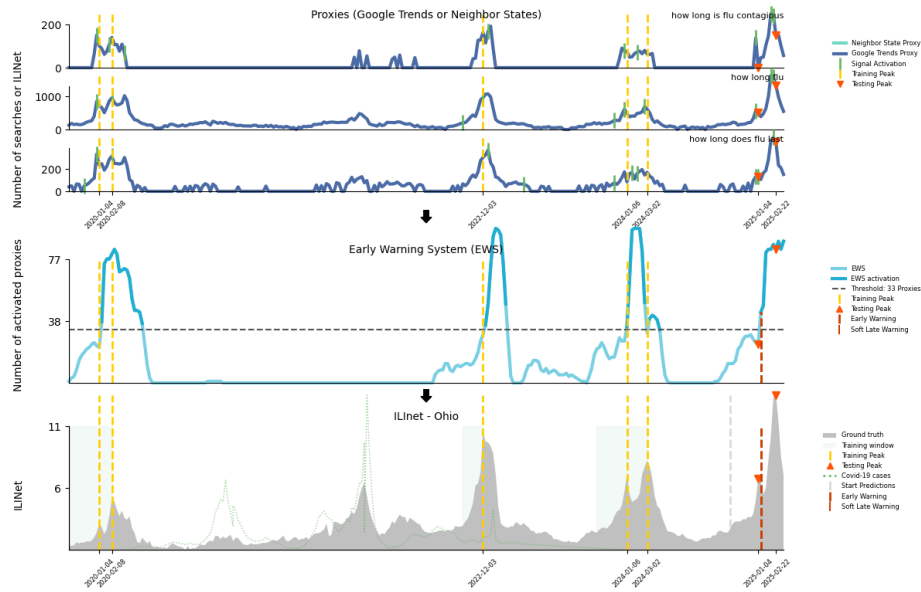


Fig. S98: Peak detection for Ohio during the 2024-2025 season

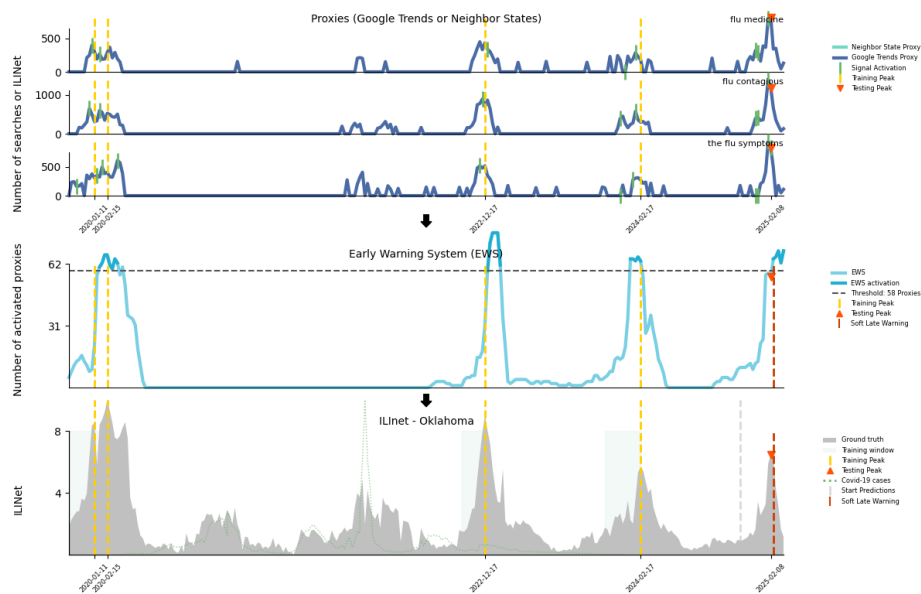


Fig. S99: Peak detection for Oklahoma during the 2024-2025 season

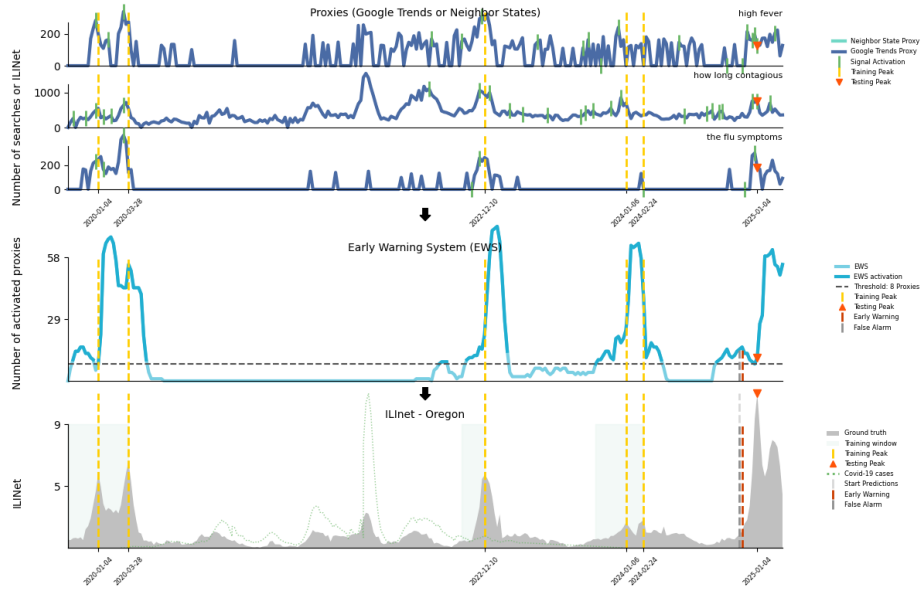


Fig. S100: Peak detection for Oregon during the 2024-2025 season

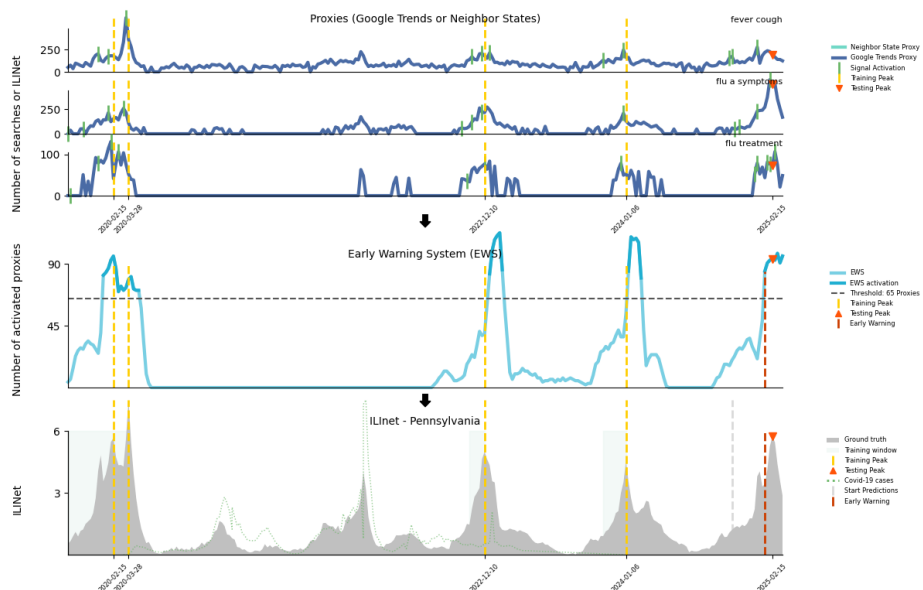


Fig. S101: Peak detection for Pennsylvania during the 2024-2025 season

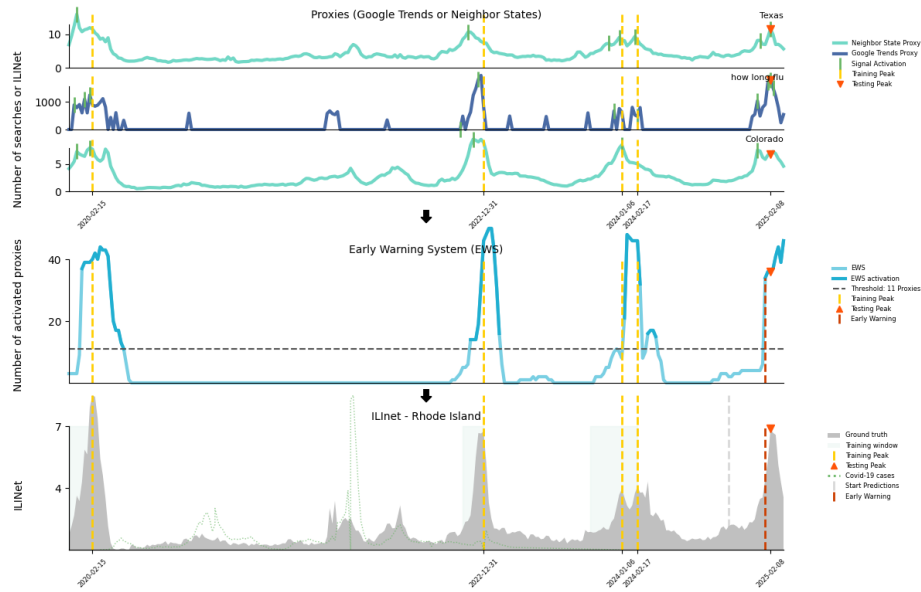


Fig. S102: Peak detection for Rhode Island during the 2024-2025 season

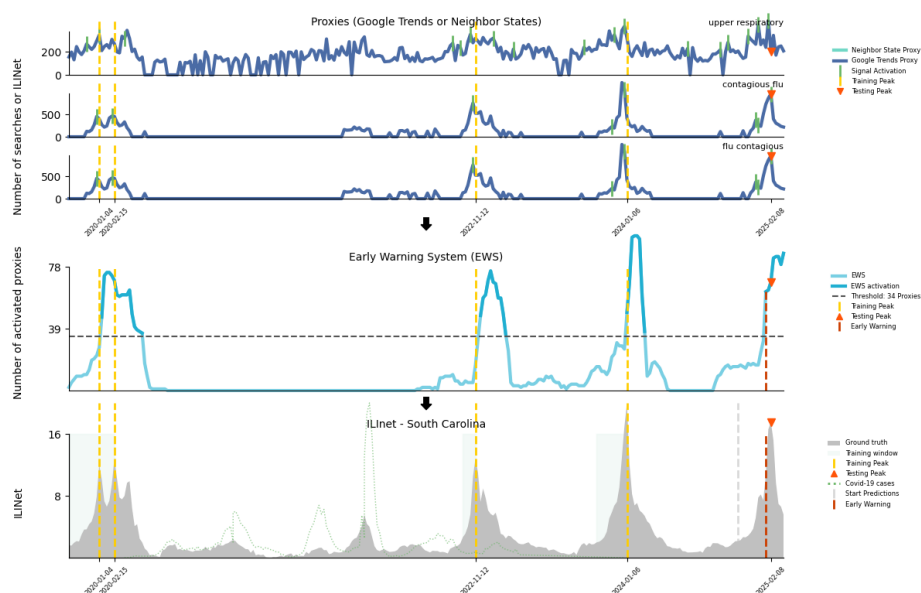


Fig. S103: Peak detection for South Carolina during the 2024-2025 season

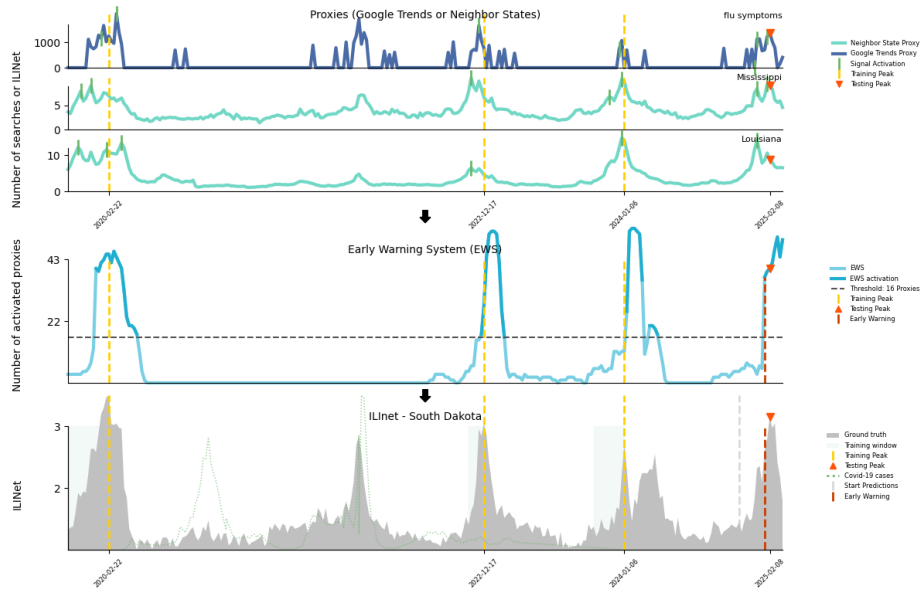


Fig. S104: Peak detection for South Dakota during the 2024-2025 season

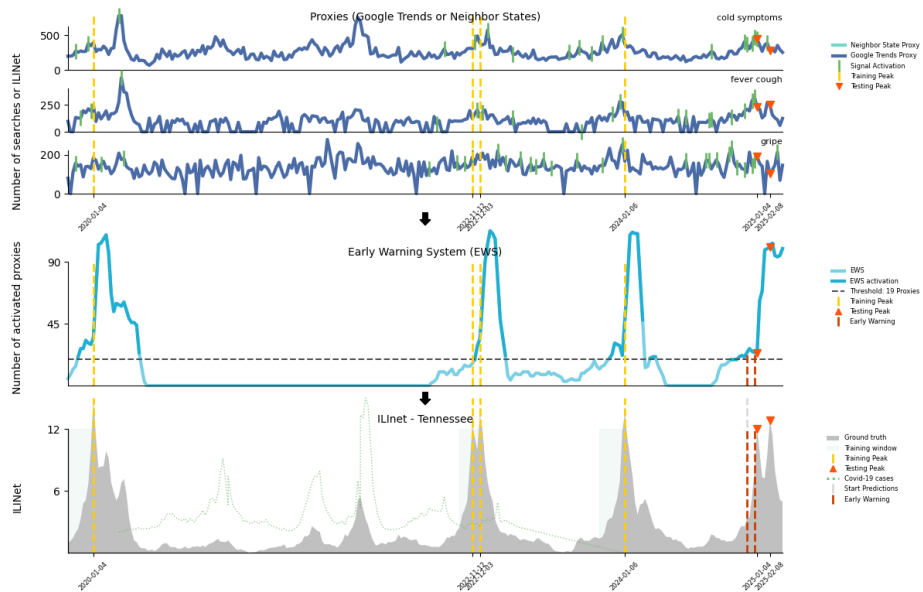


Fig. S105: Peak detection for Tennessee during the 2024-2025 season

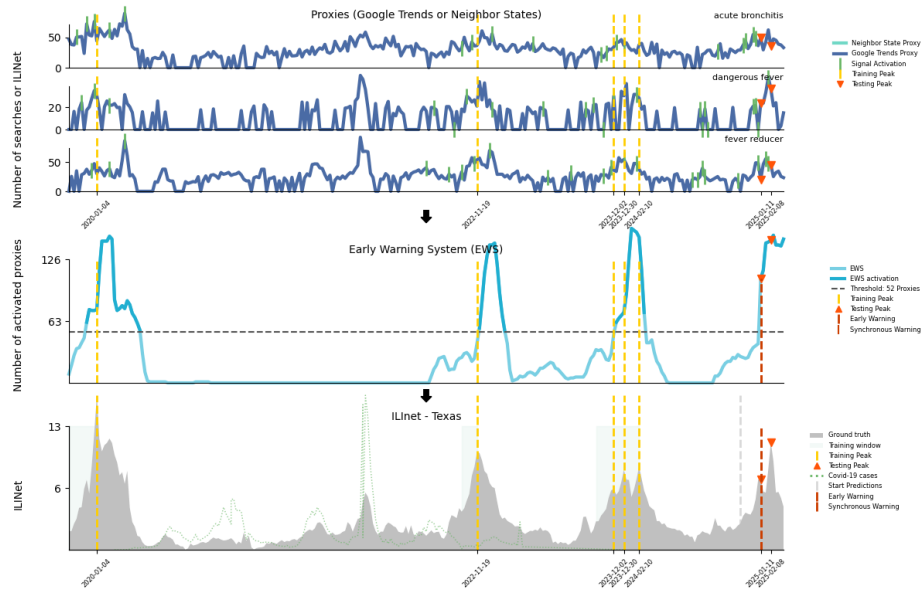


Fig. S106: Peak detection for Texas during the 2024-2025 season

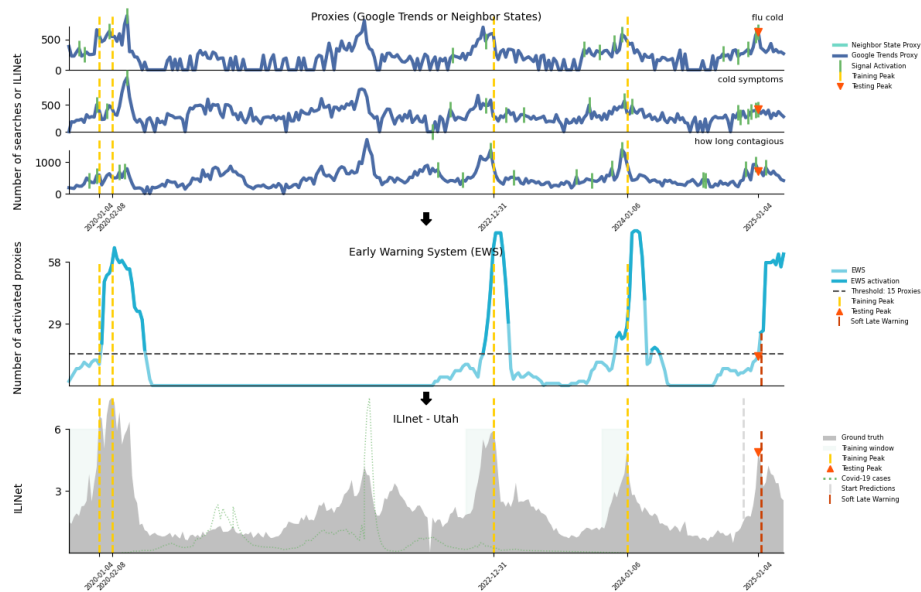


Fig. S107: Peak detection for Utah during the 2024-2025 season

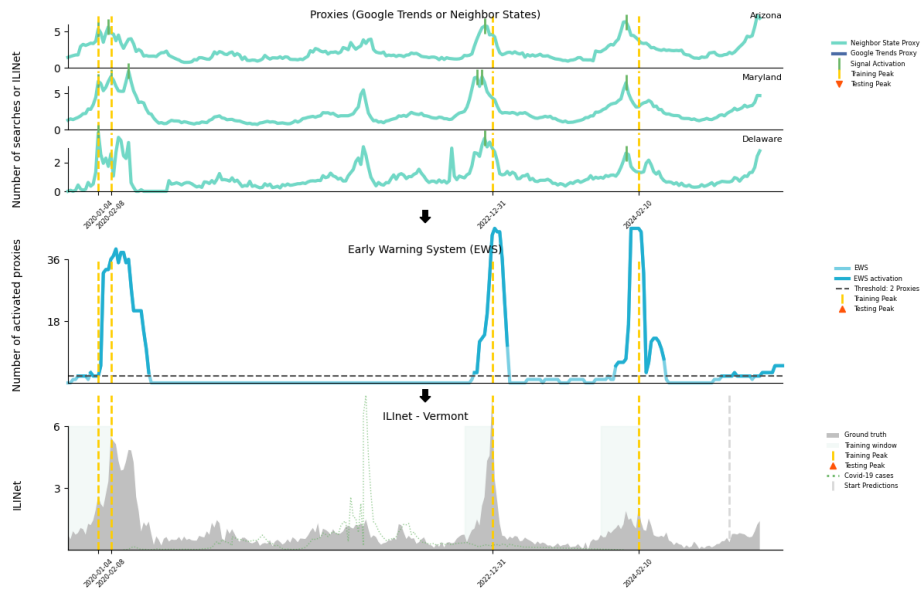


Fig. S108: Peak detection for Vermont during the 2024-2025 season

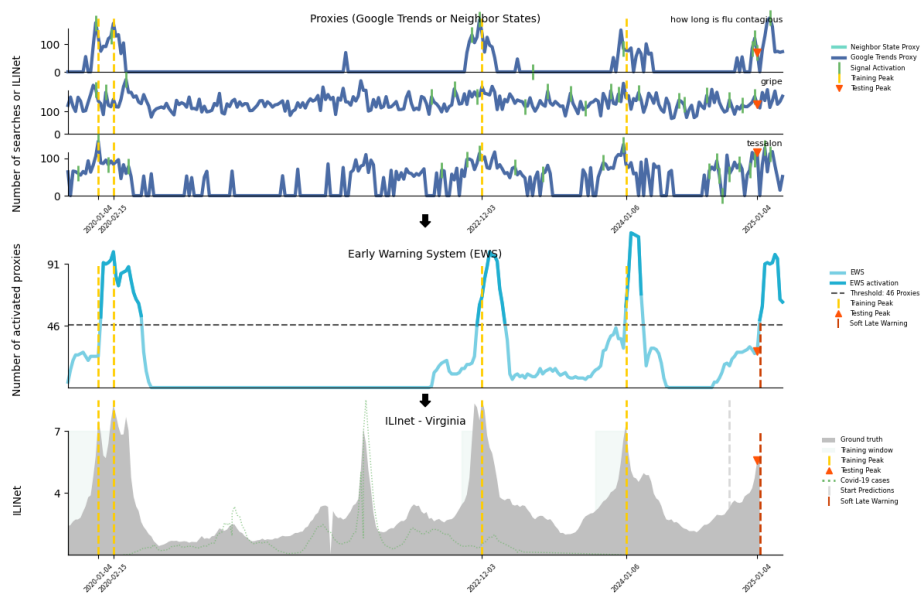


Fig. S109: Peak detection for Virginia during the 2024-2025 season

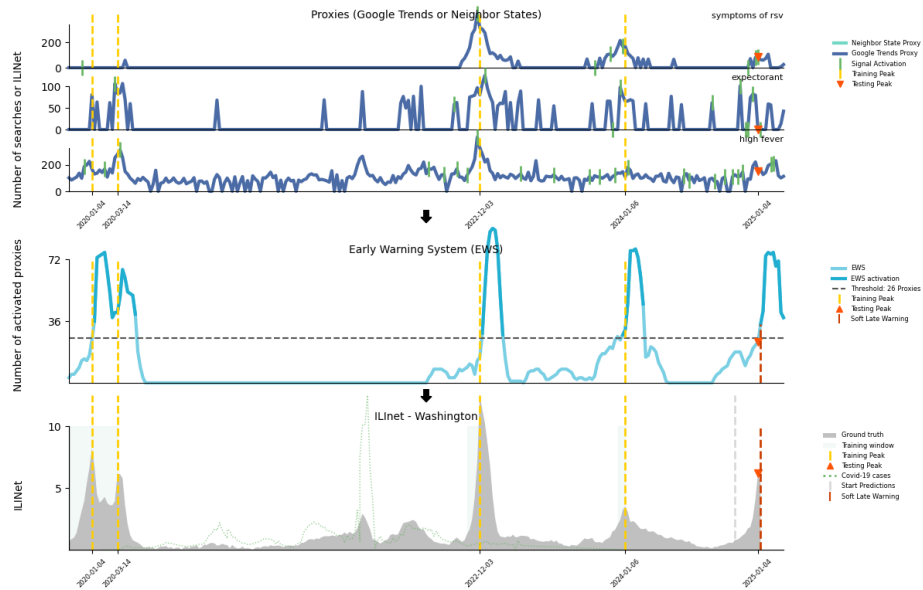


Fig. S110: Peak detection for Washington during the 2024-2025 season

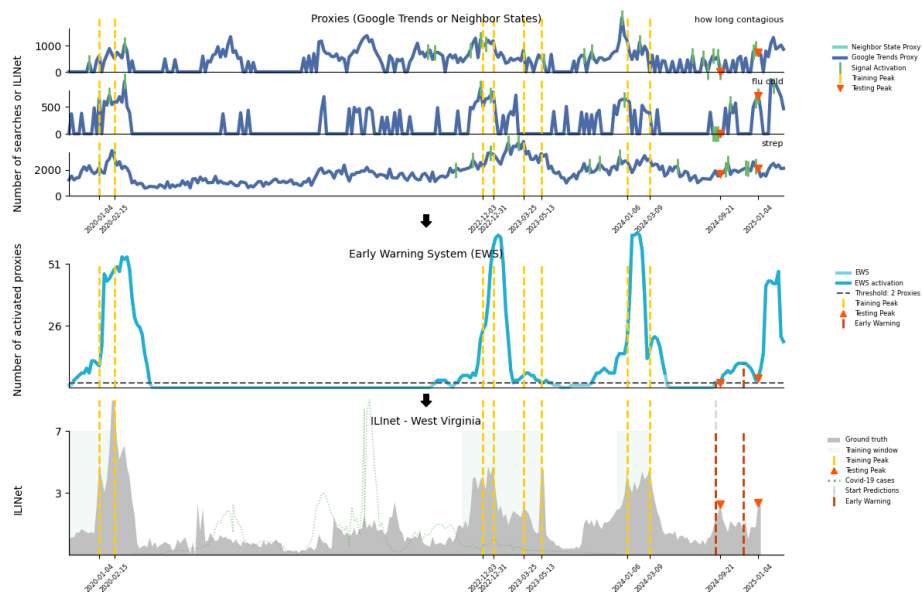


Fig. S111: Peak detection for West Virginia during the 2024-2025 season

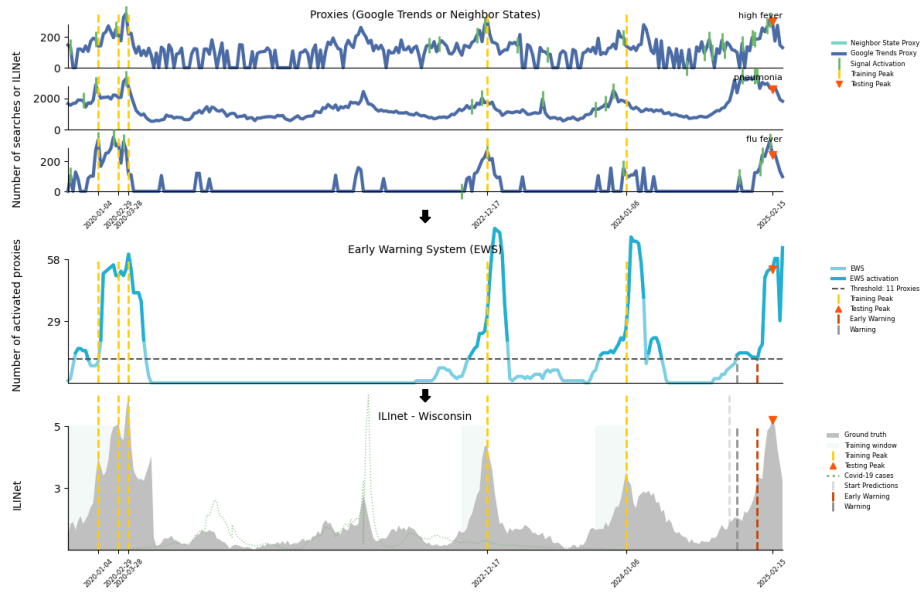


Fig. S112: Peak detection for Wisconsin during the 2024-2025 season

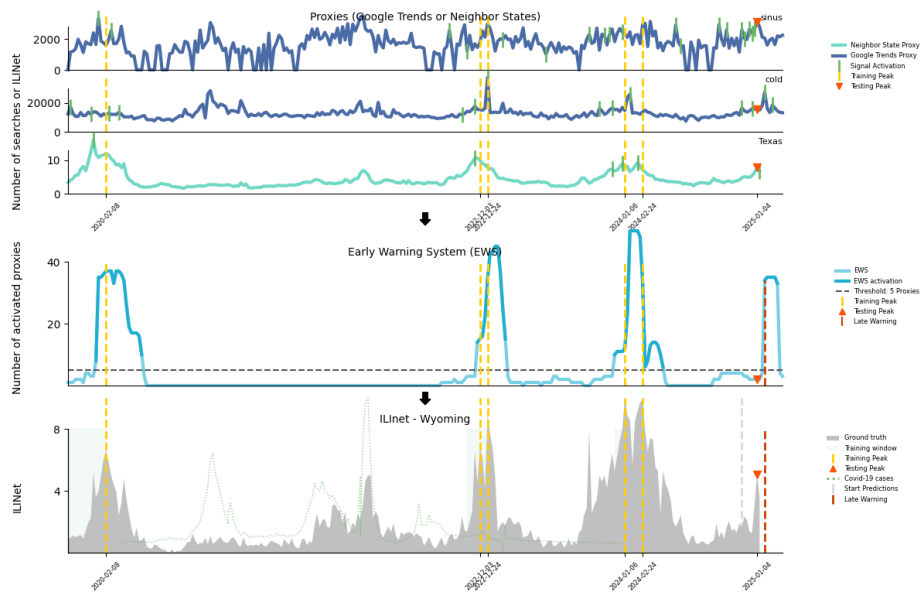


Fig. S113: Peak detection for Wyoming during the 2024-2025 season

9 Granger Causality Analysis

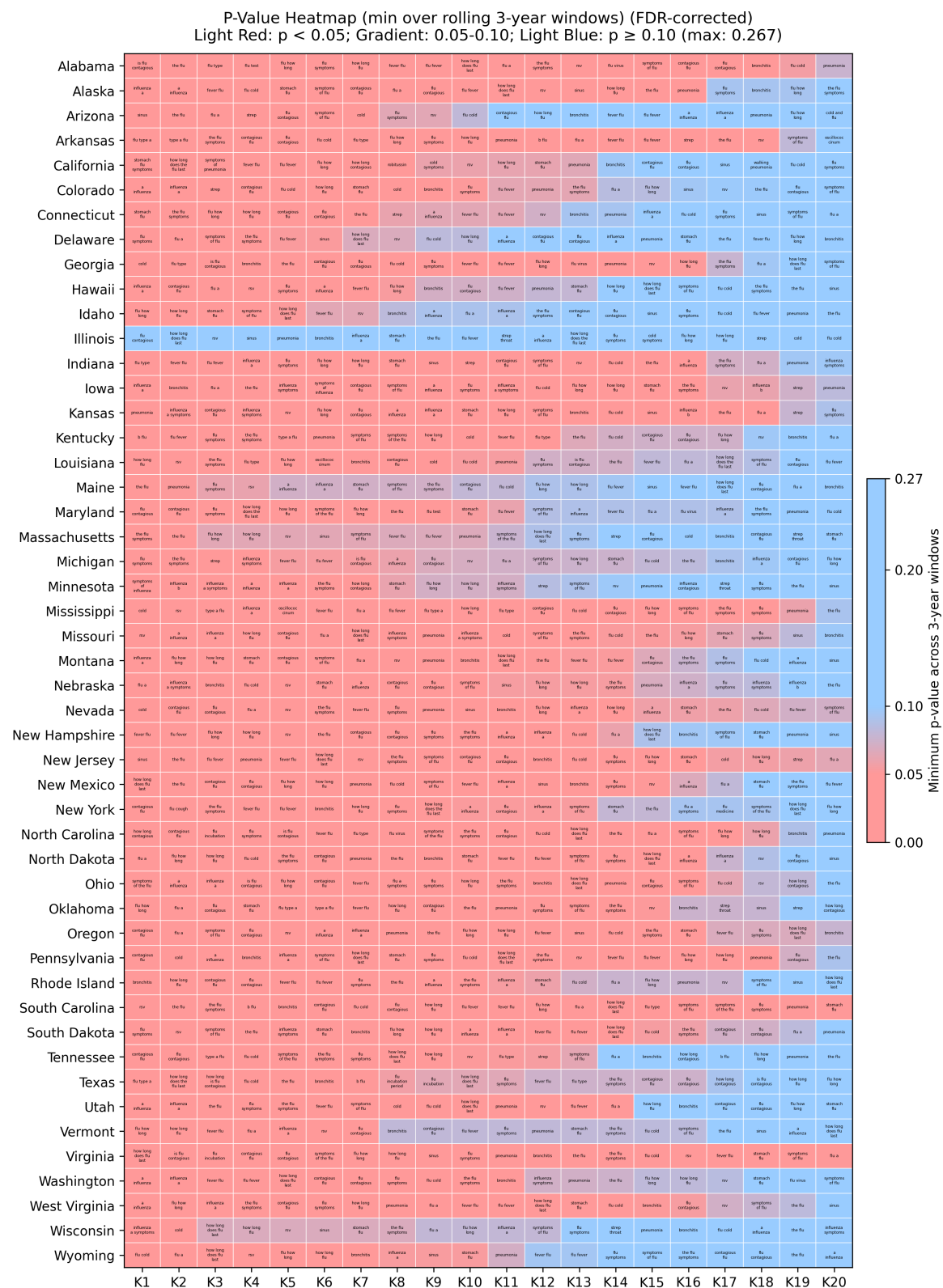


Fig. S114: Granger causality p -value heatmap (FDR-corrected). Heatmap showing the minimum p -values across rolling 3-year windows for each state (rows) and each keyword (columns), after applying false discovery rate (FDR) correction. Light red indicates statistical significance ($p < 0.05$), gradient red corresponds to $0.05 \leq p < 0.10$, and light blue indicates non-significant associations ($p \geq 0.10$).

P-Value Heatmap (min over rolling 3-year windows) (Raw)
 Light Red: $p < 0.05$; Gradient: 0.05-0.10; Light Blue: $p \geq 0.10$ (max: 0.161)

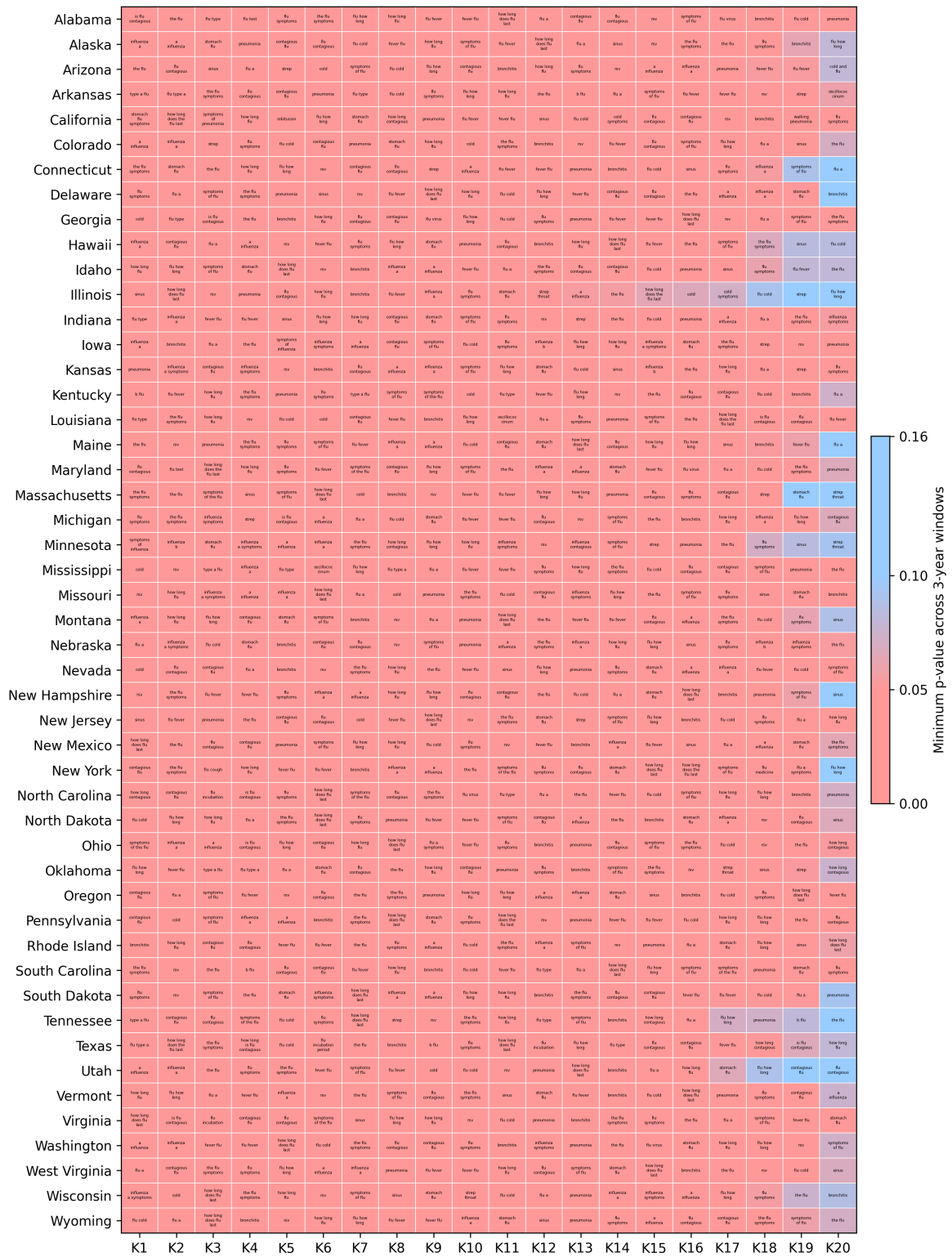


Fig. S115: Granger causality p -value heatmap (raw, uncorrected). Same as Figure S114, but showing raw p -values without FDR correction.

10 Onset Detection Methodology

Algorithm 1 Onset detection pseudocode

```

1: function GET_ONSET(target_name, lambda_vector, timeseries, onset_hypervalue=3
   (6-week window), gap_tolerance=4, min_week_length=2)
2:   Initialize empty lists: start_dates, end_dates, proxy_names, location_names
3:   for each column (proxy) in lambda_vector do
4:     Extract coefficient values and corresponding dates
5:     Convert coefficients into binary list: 1 if coefficient > 1 (growth), else 0
6:     Find consecutive windows of 1's: track start and end dates of these "onset candidate
   windows"
7:     Merge windows if they are less than gap_tolerance (4) weeks apart
8:     if column is the target location (process for targets, look into future) then
9:       for each window do
10:        if window  $\geq$  min_week_length (2) weeks long then
11:          Scan through window dates
12:          Check if cases increase on average in next onset_hypervalue (3) weeks
13:          if true then
14:            if window length >  $2 \times$  onset_hypervalue (3) weeks then
15:              Record start_date = current date + onset_hypervalue (3)
16:              Record end_date = window_end (large window, large outbreak)
17:            else
18:              Record start_date = date, end_date = window_end (short window, noisy short outbreak)
19:            end if
20:          end if
21:        end if
22:      end for
23:     else column is a predictor (mimic process for targets, without look into future)
24:       for each window (proxy column, mimic target process without looking into future) do
25:        if window length  $\geq 2 \times$  onset_hypervalue (3) then
26:          Record start_date = window_start +  $2 \times$  onset_hypervalue (total shift of 6 weeks)
27:          Record end_date = window_end
28:        end if
29:      end for
30:     end if
31:   end for
32: end function

```

11 Formal Definition of the Early Warning Algorithm

Event-level labeling (6-week window)

Let M denote the total number of proxy data sources (e.g., Google Trends queries, CDC surveillance streams). A proxy event at time $t_e^{(x_i)}$ is counted as a true positive (TP) for outbreak event $t_e^{(y)}$ if it occurs within the preceding 6 weeks:

$$\text{TP}_j^{(i)} = \mathbb{I} \left[\exists t_e^{(x_i)} \text{ s.t. } 0 \leq t_e^{(y)} - t_e^{(x_i)} \leq 6 \right]. \quad (2)$$

Equivalently, for each historical outbreak event j , define the total number of proxy true-positive votes as

$$\text{TP}_j = \sum_{i=1}^M \text{TP}_j^{(i)}. \quad (3)$$

Location-specific voting threshold

Let $\mathcal{J}_{\text{train}}$ denote the set of historical outbreak events in the training period used for threshold calibration. We define the early warning system (EWS) decision threshold for location s as the minimum number of proxy votes observed across the three most recent training events at that location:

$$\tau_s = \min_{j \in \{j_1, j_2, j_3\}} \text{TP}_j, \quad (1)$$

where $\{j_1, j_2, j_3\} \subset \mathcal{J}_{\text{train}}$ are the three most recent outbreak events for location s in the training data. This threshold is computed once during model development using only historical data, ensuring no information leakage from the prospective monitoring period.

Real-time proxy activation (3-week persistence)

Let $\mathcal{X}_s = \{x_1, x_2, \dots, x_M\}$ denote the set of M proxy data sources monitored at location s . During prospective monitoring, let t_{s, x_i} denote the most recent proxy-event time produced by proxy x_i at location s (up to time t). We define a binary activation indicator that persists for $k = 3$ weeks:

$$g(x_i, t) = \begin{cases} 1, & \text{if } t - k \leq t_{s, x_i} \leq t, \\ 0, & \text{otherwise.} \end{cases} \quad (2)$$

EWS vote count and alarm triggering

The EWS vote count at location s and time t is

$$M_{s, t} = \sum_{x_i \in \mathcal{X}_s} g(x_i, t), \quad (3)$$

and the system triggers an alarm if

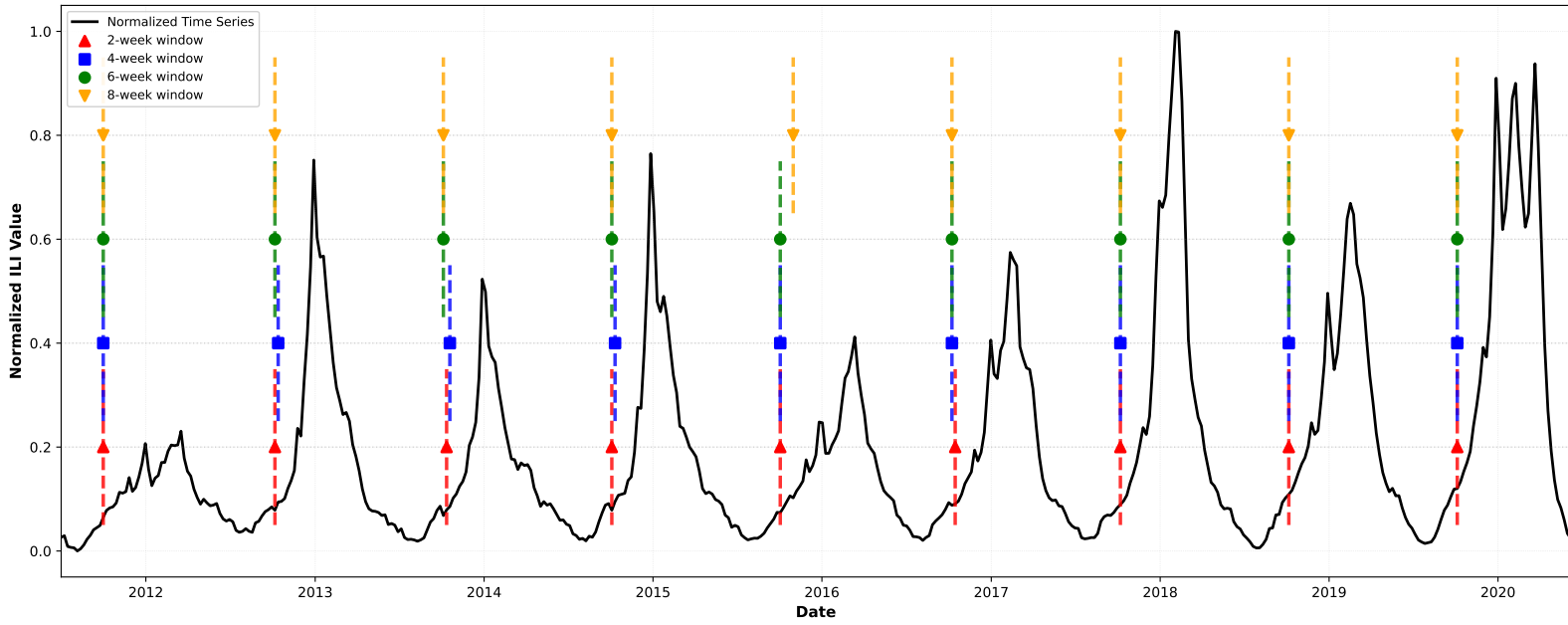
$$A_{s, t} = \mathbb{I}[M_{s, t} \geq \tau_s], \quad (4)$$

which we interpret as signaling an expected outbreak event within the next 6 weeks.

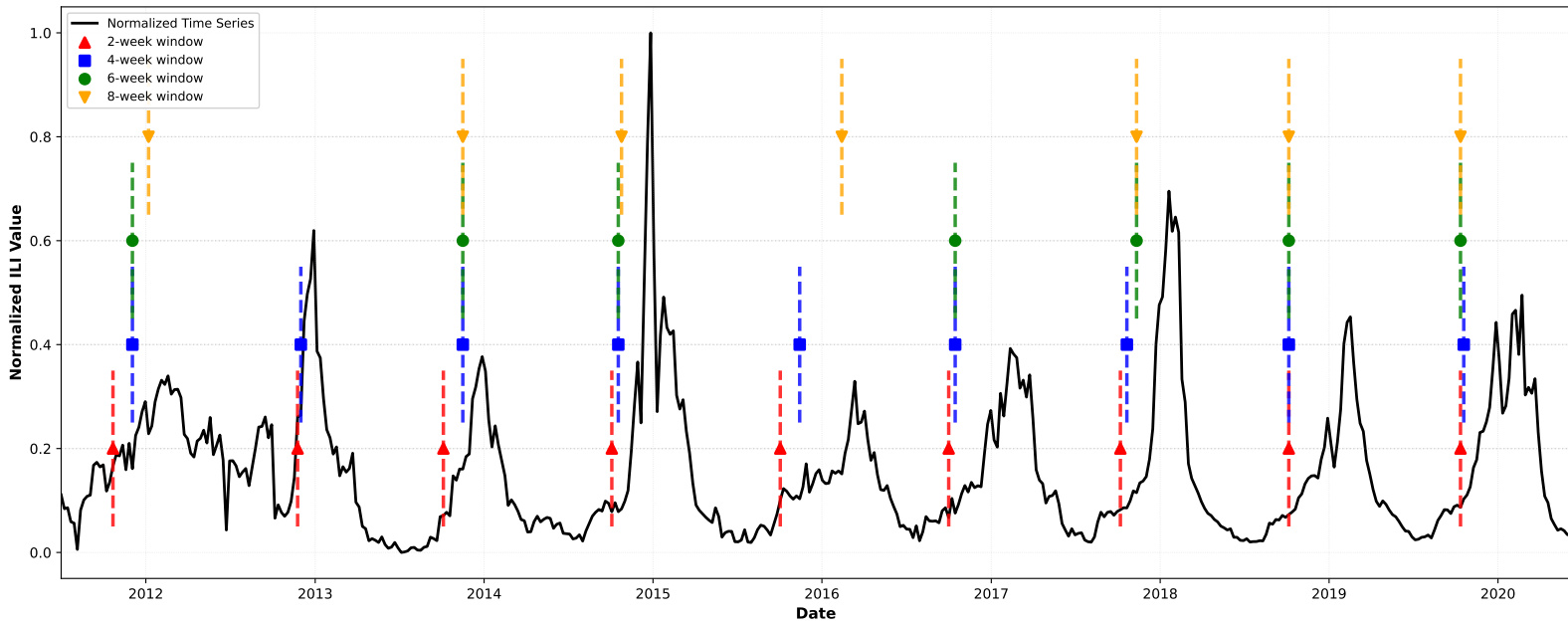
12 Sensitivity of Onset Detection to Exponential Growth Duration

The Following figures illustrate the impact of varying the exponential growth window parameter on onset detection timing for normalized ILI time series from 2011 to 2020 and Influenza and RSV time series from 2023 to 2025 across the United States. Each colored marker represents onset detection using different minimum durations of sustained exponential growth: 2 weeks (red triangles), 4 weeks (blue squares), 6 weeks (green circles), and 8 weeks (orange inverted triangles). The dashed vertical lines connect these markers to their corresponding positions on the incidence curve, demonstrating how longer required growth periods systematically delay onset detection relative to the epidemic trajectory.

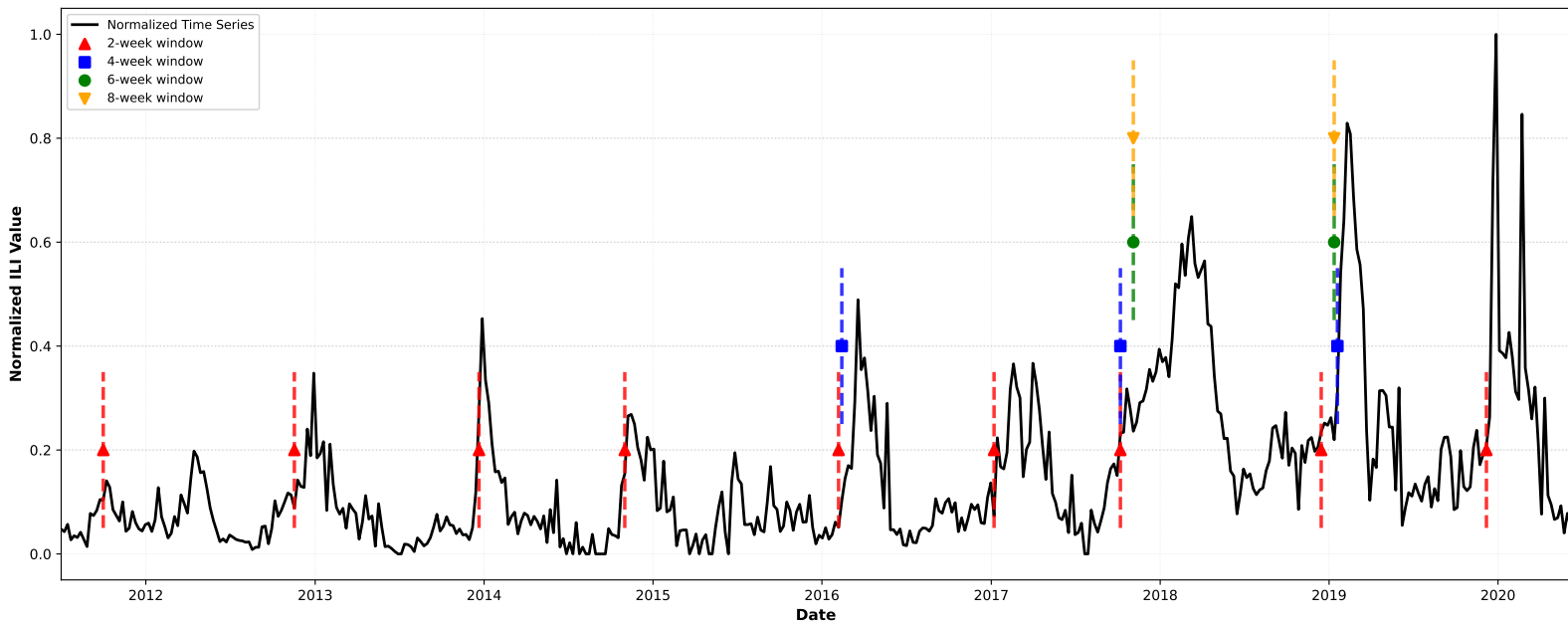
US — Normalized ILI Time Series with Onset Markers



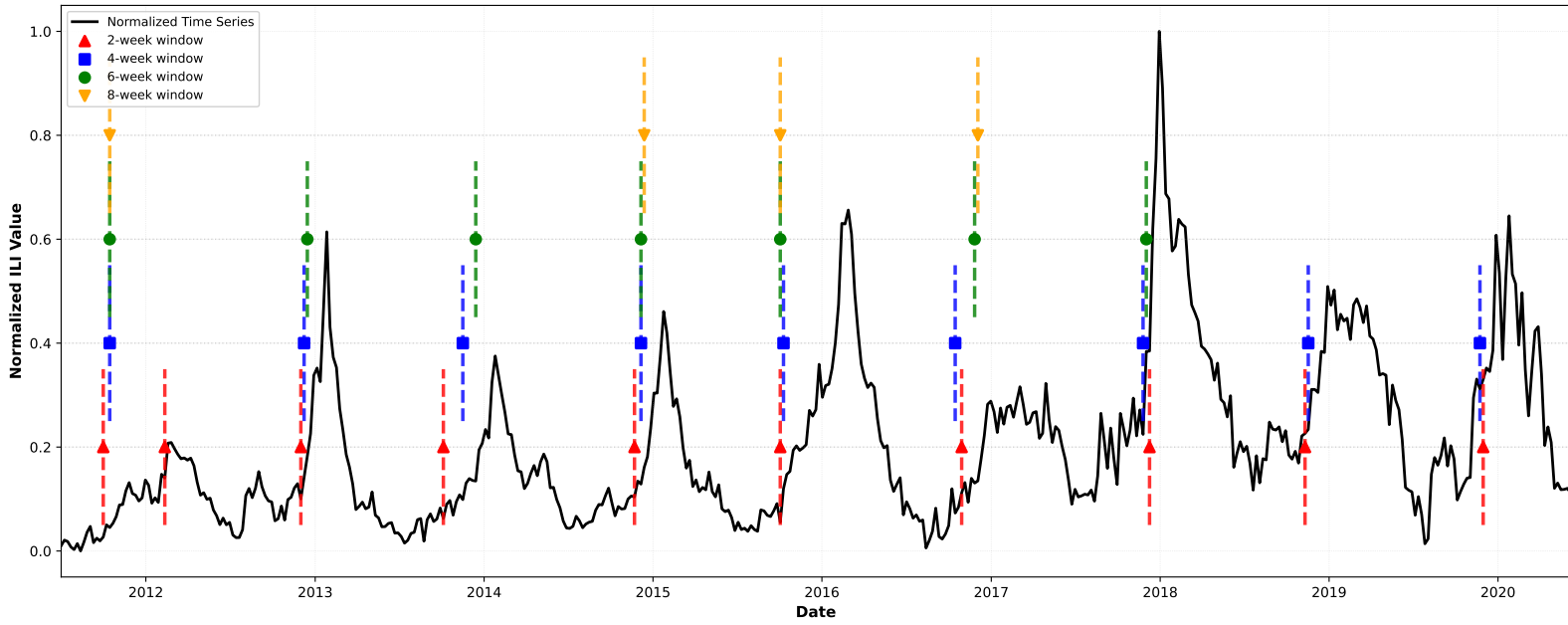
Alabama — Normalized ILI Time Series with Onset Markers



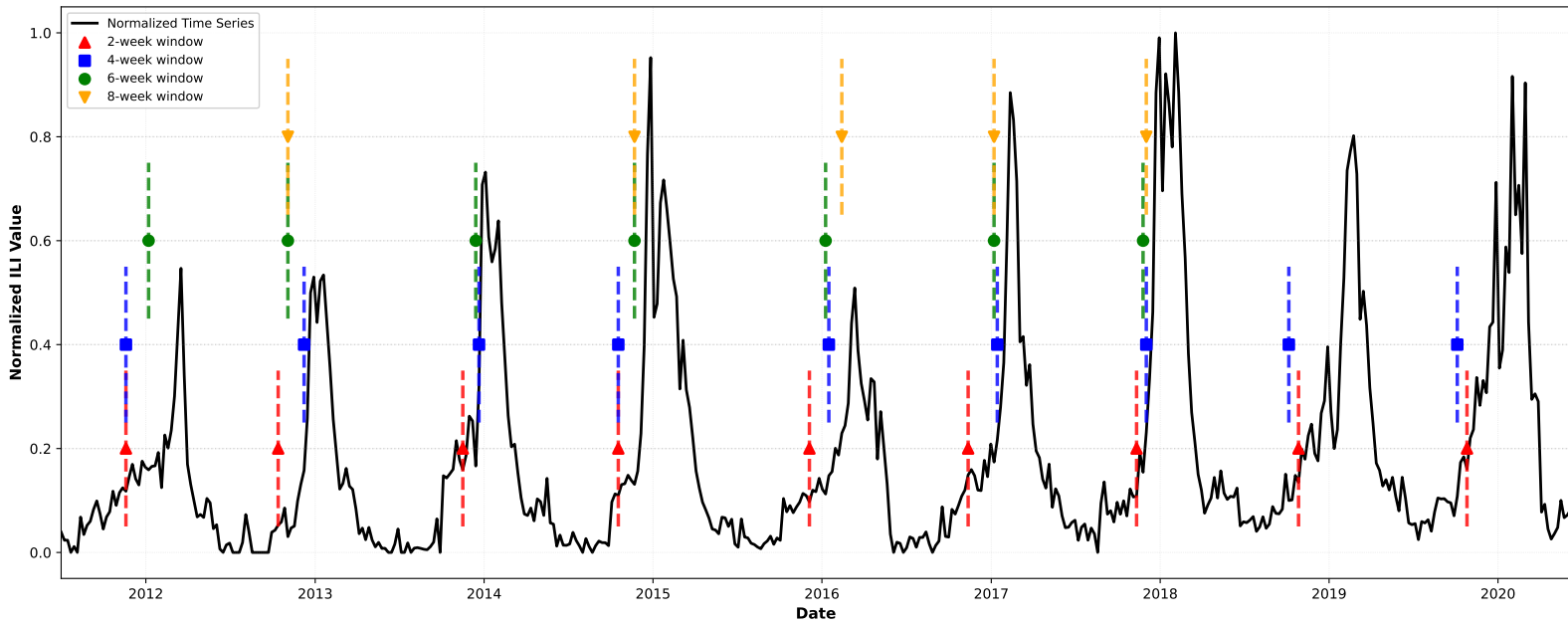
Alaska — Normalized ILI Time Series with Onset Markers



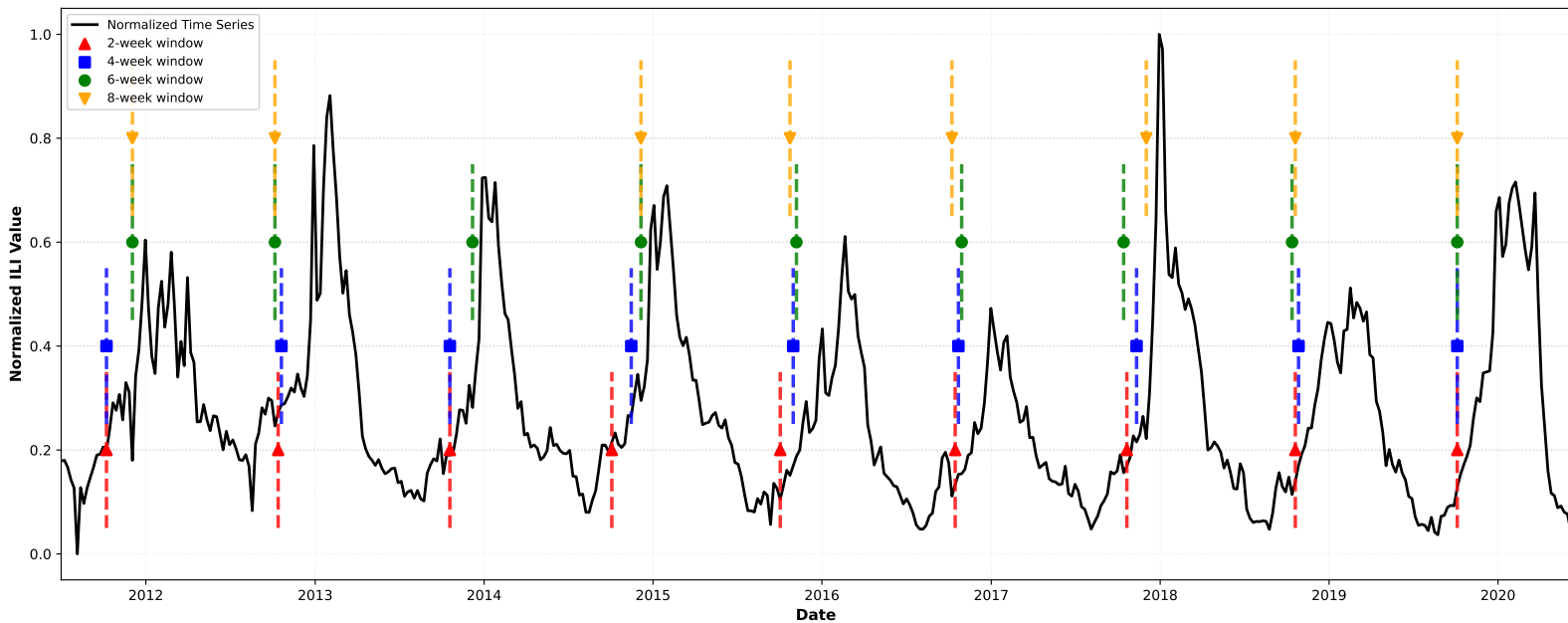
Arizona — Normalized ILI Time Series with Onset Markers



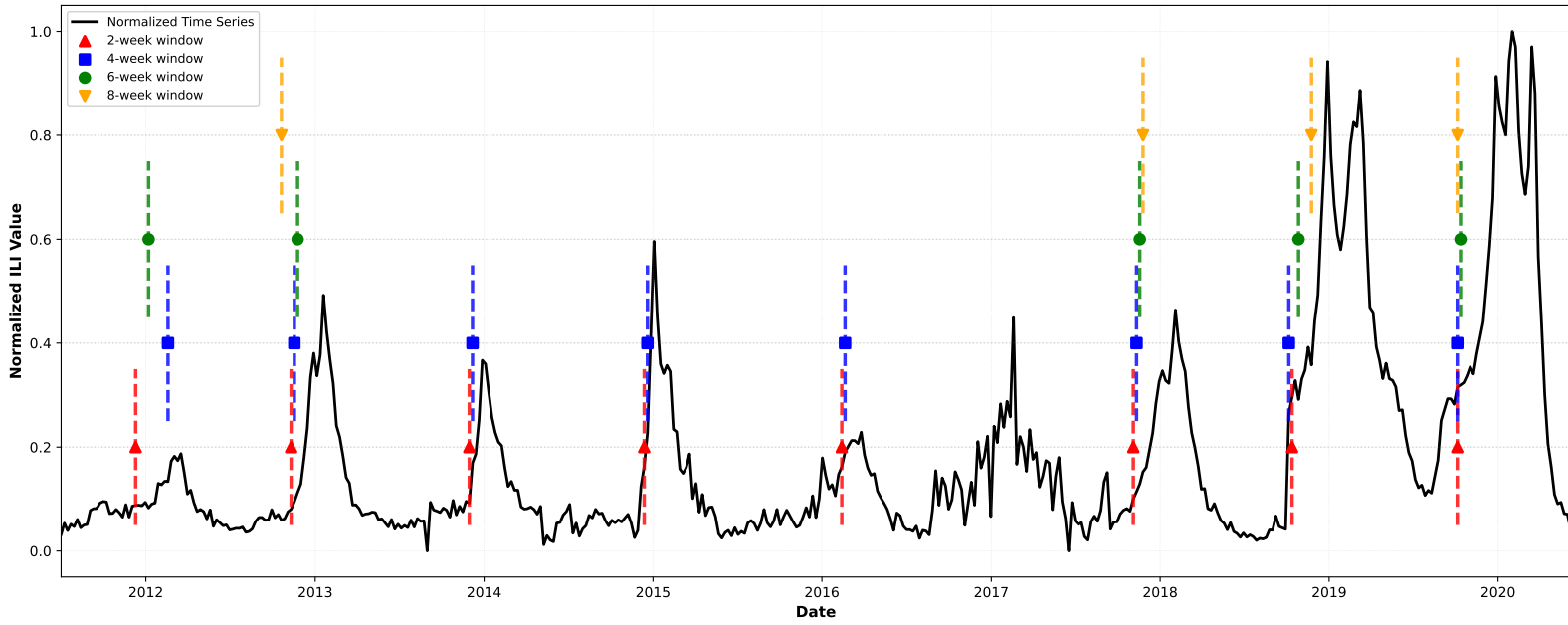
Arkansas — Normalized ILI Time Series with Onset Markers



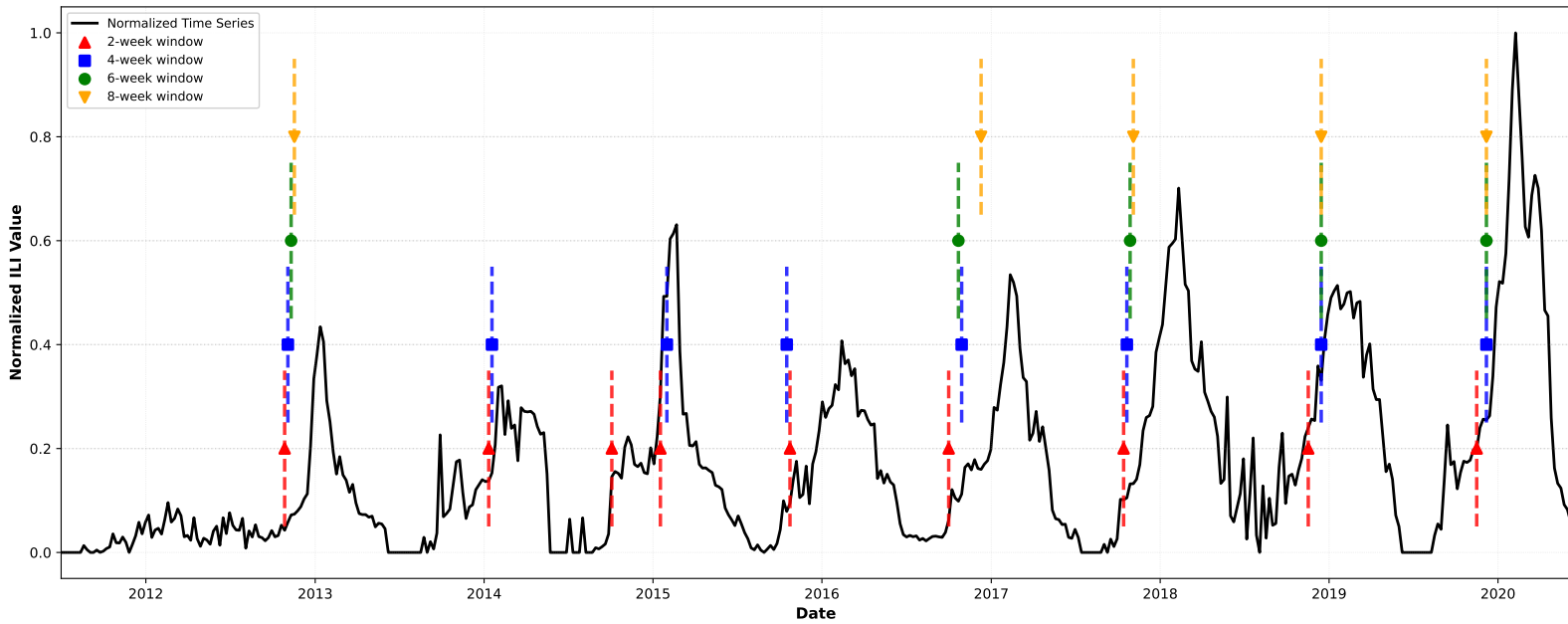
California — Normalized ILI Time Series with Onset Markers



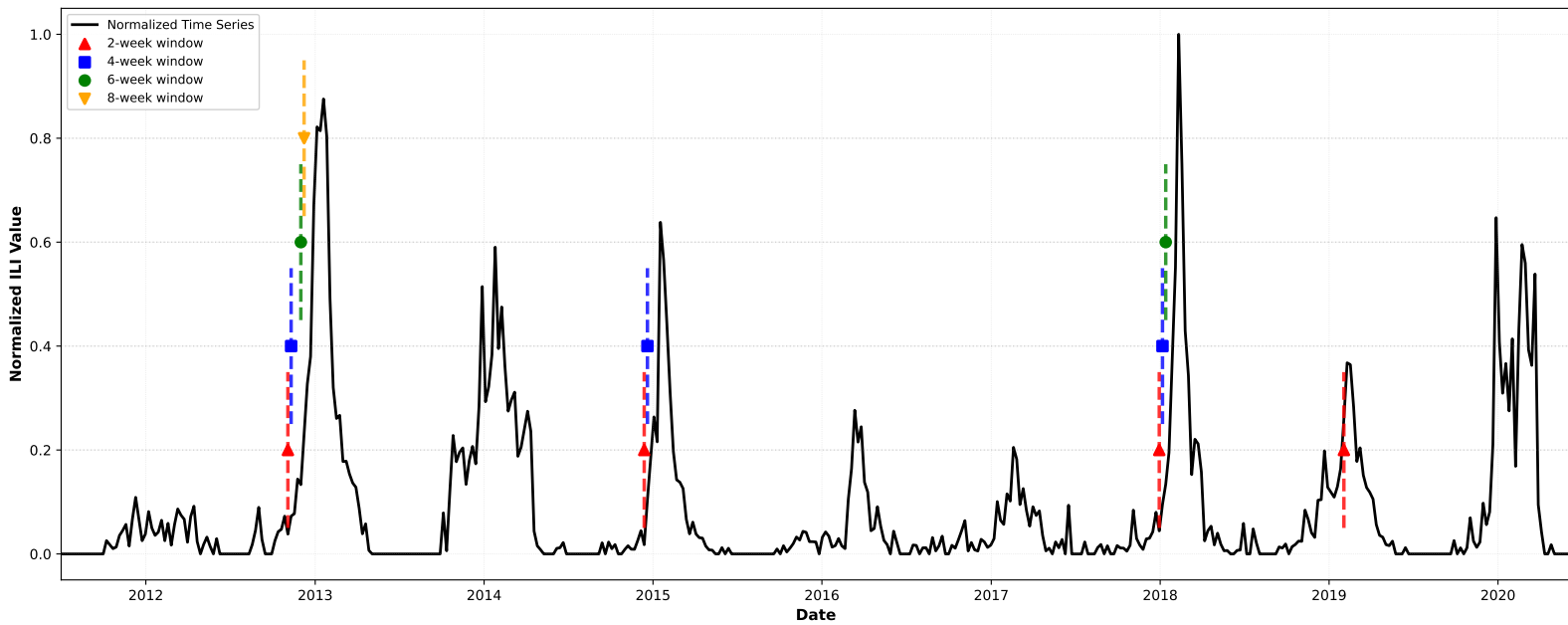
Colorado — Normalized ILI Time Series with Onset Markers



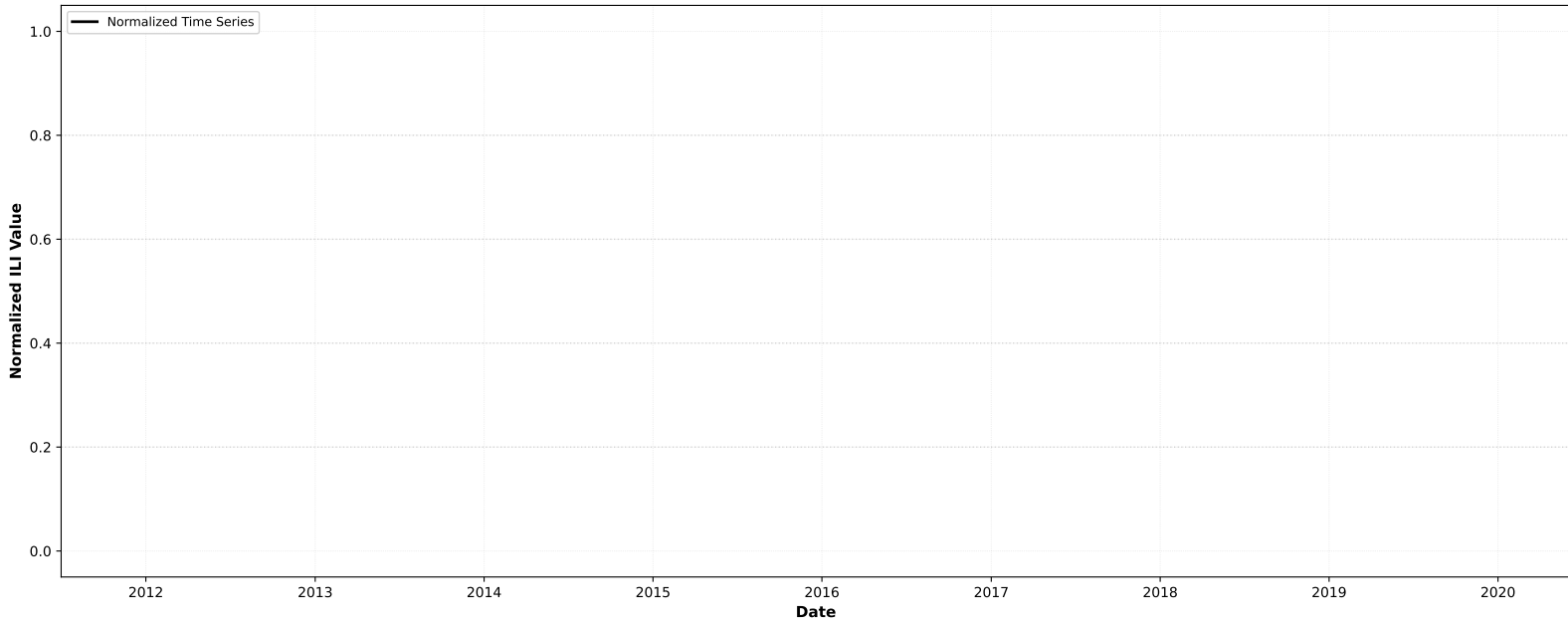
Connecticut — Normalized ILI Time Series with Onset Markers



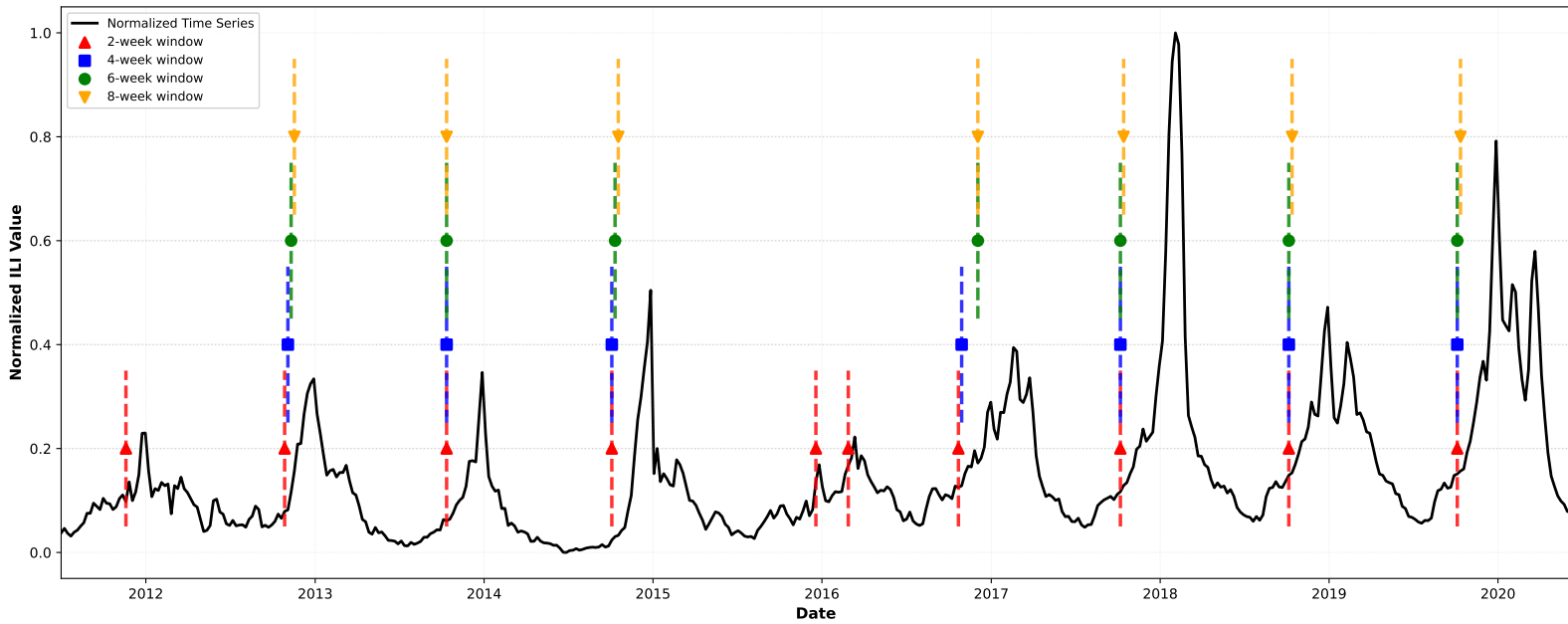
Delaware — Normalized ILI Time Series with Onset Markers



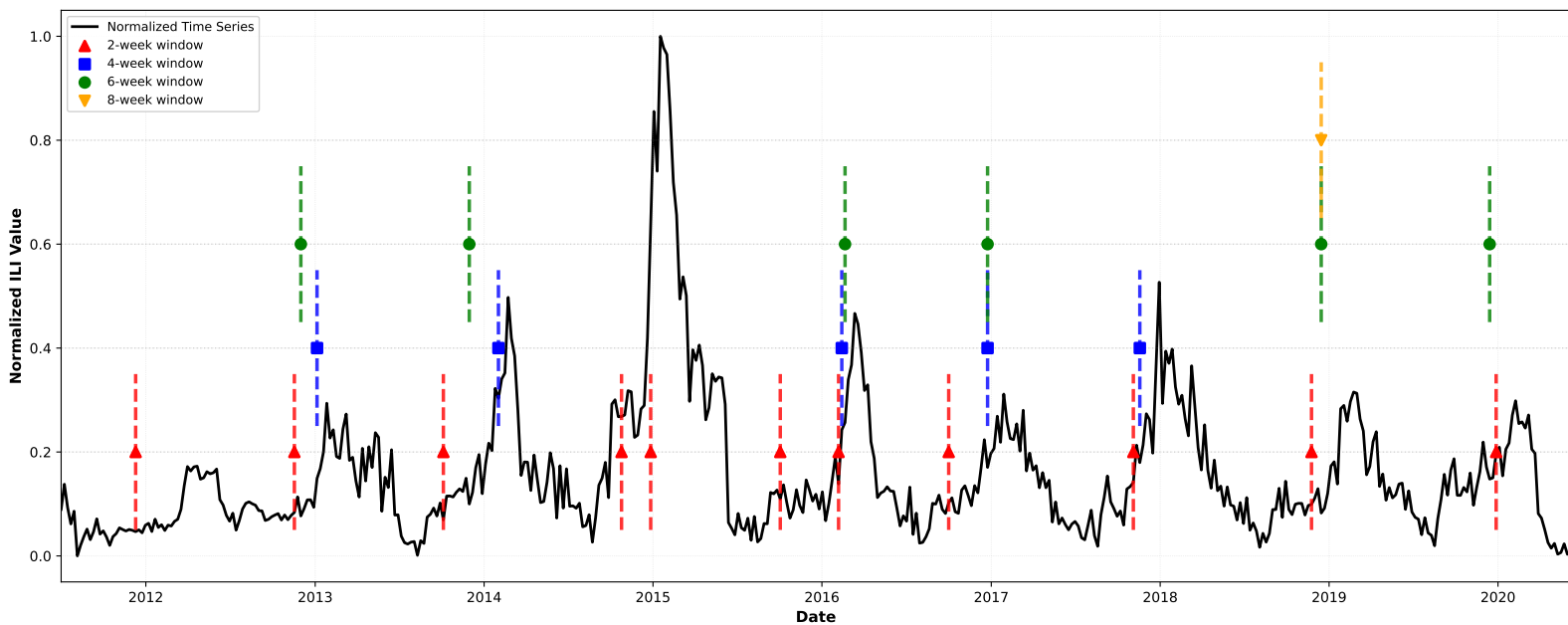
Florida — Normalized ILI Time Series with Onset Markers



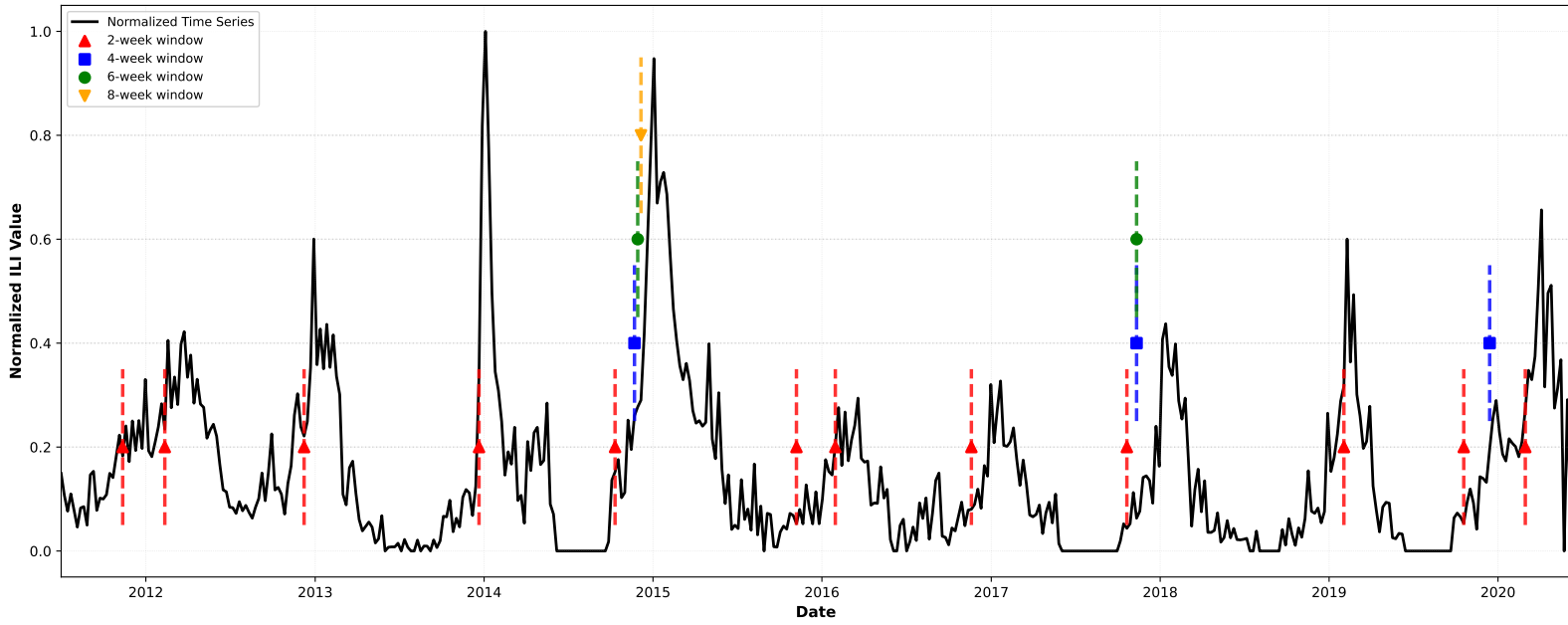
Georgia — Normalized ILI Time Series with Onset Markers



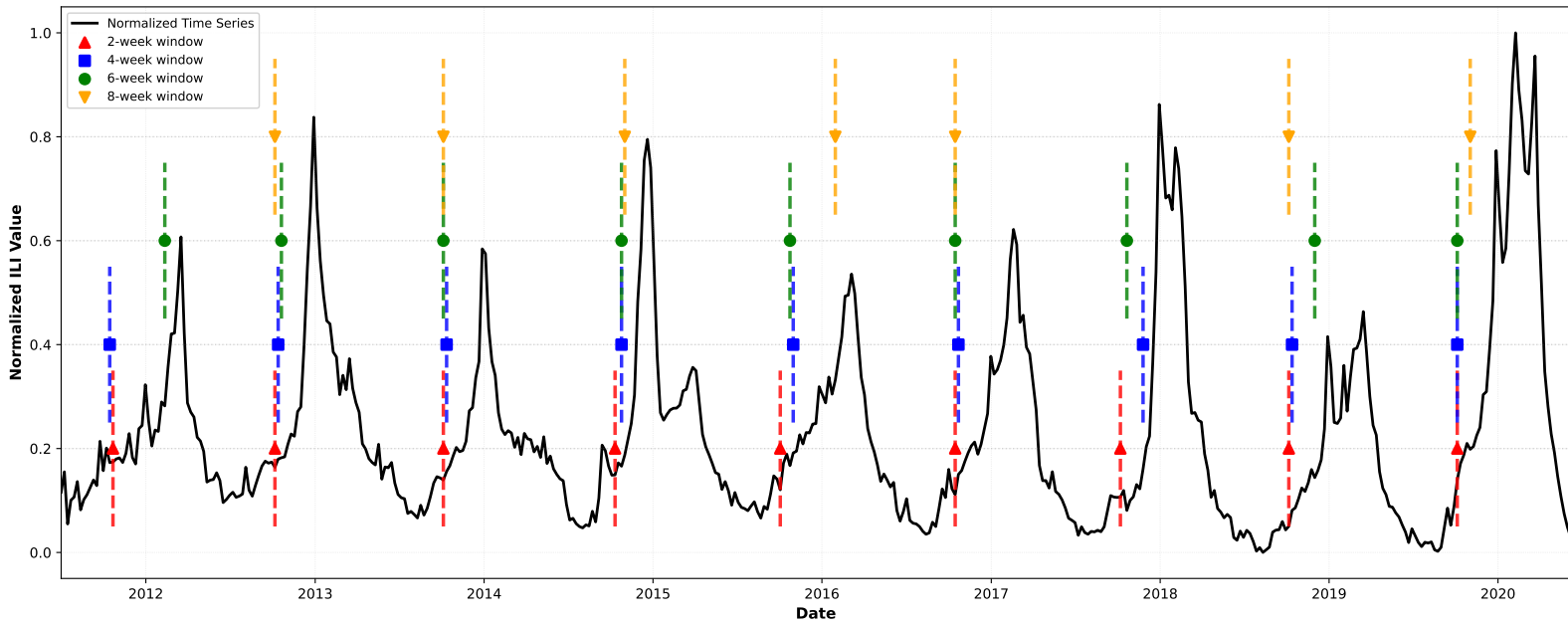
Hawaii — Normalized ILI Time Series with Onset Markers



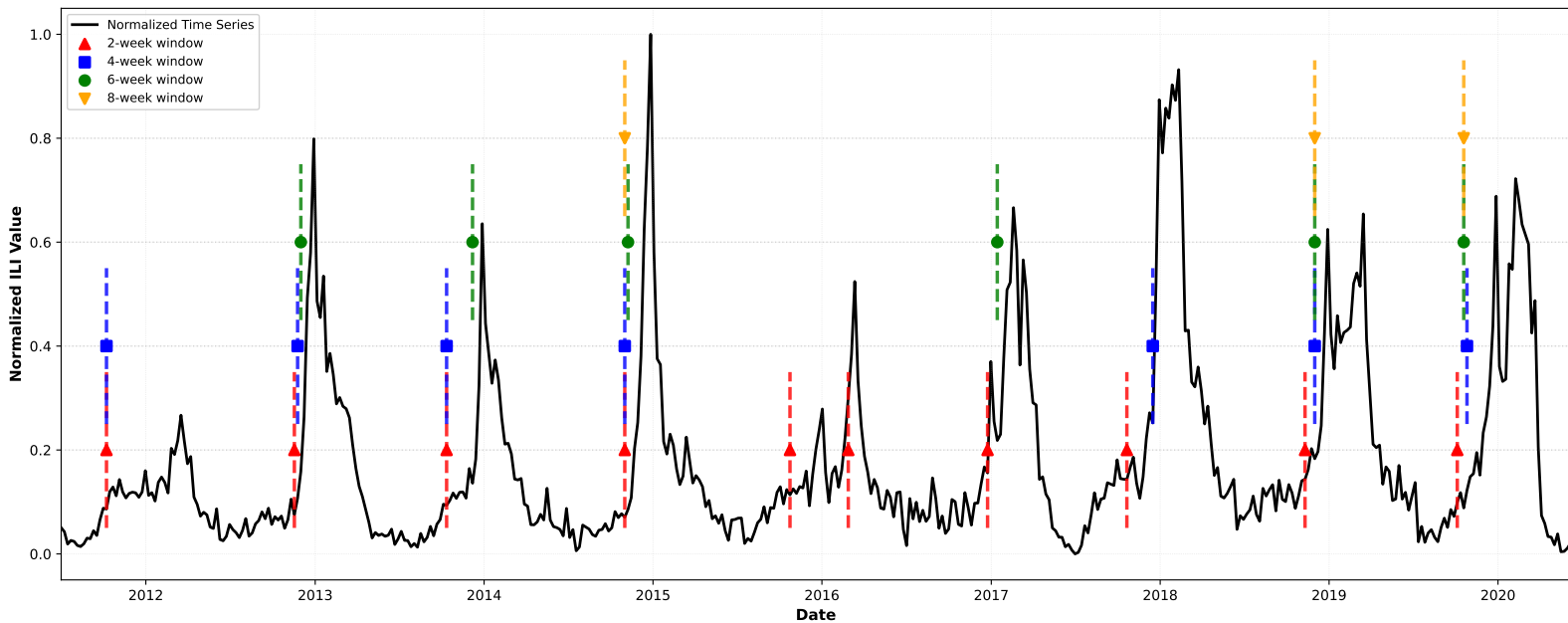
Idaho — Normalized ILI Time Series with Onset Markers



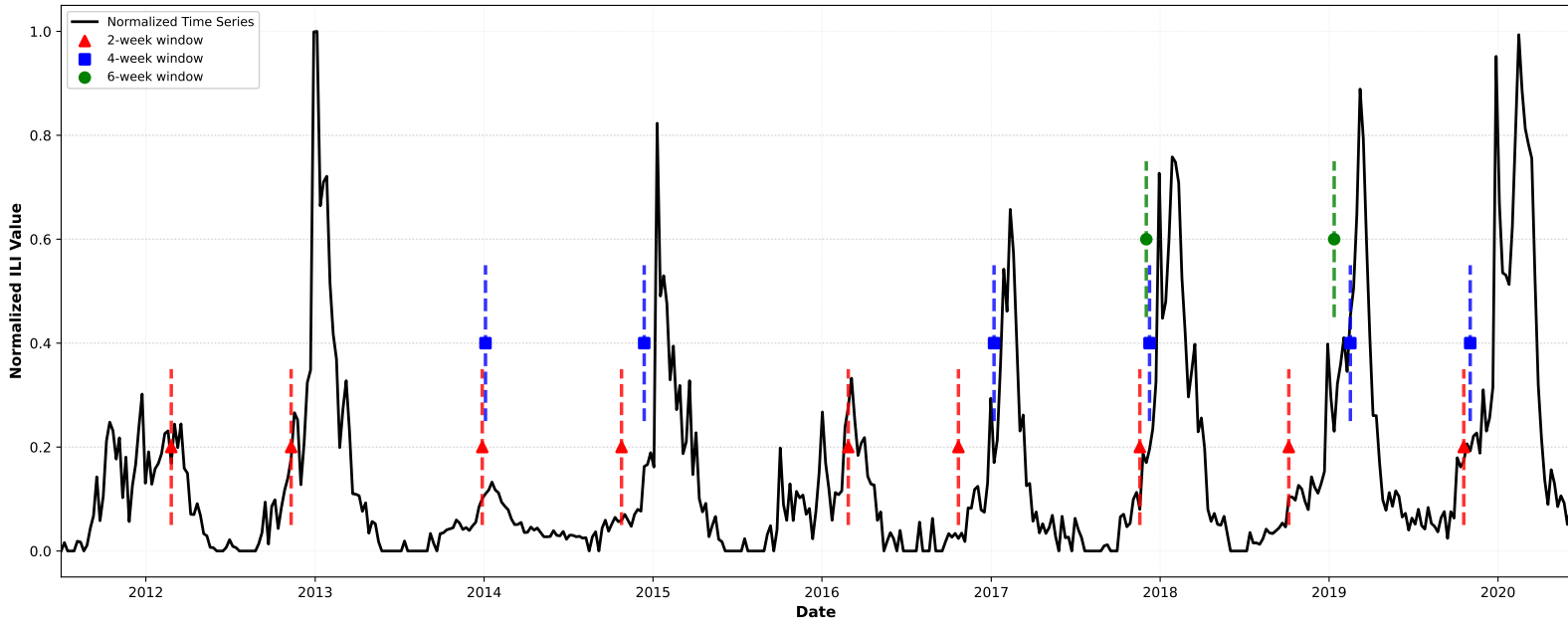
Illinois — Normalized ILI Time Series with Onset Markers



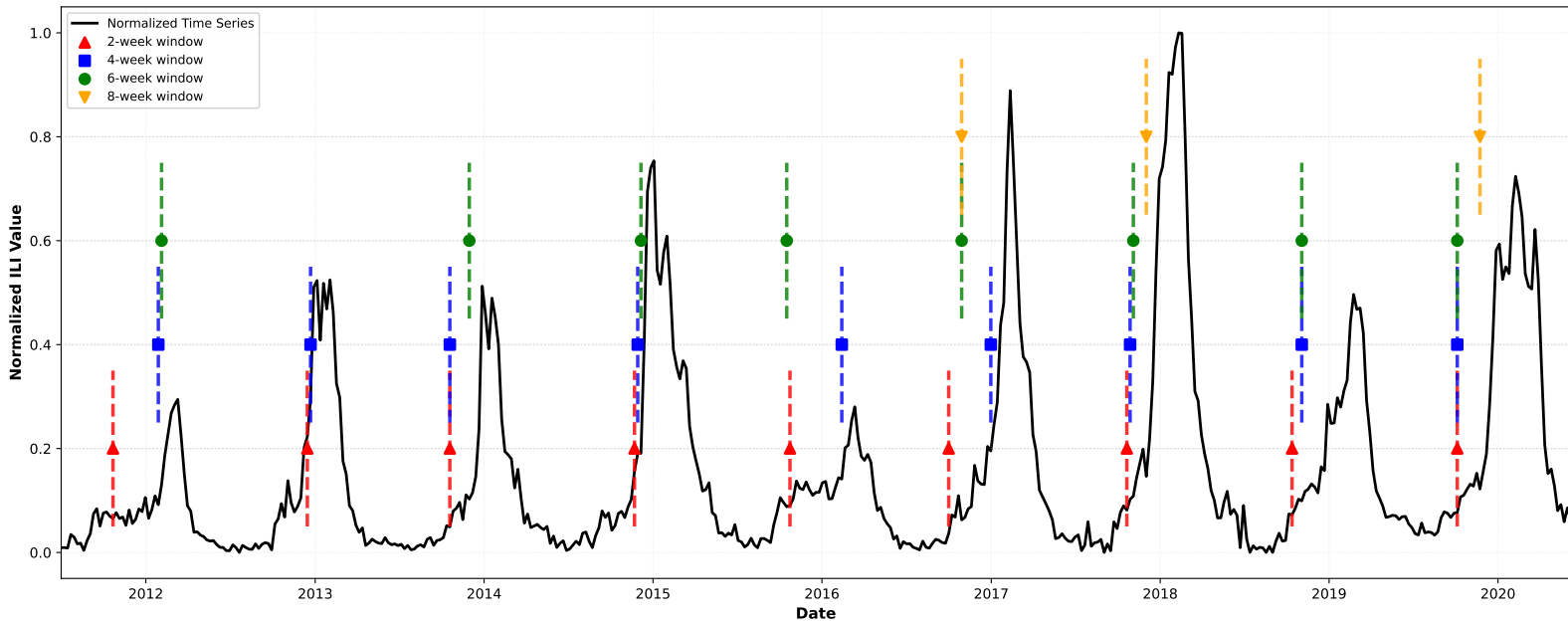
Indiana — Normalized ILI Time Series with Onset Markers



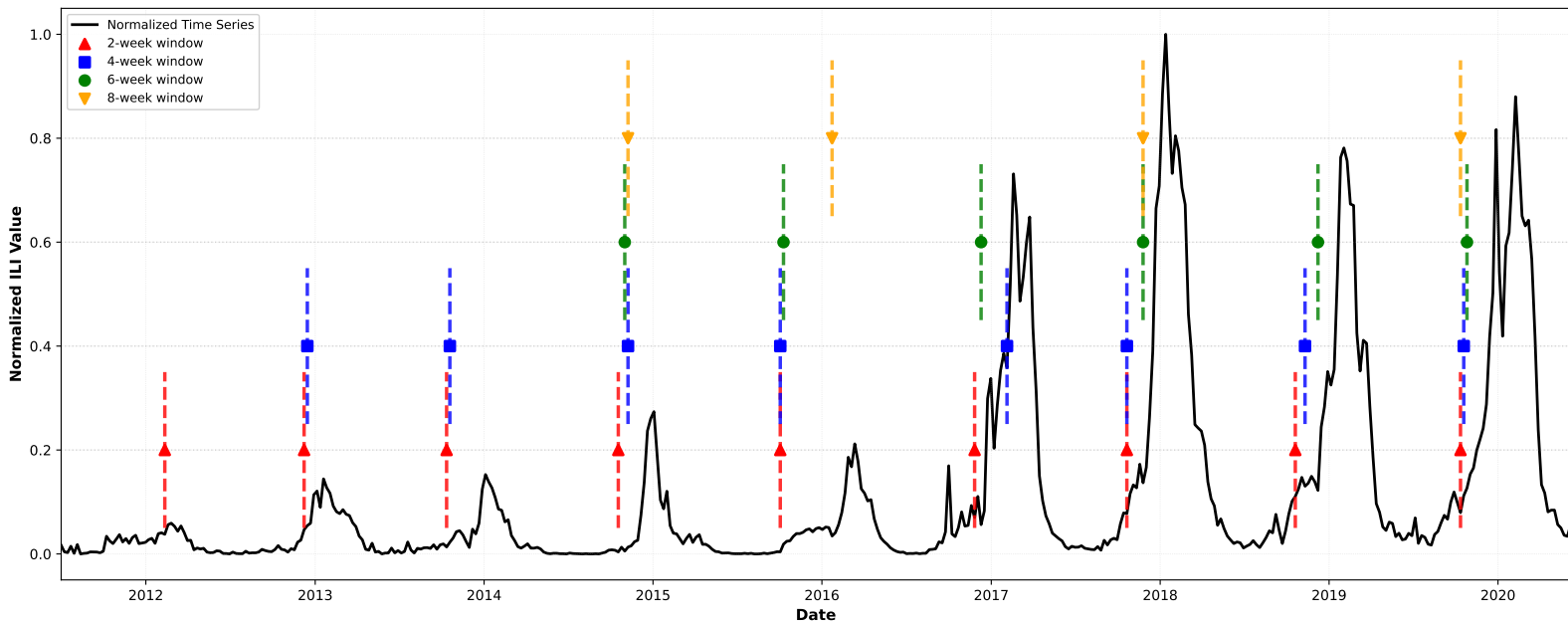
Iowa — Normalized ILI Time Series with Onset Markers



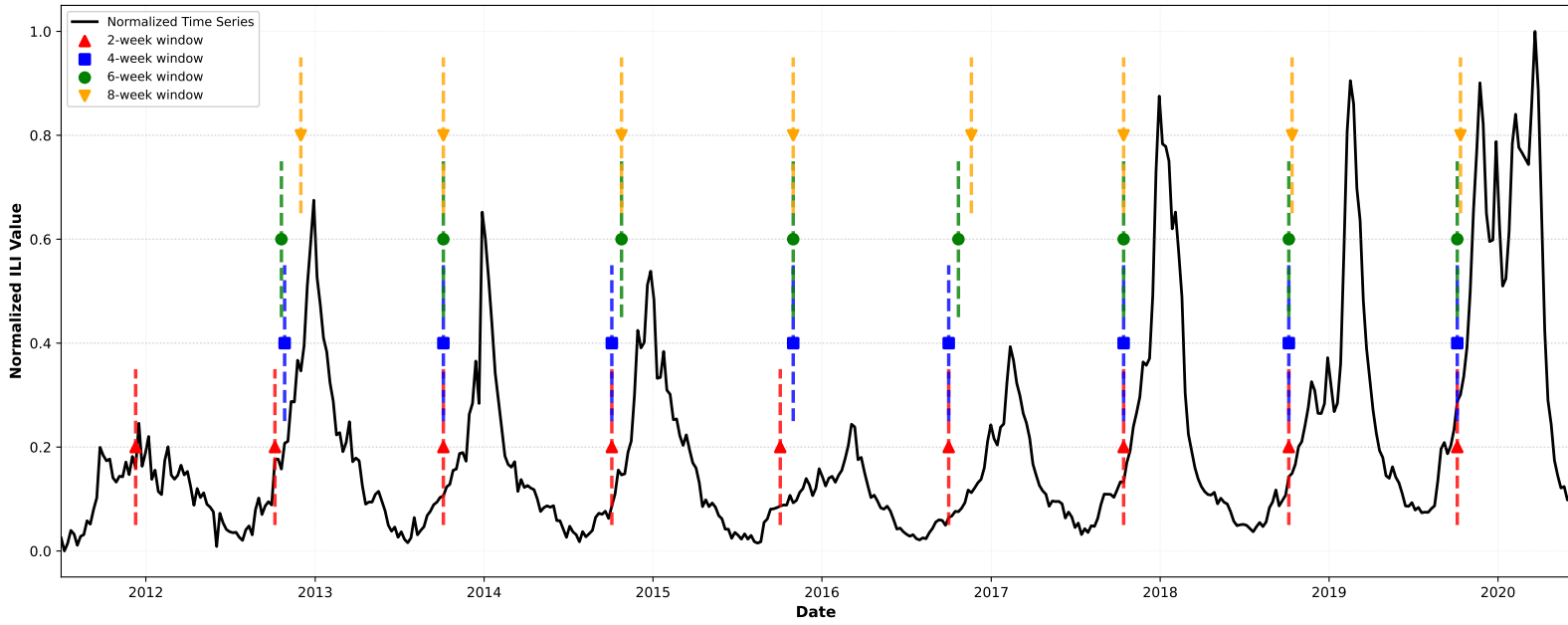
Kansas — Normalized ILI Time Series with Onset Markers



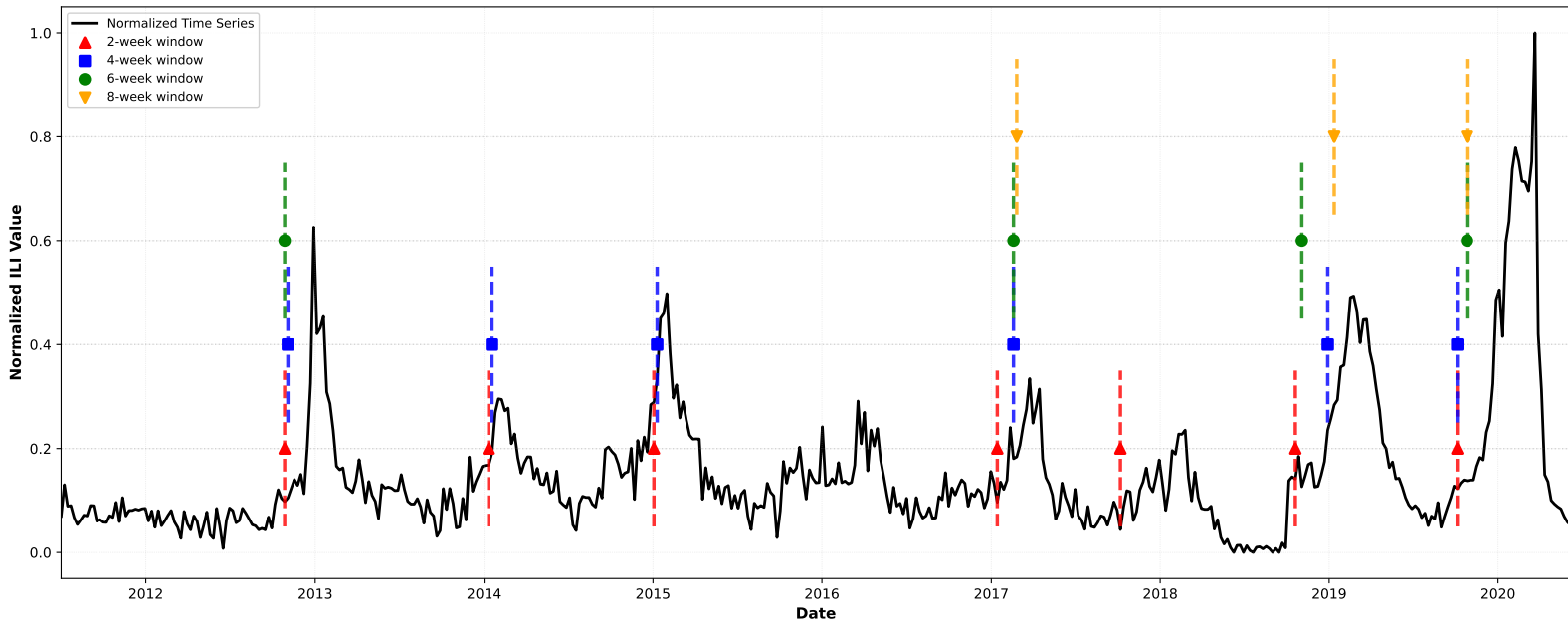
Kentucky — Normalized ILI Time Series with Onset Markers



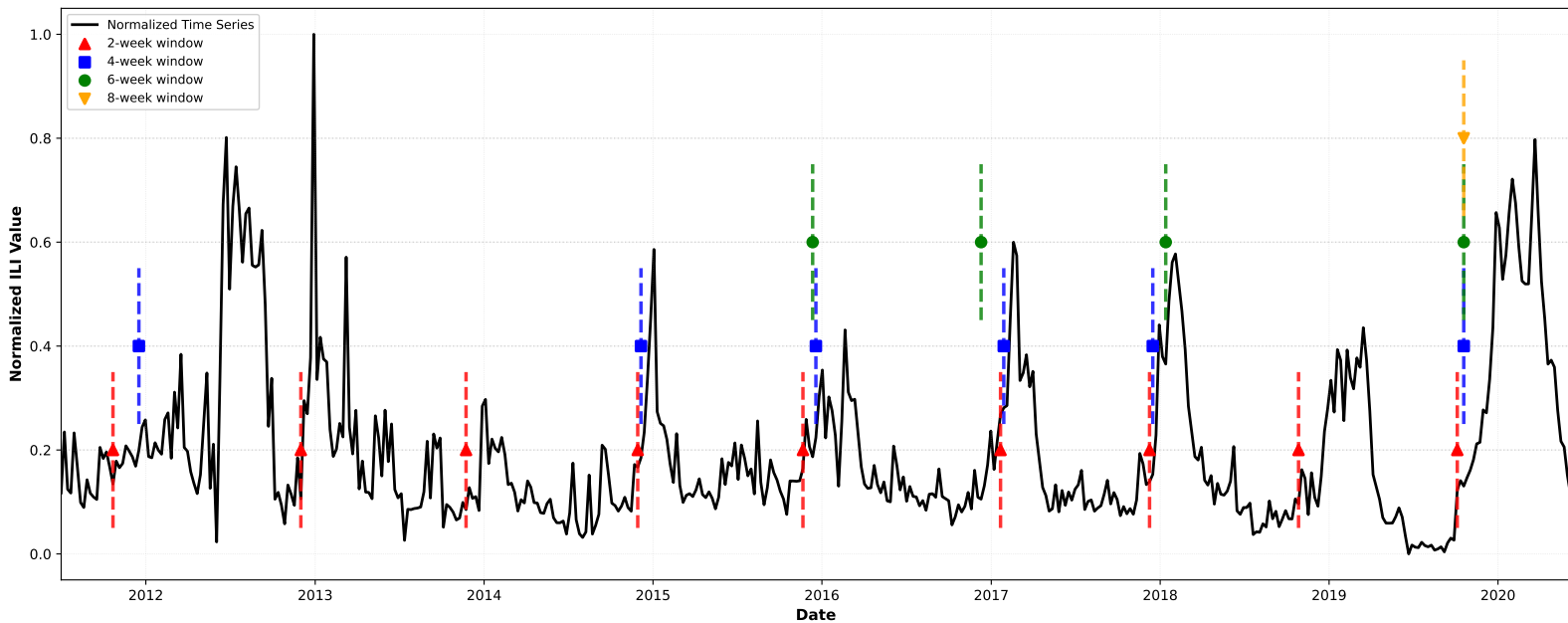
Louisiana — Normalized ILI Time Series with Onset Markers



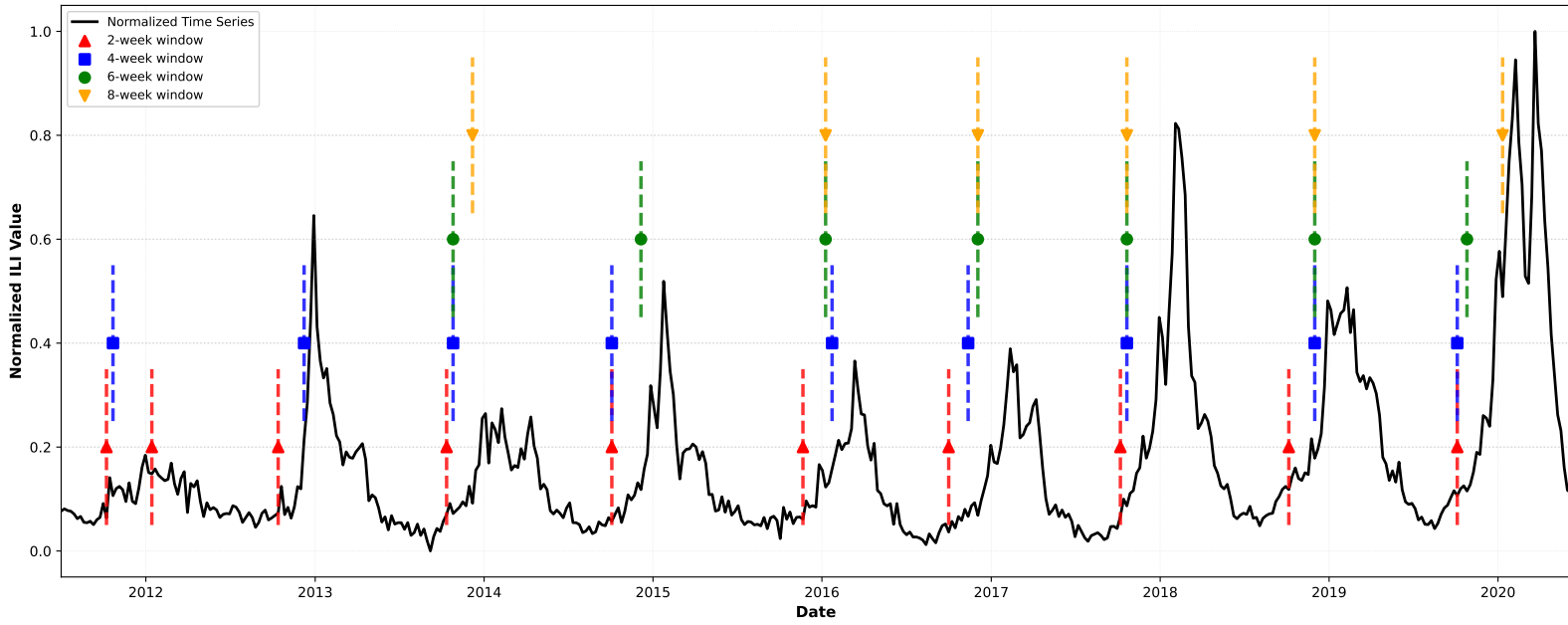
Maine — Normalized ILI Time Series with Onset Markers



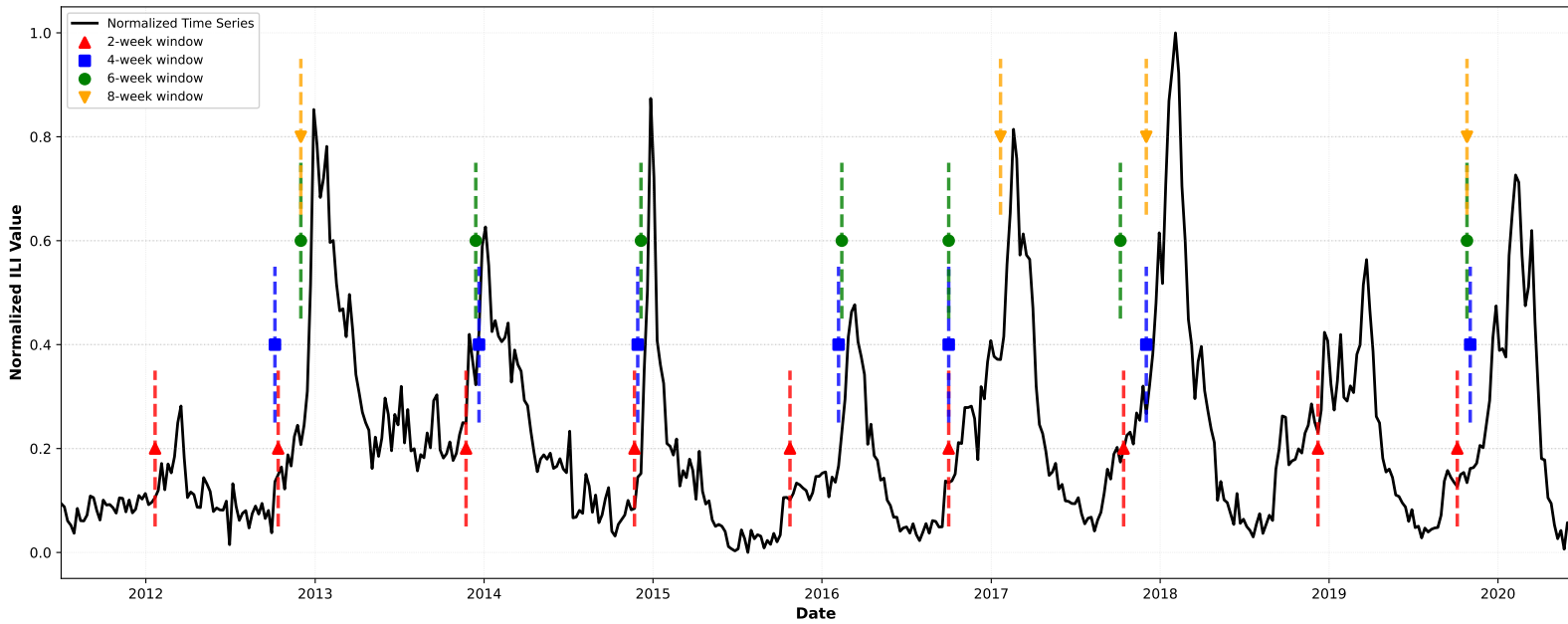
Maryland — Normalized ILI Time Series with Onset Markers



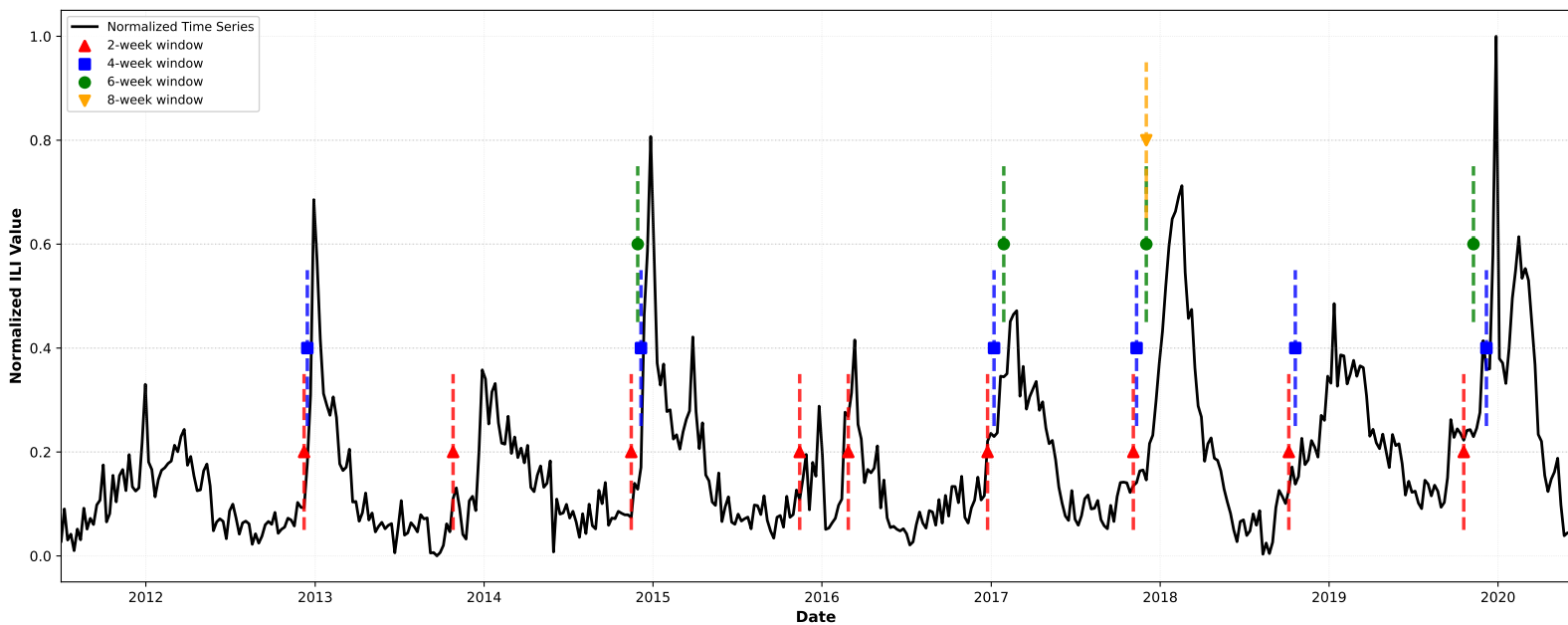
Massachusetts — Normalized ILI Time Series with Onset Markers



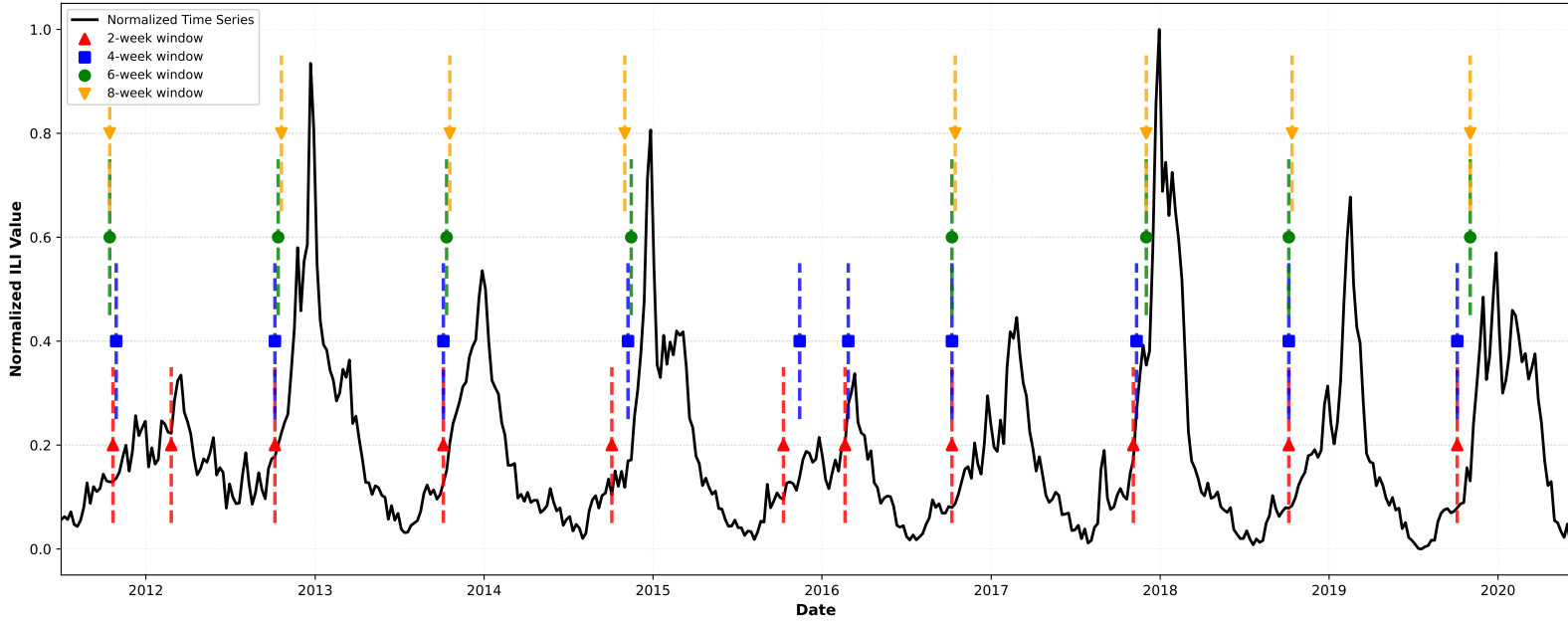
Michigan — Normalized ILI Time Series with Onset Markers



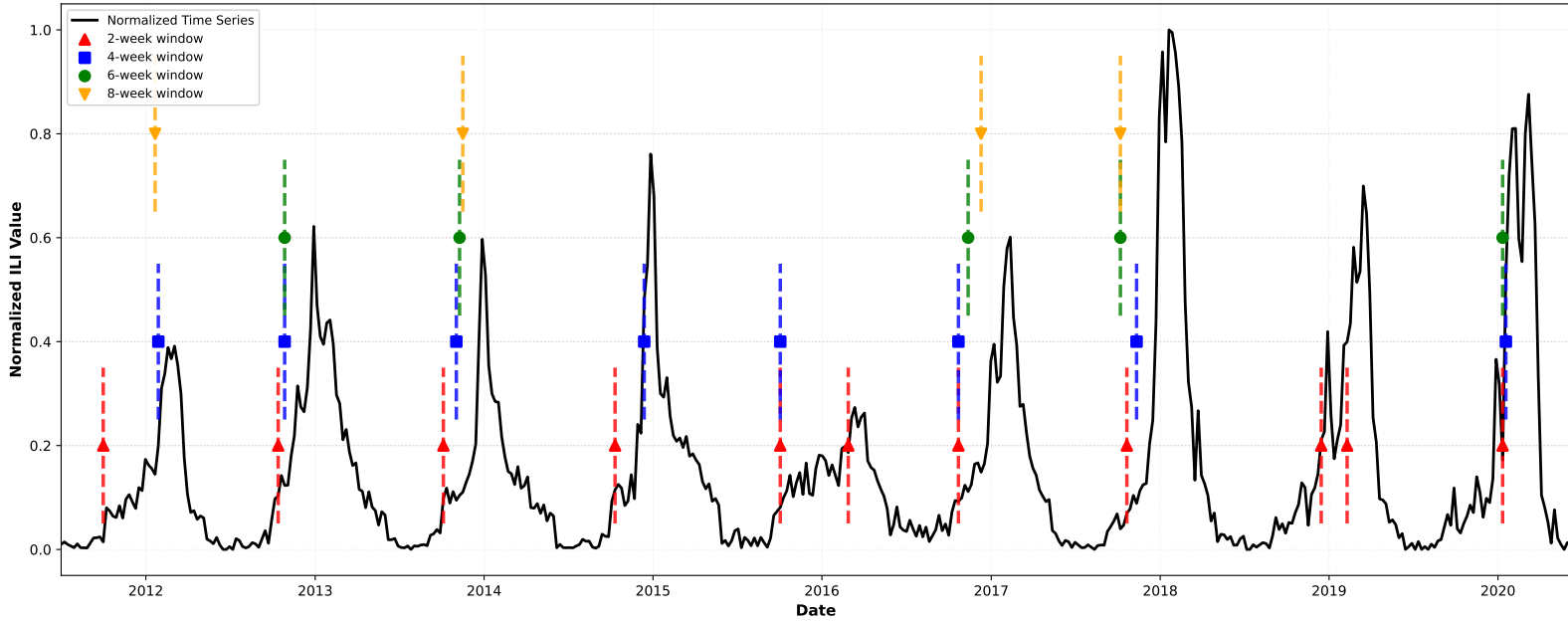
Minnesota — Normalized ILI Time Series with Onset Markers



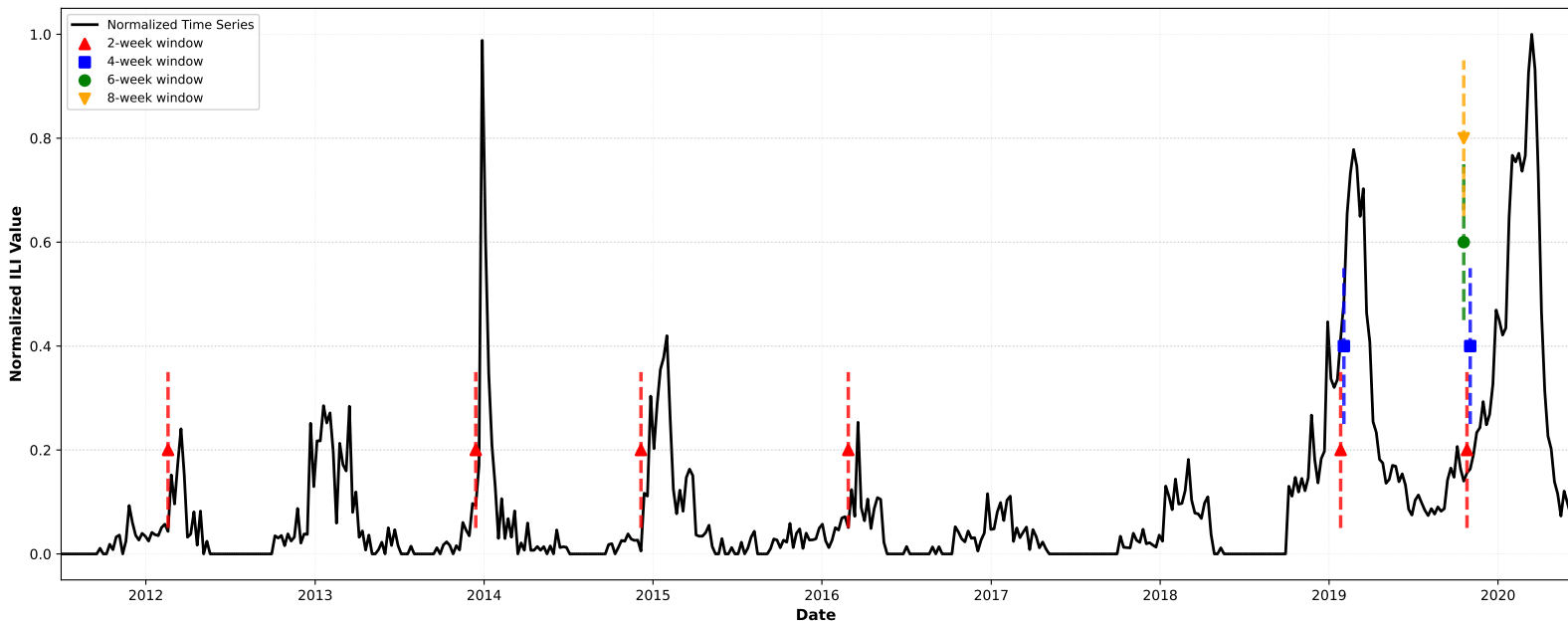
Mississippi — Normalized ILI Time Series with Onset Markers



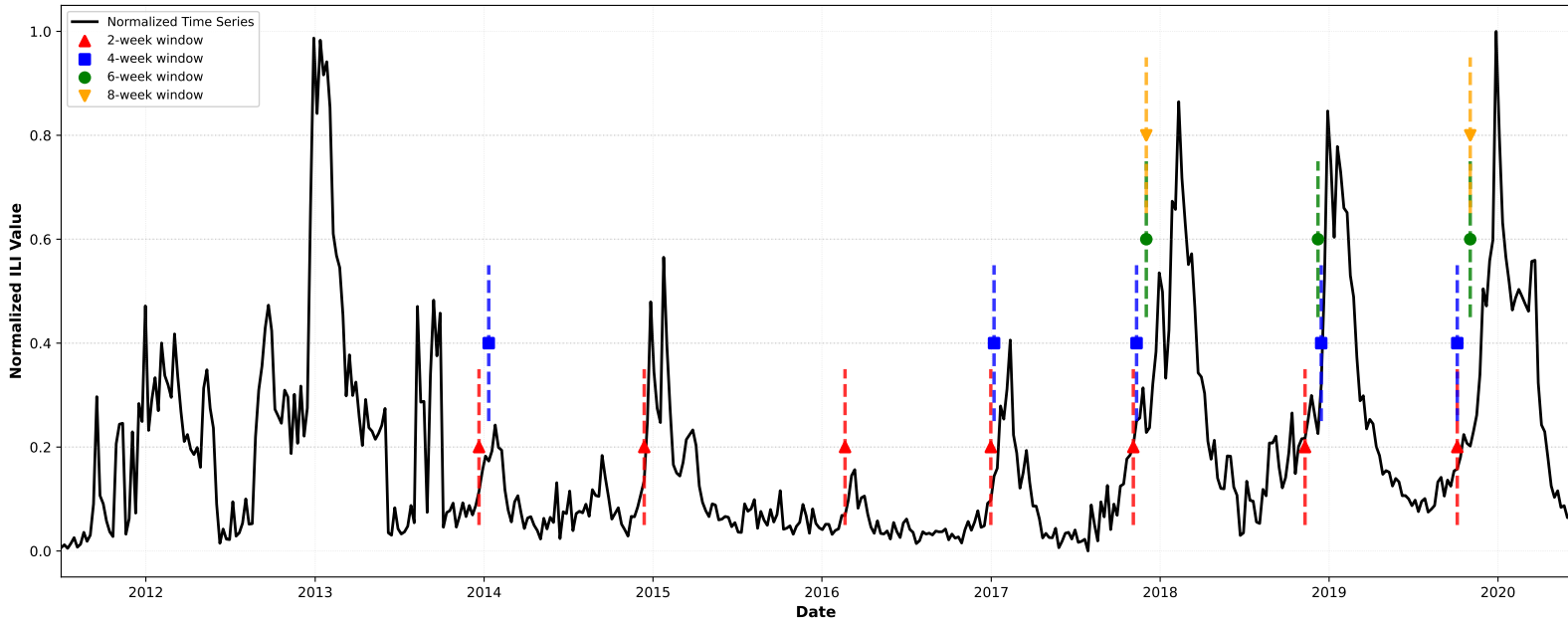
Missouri — Normalized ILI Time Series with Onset Markers



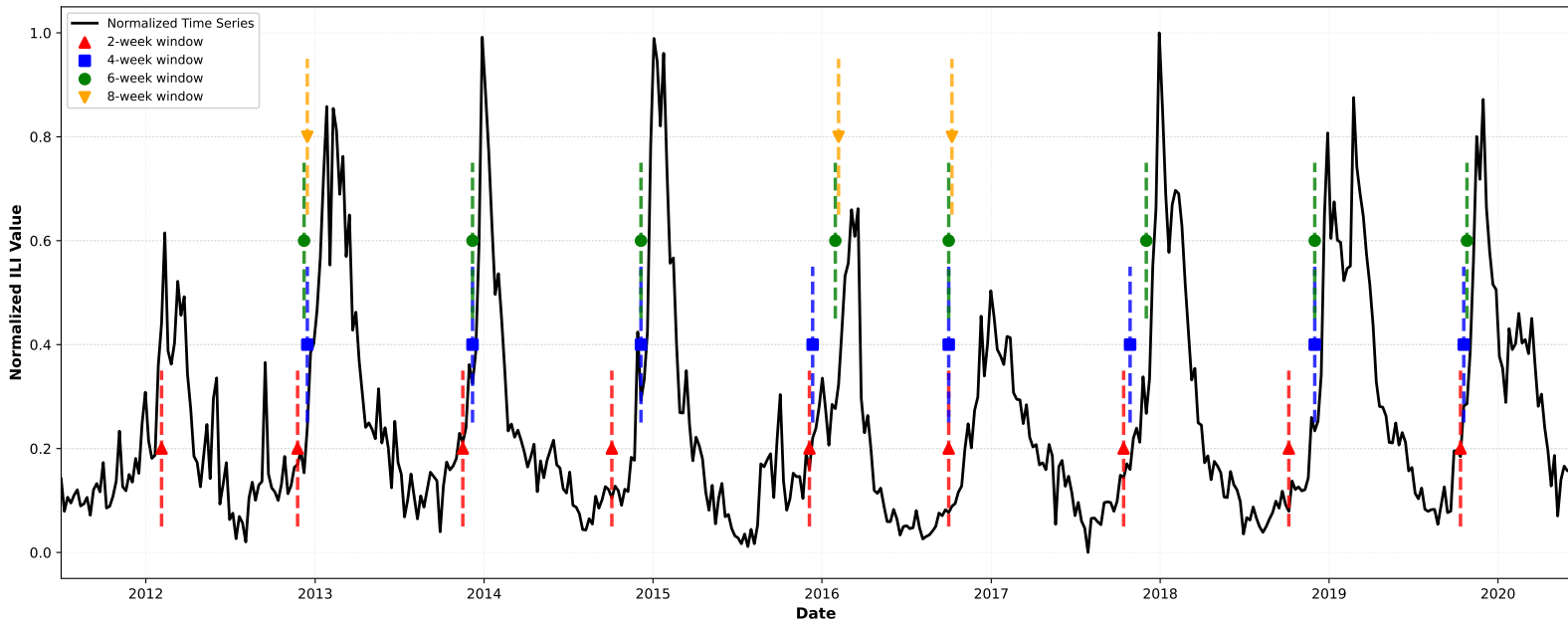
Montana — Normalized ILI Time Series with Onset Markers



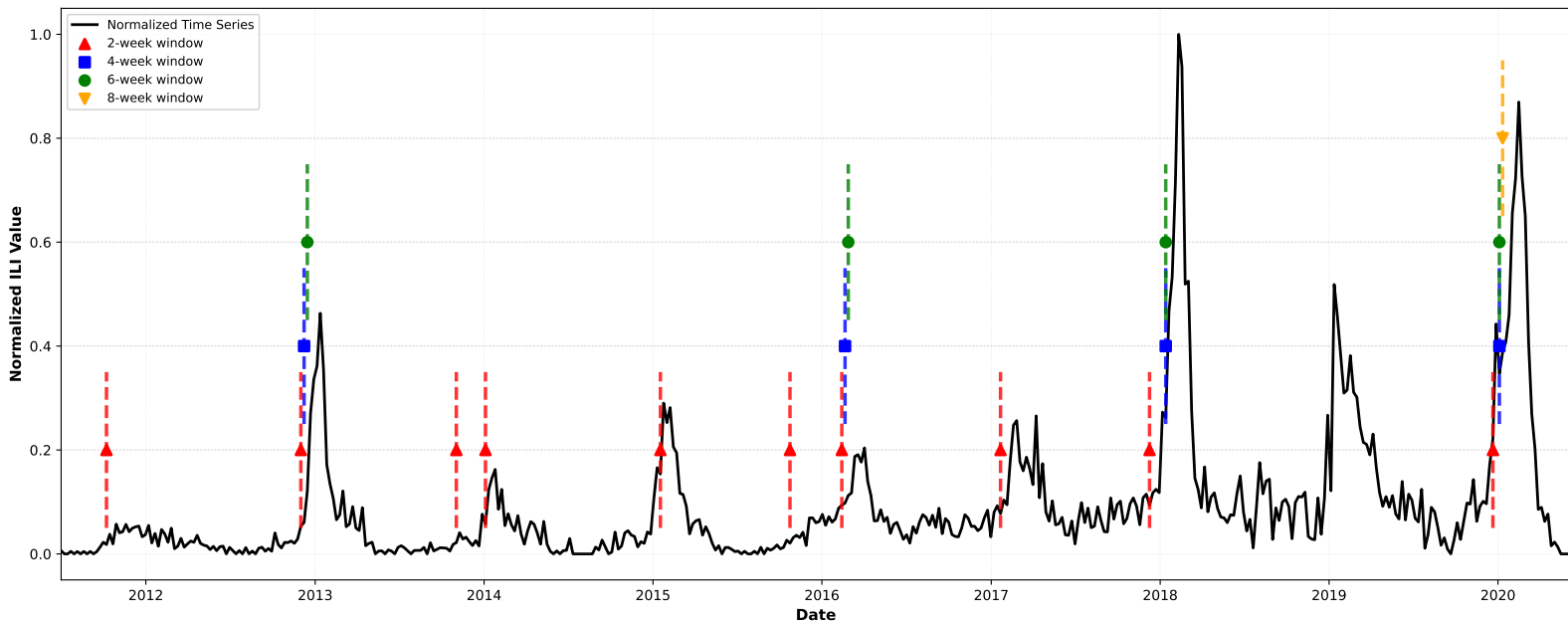
Nebraska — Normalized ILI Time Series with Onset Markers



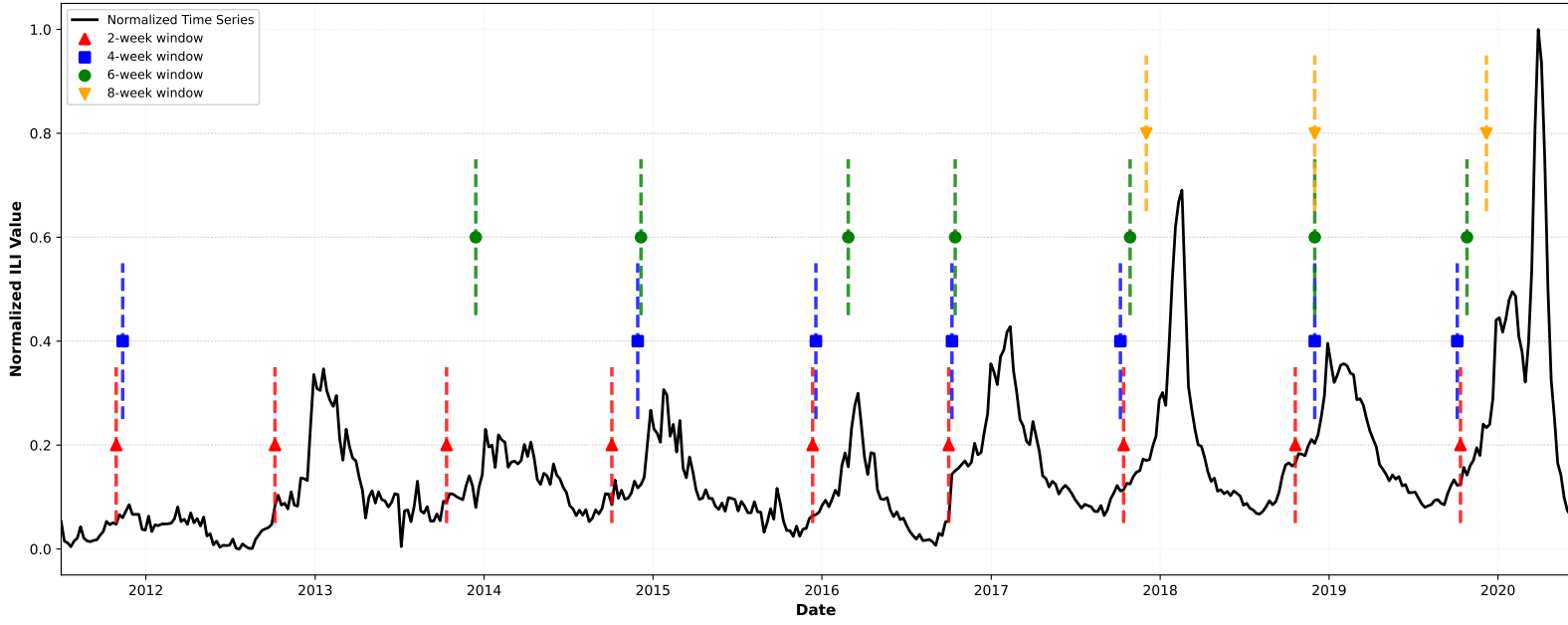
Nevada — Normalized ILI Time Series with Onset Markers



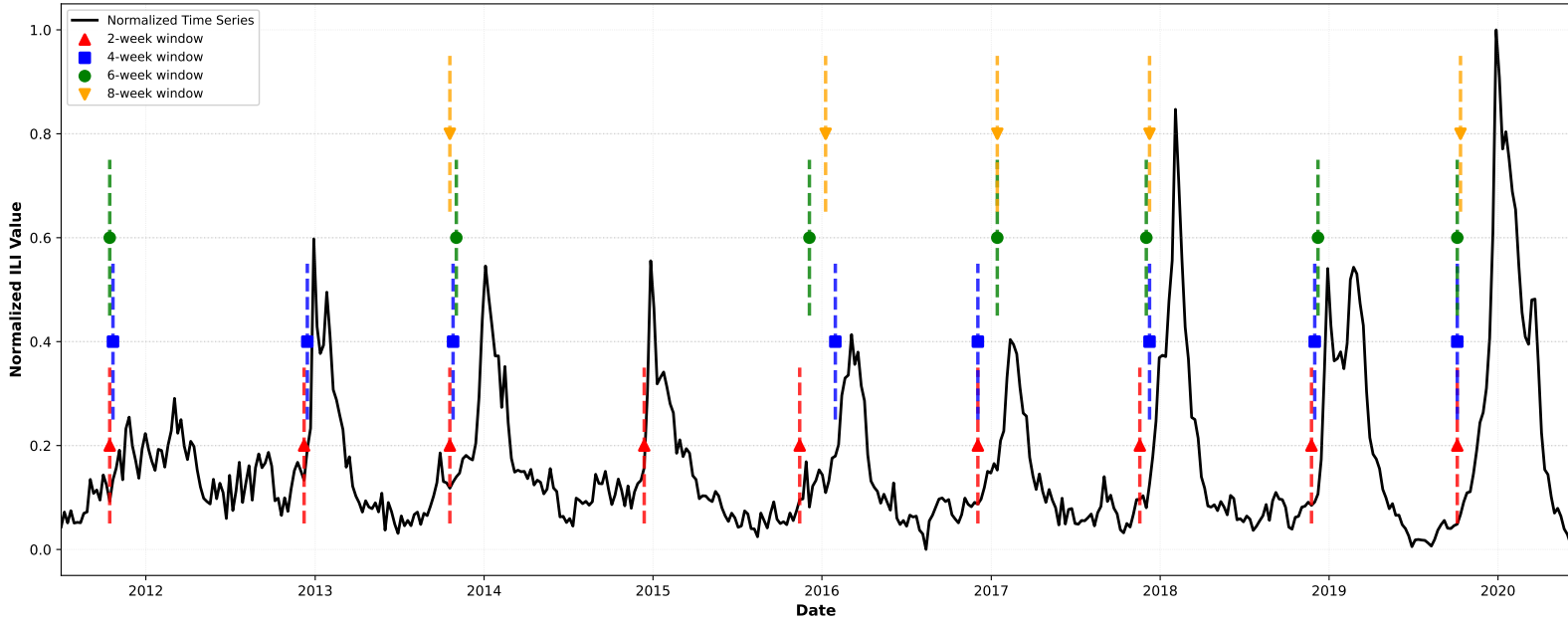
New Hampshire — Normalized ILI Time Series with Onset Markers



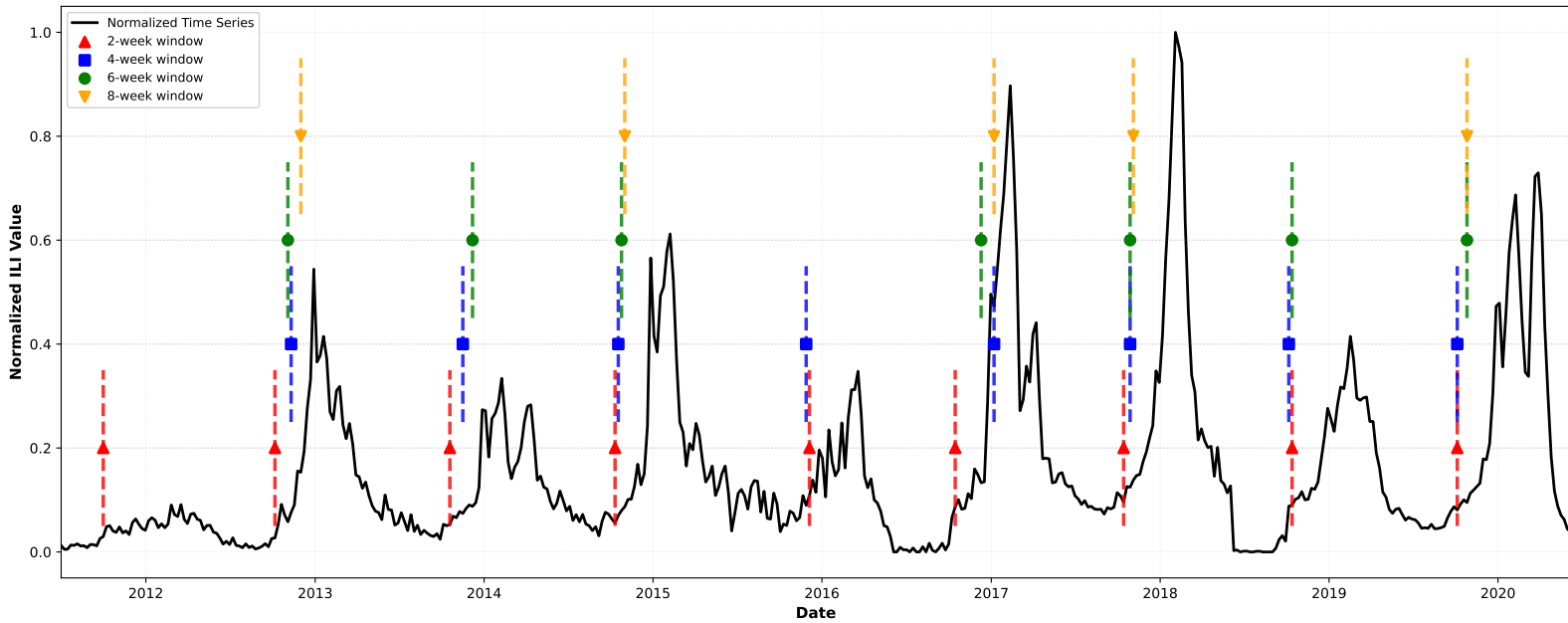
New Jersey — Normalized ILI Time Series with Onset Markers



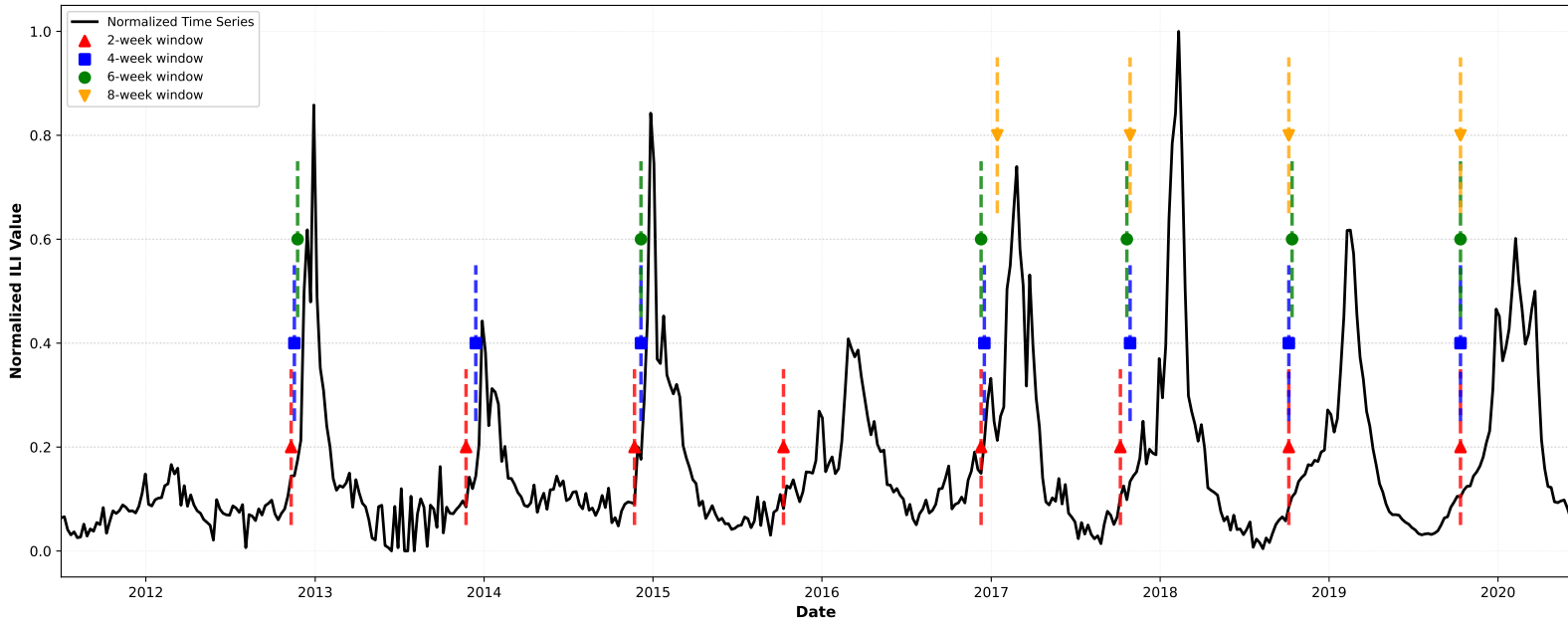
New Mexico — Normalized ILI Time Series with Onset Markers



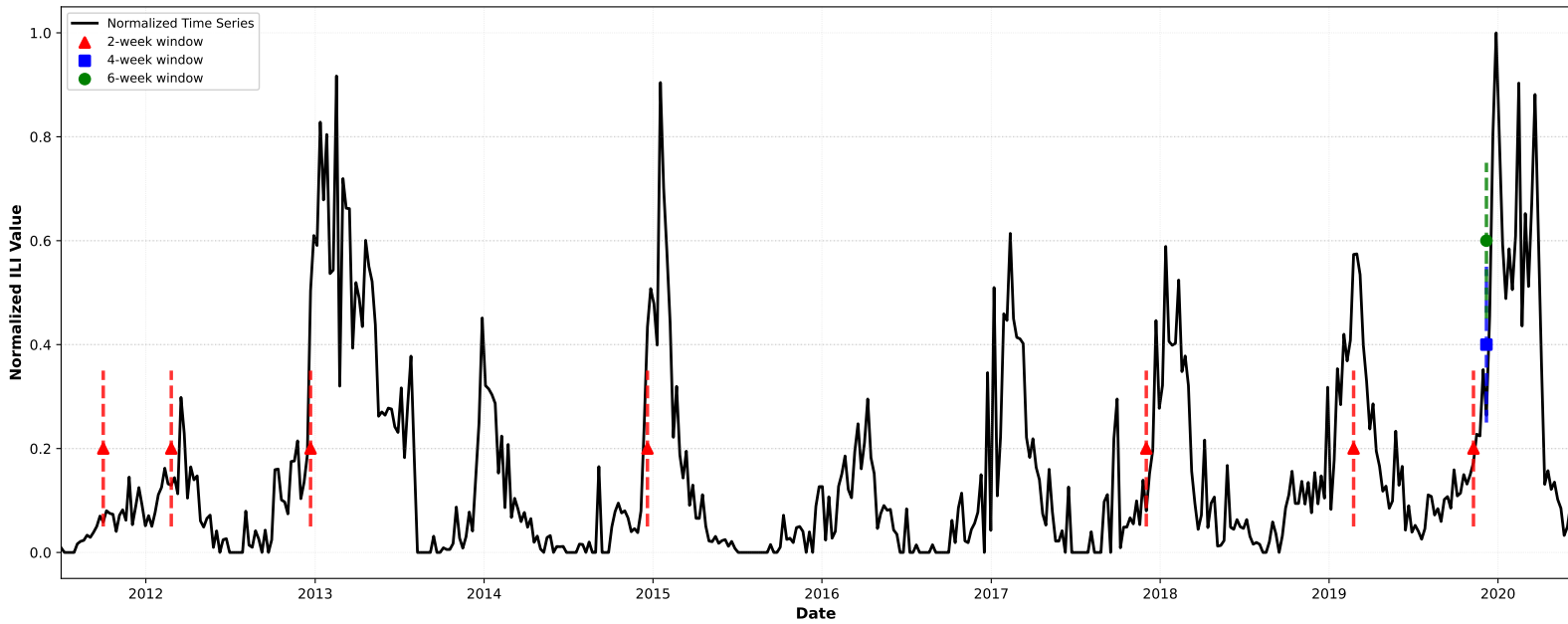
New York — Normalized ILI Time Series with Onset Markers



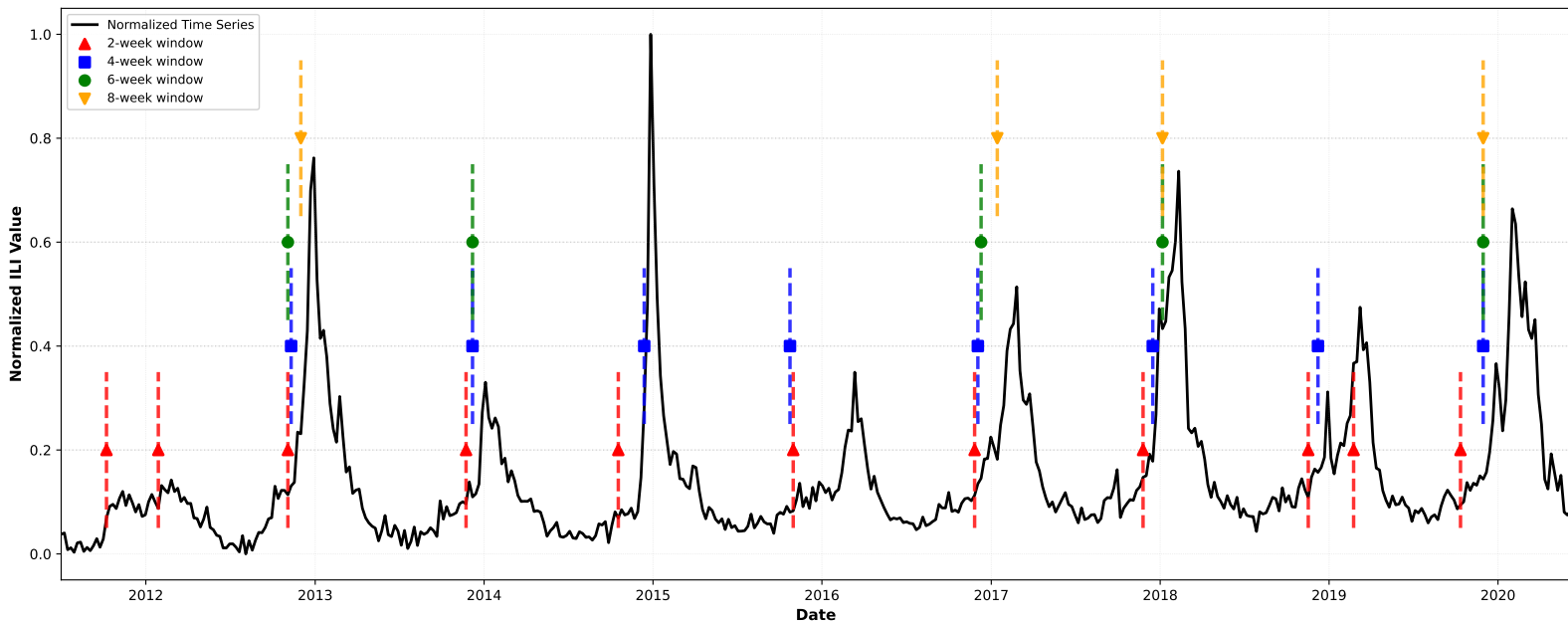
North Carolina — Normalized ILI Time Series with Onset Markers



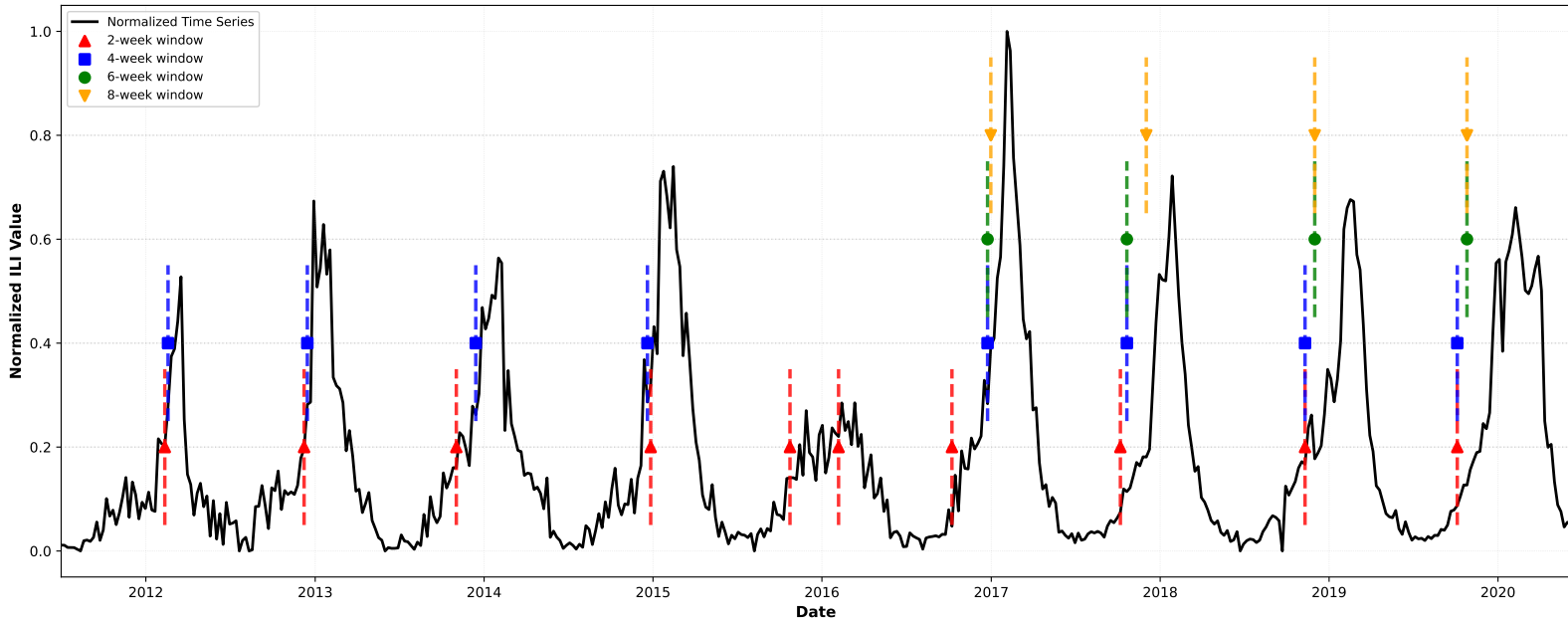
North Dakota — Normalized ILI Time Series with Onset Markers



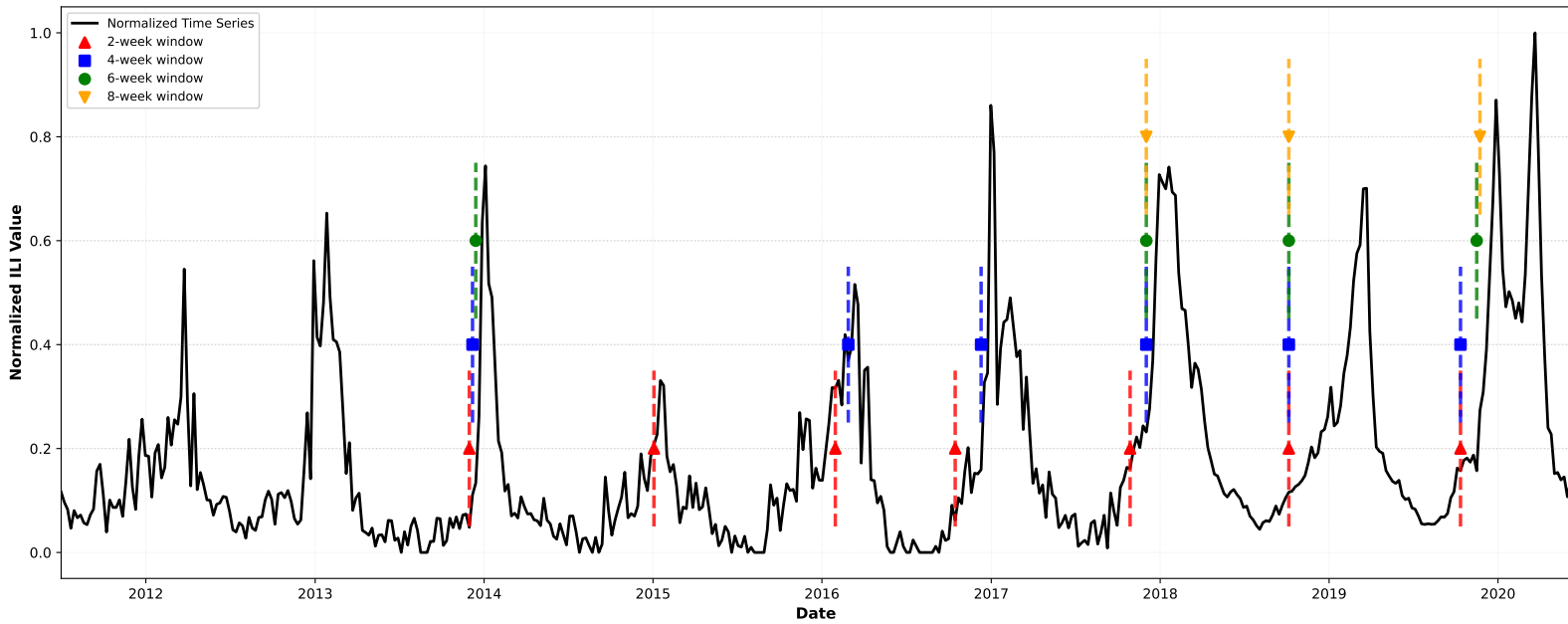
Ohio — Normalized ILI Time Series with Onset Markers



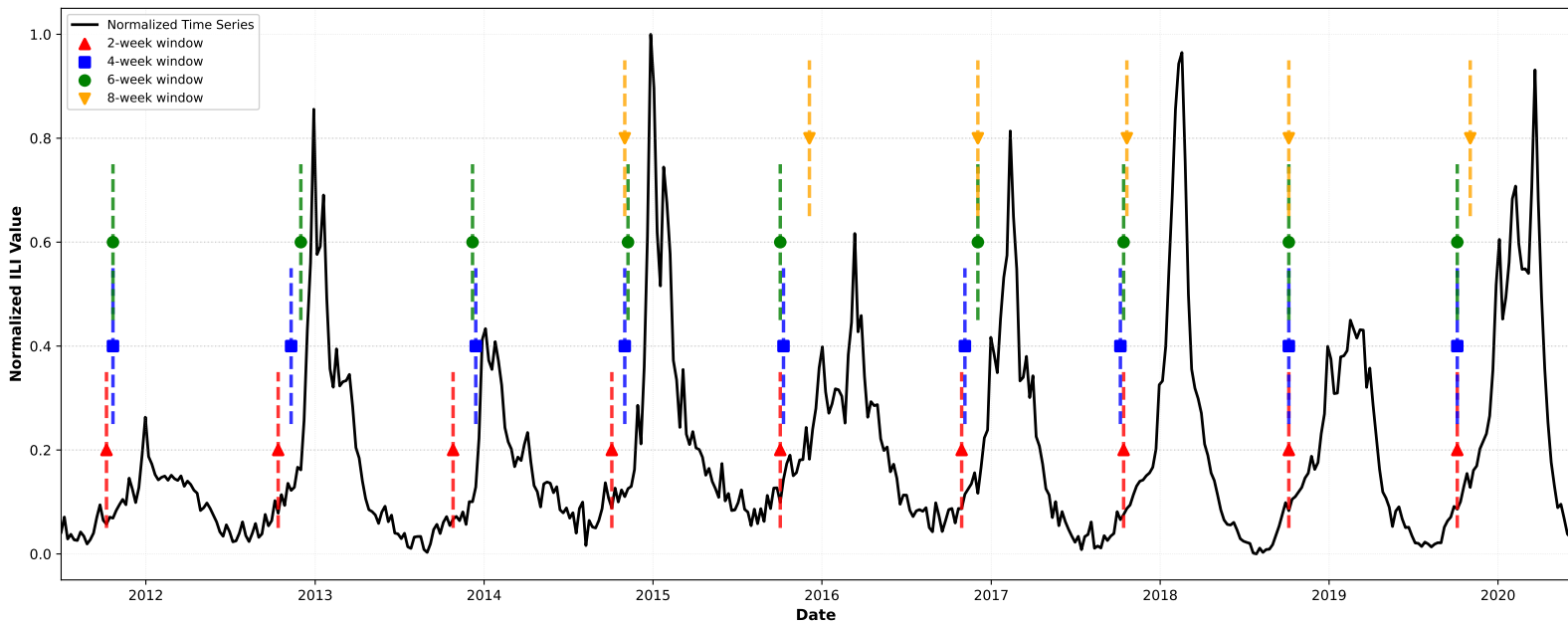
Oklahoma — Normalized ILI Time Series with Onset Markers



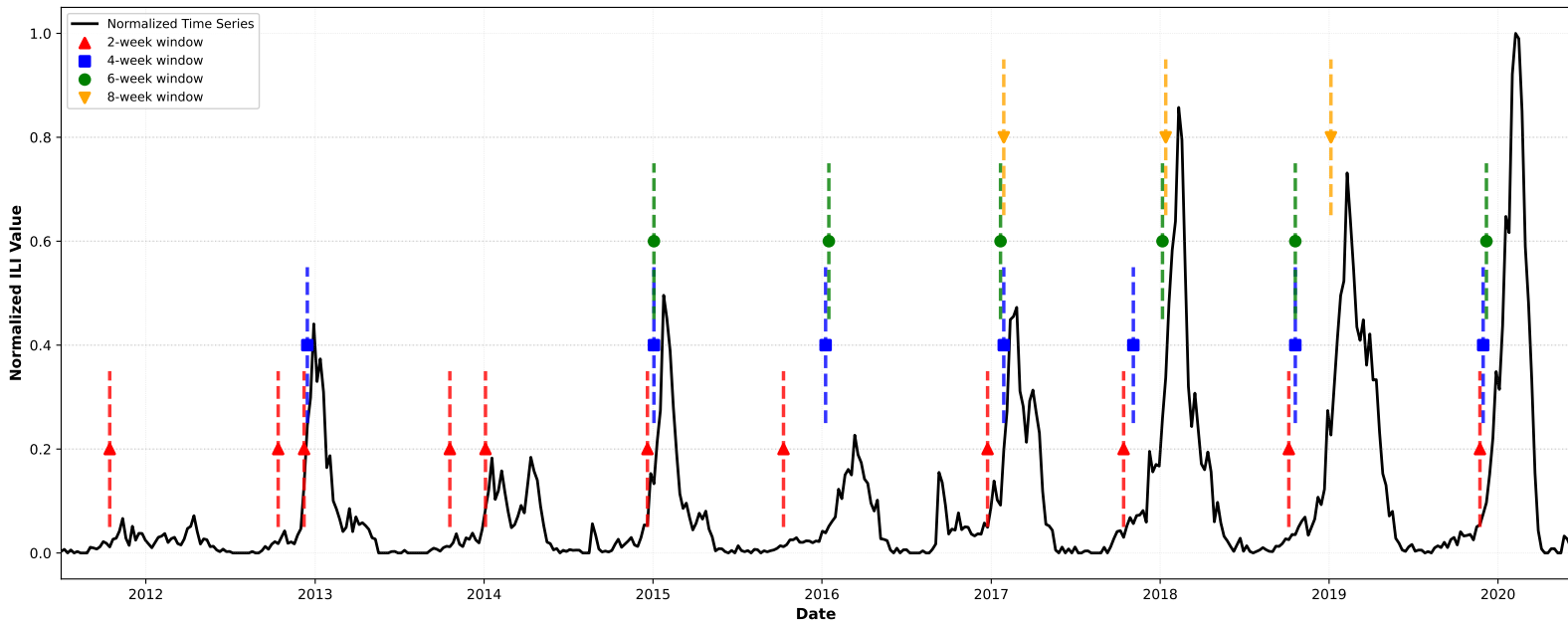
Oregon — Normalized ILI Time Series with Onset Markers



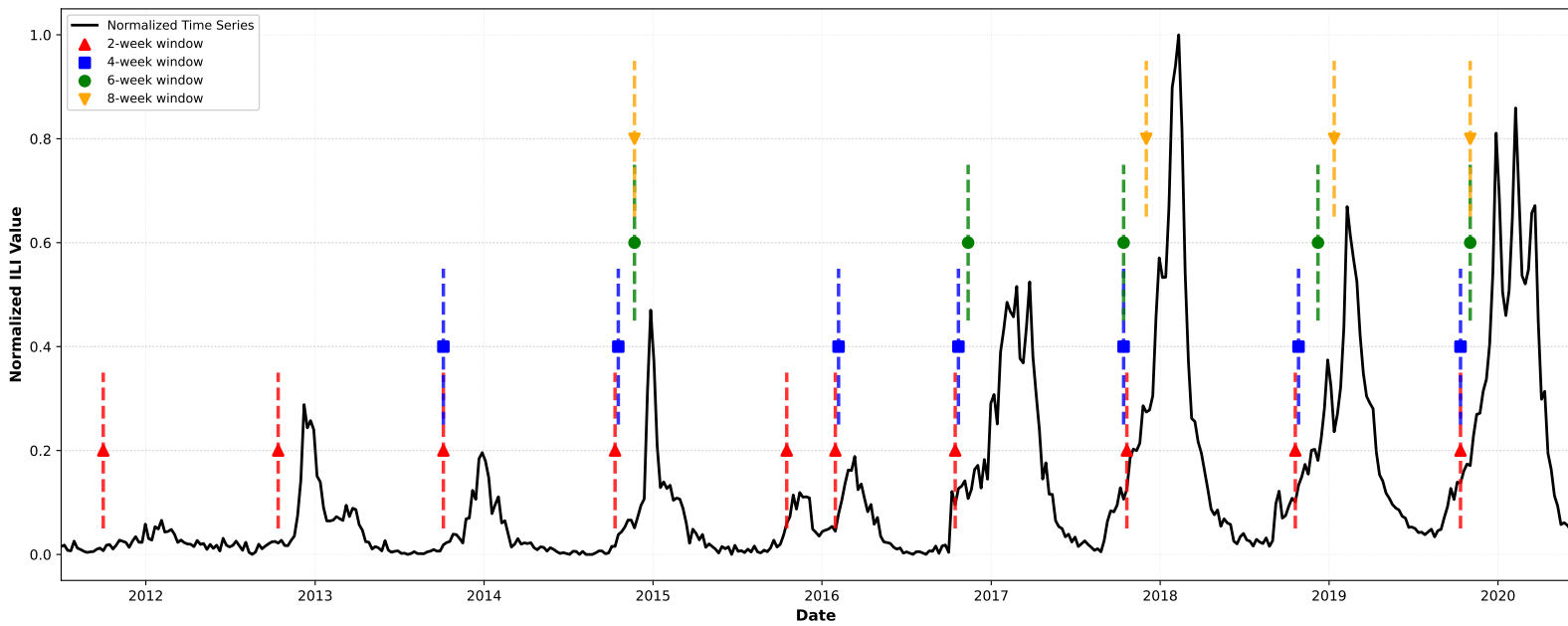
Pennsylvania — Normalized ILI Time Series with Onset Markers



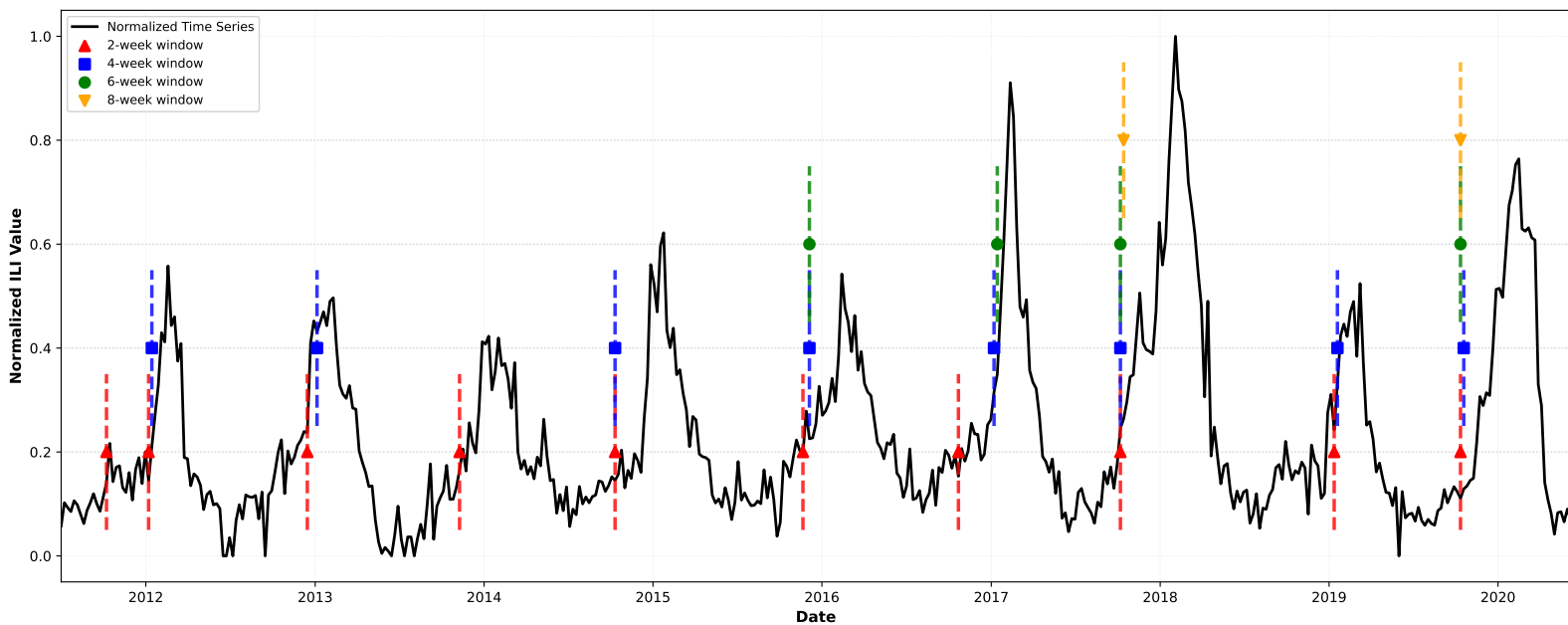
Rhode Island — Normalized ILI Time Series with Onset Markers



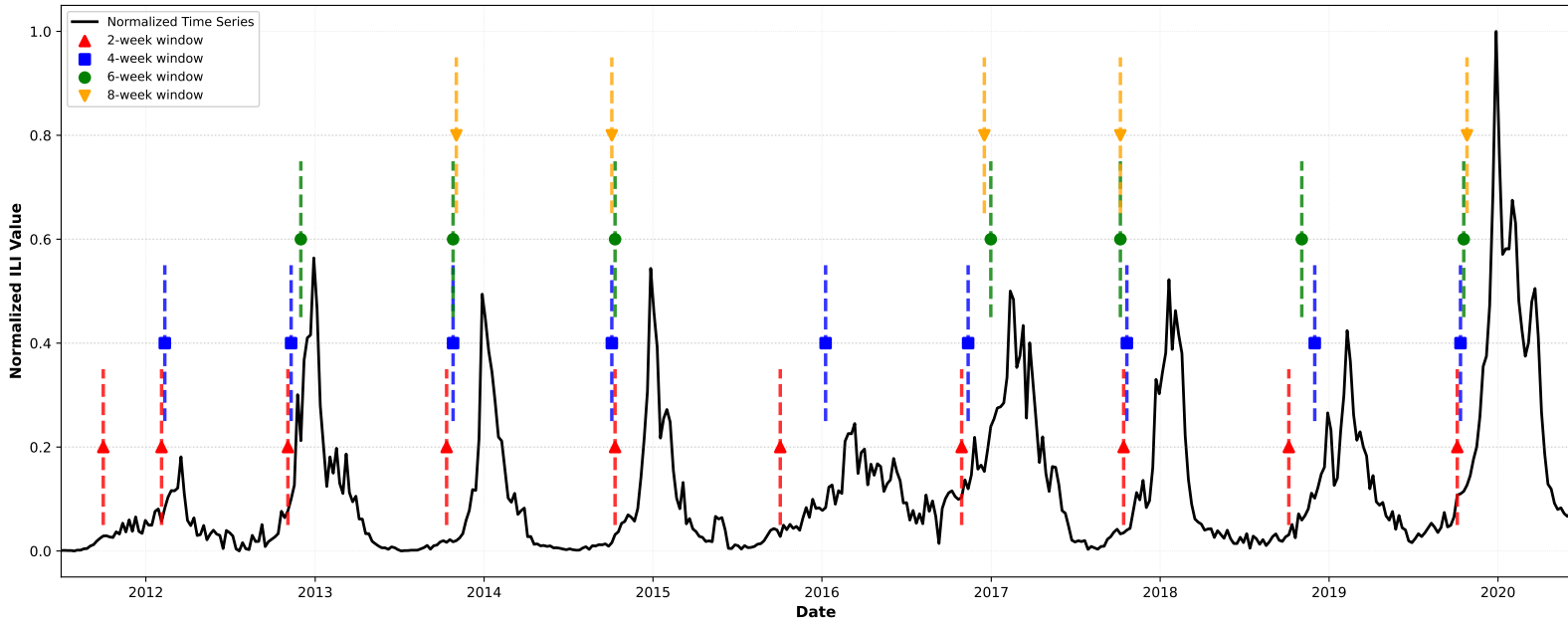
South Carolina — Normalized ILI Time Series with Onset Markers



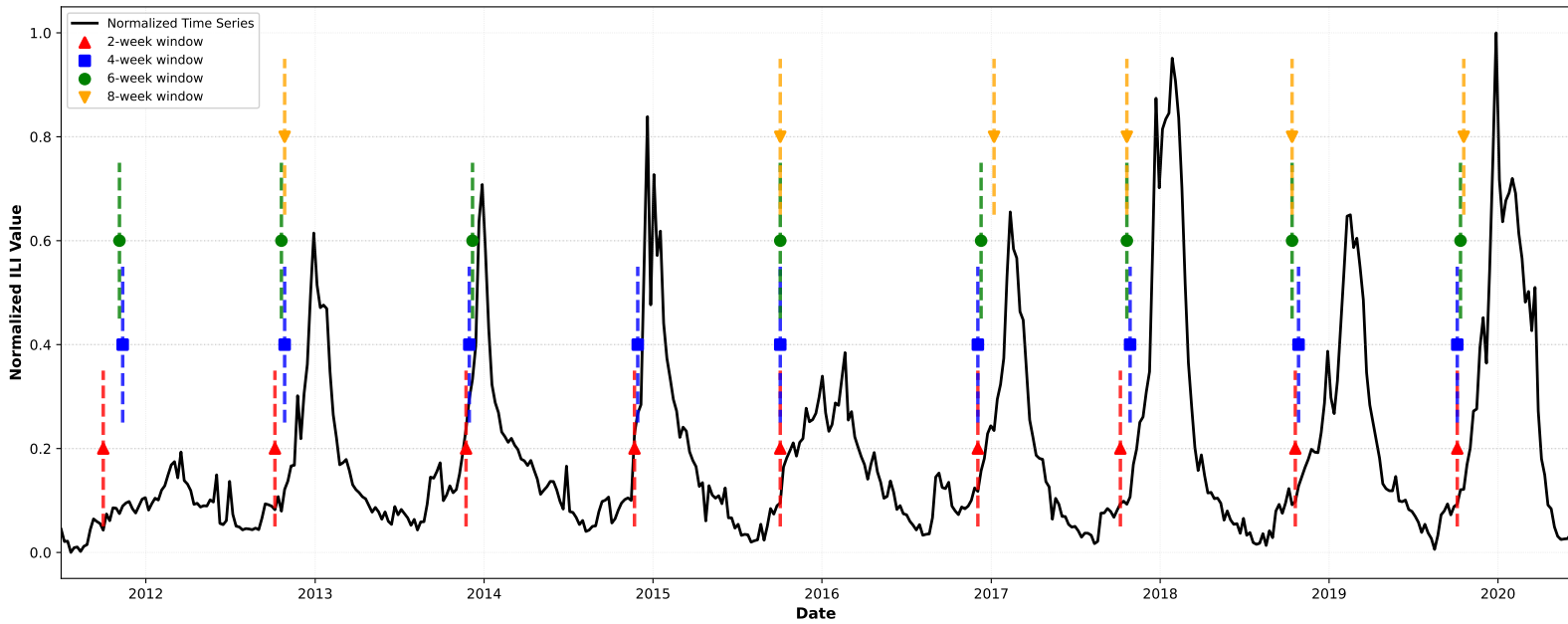
South Dakota — Normalized ILI Time Series with Onset Markers



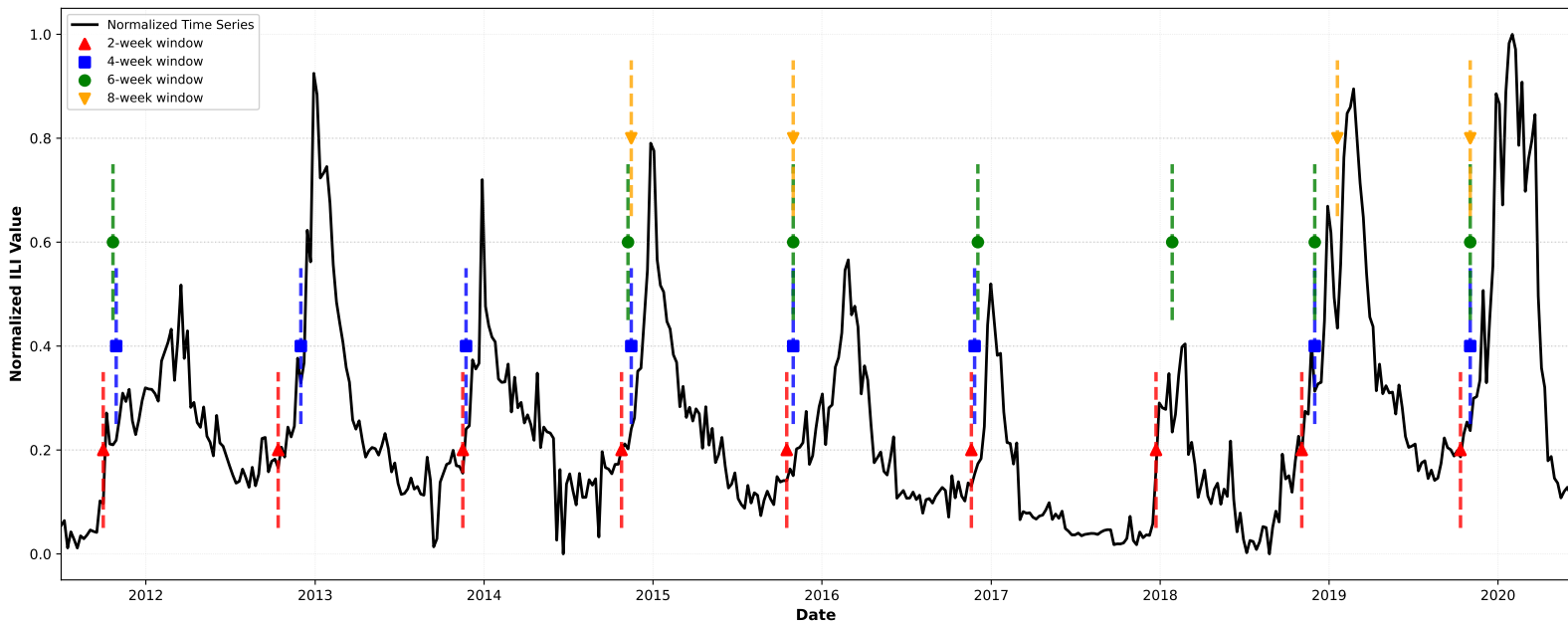
Tennessee — Normalized ILI Time Series with Onset Markers



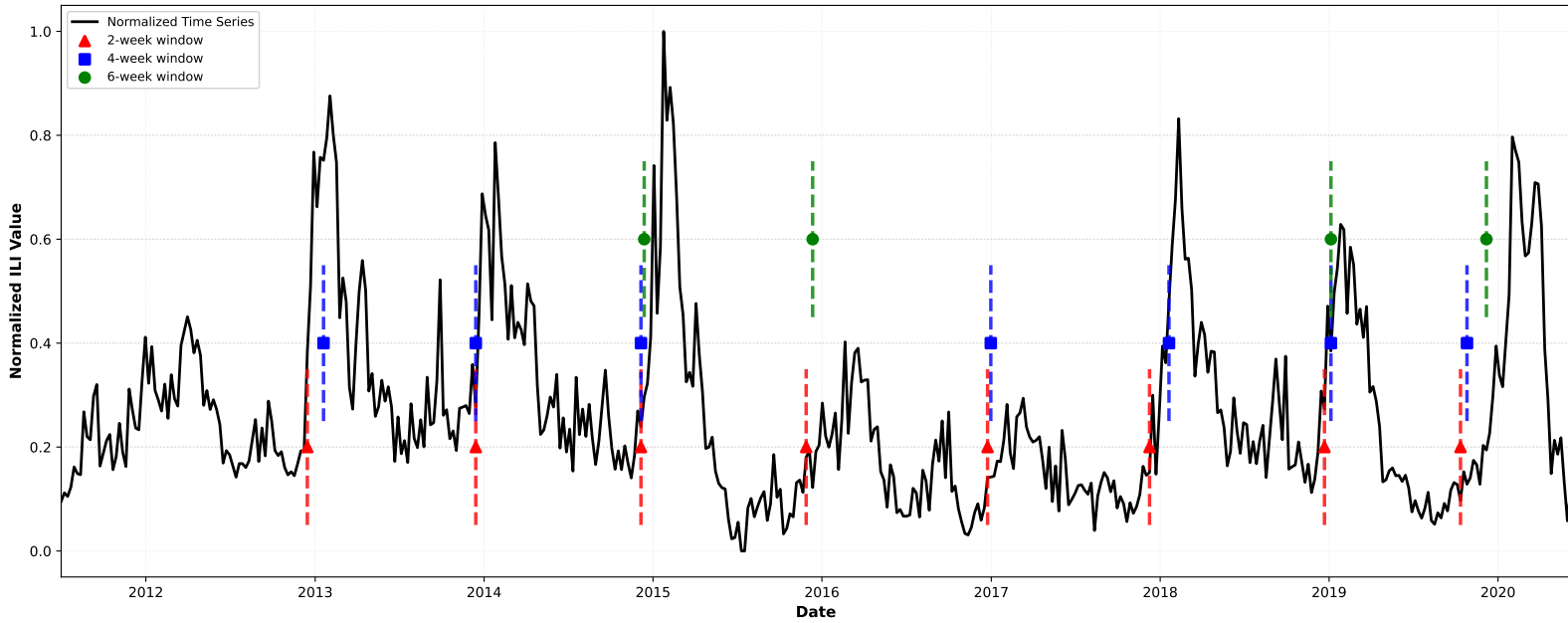
Texas — Normalized ILI Time Series with Onset Markers



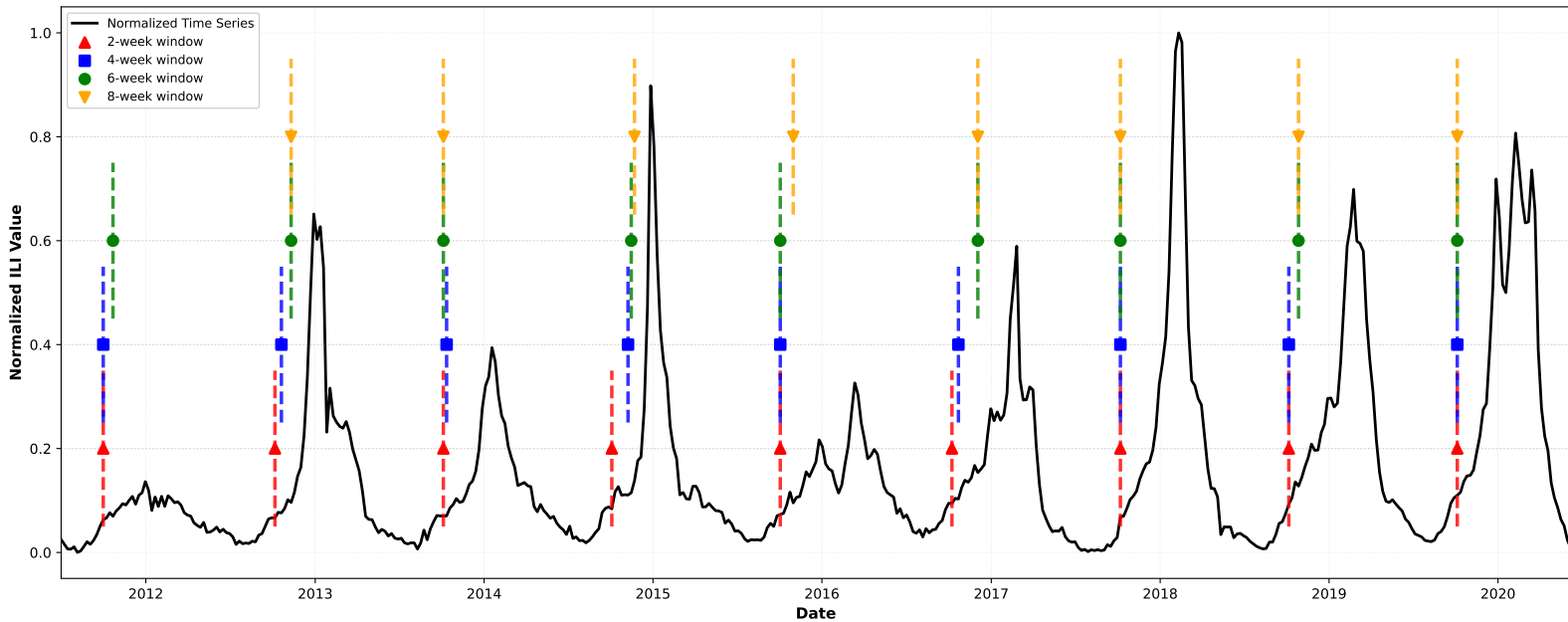
Utah — Normalized ILI Time Series with Onset Markers



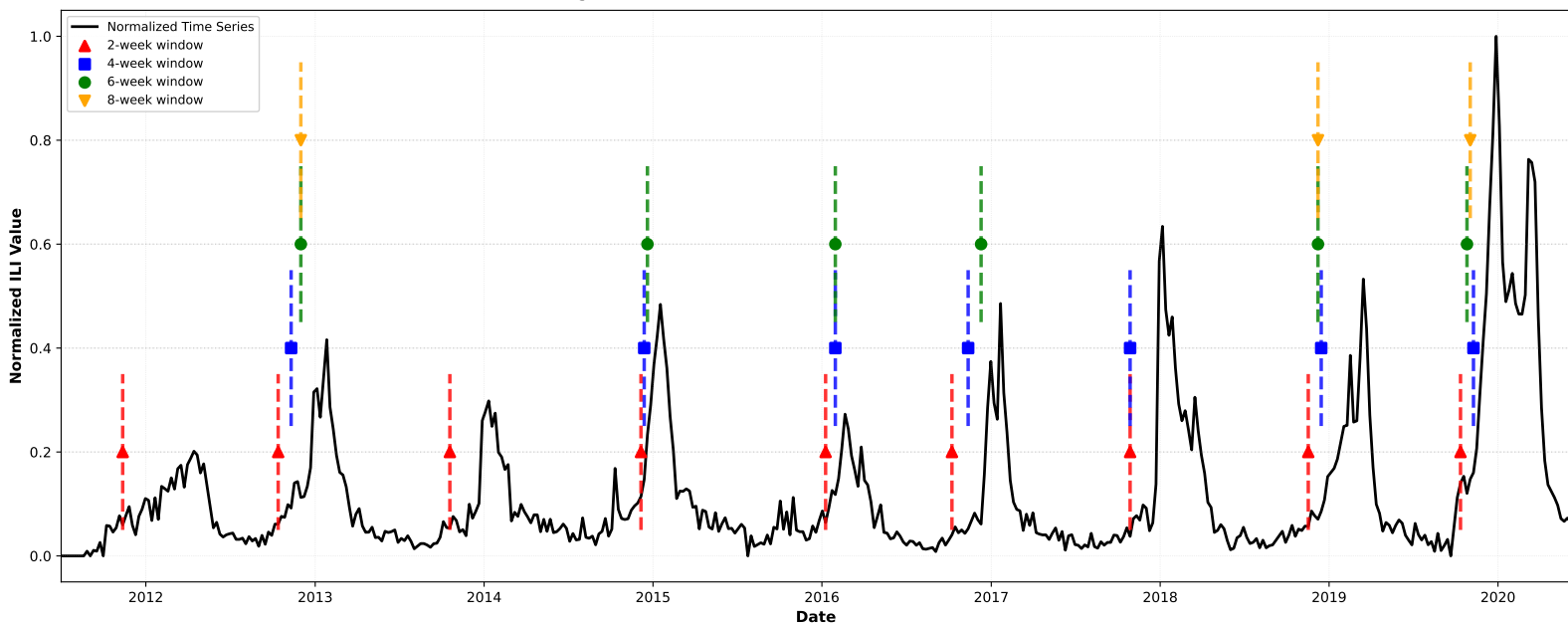
Vermont — Normalized ILI Time Series with Onset Markers



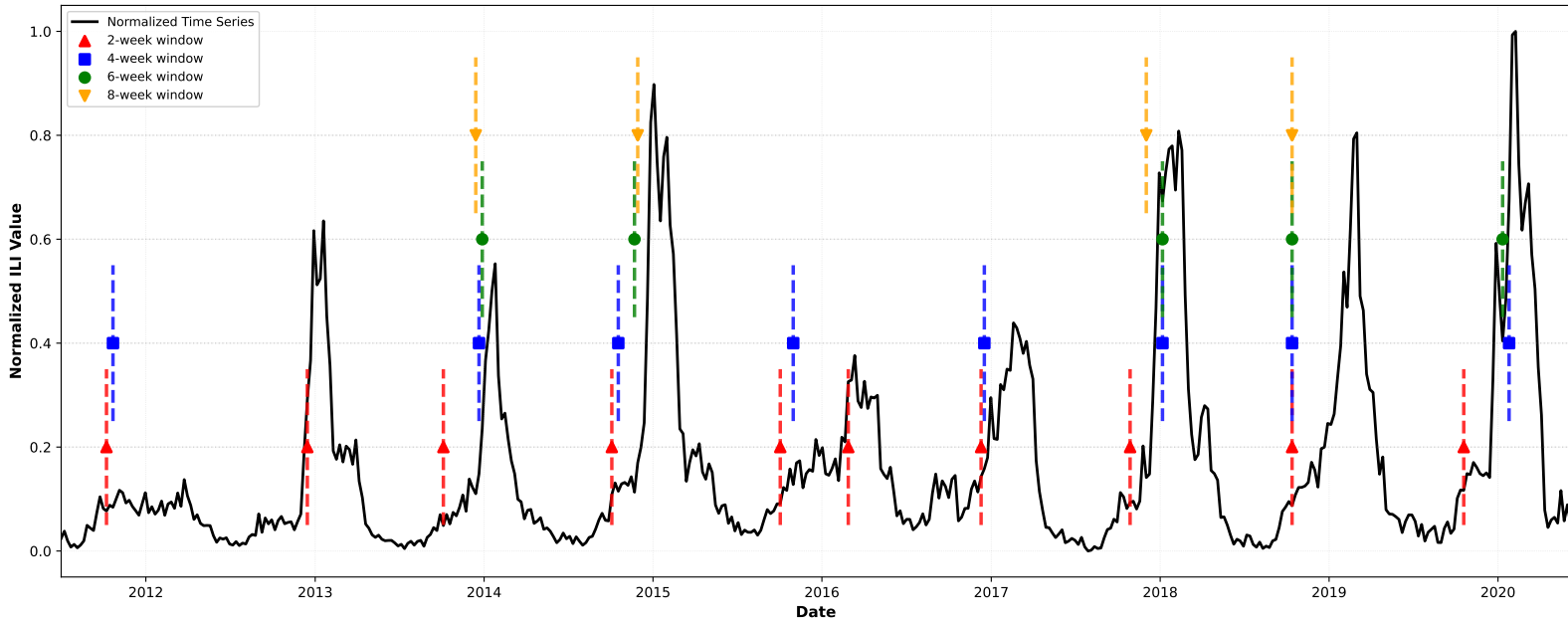
Virginia — Normalized ILI Time Series with Onset Markers



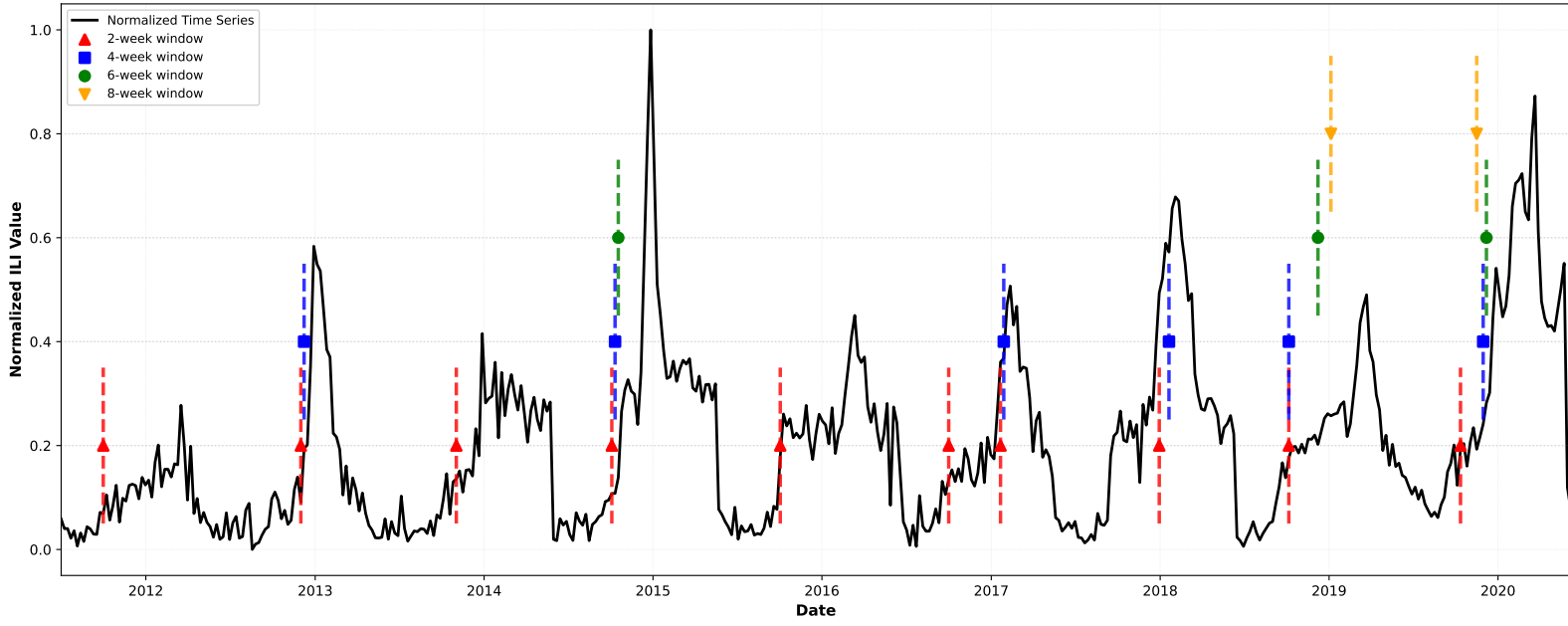
Washington — Normalized ILI Time Series with Onset Markers



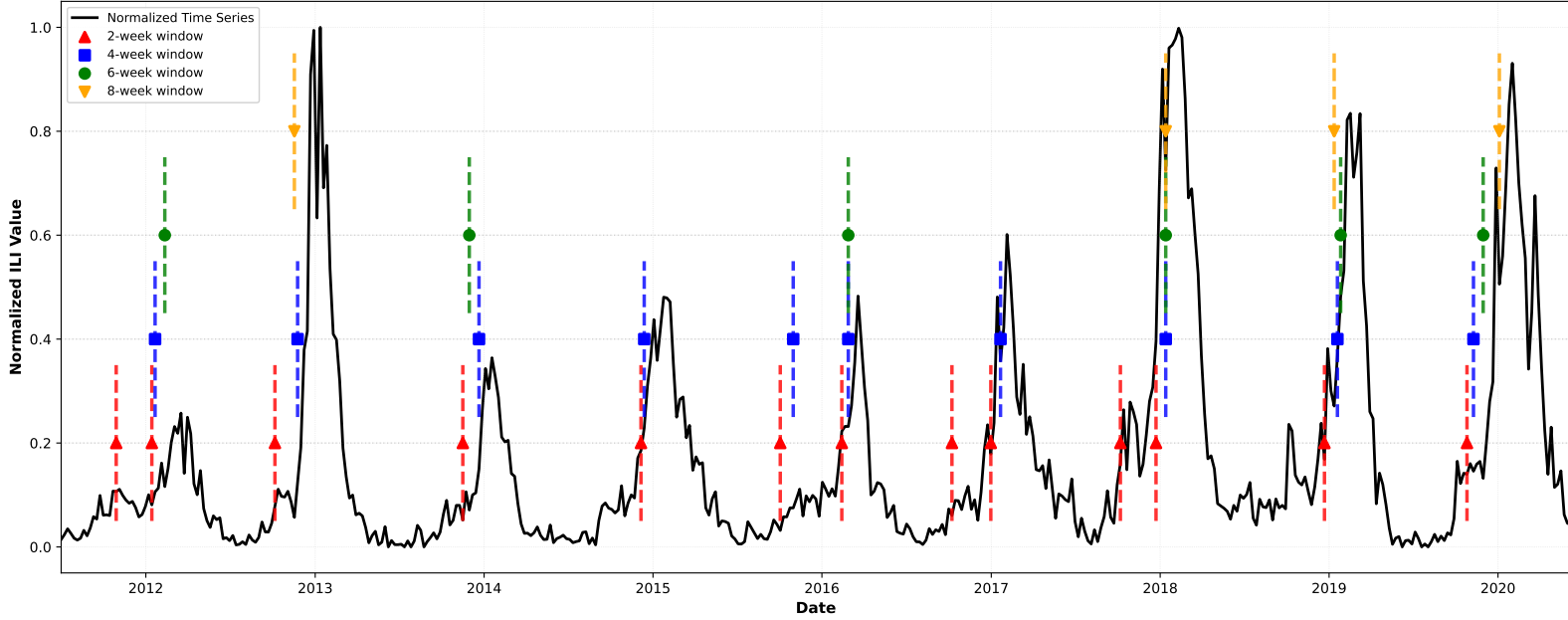
West Virginia — Normalized ILI Time Series with Onset Markers



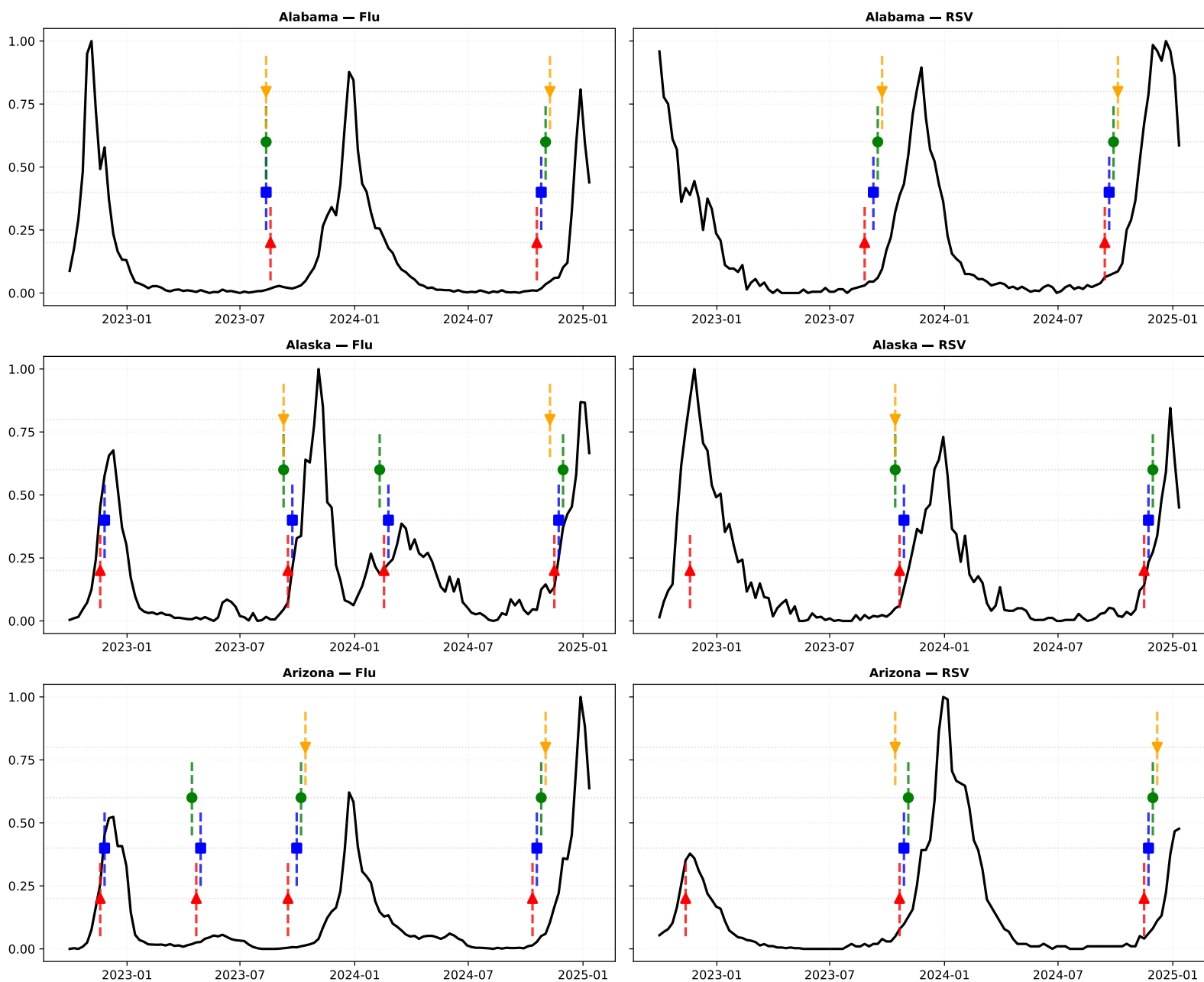
Wisconsin — Normalized ILI Time Series with Onset Markers



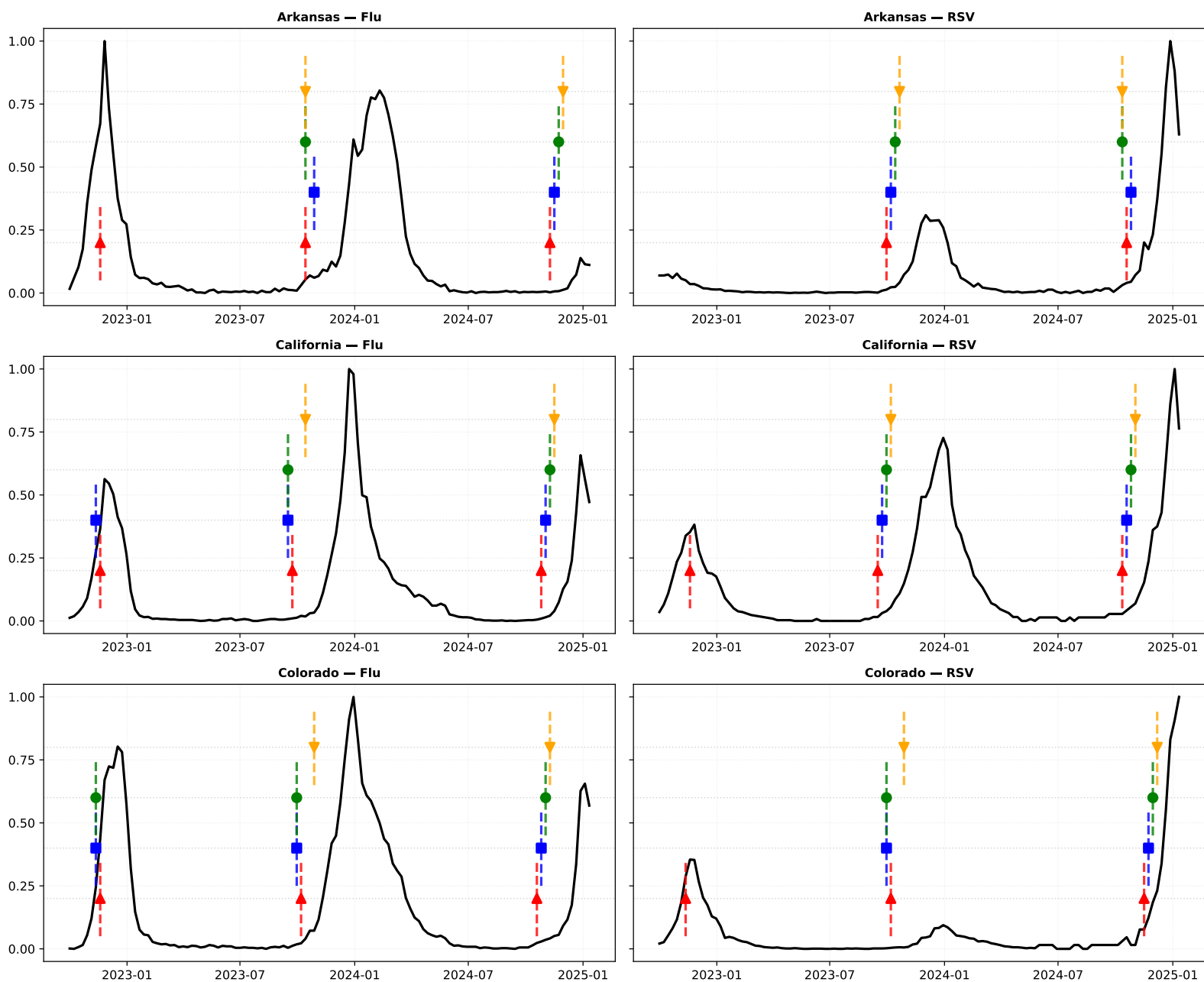
Wyoming — Normalized ILI Time Series with Onset Markers



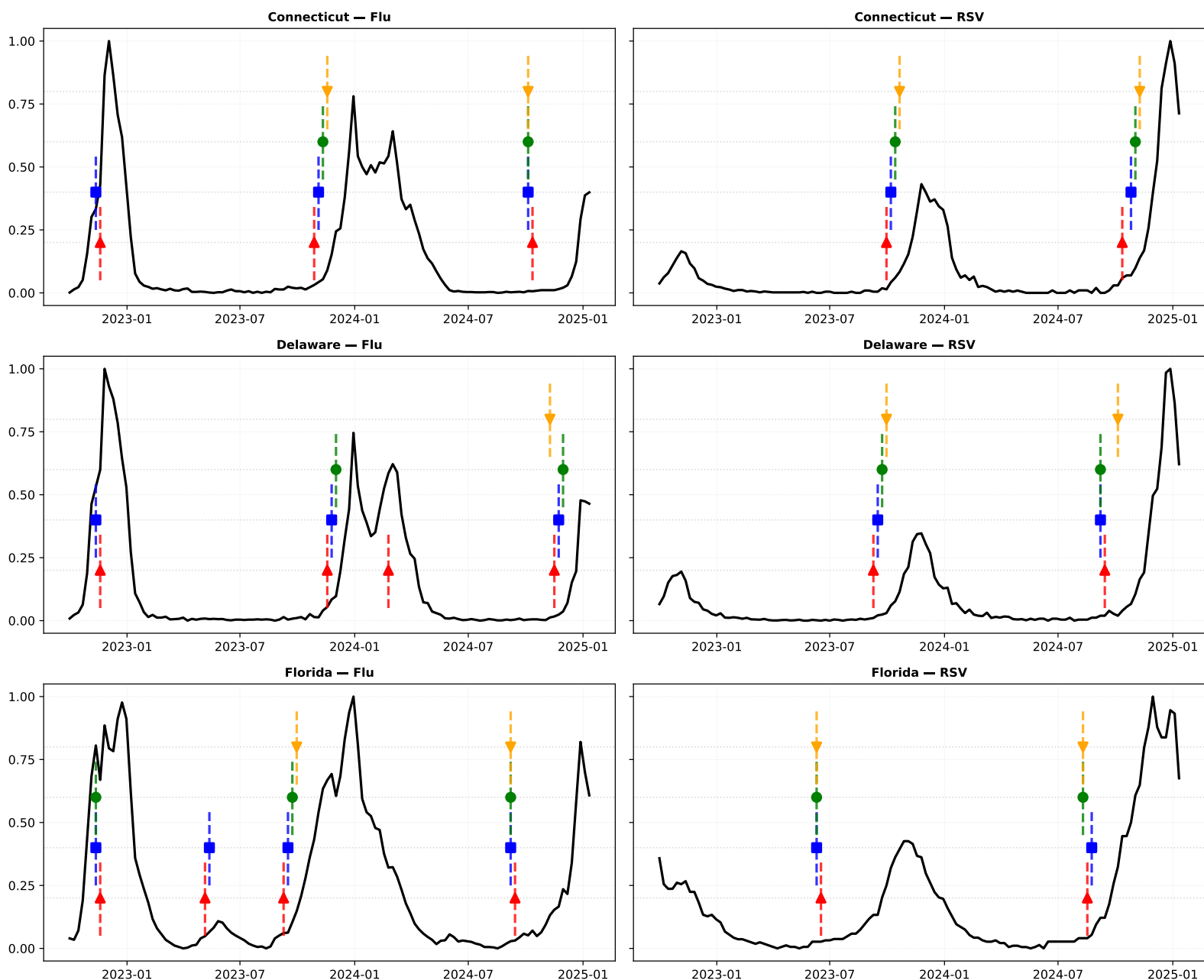
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window



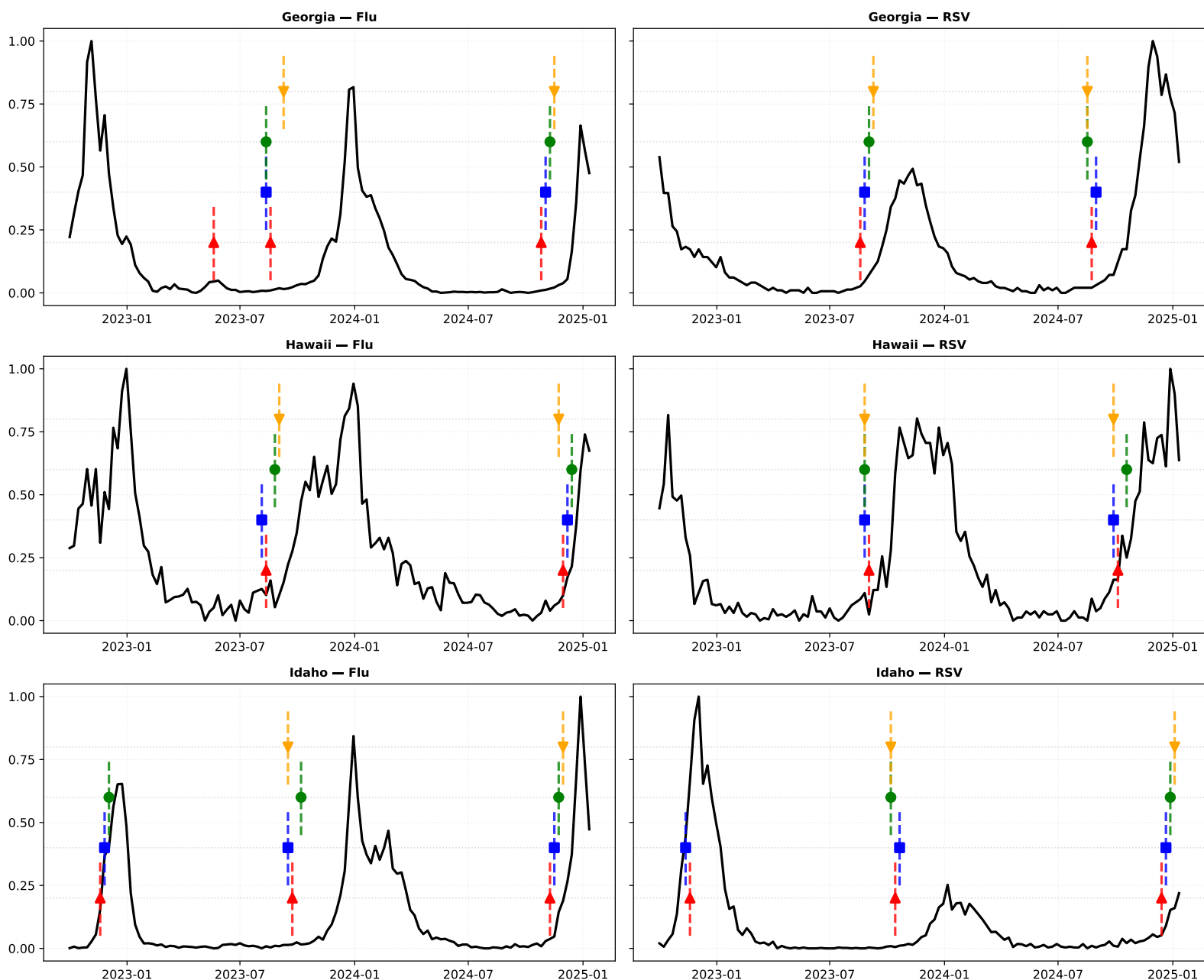
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window



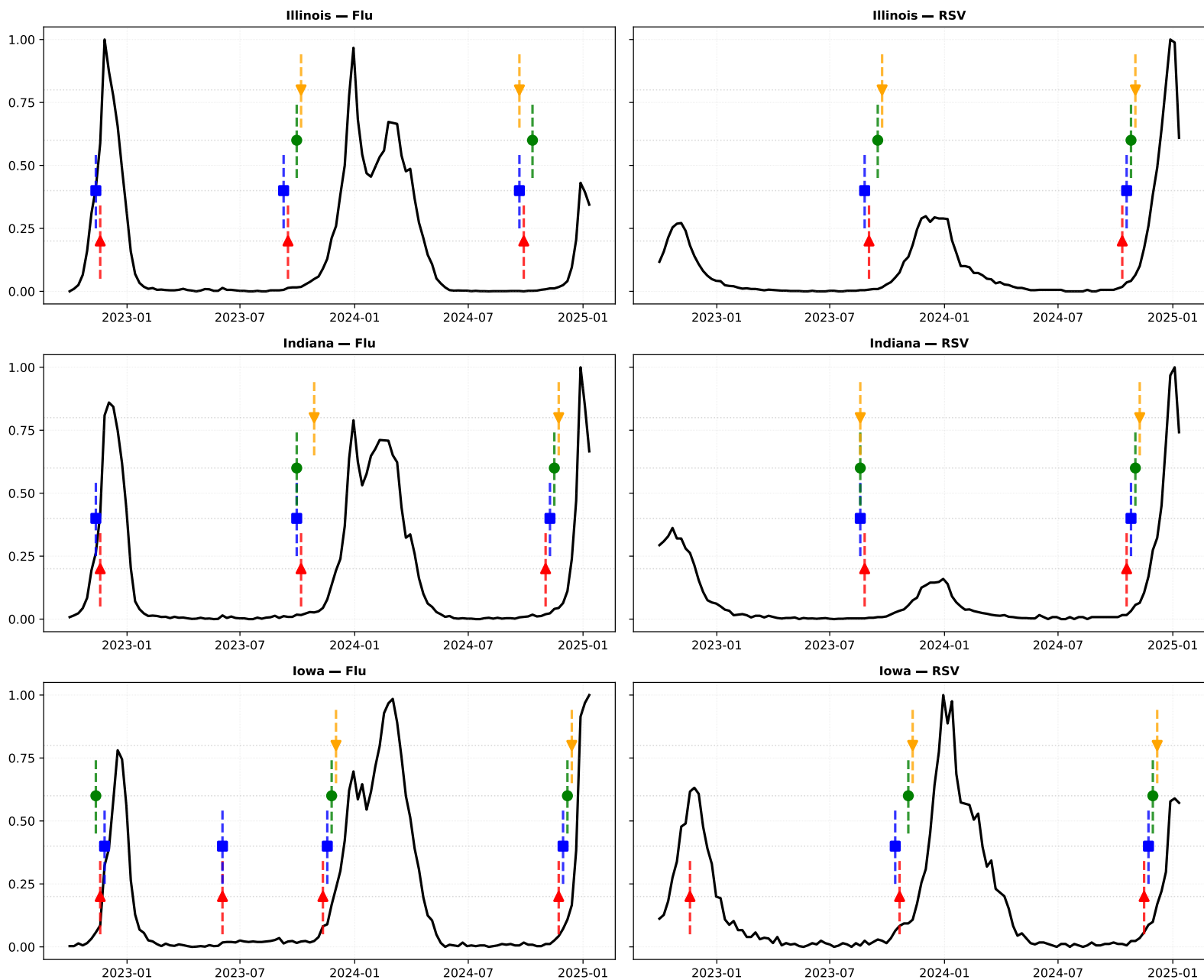
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window



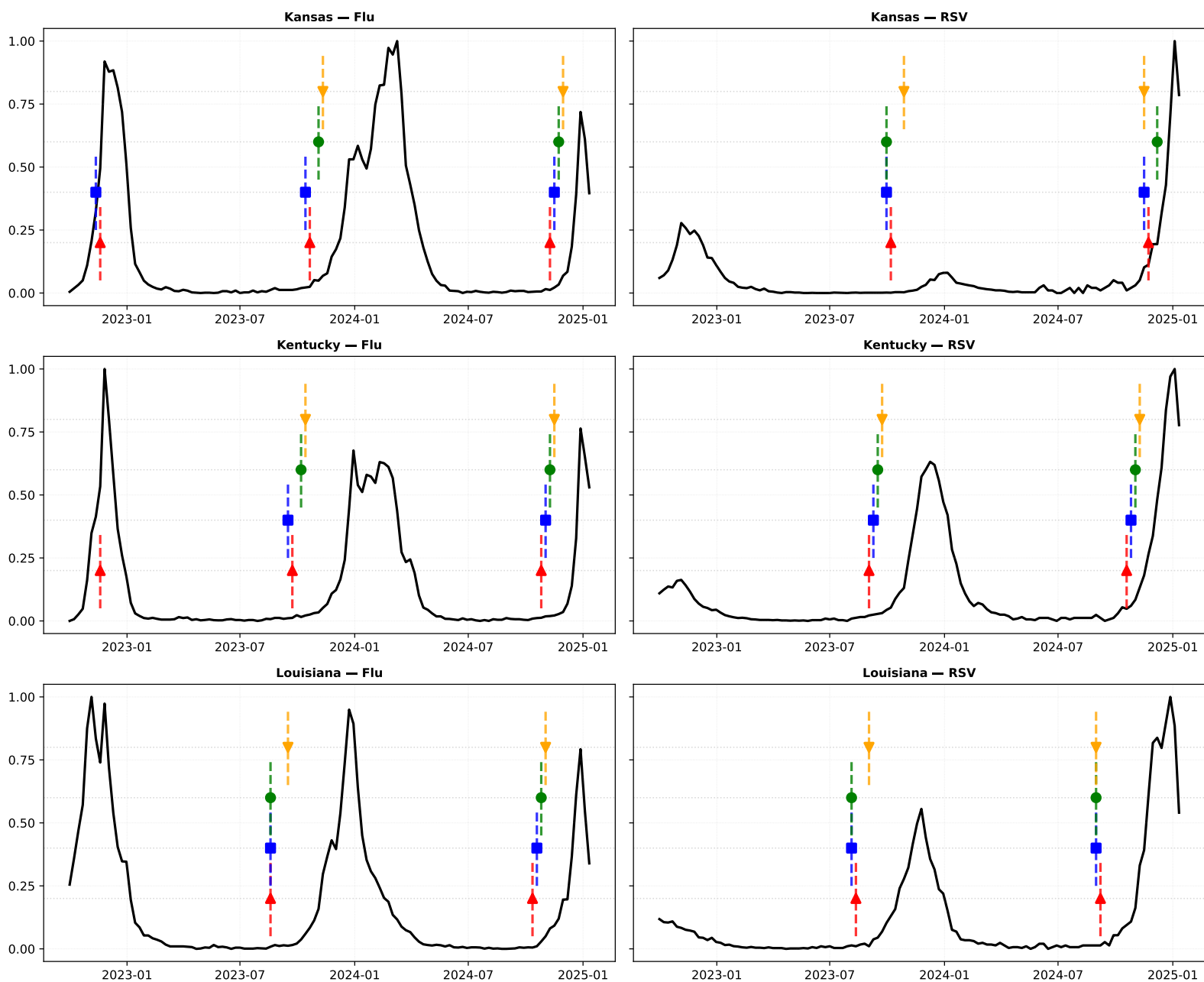
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window

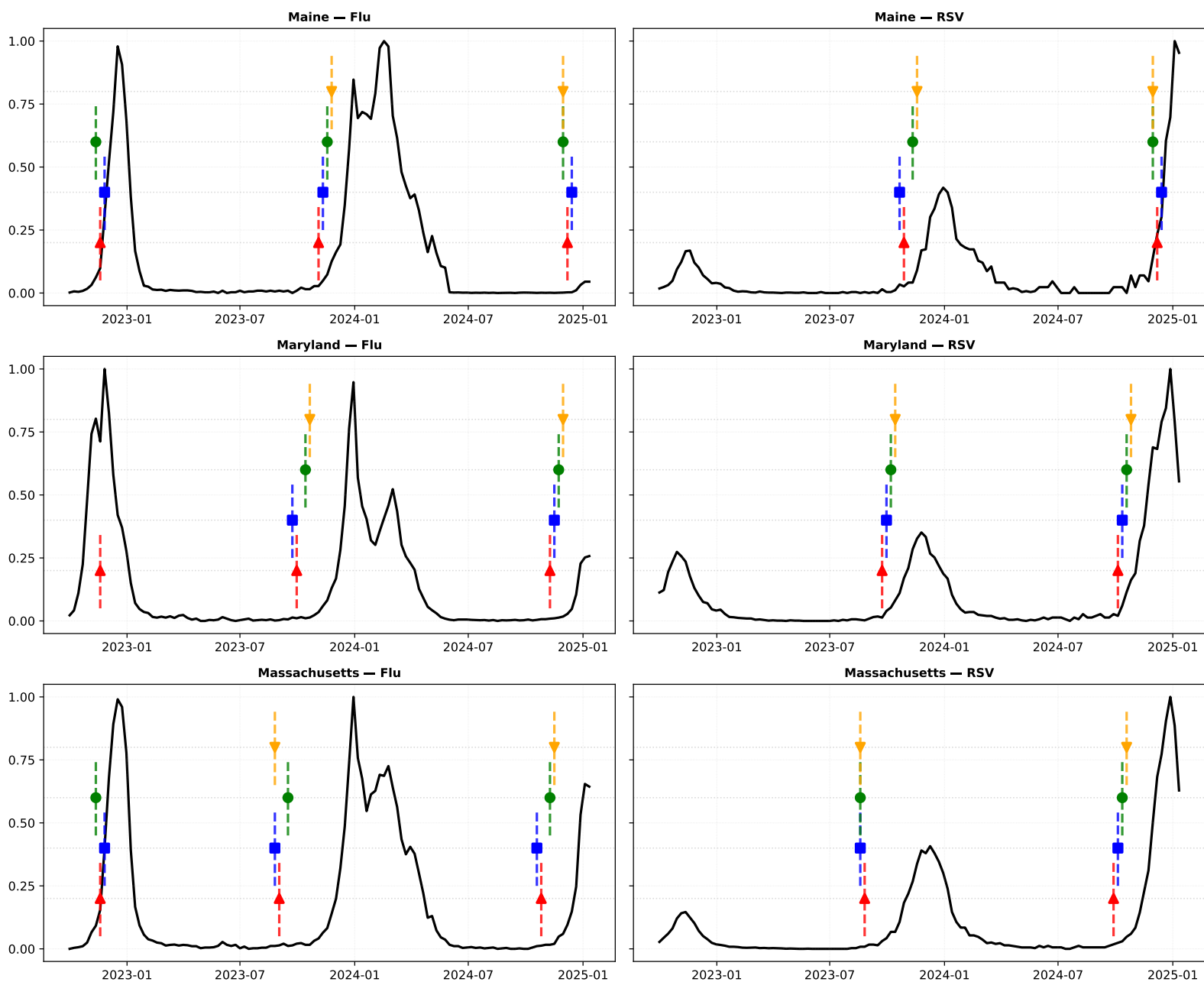


—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window

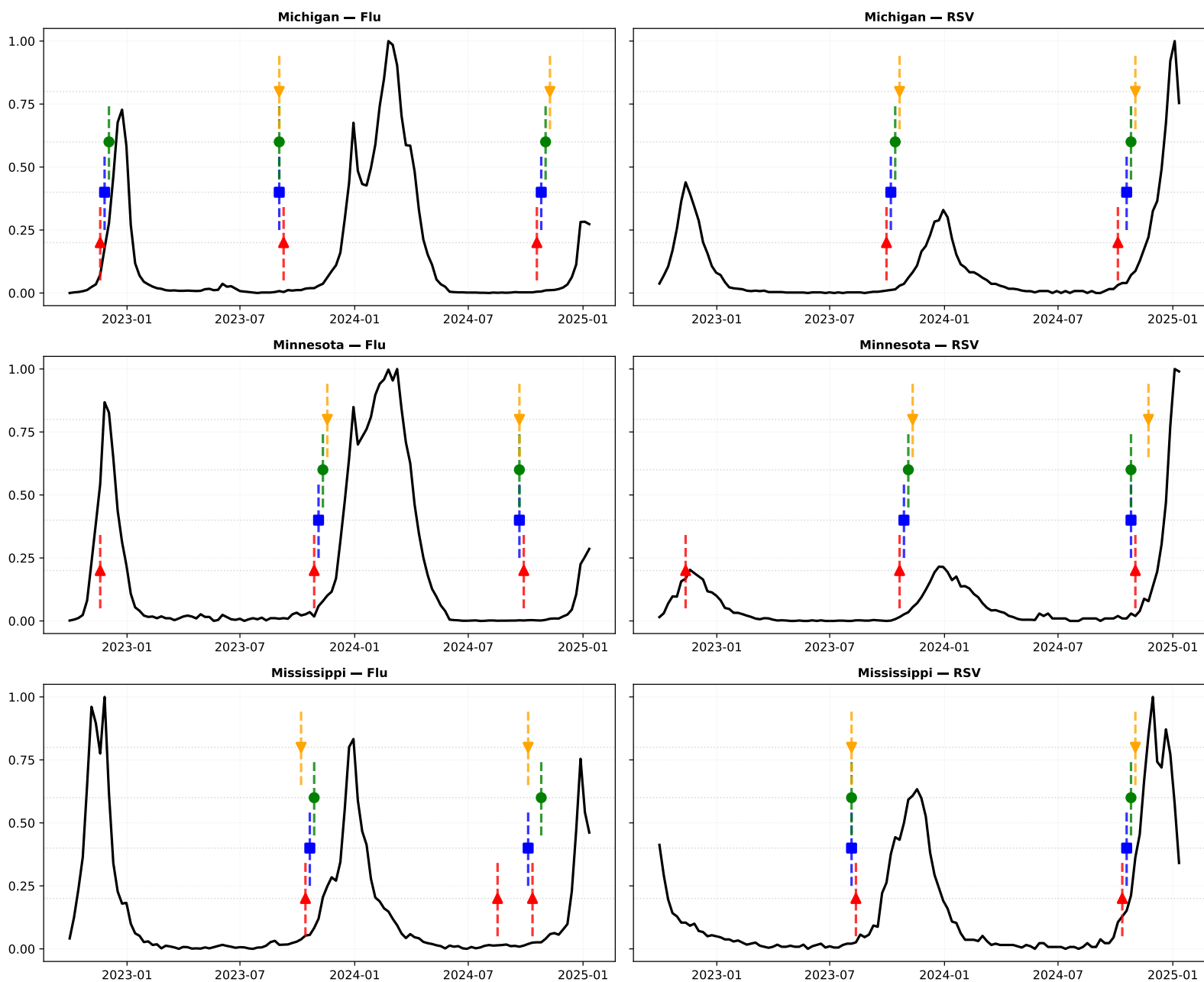


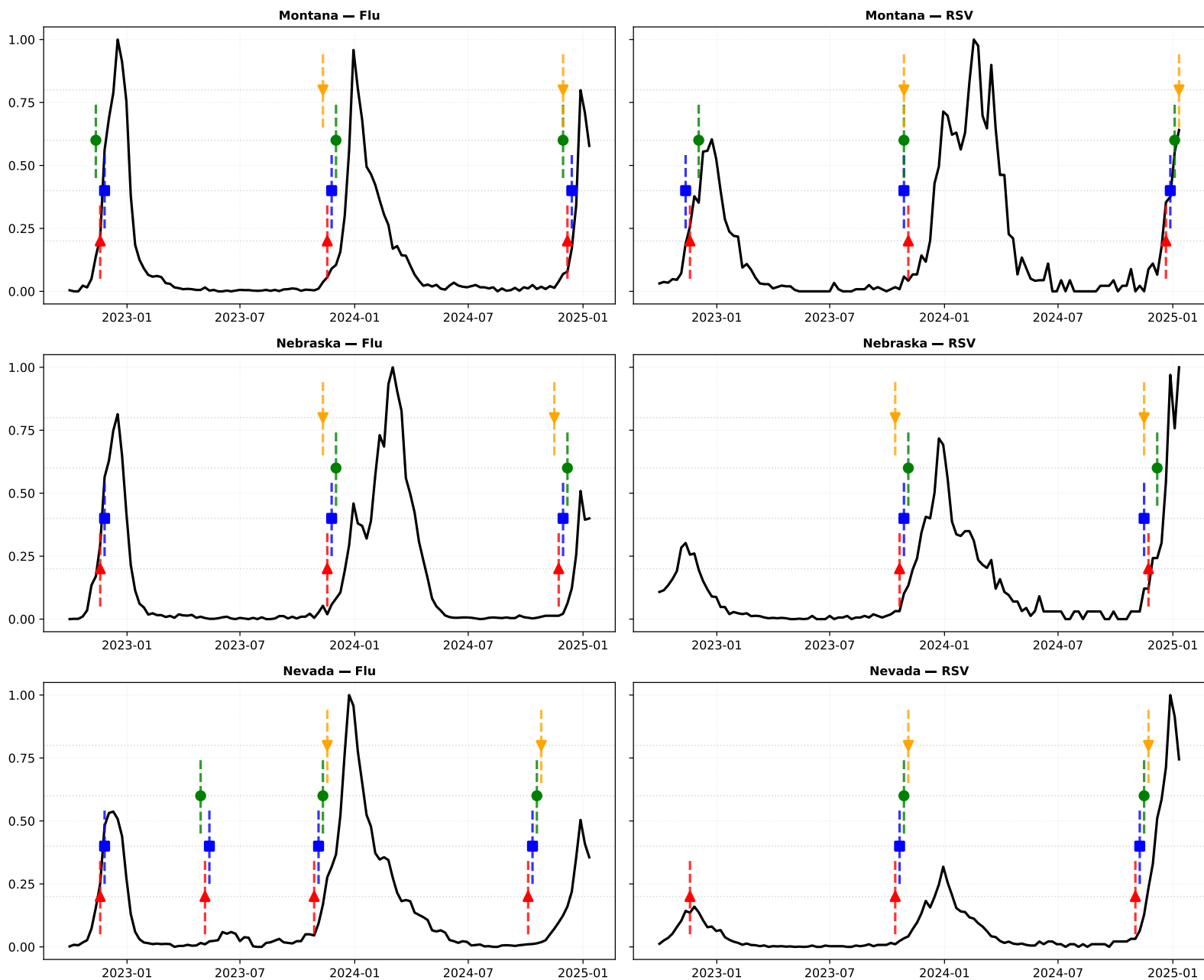
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window



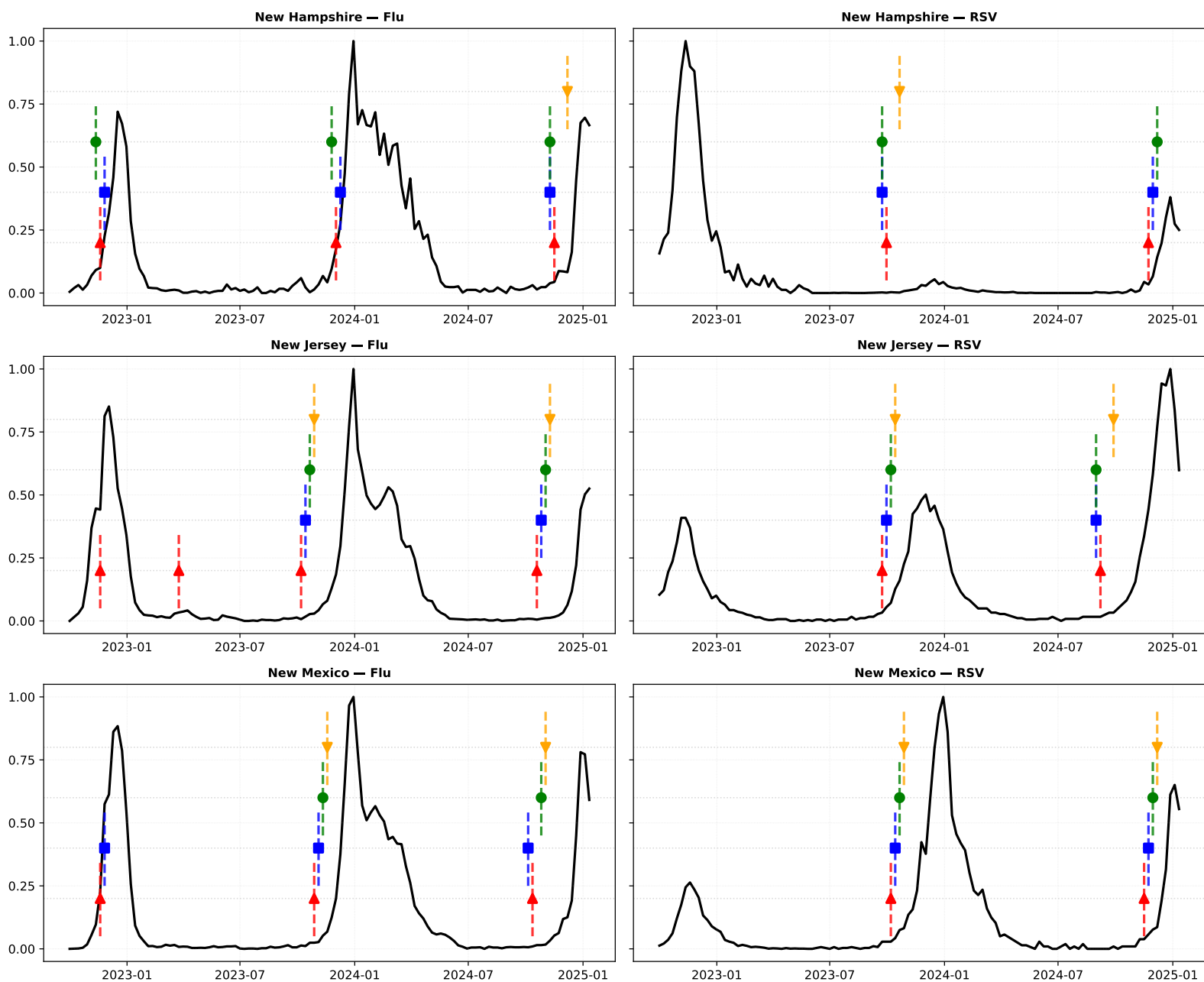


—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window

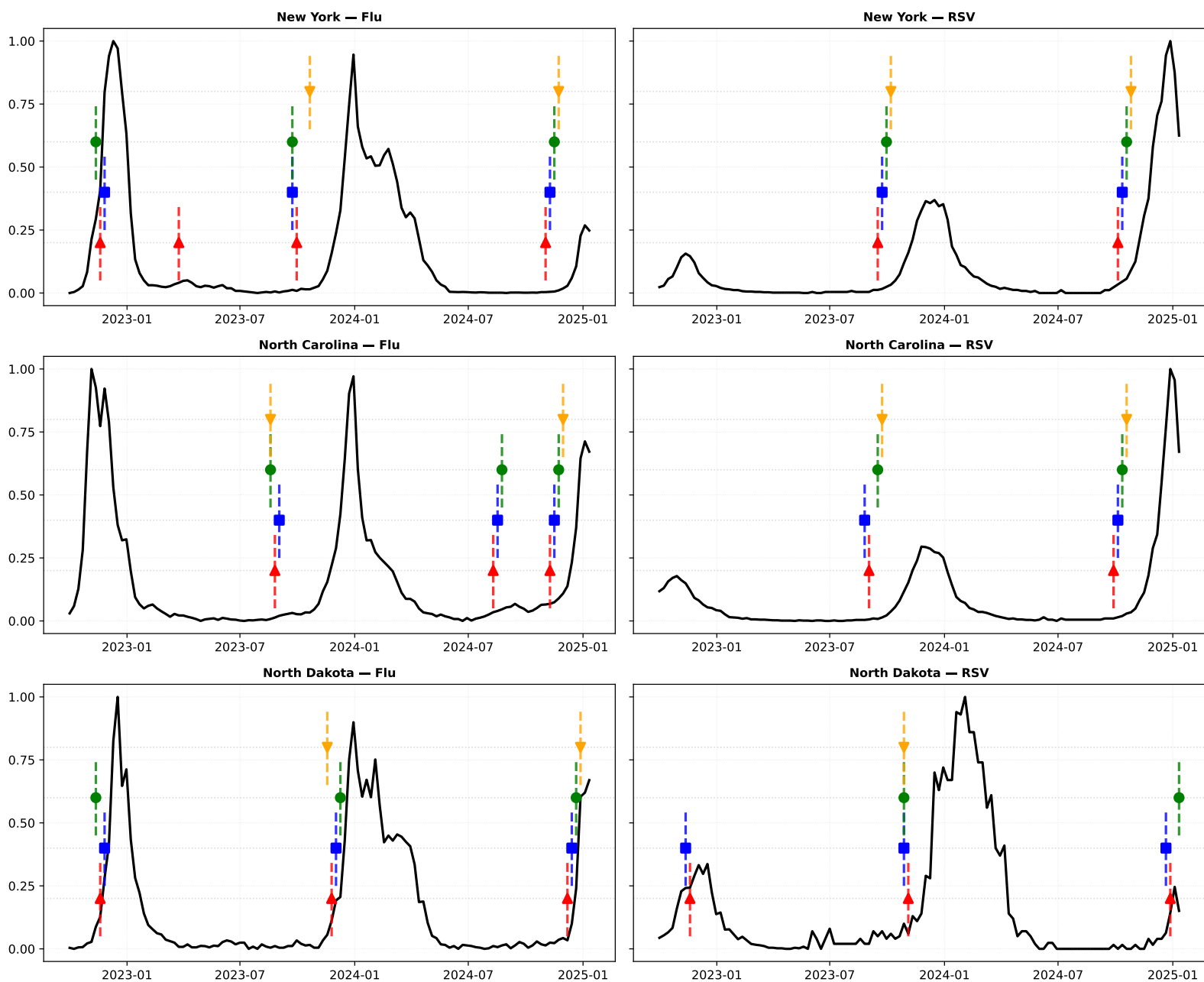


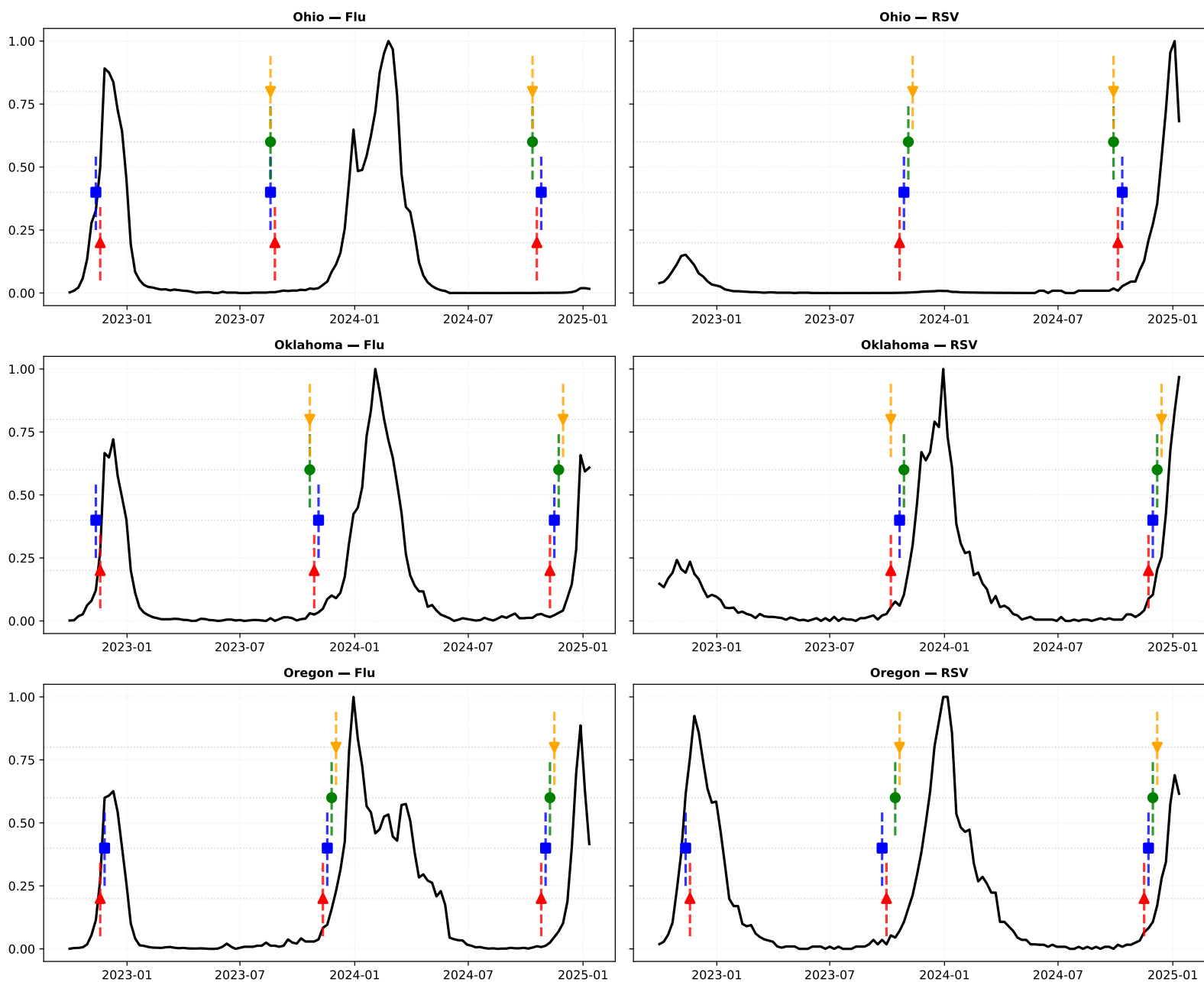


2-week window 4-week window 6-week window 8-week window

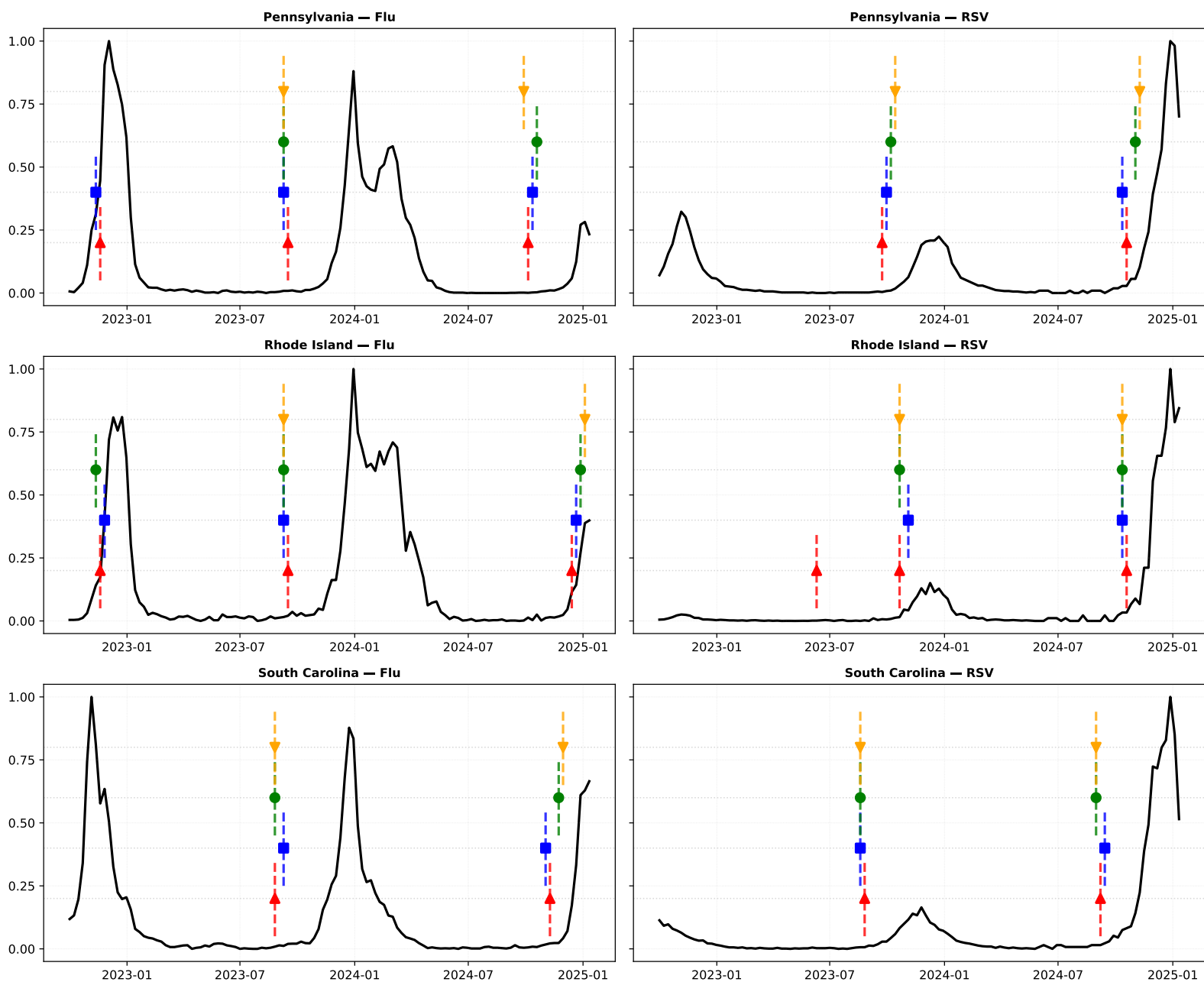


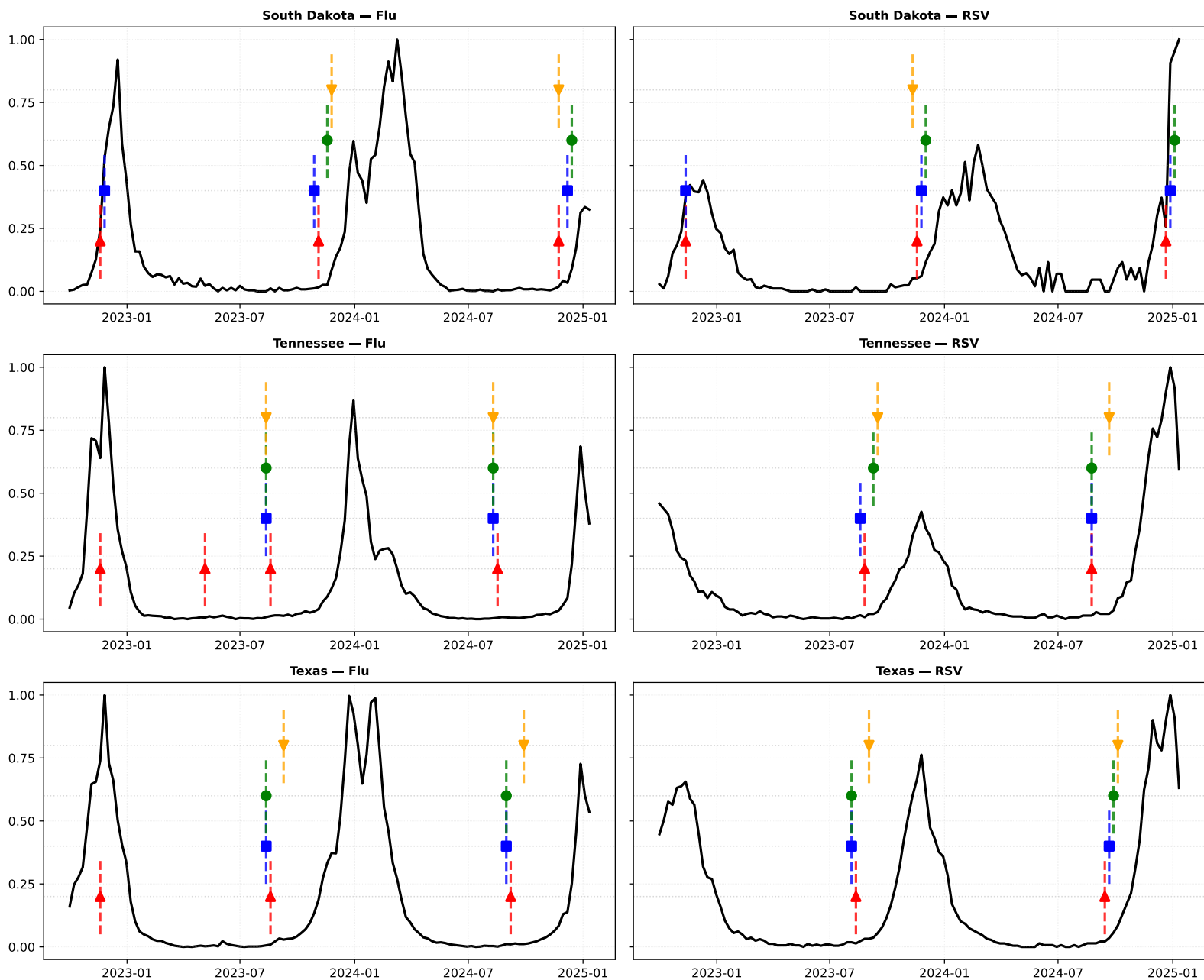
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window

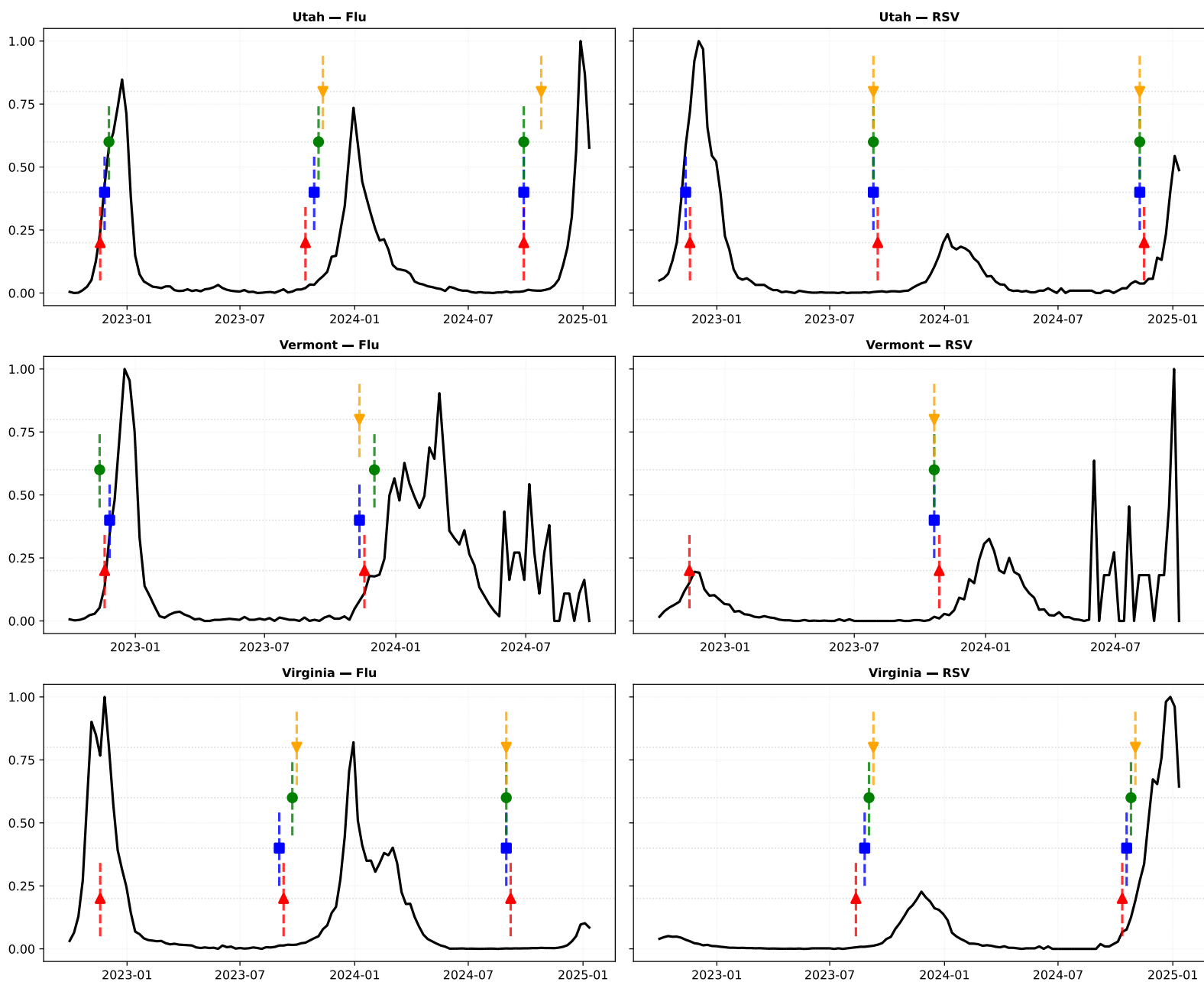




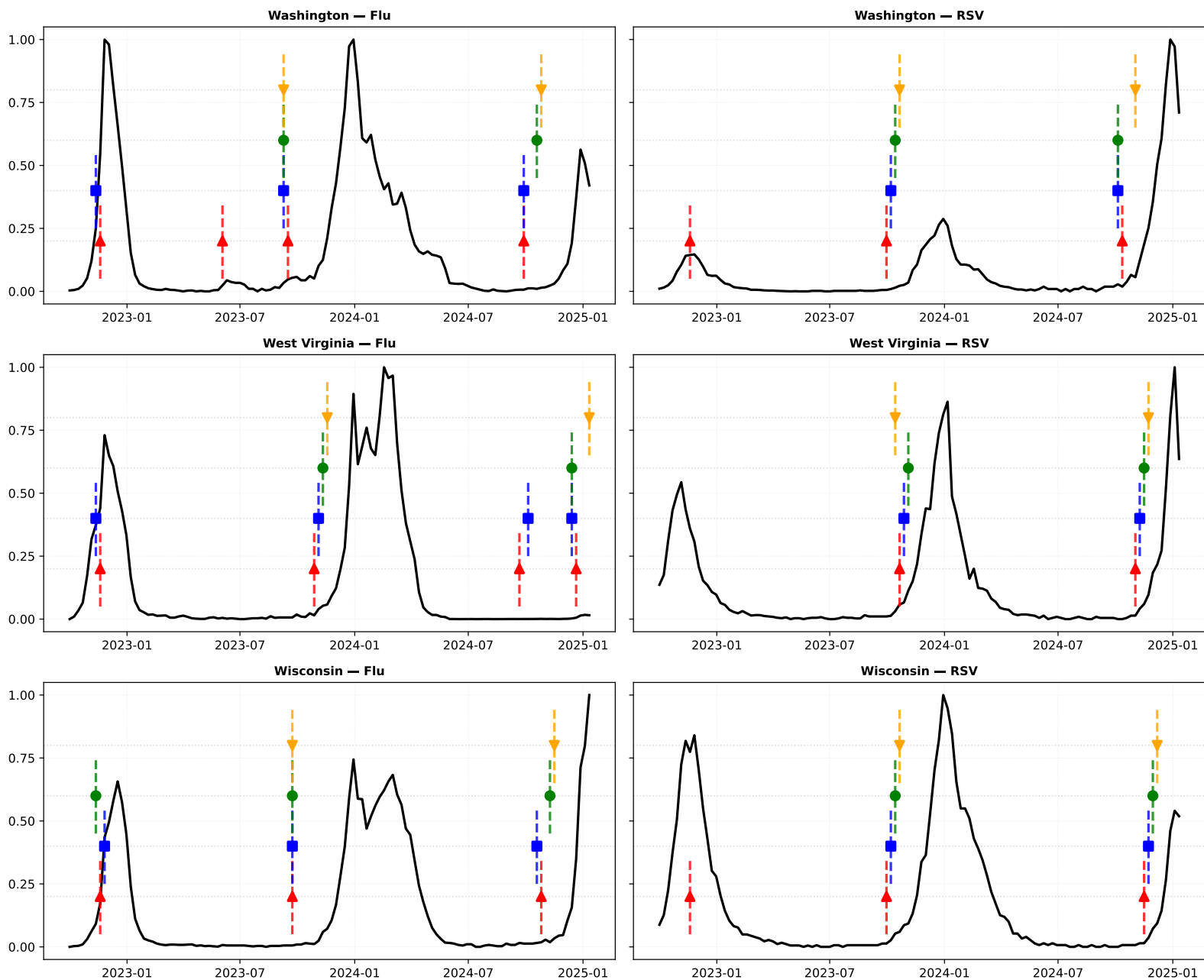
—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window

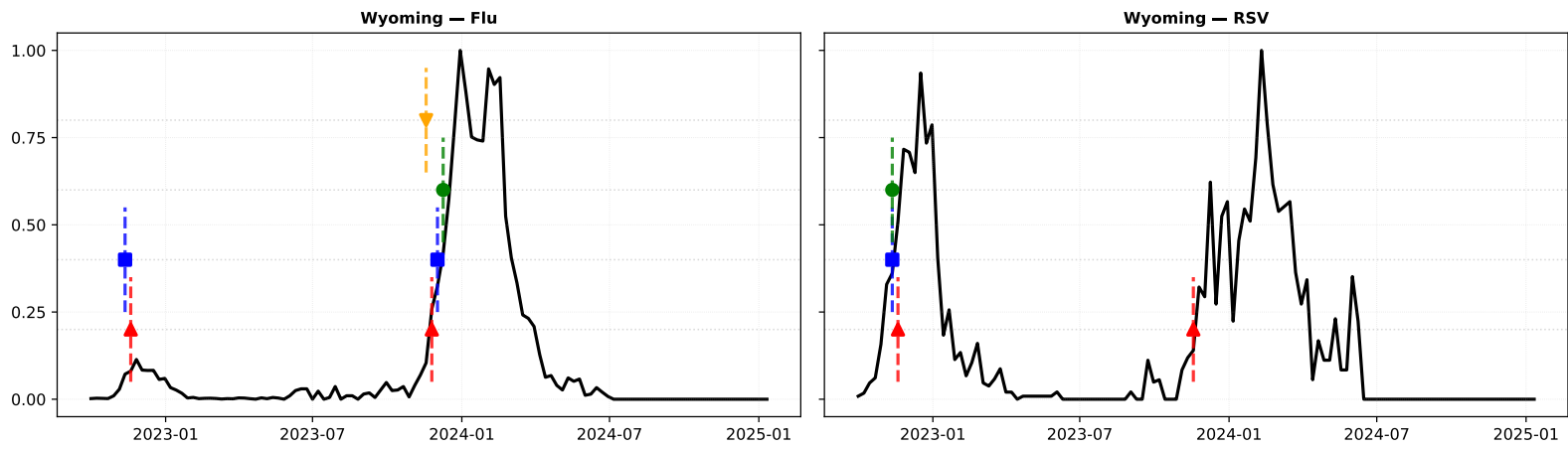






—▲— 2-week window —■— 4-week window —●— 6-week window —▼— 8-week window



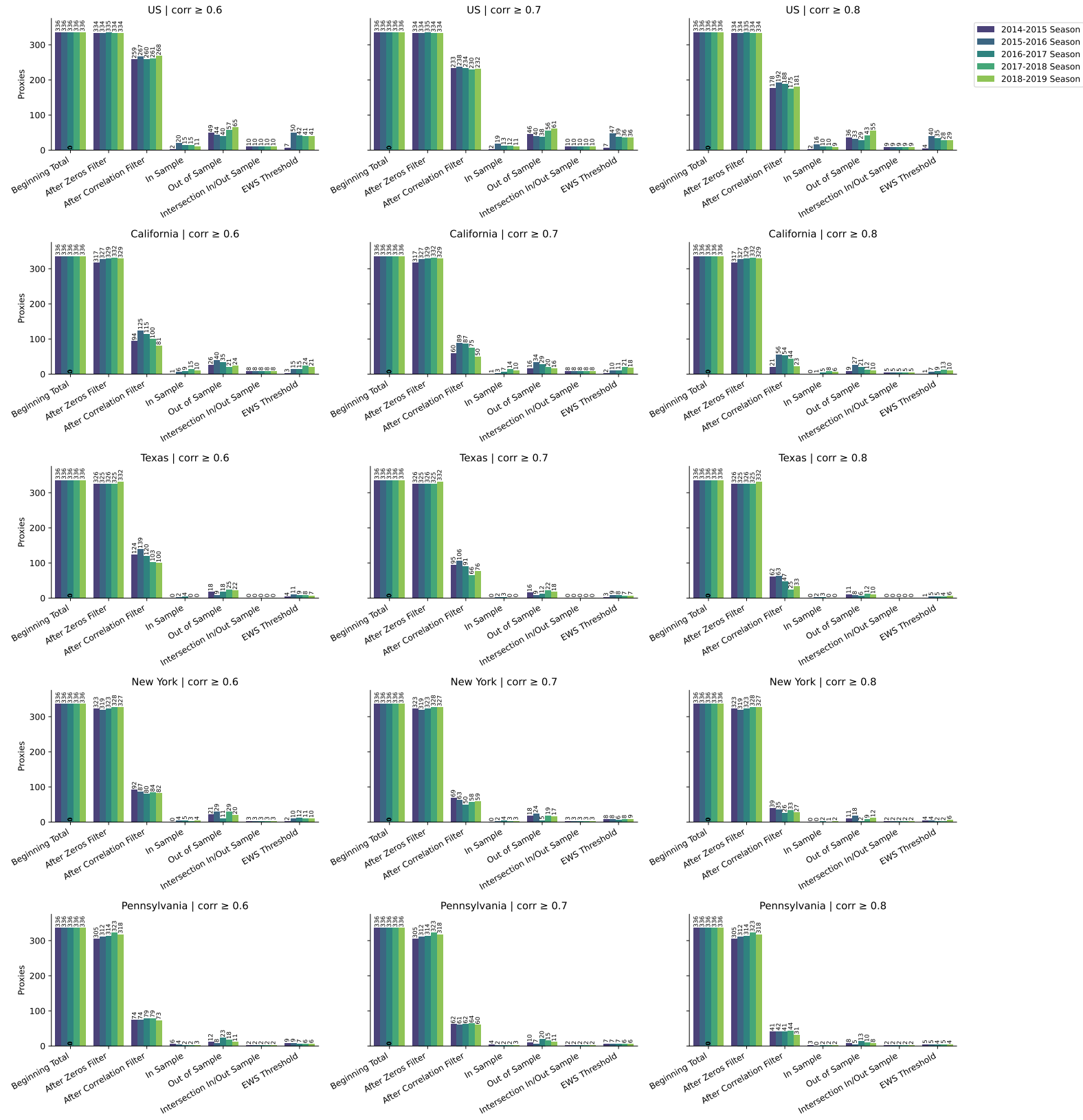


13 Sensitivity of Correlation Threshold

The following figures illustrate the sensitivity of the early warning system to the choice of correlation threshold used for proxy selection, evaluated on normalized ILI time series from 2011–2020. Lower correlation thresholds admit a larger number of proxy signals, increasing sensitivity but also introducing noisy and weakly informative trends driven by transient behavioral fluctuations. In contrast, overly restrictive thresholds exclude potentially informative signals and reduce robustness under distributional or behavioral shifts.

Across all datasets and validation periods, a correlation threshold of 0.7 emerges as a practical balance between these extremes. At this value, the system effectively filters spurious or unstable proxy signals while retaining a sufficiently diverse set of indicators to preserve early detection performance in the presence of evolving search behavior. Thresholds above 0.7 lead to marginal gains in noise reduction but at the cost of reduced proxy coverage and increased vulnerability to behavioral drift, whereas thresholds below 0.7 admit excess noise without consistent gains in lead time or detection reliability. Based on this empirical trade-off, we adopt a correlation threshold of 0.7 as the default setting, as it yields the most stable and robust performance across diseases, seasons, and deployment regimes.

Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



Proxy Selection Across Correlation Thresholds



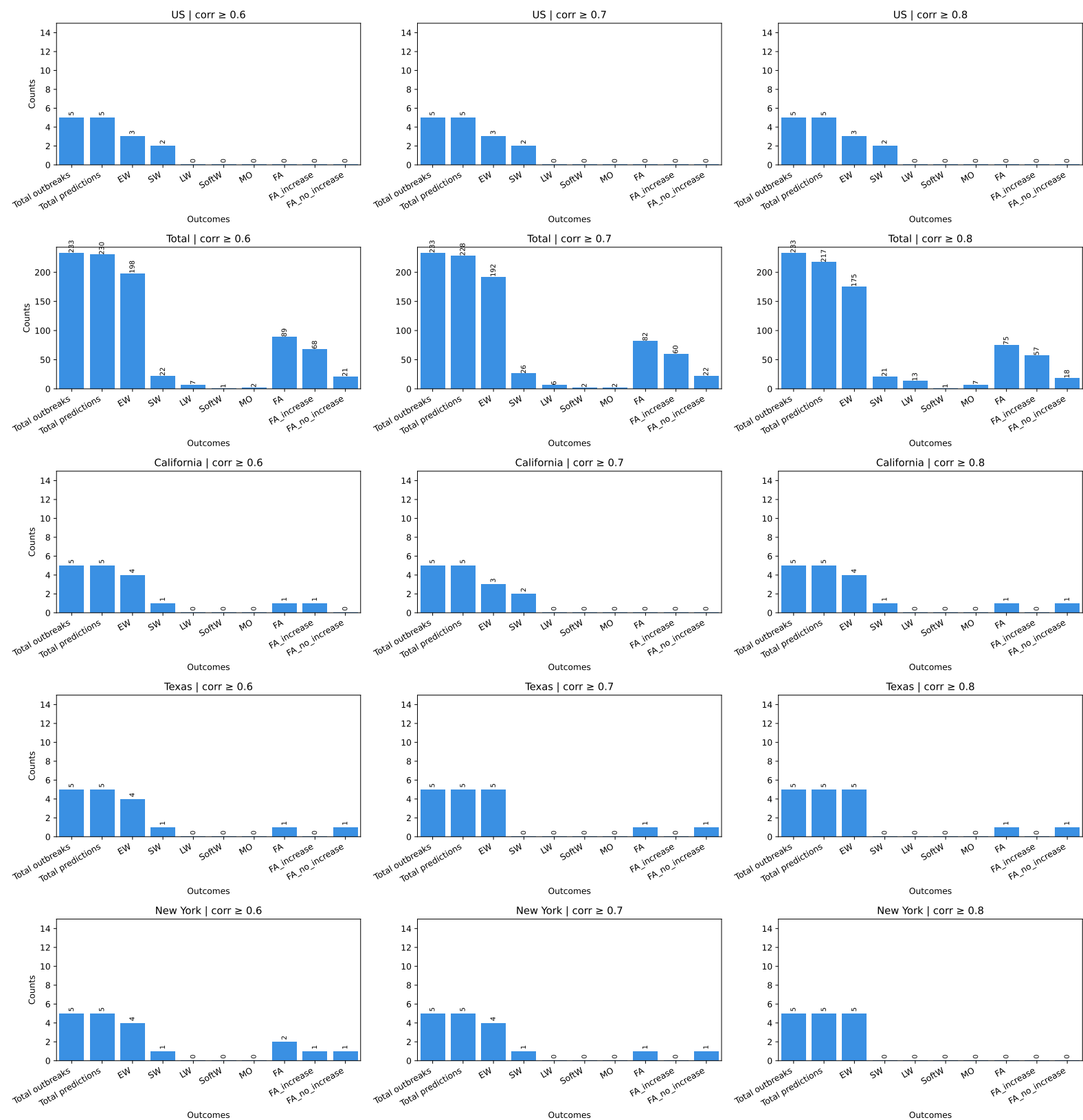
Proxy Selection Across Correlation Thresholds



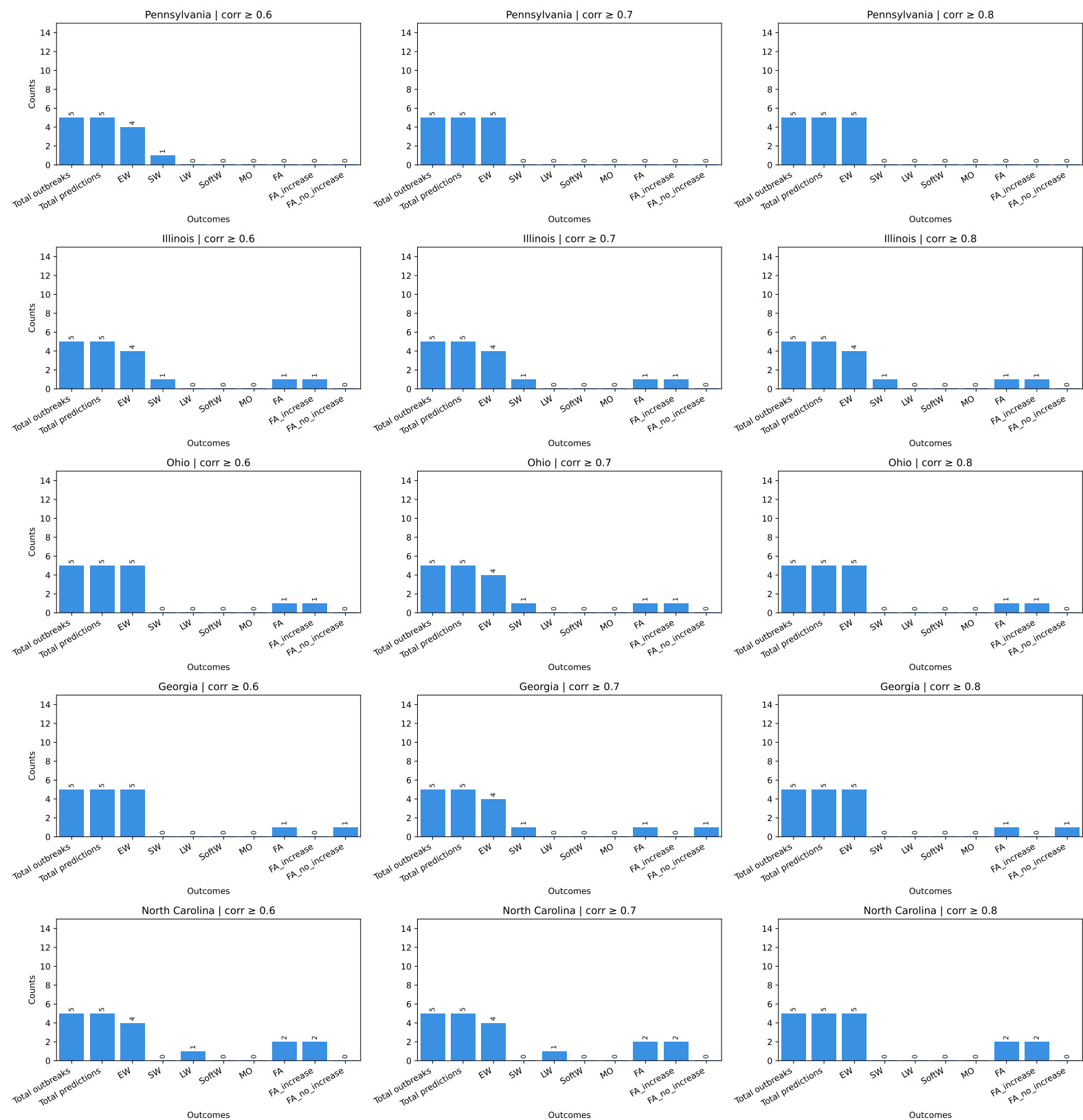
Proxy Selection Across Correlation Thresholds



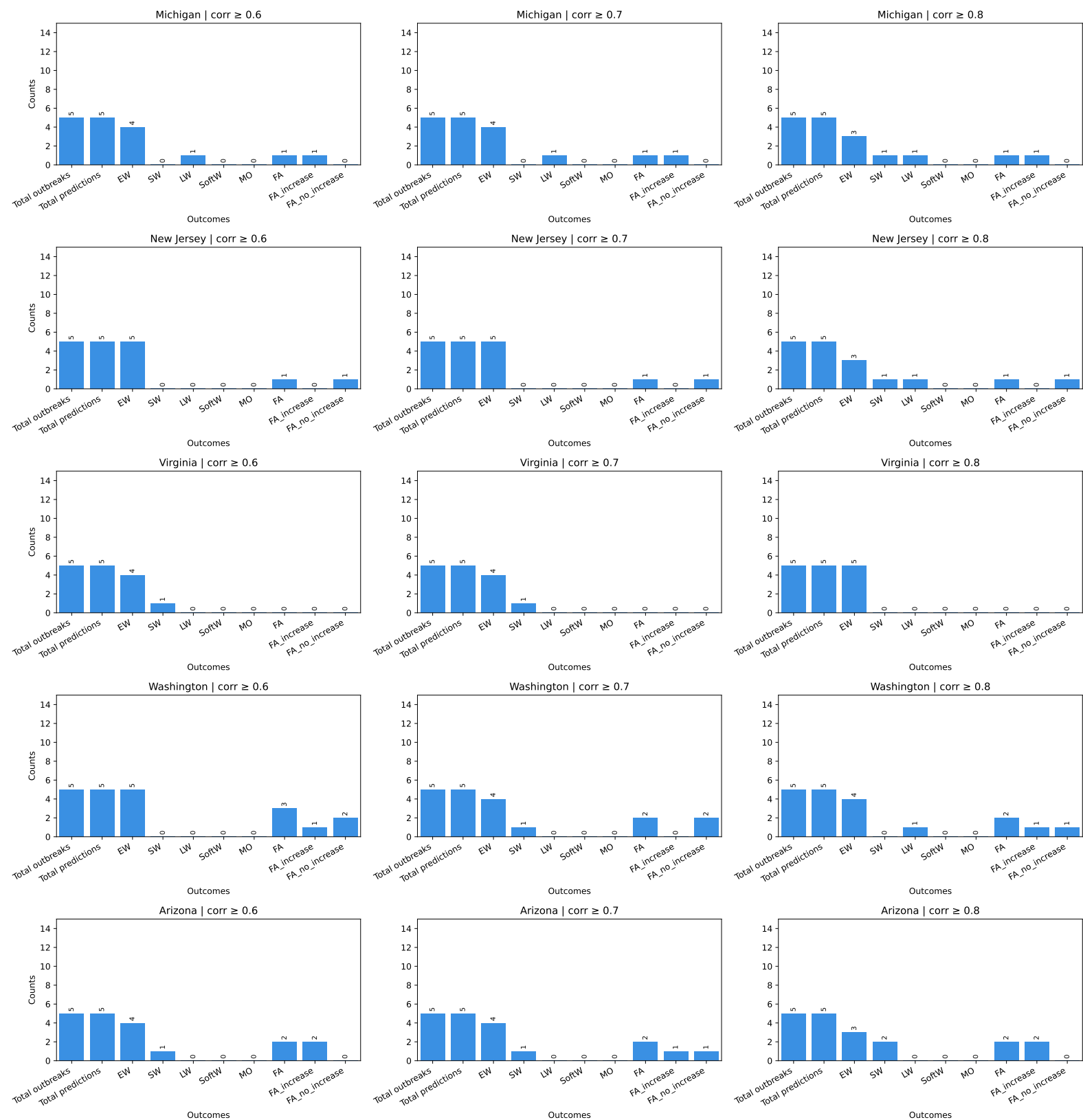
Performance Comparison Across Correlation Thresholds



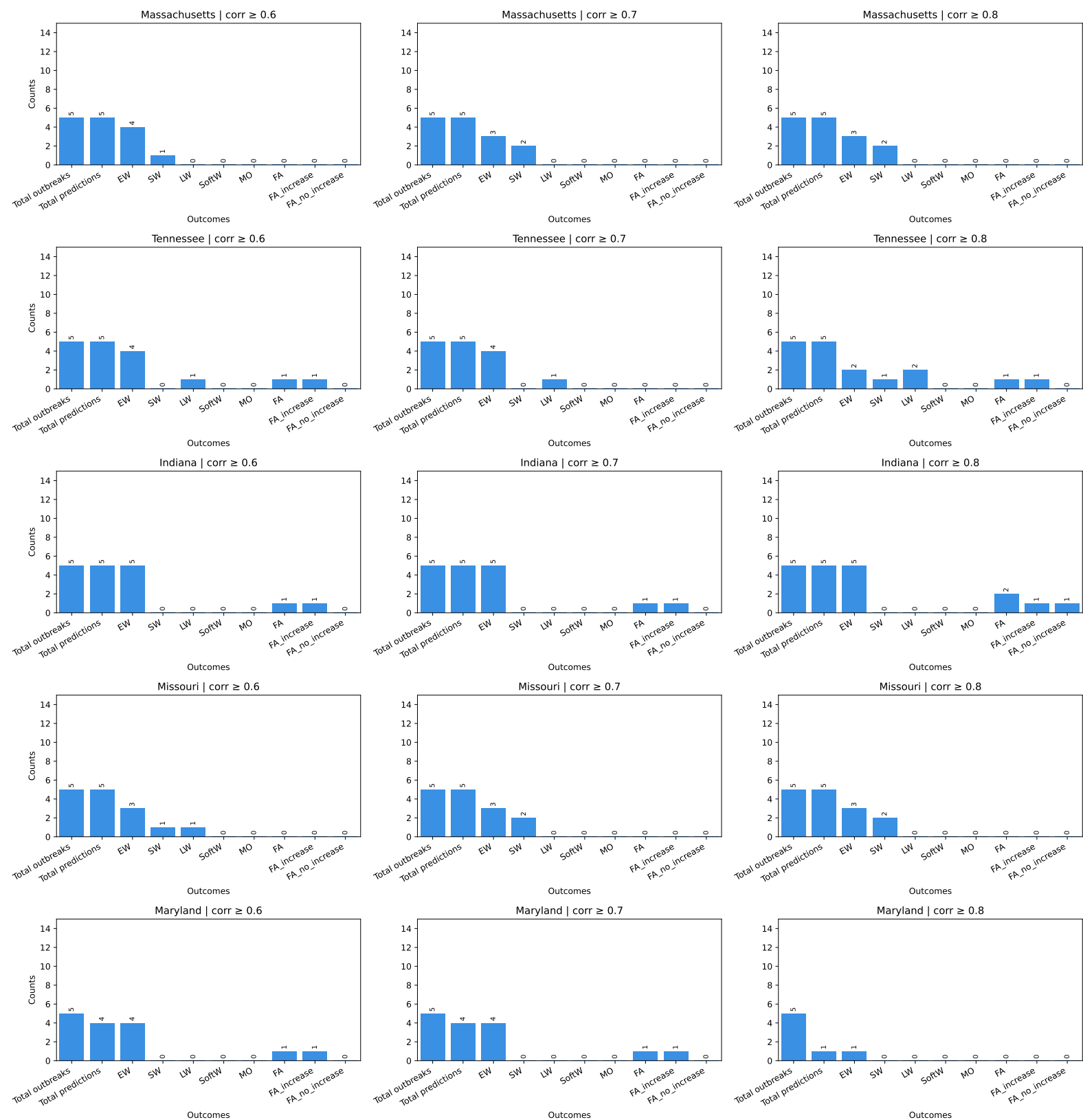
Performance Comparison Across Correlation Thresholds



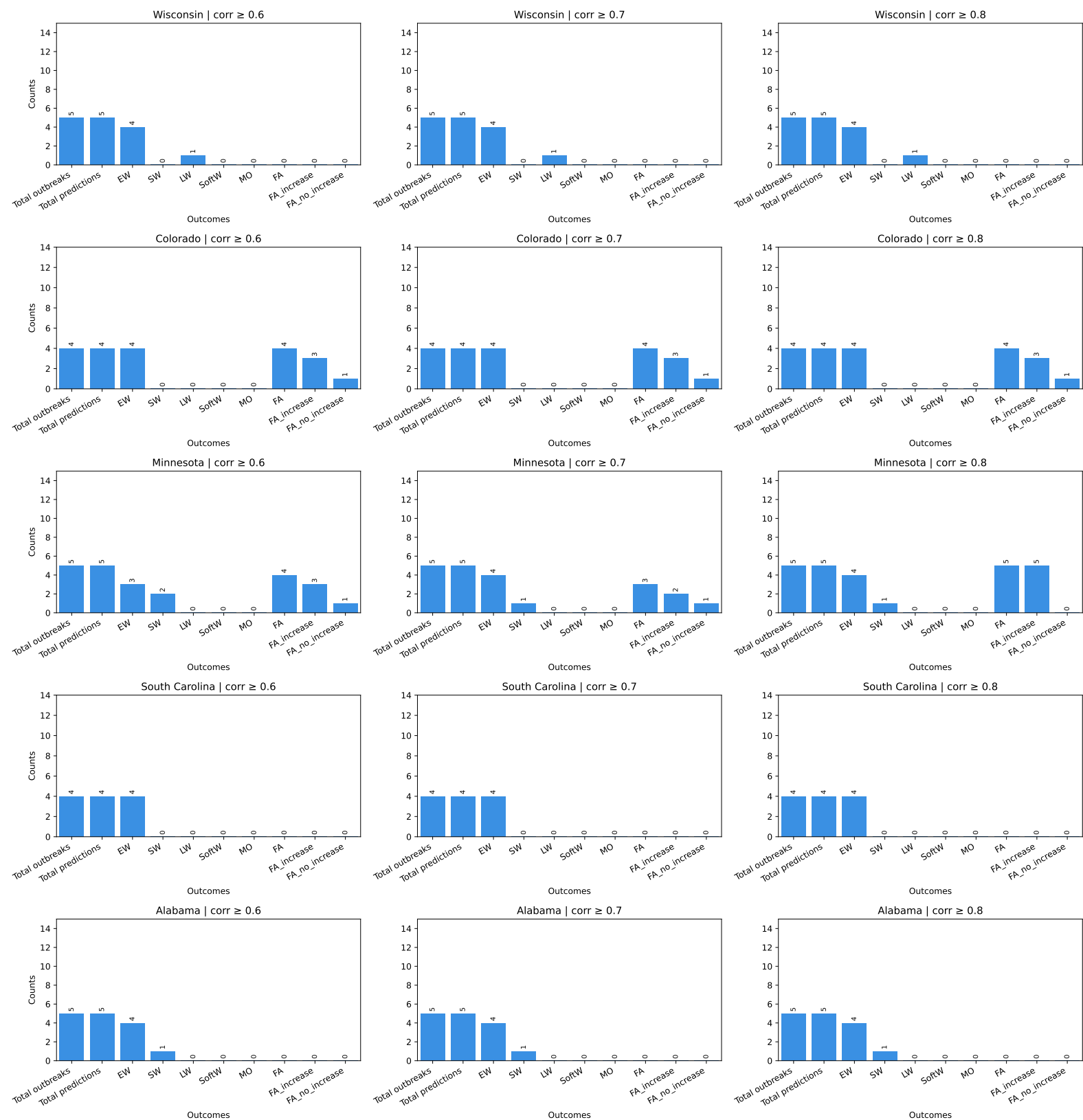
Performance Comparison Across Correlation Thresholds



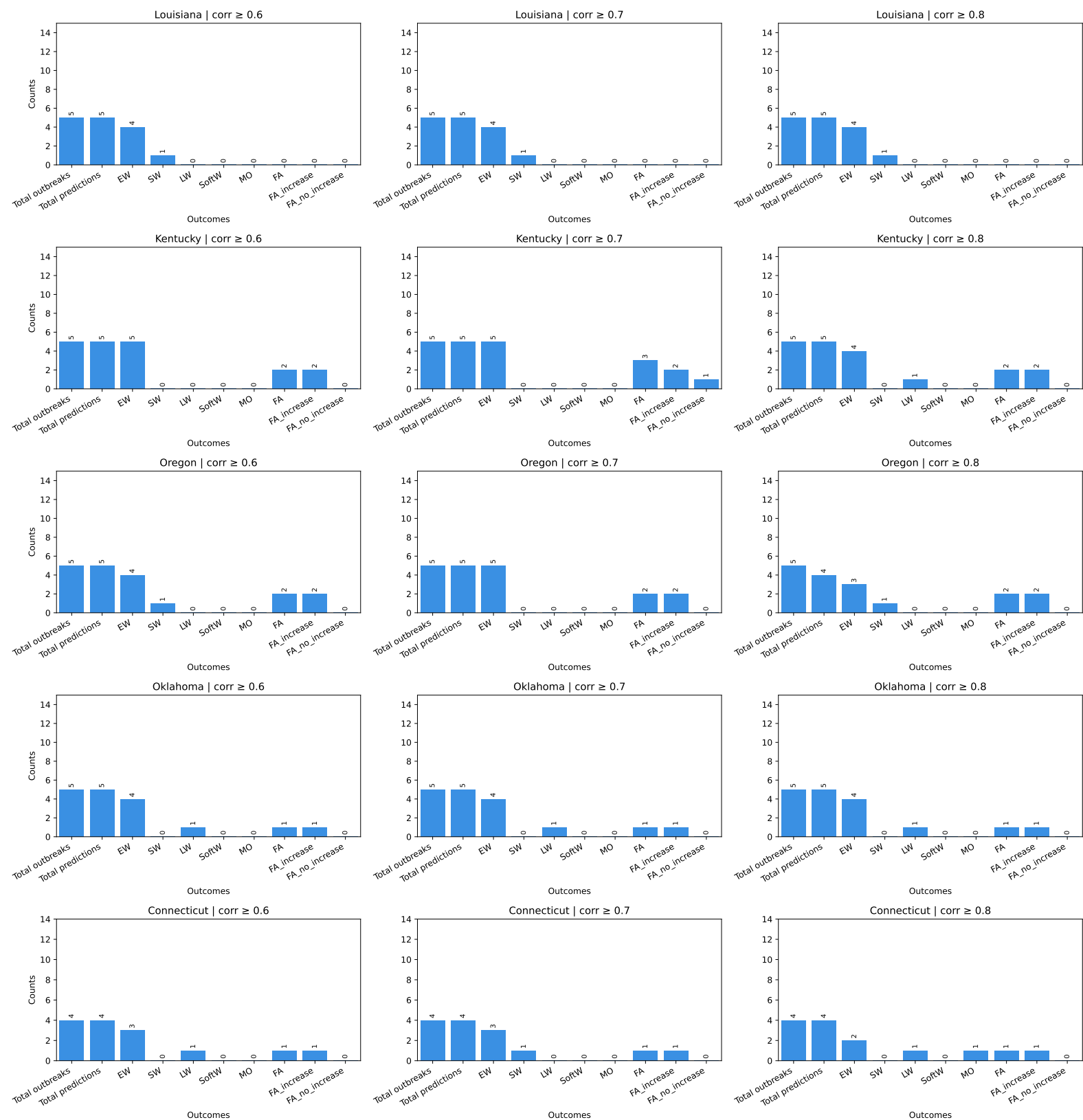
Performance Comparison Across Correlation Thresholds



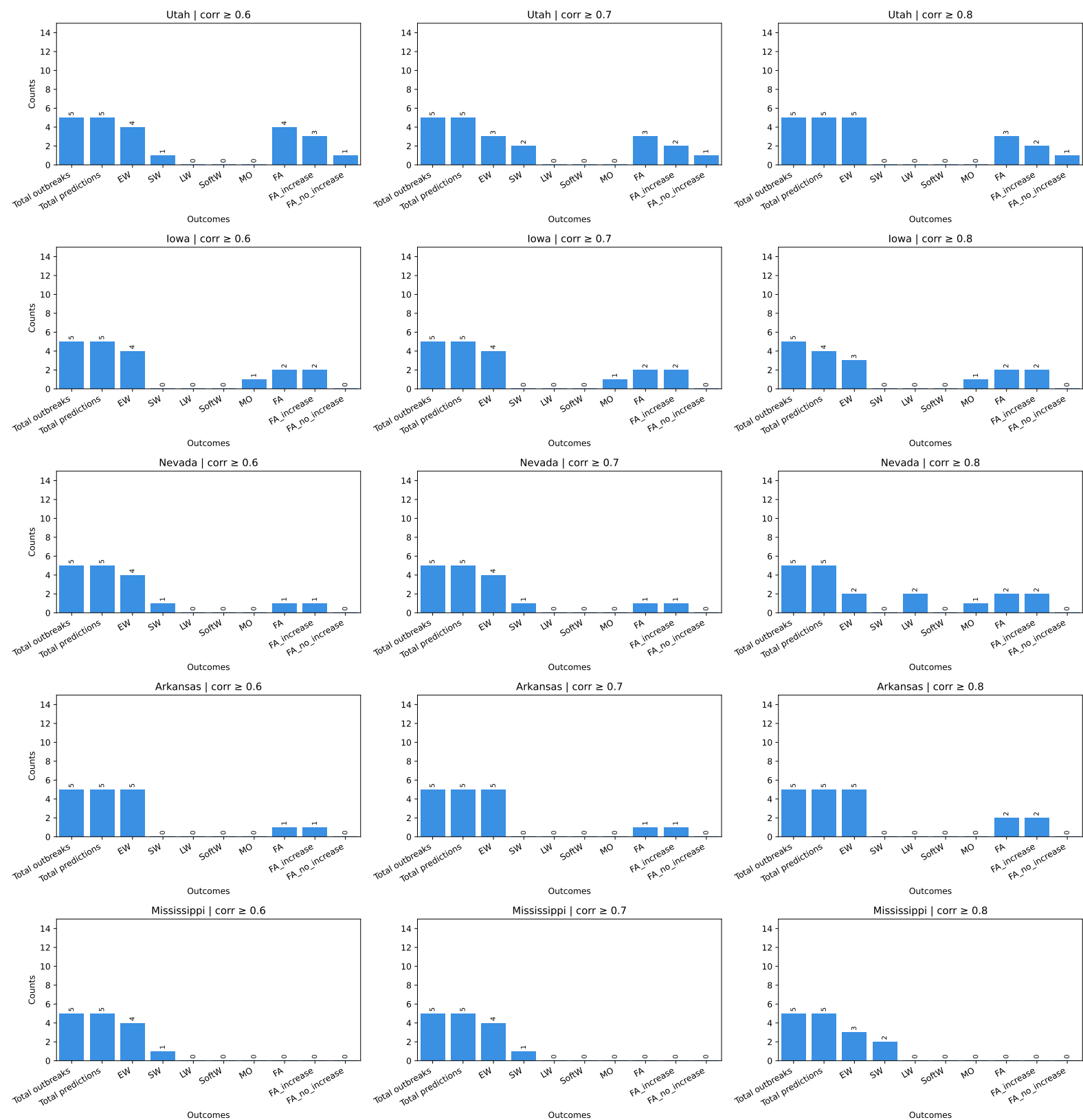
Performance Comparison Across Correlation Thresholds



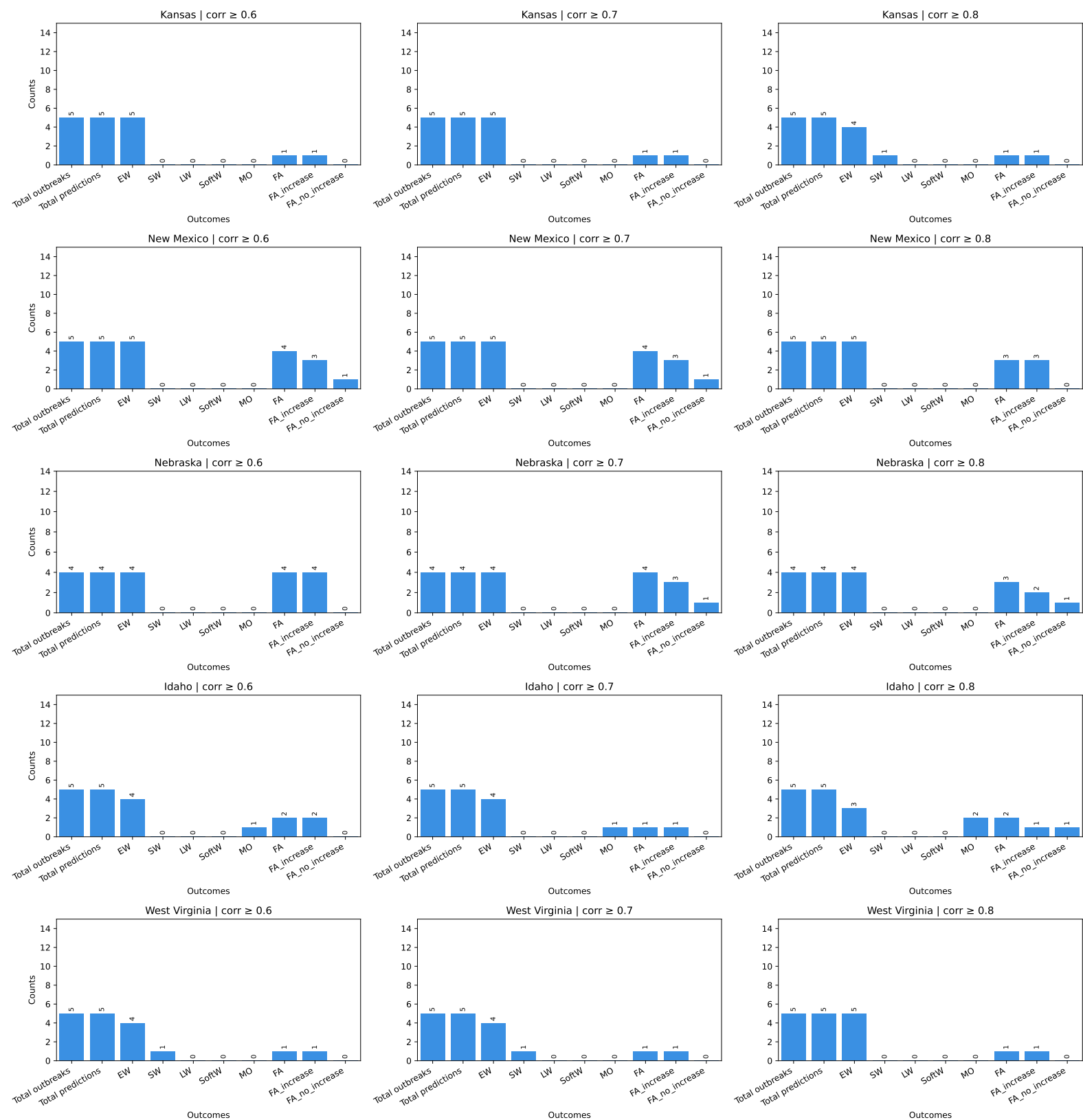
Performance Comparison Across Correlation Thresholds



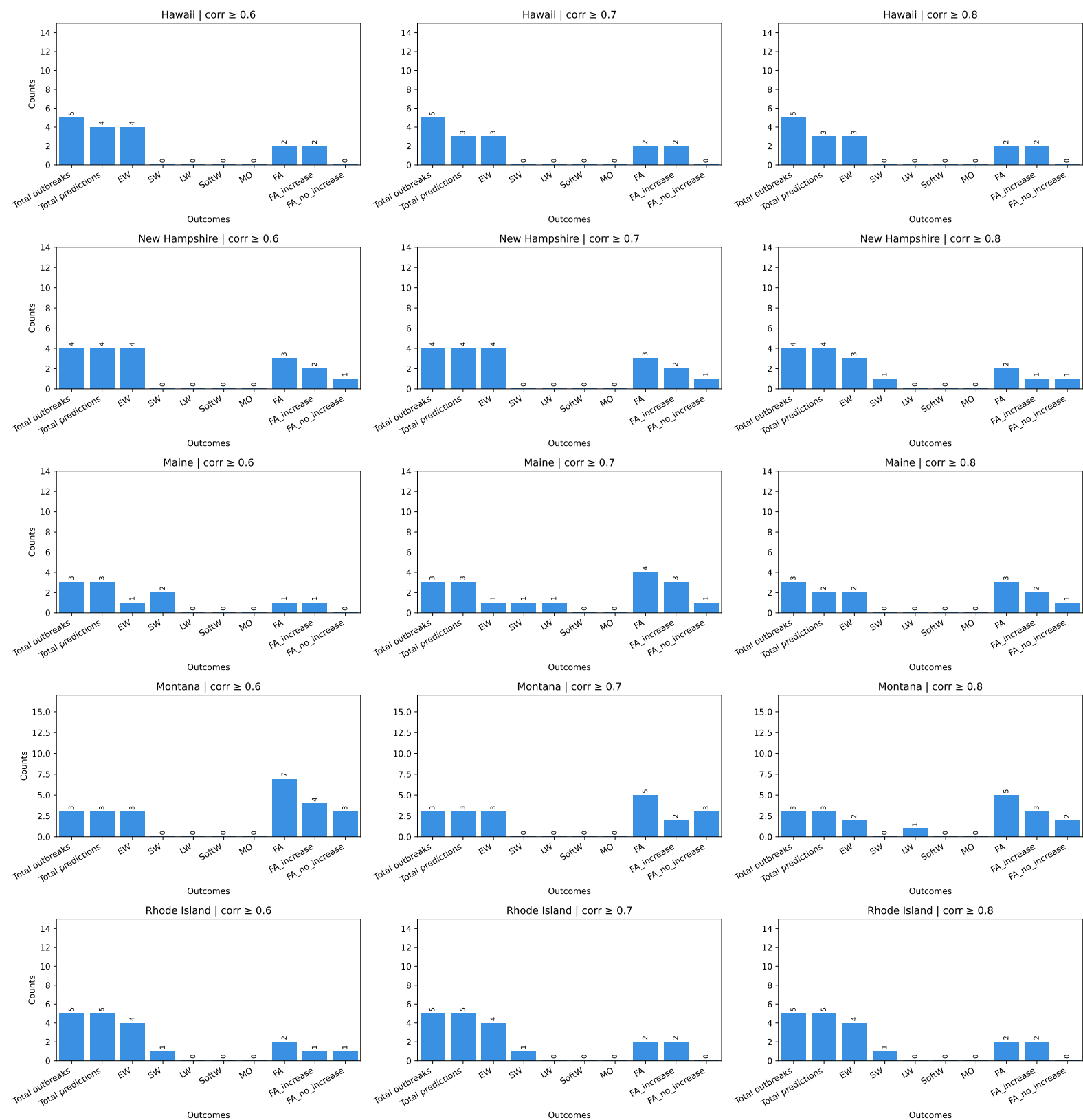
Performance Comparison Across Correlation Thresholds



Performance Comparison Across Correlation Thresholds



Performance Comparison Across Correlation Thresholds



Performance Comparison Across Correlation Thresholds

