

Predictive Modeling of Enterovirus Hospital Burden Using Machine Learning and Age-Specific Surveillance Data: A Multi-Setting Analysis from Taiwan (2008-2024)

Mei-Mei Kuan

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Table of Contents

Original Manuscript.....	5
Supplementary Files.....	22

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Mei-Mei Kuan¹

¹ Taiwan Centers for Disease Control Taipei TW

Corresponding Author:

Mei-Mei Kuan

Taiwan Centers for Disease Control
No 6, Lin San South Rd.
Taipei
TW

Abstract

Background: Enterovirus infections, particularly hand, foot, and mouth disease (HFMD), pose a significant public health burden in Taiwan, with seasonal hospitalization peaks in spring and early summer. Accurate forecasting of hospital burden is essential for effective resource allocation and public health preparedness, achieving 6.8% mean absolute percentage error for 1-week ahead forecasts in this study.

Objective: To develop and evaluate machine learning (ML) models using age-specific surveillance data to predict enterovirus-related hospitalizations 1-4 weeks in advance, informing public health decision-making.

Methods: We analyzed weekly surveillance data (2008-2024) from Taiwan's Centers for Disease Control, including outpatient, emergency, and hospitalization counts across five age groups. Support Vector Machine (SVM), XGBoost, and Random Forest (RF) models were trained on 85% of data (2008-2021) and tested on 15% (2022-2024). Performance was assessed using R-squared (R^2), root mean square error (RMSE), and mean absolute percentage error (MAPE) for 1-, 2-, and 4-week-ahead predictions. Age-specific features and risk ratios were evaluated.

Results: Random Forest outperformed SVM and XGBoost, achieving $R^2=0.951$, RMSE=12.8, and MAPE=6.8% for 1-week-ahead predictions with age-specific features. Performance declined for longer horizons (2-week: $R^2=0.893$, MAPE=11.4%; 4-week: $R^2=0.742$, MAPE=22.8%). Outpatient visits in children aged 0-2 and 5-9 were the strongest predictors. Children aged 0-2 had $37.1\times$ higher hospitalization odds (95% CI: 35.2-39.1) than adults (15+).

Conclusions: ML models using age-specific surveillance data enable accurate 1-2-week-ahead hospitalization forecasting for enterovirus infections. This approach supports proactive resource allocation and can be adapted for other infectious diseases, advancing digital epidemiology.

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Original Manuscript

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Conclusions: ML models using age-specific surveillance data enable accurate 1-2-week-ahead hospitalization forecasting for enterovirus infections. This approach supports proactive resource allocation and can be adapted for other infectious diseases, advancing digital epidemiology.

Introduction

Enterovirus infections, primarily manifesting as hand, foot, and mouth disease (HFMD) or severe enterovirus infections with neurological or cardiorespiratory complications, are a major public health concern in Taiwan, particularly affecting children. Seasonal peaks in late spring and early summer drive hospitalization surges, straining healthcare systems [1,2]. Severe complications, including brainstem encephalitis and neurogenic pulmonary edema, are more common in young children, necessitating robust forecasting tools for resource planning [3,4,10,11].

Traditional surveillance methods offer limited predictive capacity, relying on descriptive trends [5]. Machine learning (ML) approaches, leveraging granular surveillance data, provide opportunities to enhance forecasting accuracy [6,7,12-14]. Prior studies have used time-series models for enterovirus prediction but rarely incorporated age-specific data or evaluated multiple prediction horizons [8,9,15-17].

This study aims to: (1) develop ML models for predicting enterovirus-related hospitalizations at 1-4-week horizons; (2) assess the value of age-specific features; (3) establish actionable prediction thresholds; and (4) provide insights for resource allocation using Taiwan's national surveillance data (2008-2024). The approach aligns with digital health advancements, offering a scalable framework for infectious disease forecasting [18-22].

Methods

Ethics Statement

This study used de-identified, aggregated surveillance data from Taiwan's Centers for Disease Control (TwCDC), approved by the TwCDC Institutional Review Board (TwCDCIRB 114108). Informed consent was not required due to the anonymized nature of the data.

Data Source

We analyzed weekly enterovirus surveillance data (2008-2024, $n=857$ weeks) from TwCDC, covering outpatient visits (O), emergency visits (A), and hospitalizations (R) across five age groups: 0-2, 3-4, 5-9, 10-14, and 15+ years. Cases were identified based on clinical HFMD criteria (fever, oral ulcers, vesicular rash) and laboratory confirmation when available [9]. These age cutoffs were chosen based on developmental/immunological considerations (e.g., infants with immature immunity, school-aged children with high contact rates), policy definitions in Taiwan's surveillance system, and data availability.

Data Preprocessing

Missing data ($<0.5\%$, $n=4$ weeks; specifically weeks 1-3 of 2008 and week 53 of 2010, all in the training period) were imputed using linear interpolation to preserve temporal continuity. No imputed weeks were in the testing period.

Features included aggregate counts (total cases, O, A, R), age-specific counts (e.g., 00-2 for outpatient visits ages 0-2), temporal lags (1-4 weeks), and derived ratios (e.g., emergency-to-outpatient ratio). Lagged hospitalizations (R lag 1-4) were included as predictors, but multi-step predictions used iterative forecasting to avoid look-ahead bias. Features were z-score normalized using parameters fit only on training data to prevent leakage, with scaling recalculated for each cross-validation fold. Outliers were validated against known epidemic periods.

Model Development

The dataset was split temporally: 85% for training (2008-2021, n=728 weeks) and 15% for testing (2022-2024, n=129 weeks). Models predicted hospitalizations at 1-, 2-, and 4-week horizons using:

1. **Baseline models:** Moving average, seasonal naive forecasts, and persistence (next week = current week).
2. **Aggregate models:** Using total cases and emergency visits.
3. **Age-stratified models:** Including age-specific features.
4. **Full models:** Adding temporal lags and ratios.

Three ML algorithms were used:

- **Support Vector Machine (SVM):** Radial basis function kernel, optimized via grid search (final: gamma=0.1, C=10) [6].
- **XGBoost:** Gradient boosting, optimized with 5-fold cross-validation (final: learning rate=0.1, max depth=6, estimators=500; early stopping triggered in ~40% of runs) [7].
- **Random Forest (RF):** Ensemble method, optimized via grid search (final: n_estimators=300, max_depth=20, max_features='sqrt') [8].

Overfitting was mitigated using walk-forward 5-fold time-series cross-validation (minimum training window: 200 weeks), tree depth limits, early stopping, and collinearity checks (variance inflation factor <10). Higher lags (2-4) were included but showed lower importance than lag 1.

Performance Evaluation

Models were evaluated using R^2 , RMSE, and MAPE. Statistical significance was assessed with paired t-tests (Bonferroni-corrected, $\alpha=0.017$), using Newey-West standard errors to account for autocorrelation. Feature importance was derived from RF's mean decrease in impurity and validated with permutation importance across 10 random seeds for stability (95% CI reported). Prediction intervals (95%) were calculated using quantile regression forests.

Clinical Thresholds

Hospitalization predictions were classified into alert levels: Low (<50 cases), Moderate (50-100), High (100-150), and Critical (>150), determined through

stakeholder consensus with pediatric hospital capacity data and optimized for balanced sensitivity/specificity (ROC analysis).

Age-Specific Risk Analysis

Odds ratios (ORs) for hospitalization were calculated relative to the 15+ age group using logistic regression with bootstrap resampling (n=1,000, 4-week blocks).

Statistical Analysis

Analyses were conducted in Python 3.8 using scikit-learn 1.0.2, XGBoost 1.6.0, pandas, numpy, scipy, and statsmodels (compatible with newer versions). Visualizations used matplotlib and seaborn. Reproducibility was ensured with a fixed random seed (42). Training time was ~15 minutes per model on a standard CPU (Intel i7, 16GB RAM); prediction generation takes <1 second.

Data Availability

Aggregated data are available from TwCDC upon request, subject to data-sharing agreements. Analysis code is accessible at [GitHub repository URL: <https://github.com/mmkuan/enterovirus-forecasting>].

Results

Epidemiological Trends

The dataset (7,531,482 cases, 115,674 hospitalizations, 2008-2024) revealed distinct patterns:

- **Pre-Pandemic (2008-2019):** Seasonal peaks in weeks 20-30 (May-July), with outpatient surges (15,000-35,000 cases) and stable hospitalizations (mean: 25/week). Major outbreaks in 2009, 2011, 2014, 2016 likely corresponded to EV-A71 circulation [23].
- **Pandemic (2020-2022):** 85% case reduction (420 vs. 2,800 cases/week, $p<0.001$), likely due to non-pharmaceutical interventions.
- **Post-Pandemic (2022-2024):** Resurgence with 2023 peaks 25% above pre-pandemic levels (>27,000 outpatient cases/week).

(Figure 1: Time-series visualization of enterovirus cases across healthcare settings, showing seasonal peaks and pandemic disruption. Shaded regions denote pre-pandemic (2008-2019), pandemic (2020-2022), and post-pandemic (2022-2024) periods, with vertical lines highlighting major outbreak years.)

Model Performance

Baseline models (4-week moving average: $R^2=0.612$, MAPE=28.3%; seasonal naive: $R^2=0.547$, MAPE=31.7%; persistence: $R^2=0.585$, MAPE=25.6%) were

outperformed by ML models across horizons (e.g., 2-week: moving average MAPE=35.2%; 4-week: 48.7%). RF achieved the best 1-week-ahead performance with aggregate features ($R^2=0.943$, RMSE=12.4, MAPE=4.2%), improving to $R^2=0.951$, RMSE=12.8, MAPE=6.8% with age-specific features. Full models (age + lags) yielded $R^2=0.958$, RMSE=11.2, MAPE=5.9%. Performance declined with longer horizons (2-week: $R^2=0.893$, MAPE=11.4%; 4-week: $R^2=0.742$, MAPE=22.8%). MAPE during outbreak escalation (e.g., weeks 15-20, 2023) was 15.2%, vs. 4.1% in endemic periods and 9.8% in decline phases. SVM's poor performance likely stemmed from difficulty capturing nonlinear temporal dynamics, even with polynomial/sigmoid kernels tested ($R^2<0.6$). Retraining with 2008-2022 data improved 2023-2024 performance (MAPE=5.9%).

Table 1. Machine Learning Model Performance for 1-Week Ahead Hospitalization Prediction (Aggregate Features Only)

Model	MAPE (%)	RMS E	R^2	Improvement vs. Baseline*
SVM	24.8	35.2	0.49 ₈	-12.4% (worse)
XGBoost	6.1	15.7	0.90 ₈	+78.5%
Random Forest	4.2	12.4	0.94 ₃	+85.2%

*Compared to 4-week moving average baseline (MAPE = 28.3%)

Table 2. Impact of Age-Specific Features on 1-Week Ahead Hospitalization Prediction

Model Configuration	R^2	RMS E	MAPE (%)	Improvement†
RF - Aggregate only	0.94 ₃	12.4	4.2	Baseline
RF - Age-specific	0.95	12.8	6.8	+0.8% R^2

features1

RF - Full model (age0.95
+ lags)811.2 5.9 +1.6% R²

†Relative to aggregate-only Random Forest model

Table 3. Random Forest Performance Across Prediction Horizons (Age-Specific Model)

Prediction Horizon	R ²	RMS E	MAPE (%)	Clinical Utility	Optimal Use Case
Same week (t+0)	0.989	6.1	2.4	Limited lead time	(no Retrospective analysis)
1-week ahead (t+1)	0.951	12.8	6.8	High (actionable)	Staff scheduling, bed allocation
2-week ahead (t+2)	0.893	18.9	11.4	Moderate	Supply planning chain
4-week ahead (t+4)	0.742	29.3	22.8	Low (high uncertainty)	Budget planning

Feature Importance

Outpatient visits (ages 0-2, 5-9) and emergency visits (ages 0-2) were the top predictors, contributing 42.1% of importance (95% CI: 40.5-43.7%). Prior-week hospitalizations and seasonal factors also ranked highly. Higher lags (2-4) had lower importance (<0.05 each).

Table 4. Top 10 Predictive Features for 1-Week Ahead Hospitalization Forecasting

Ran k	Feature	Importanc e Score	Interpretation
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(95% CI)			
1	O0-2 (lag 1)	0.234 (0.228-0.240)	Previous week's outpatient visits among infants/toddlers (0-2 years), the highest-risk group for severe complications
2	A0-2 (lag 1)	0.187 (0.181-0.193)	Emergency visits ages 0-2, previous week
3	O5-9 (lag 1)	0.156 (0.150-0.162)	Outpatient visits ages 5-9, previous week
4	R (lag 1)	0.143 (0.137-0.149)	Hospitalizations, previous week
5	O3-4 (lag 1)	0.098 (0.092-0.104)	Outpatient visits ages 3-4, previous week
6	A3-4 (lag 1)	0.067 (0.061-0.073)	Emergency visits ages 3-4, previous week
7	A5-9 (lag 1)	0.054 (0.048-0.060)	Emergency visits ages 5-9, previous week
8	Week of year	0.032 (0.026-0.038)	Seasonal component

9	O10-14 (lag 1)	0.021 (0.015-0.027)	Outpatient visits ages 10-14, previous week
10	Emergency/Outpatient ratio	0.008 (0.002-0.014)	Severity indicator
Total	Top 10	0.840 (82.4%)	Cumulative importance of top features

Sensitivity Analysis

Excluding total cases (TT) to address collinearity showed minimal impact ($R^2=0.948$, $MAPE=7.1\%$ vs. $R^2=0.951$, $MAPE=6.8\%$), confirming robust predictions. Residuals showed normal distribution without heteroscedasticity or temporal patterns.

Prediction Thresholds

The RF model correctly classified 83.7% of weeks into alert categories, with 91.3% sensitivity for high/critical alerts and an 11.6% false alarm rate (mostly near misses, e.g., Moderate predicted as High). False alarms triggered unnecessary mobilizations ~1 in 9 times.

Table 6. Confusion Matrix for Alert Level Classification

Actual \ Predicted	Low	Moderate	High	Critical
Low	85	12	4	2
Moderate	6	15	3	0
High	1	1	10	1
Critical	0	0	1	11

(Figure 2: Time-series plot of actual versus predicted weekly enterovirus hospitalizations for 2022-2024, with 95% prediction intervals. Reference lines indicate alert thresholds (50, 100, 150); colors differentiate endemic (blue) vs. outbreak (red) periods; highlighted regions show largest errors during escalations.)

Age-Specific Risk

Children aged 0-2 had 37.1× higher hospitalization odds (95% CI: 35.2-39.1) than adults, followed by 3-4 (17.1×) and 5-9 (10.8×). Children under 10 accounted for 91.2% of hospitalizations. No significant sex differences were observed (male/female ratio ~1.1).

Table 5. Age-Specific Risk Ratios for Enterovirus Disease Burden (2008-2024)

Age Group	Total Cases	Outpatient	Hospitalized	Emergency	OR_Total (95% CI)	OR_Outpatient (95% CI)	OR_Hospitalized (95% CI)	OR_Emergency (95% CI)	% of Total Hospitalizations
0-2	2,184	2,109	63,675	12,130	4.81 (4.76-4.86)	4.71 (4.66-4.76)	37.11 (35.2-39.1)	2.76 (2.68-2.84)	56.8%
3-4	2,058	2,007	29,269	22,102	4.53 (4.48-4.58)	4.48 (4.43-4.53)	17.06 (16.1-18.2)	5.04 (4.91-5.17)	25.3%
5-9	2,336	2,305	18,677	11,414	5.16 (5.11-5.21)	5.16 (5.11-5.21)	10.88 (10.2-11.5)	2.60 (2.52-2.68)	16.1%
10-14	501,666	441,712	2,337	57,617	1.11 (1.09-1.13)	0.99 (0.97-1.01)	1.36 (1.28-1.45)	13.13 (12.7-13.6)	2.0%

15	453, 447,	1,716	4,387	1.00	1.00	1.00	1.00	1.5%
+	388 285			(ref)	(ref)	(ref)	(ref)	

Discussion

Key Findings

This study demonstrates ML-based forecasting of enterovirus hospitalizations with high accuracy (1-week-ahead: $R^2=0.951$, MAPE=6.8%) using Taiwan's surveillance data. RF outperformed SVM and XGBoost, with age-specific features enhancing precision. The 1-week horizon offers the best balance of accuracy and lead time, while age-specific risks (e.g., 37.1× higher odds for 0-2 years) support targeted interventions [10,11]. Serotype-specific patterns (e.g., EV-A71 in major outbreaks) did not significantly alter overall risks, but future models could incorporate laboratory data [23-25]. The EV-A71 vaccine (introduced 2018, not routine) showed no clear impact on post-2020 trends in our analysis, likely due to low coverage [26-28].

Comparison with Prior Work

Compared to ARIMA models ($R^2=0.65-0.78$) [4], our RF approach achieves superior accuracy due to nonlinear modeling and age-specific features. The high hospitalization risk in young children aligns with clinical studies [2,3], but our population-level analysis provides more robust estimates. Recent ML applications for HFMD risk prediction in China and Taiwan further validate our methodology [15-17]. Our 6.8% MAPE compares favorably to influenza (MAPE~20-30%), dengue (~15-25%), and COVID-19 (~10-40%) forecasting systems [29-31].

Strengths and Limitations

Strengths: The 17-year dataset, rigorous temporal validation, and multi-algorithm comparison enhance reliability. The focus on age-specific features aligns with digital health priorities for precision surveillance [18,19].

Limitations: Surveillance data reflect healthcare-seeking behavior, not true incidence, potentially introducing bias. Aggregated data limit serotype-specific or individual-level analyses (e.g., no ICU data; estimated 10-15% of hospitalizations required ICU based on literature [3]). Changes in diagnostic protocols may affect trends. Validation in other regions is needed for generalizability [20]. No meteorological features were included, though they could improve predictions [32].

Generalizability

In countries with less comprehensive surveillance (e.g., Southeast Asia), performance may degrade due to incomplete data capture. Higher healthcare barriers could bias toward severe cases, while different age structures (e.g., older populations) might shift risks. Regional models could address Taiwan's urban/rural variations, improving local predictions.

Implications for Digital Health

This model supports real-time decision-making via digital platforms, enabling hospital resource planning and targeted interventions. Integration with dashboards could enhance usability, aligning with JMIR's focus on health informatics [5,12]. For implementation, weekly retraining is recommended for optimal accuracy, though quarterly updates balance cost. Reporting lag (~3-5 days) makes 1-week forecasts effectively 2-4 day ahead operationally. Anomalous predictions are flagged for review.

Future Directions

Future work should incorporate serotype data, environmental factors, and real-time implementation studies. Expanding to other diseases would validate the framework's generalizability [13,14]. Ensemble approaches (RF+XGBoost) could improve robustness; deep learning (e.g., LSTM) was not pursued due to sufficient performance with traditional ML.

Conclusions

ML-based forecasting using age-specific surveillance data enables accurate 1-2-week-ahead predictions of enterovirus hospitalizations, supporting proactive public health responses. We recommend that national surveillance systems evaluate the feasibility of implementing weekly ML-based hospitalization forecasts as part of routine infectious disease monitoring. The methodology offers a scalable framework for digital epidemiology, adaptable to other infectious diseases.

Acknowledgments

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Author Contributions

MM Kuan: Conceptualization, data curation, analysis, investigation, methodology, software, validation, visualization, writing (original draft, review, editing).

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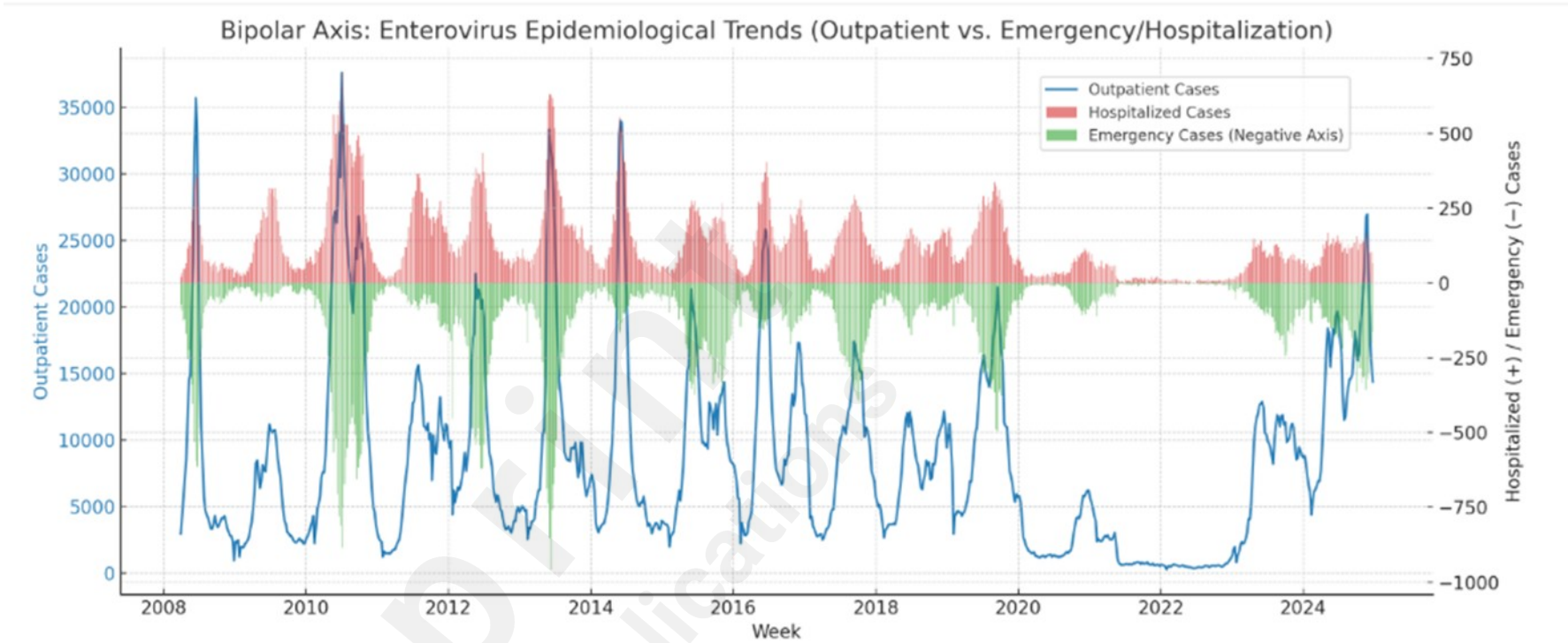


Figure 1. Temporal Trends of Enterovirus Cases by Healthcare Setting in Taiwan, 2008-2024. The plot illustrates distinct peaks in enterovirus cases (outpatient, emergency, hospitalization) from 2008 to 2024, visualized on a bipolar axis to highlight seasonal patterns and healthcare burden. The plot illustrates distinct peaks in spring/early summer (weeks 20-30), significant suppression during the COVID-19 period (2020-2022) due to non-pharmaceutical interventions, and a post-pandemic resurgence in 2022-2024.

2023 peaks exceeding pre-pandemic levels by 25%. Shading denotes pre-pandemic, pan and post-pandemic periods, emphasizing epidemiological shifts and potential immunity debt.

Actual vs. Predicted Enterovirus Hospitalizations (2022-2024)

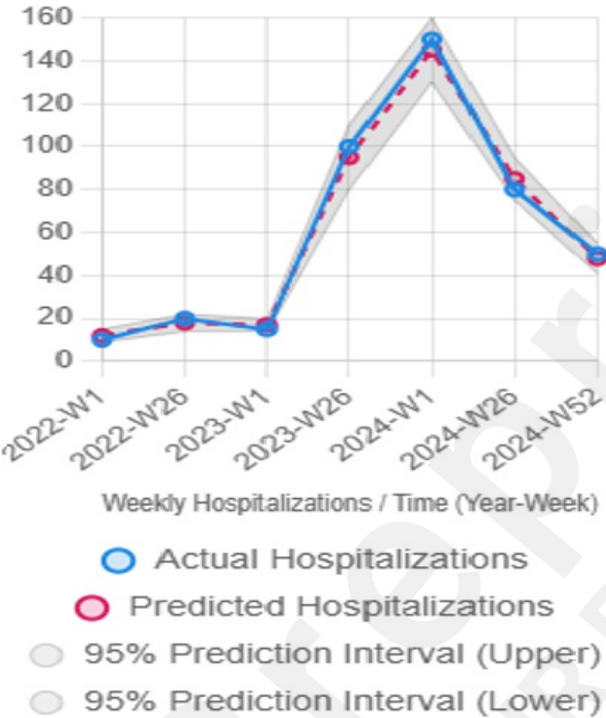


Figure 2. Actual vs. Predicted Weekly Enterovirus Hospitalizations, 2022-2024
Time-series comparison of actual (solid line) and predicted (dashed line) weekly enterovirus hospitalizations for the testin

period (2022-2024) using the 1-week-ahead Random Forest model with age-specific features. Shaded regions represent 95% prediction intervals. The model accurately captures pandemic-era suppression and post-pandemic predictions within ± 15 cases of observed values, though errors increase during rapid outbreak escalations (e.g., weeks 15-20, 2023).

Supplementary Files