Preplanned Studies

Comparison of Three Influenza Surveillance Data Sources for Timely Detection of Epidemic Onset — Chengdu City, Sichuan Province and Beijing Municipality, China, 2017–2023

Mingyue Pan[1]; Ying Shen[1,2]; Yao Wang[3]; Lu Long[3]; Xunbo Du[3]; Ying Sun[1,2]; Daitao Zhang[1,2]; Hui Yao[1]; Yonghong Liu[1]; Peng Yang[1,2]; Quanyi Wang[1,2]; Xiaoli Wang[1,2,#]; Liang Wang[3,#]

Summary

What is already known about this topic?

The syndromic surveillance system, exemplified by the influenza-like illness (ILI) surveillance system, has long been crucial in providing early warnings of influenza epidemics.

What is added by this report?

The analysis revealed that employing reported influenza case data from the nationwide Notifiable Infectious Diseases Reporting Information System (NIDRIS) enhanced the early detection of influenza epidemics, particularly within the context of multiple respiratory pathogens circulating concurrently.

What are the implications for public health practice?

The NIDRIS, characterized by its extensive coverage, obligatory reporting, high specificity, and real-time data transmission, offers a valuable tool for the effective early detection of influenza epidemics. Utilizing this system could enhance preparedness and responses to such health crises, potentially mitigating their impact on public health.

The influenza-like illness (ILI) surveillance system in China plays a crucial role in the syndromic surveillance infrastructure, serving as an essential tool for the early warning of influenza epidemics (*1*–*2*). Despite its historical significance, the effectiveness of this system is often compromised during periods when multiple respiratory pathogens are present, which may obscure the specific activities of the influenza virus (*3*–*4*).

In addition to the ILI surveillance system, China employs two other primary systems for influenza monitoring: the nationwide Notifiable Infectious Diseases Reporting Information System (NIDRIS) and the Virological Surveillance System (*5*). A notable challenge within these systems is the potential for undiagnosed or misdiagnosed influenza cases, particularly during non-epidemic periods and in the absence of laboratory confirmation. Nevertheless, NIDRIS requires the nationwide reporting of all confirmed influenza cases, providing a comprehensive dataset for analysis. On the other hand, the Virological Surveillance System, while offering highly accurate tracking of viral activities, is hampered by its time-intensive processes and lack of immediate data availability.

This study aimed to compare the effectiveness of these three surveillance datasets in detecting the timely onset of influenza epidemics. We employed the exponentially weighted moving average (EWMA) and a modified version of the Cumulative Sum (modified-CUSUM) to assess the performance of each dataset.

The findings from our evaluation suggested that the data derived from NIDRIS demonstrated superior performance in the early detection of influenza epidemics, particularly in scenarios involving the co-circulation of various respiratory pathogens. Based on these results, we recommend that public health practitioners in China prioritize the use of NIDRIS-reported case data to enhance the accuracy and timeliness of influenza epidemic detection. This approach could significantly improve the responsiveness and effectiveness of public health interventions against influenza outbreaks.

We analyzed three datasets covering the period from 2017 to 2023 to facilitate early detection of influenza epidemics in Chengdu City, Sichuan Province and Beijing Municipality, cities emblematic of the southern and northern China, respectively. The first dataset comprised the daily count of reported influenza cases from the NIDRIS. The second dataset included daily reports of ILI cases from an ILI surveillance network, drawing data from 144 sentinel hospitals in Beijing and 11 in Chengdu. Finally, the third dataset was constructed by multiplying weekly ILI reports by the influenza positivity rate (PR) (ILIs*PR), as determined from the Virological Surveillance System active in Beijing and Chengdu.

We utilized two widely accepted outbreak detection algorithms, the EWMA and the modified-CUSUM, to facilitate early warnings of influenza epidemics (Supplementary Material, available at https://weekly.chinacdc.cn/). The EWMA algorithm is designed for analyzing time series data by applying exponentially decreasing weights to older observations. An alert is triggered when the moving average surpasses a predefined threshold. Similarly, the modified-CUSUM algorithm monitors the cumulative difference between observed and expected values, issuing an alert when this deviation exceeds its respective threshold (*6*). The benchmark for these analyses was the influenza PR, which we deemed the gold standard. We defined the influenza season as spanning from the 27th week of one year to the 26th week of the following year. The threshold for an alert was set when the PR exceeded 40% of its peak value (*7*).

To assess model performance, we employed evaluation criteria including sensitivity, specificity, and the Youden Index to optimize parameters. Sensitivity measures the model's ability to correctly identify true positive instances when an alert is warranted, calculated as the ratio of true positives to all instances that should trigger an alarm. Specificity, in contrast, evaluates the model's accuracy in identifying true negative instances where no alert is needed, computed as the ratio of true negatives to all instances without an alarm (*8*). The Youden Index is derived by summing the sensitivity and specificity and then subtracting one, providing a single statistic that balances both metrics.

Data for each season were partitioned into training and test sets to facilitate early warnings. For the 2021–2022 season, for instance, all preceding data was utilized as the training set, while data from the 2021–2022 season comprised the test set. This approach was uniformly adopted for subsequent seasons. We optimized parameter values using the training sets, employing evaluation metrics such as sensitivity, specificity, and the Youden Index to determine effectiveness. Subsequently, the model demonstrating the highest performance with these optimized parameters was selected for early signal detection in the test sets.

In the case of the ILIs*PR dataset, the PR for the most recent week was only available on the final day of that week. Consequently, we employed a Long Short-Term Memory (LSTM) model (*9*) to forecast the latest PR in the test sets. The LSTM network, a variant of recurrent neural network, is particularly adept at longitudinal data prediction. It effectively retains critical data over time, which is essential for capturing long-term dependencies that enhance the accuracy of both current and future predictions.

Prediction accuracy was quantified using the mean squared error (MSE). All analyses were conducted using R (Version 4.3.1, R Foundation for Statistical Computing, Vienna, Austria), except for the LSTM model which was implemented using Python (Version 3.8.13, Python Software Foundation, Beaverton, USA).

Surveillance data from Beijing revealed a consistent annual peak in ILIs each January up until 2020. However, the emergence of the coronavirus disease 2019 (COVID-19) pandemic and the simultaneous circulation of multiple respiratory pathogens disrupted this established seasonal trend. Notably, an atypical peak occurred in 2023, occurring despite limited influenza virus activity (Figure 1). In contrast, the combination of reported ILI cases and virus PRs provided a more accurate reflection of influenza virus activity when the virus was actively circulating.

During periods of concurrent circulation of multiple respiratory pathogens, both reported cases and ILIs*PR demonstrated superior performance compared to ILIs alone. Specifically, across the last three seasons in Beijing, reported cases and ILIs*PR consistently exhibited good sensitivity, with reported cases also displaying strong specificity. The composite Youden Index for these three seasons indicated that reported cases achieved the best overall performance (0.905), followed by ILIs*PR (0.844), and ILIs (0.566). In Chengdu, reported cases consistently exhibited better sensitivity and specificity. Conversely, the performance of ILIs and ILIs*PR was found to be suboptimal, achieving overall Youden Index scores of only 0.49 and 0.74, respectively, as shown in Table 1.

The somewhat reduced specificity observed in reported cases and ILIs*PR can be primarily attributed to the prompt issuance of early warnings, which, in turn, led to a rise in the number of false positives. In scenarios where the prioritization of early warnings is critical, such performance might be deemed beneficial. Notably, an increase in false positives for ILIs was particularly evident during periods of low influenza activity, underscoring that in the presence of co-circulating pathogens, this dataset might not represent the optimal choice (Figure 2).

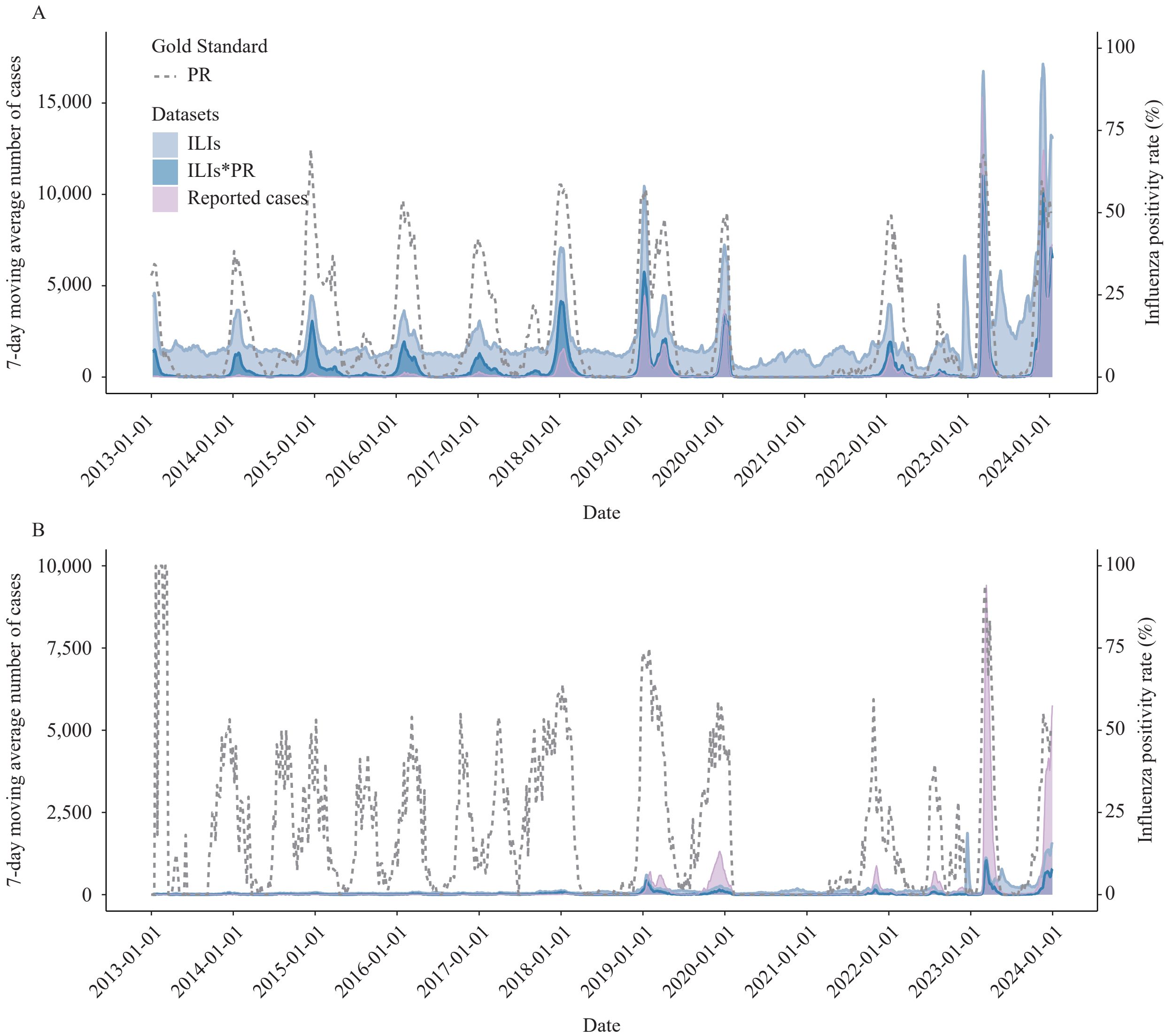

FIGURE 1. The 7-day moving average of the daily number of new cases in the three datasets and the weekly influenza positivity rate, 2013–2023. (A) In Beijing Municipality; (B) In Chengdu City, Sichuan Province.

Note: This figure illustrates the trends in the 7-day moving average of reported influenza cases, ILI cases, ILI cases adjusted for influenza positivity rate, and the weekly influenza positivity rate. The light blue shaded area represents the trend in ILI cases, while the dark blue shaded area indicates the trend in ILI cases adjusted by the influenza positivity rate. The pink shaded area depicts the trend in reported cases derived from the nationwide NIDRIS. The dotted line displays the weekly influenza positivity rate. Reported cases indicate the number of reported cases from the nationwide NIDRIS; ILIs*PR indicates the number of cases of influenza-like illness multiplied by the positivity rate of the influenza virus.

Abbreviation: PR=positivity rate; NIDRIS=Notifiable Infectious Diseases Reporting Information System; ILI=influenza-like illness.

DISCUSSION

This study revealed that data reported through NIDRIS provided a superior early warning of influenza epidemics in both Beijing and Chengdu, particularly in the presence of concurrent respiratory pathogen co-circulation. This was indicated by the highest Youden index values among the three datasets examined. Since the 2017–2018 and 2018–2019 influenza seasons, Beijing and Chengdu have enhanced the reporting of clinically diagnosed influenza cases within the NIDRIS system. The data from this system demonstrated a robust capability to accurately capture influenza activity, correlating closely with the influenza PR.

In contrast, the count of ILI cases exhibited diminished effectiveness as an early warning indicator. This trend was particularly pronounced during the 2022–2023 influenza season, during which the Youden

TABLE 1. Performance of three datasets for the early warning of influenza epidemic in Beijing Municipality and Chengdu City, Sichuan Province, using test sets, 2021–2024.

City	Datasets	Evaluation Metrics	Influenza Season*			Total
			2021–2022	2022–2023	2023–2024	
Beijing	Reported cases	Sensitivity	0.959	1.000	1.000	0.982
		Specificity	0.982	0.903	0.881	0.923
		Youden Index	0.941	0.903	0.881	0.905
	ILIs	Sensitivity	0.714	1.000	0.914	0.848
		Specificity	0.946	0.538	0.754	0.718
		Youden Index	0.661	0.538	0.668	0.566
	ILIs*PR	Sensitivity	1.000	1.000	1.000	1.000
		Specificity	0.863	0.866	0.778	0.844
		Youden Index	0.863	0.866	0.778	0.844
Chengdu	Reported cases	Sensitivity	1.000	1.000	1.000	1.000
		Specificity	0.879	0.771	0.865	0.819
		Youden Index	0.879	0.771	0.865	0.819
	ILIs	Sensitivity	0.857	0.893	1.000	0.912
		Specificity	0.725	0.498	0.619	0.578
		Youden Index	0.582	0.391	0.619	0.490
	ILIs*PR	Sensitivity	0.829	0.964	1.000	0.923
		Specificity	0.802	0.857	0.754	0.817
		Youden Index	0.631	0.821	0.754	0.740

Note: Reported cases indicate the number of cases reported through the nationwide NIDRIS; ILIs*PR indicates the number of cases of influenza-like illness multiplied by the positivity rate of the influenza virus.
Abbreviation: NIDRIS=Notifiable Infectious Diseases Reporting Information System; ILI=influenza-like illness; PR=positivity rate.
* The influenza season was defined as the period from the 27th week of one year to the 26th week of the next year.

Index in Chengdu dropped below 0.4. Prior to the COVID-19 pandemic, the daily count of ILI cases reported in Beijing closely corresponded with the influenza PRs. However, a marked divergence between ILI case numbers and influenza PRs emerged from 2020 to 2023, a period characterized by the co-circulation of multiple respiratory pathogens including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Mycoplasma pneumoniae, and respiratory syncytial virus (RSV). This discrepancy was similarly noted in data from the United Kingdom and the United States (*10*–*11*). Consequently, ILI counts may be less reliable as indicators of influenza virus activity.

Our findings indicate that the dataset created by multiplying the number of reported ILI cases by the influenza PR exhibited strong early warning capabilities. Its performance, as measured by the Youden Index, surpassed that of using ILI counts alone. It appears that, in theory, this dataset could most effectively track daily increments in influenza cases. However, the reliance on laboratory testing data to ascertain PRs constrains its timeliness. To overcome this limitation and enhance the ability to provide real-time alerts, we integrated a predictive model employing LSTM techniques to approximate the most current influenza PRs. This predictive model demonstrated a low MSE, recording values of 0.0012 in Beijing and 0.0059 in Chengdu, which indicates its promising utility for the early detection of influenza outbreaks.

This study was subject to several limitations. First, both Beijing and Chengdu enhanced their reporting of influenza cases in NIDRIS starting from 2018, which resulted in a paucity of historical data. This limited dataset may have affected the robustness of optimal model selection in the training sets, potentially impacting the models' ability to detect epidemics early in the test sets. Second, a significant disparity in the number of sentinel hospitals between Beijing and Chengdu resulted in the early warning models performing better in Beijing, based on reported ILI case numbers. This discrepancy in the daily ILI case reports between the two cities may pose challenges when assessing their performance in early warning

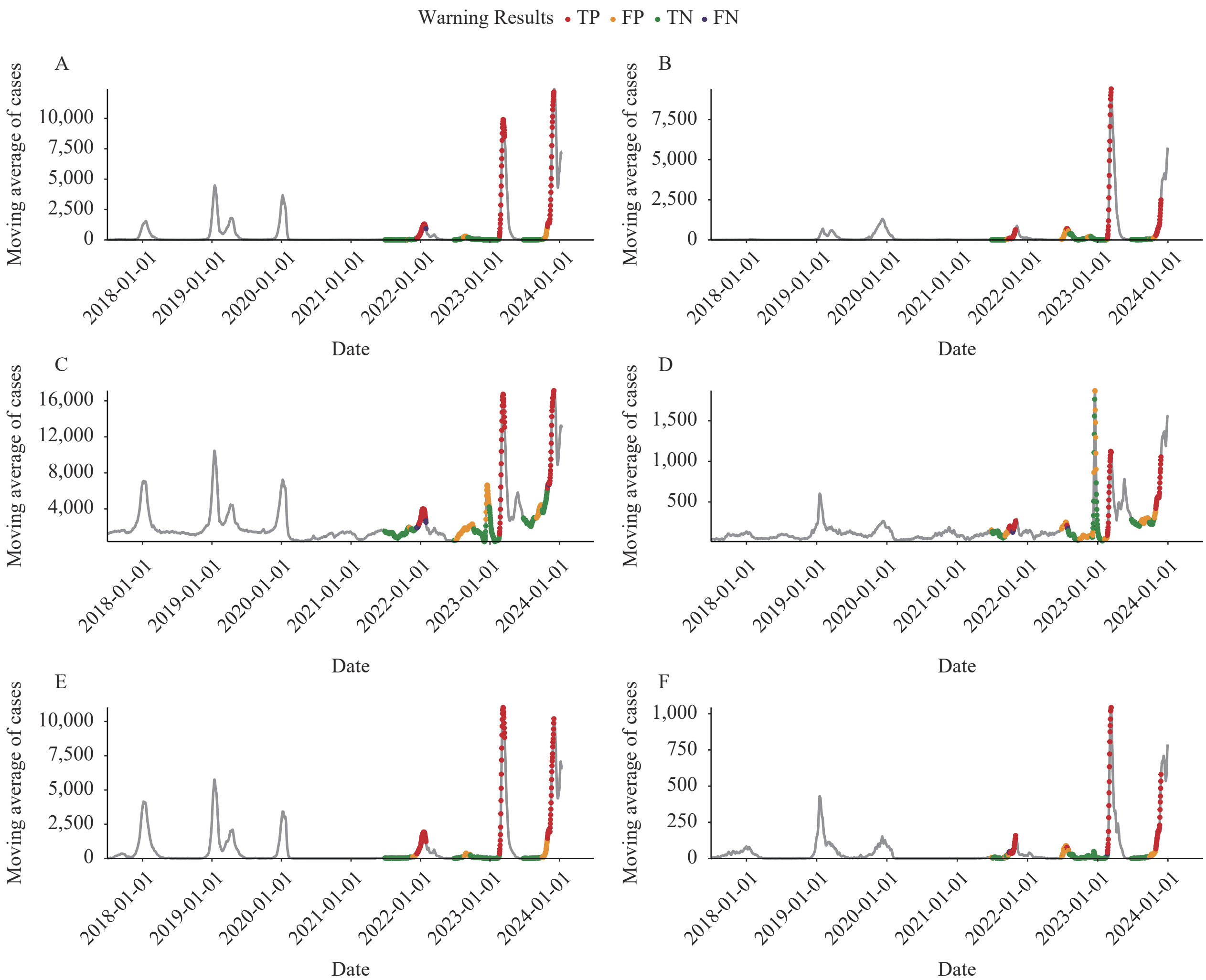

FIGURE 2. Warning results of the optimal model across three datasets for the early warning of influenza epidemic in Beijing Municipality and Chengdu City, Sichuan Province, 2021–2024. (A) Reported cases in Beijing; (B) Reported cases in Chengdu; (C) ILIs in Beijing; (D) ILIs in Chengdu; (E) ILIs*PR in Beijing; (F) ILIs*PR in Chengdu.

Note: This figure shows the performance of the three datasets for the early warning of influenza epidemics. For season 2021–2022, all data before 2021–2022 served as the training set, with data for 2021–2022 as the test set. This approach was consistently followed for subsequent seasons. The gray line represents the 7-day moving average number of corresponding cases. The red dots indicate TP, where the model accurately predicted an impending influenza epidemic; the orange dots represent FP, where the model incorrectly predicted an epidemic; the green dots signify TN, where the model correctly predicted the absence of an epidemic; and the purple dots represent FN, where the model failed to predict an actual influenza epidemic. Reported cases indicate the number of reported cases from the nationwide NIDRIS; ILIs*PR indicates the number of cases of influenza-like illness multiplied by the positivity rate of the influenza virus.

Abbreviation: PR=positivity rate; NIDRIS=Notifiable Infectious Diseases Reporting Information System; ILI=influenza-like illness; TP=true positive; FP=false positive; TN=true negative; FN=false negative.

using ILI numbers. Third, our study utilized data collected during the COVID-19 pandemic. Nonpharmaceutical interventions (NPIs) were implemented prior to the downgrading of COVID-19 management according to the law on prevention and treatment of infectious disease in China. These interventions could have affected case numbers across the three datasets, thus potentially introducing biases into our analysis.

In summary, the NIDRIS, known for its comprehensive national coverage, obligatory reporting, high specificity, and consistent, real-time reporting capabilities, holds promise as a valuable early-warning tool for the onset of influenza epidemics. This is particularly relevant in regions where there is a lack of adequate ILI surveillance systems. As China places an increasing emphasis on early-warning capabilities, improvements in data quality and system informatization of NIDRIS are anticipated. These enhancements are expected to expand its utility in providing early warnings not only for influenza but for other infectious diseases, such as enterovirus infections as well. However, it is crucial to recognize that ILI surveillance remains vital for assessing the impact of concurrent circulation of respiratory pathogens on healthcare resource utilization. Therefore, it continues to provide a critical foundation for informed decision-making in the preparation and allocation of medical supplies and resources.

Conflicts of interest: No conflicts of interest.

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Corresponding authors: Xiaoli Wang, wangxiaoli198215@163.com; Liang Wang, 363686849@qq.com.

[1] Beijing Center for Disease Prevention and Control, Beijing, China; [2] Beijing Research Center for Respiratory Infectious Diseases, Beijing, China; [3] Chengdu Center for Disease Control and Prevention, Chengdu City, Sichuan Province, China.

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SUPPLEMENTARY MATERIAL

Model Development and Performance Assessment

Early warning models: To provide early detection of influenza epidemic onset, we utilized two established outbreak detection algorithms: the Exponentially Weighted Moving Average (EWMA) and the modified Cumulative Sum (modified-CUSUM). We considered a T-day time series = $(X_1, \ldots, X_T)^\top$, where X_t is the influenza case counts for the t-th day. The distribution of cases was assumed to follow $X_t \sim N(\mu, \sigma^2)$.

EWMA model was defined as follows:

$$
\begin{aligned}
Z_1 &= X_1, \\
Z_t &= \lambda X_t + (1-\lambda) Z_{t-1}, \\
\mathrm{UCL_t} &= \widehat{\mu_\mathrm{t}} + \mathrm{k}\widehat{\sigma_\mathrm{t}}\sqrt{\frac{\lambda}{2-\lambda}},
\end{aligned}
$$

where X_t represents the case counts for the t-th day, Z_t denotes the weighted daily counts, $\lambda\,(0<\lambda<1)$ denotes the weighting factor, and k denotes the control limit coefficient. Let t_{move} be the moving period, and then the mean and standard deviation of $(X_{t-2-t_{move}}, \ldots, X_{t-3})^\top$ was calculated as $\widehat{\mu_t}$ and $\widehat{\sigma_t}$, denoting the estimated value of μ and σ. The set of days that should trigger an alarm is $\mathcal{T} = \{t: Z_t > UCL_t\}$.

In the modified-CUSUM analysis, three models — C1, C2, and C3 — were evaluated. The definitions of these models are as follows:

$$
\begin{aligned}
C1_0^{'} &= C2_0^{'} = 0, \\
C1_t^{'} &= \max\{0, X_t - (\widehat{\mu_t} + k\widehat{\sigma_t}) + C1_{t-1}^{'}\}, \\
C2_t^{'} &= \max\{0, X_t - (\widehat{\mu_t} + k\widehat{\sigma_t}) + C2_{t-1}^{'}\}, \\
C3_t^{'} &= C2_t^{'} + C2_{t-1}^{'} + C2_{t-2}^{'}, \\
H_t &= h\widehat{\sigma_t},
\end{aligned}
$$

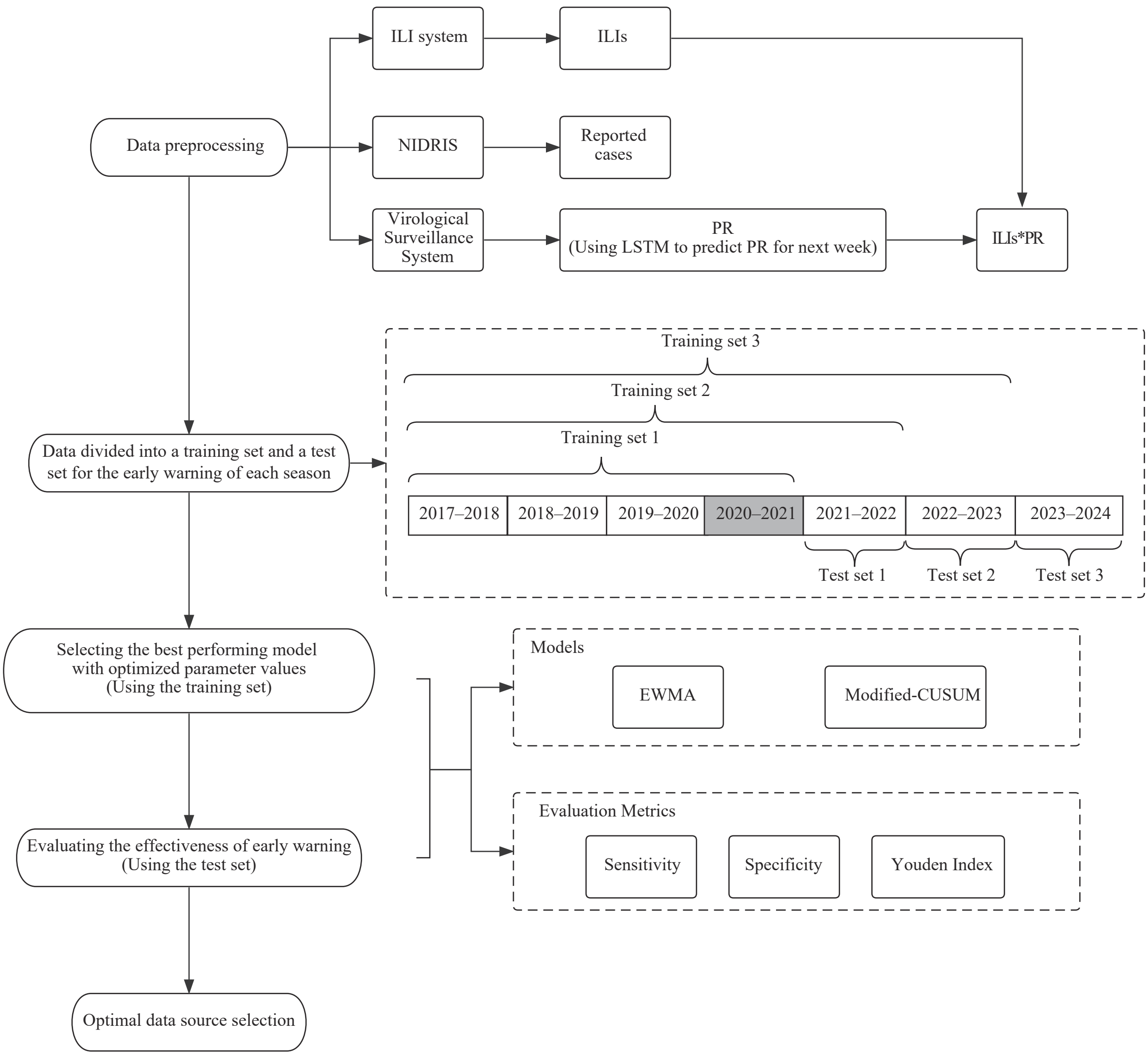
where $C1^{'}$, $C2^{'}$ and $C3^{'}$ denote the modified cumulative sum of daily counts in C1, C2 and C3 models, k denotes the control limit coefficient, and h denotes the threshold coefficient. Let t_{move} be the moving period. In C1 model, the mean and standard deviation of $(X_{t-t_{move}}, \ldots, X_{t-1})^\top$ were calculated as $\widehat{\mu_t}$ and $\widehat{\sigma_t}$. And in C2 model, $\widehat{\mu_t}$ and $\widehat{\sigma_t}$ were calculated by the mean and standard deviation of $(X_{t-2-t_{move}}, \ldots, X_{t-3})^\top$. The sets of days that should trigger an alarm for $C1^{'}$, $C2^{'}$ and $C3^{'}$ are $\mathcal{T}_1 = \{t: C1_t^{'} > H_t\}$, $\mathcal{T}_2 = \{t: C2_t^{'} > H_t\}$ and $\mathcal{T}_3 = \{t: C3_t^{'} > H_t\}$, respectively.

Model Optimization and Evaluation: In both the EWMA and modified-CUSUM models, we segmented each dataset into training and test sets to provide season-specific early warnings. For Beijing, Training Set 1 encompassed influenza seasons from 2017–2018 through 2020–2021, with Test Set 1 covering the season of 2021–2022. Training Set 2 constituted the seasons from 2017–2018 to 2021–2022, with Test Set 2 including the 2022–2023 season. Finally, Training Set 3 spanned from the 2017–2018 season through the 2022–2023 season, with Test Set 3 comprising the 2023–2024 season.

In Chengdu, the partitioning of training and test sets mirrored that of Beijing, except that all training sets began with the 2019–2020 season. Notably, the absence of influenza epidemics in both Beijing and Chengdu during the 2020–2021 season meant that the gold standard for alerts for that period was set to ‘no alerts.’

Parameters such as t_{move}, λ and k in EWMA, and t_{move}, k and h in in modified-CUSUM, were optimized using training datasets based on evaluation criteria that included sensitivity, specificity, and the Youden Index. The model demonstrating the highest performance, with optimized parameter values, was subsequently applied to detect early warning signals in the test datasets. Analyses involving case numbers utilized a 7-day moving average to mitigate effects associated with day of the week variations.

The entire analysis process is depicted in Supplementary Figure S1. The outcomes of the model selection are presented in Supplementary Table S1.



SUPPLEMENTARY FIGURE S1. Flowchart of early warning model construction and performance evaluation.
Note: The gray box indicates that the 2020–2021 season had no alerts in the gold standard, based on the absence of influenza epidemics. Reported cases indicate the number of reported cases from the nationwide NIDRIS; ILIs*PR indicates the number of cases of influenza-like illness multiplied by the positivity rate of the influenza virus.
Abbreviation: ILI=influenza-like illness; NIDRIS=Nationwide Notifiable Infectious Diseases Reporting Information System; PR=positivity rate; LSTM=long short-term memory; EWMA=exponentially weighted moving average; modified-CUSUM=modified Cumulative Sum.

SUPPLEMENTARY TABLE S1. The best performing model and its optimized parameter values for each test set.

City	Influenza season	Datasets	Model	Optimized parameters			
				λ	**h**	**k**	t_{move}
Beijing	2021–2022	ILIs	EWMA	0.1	−	7.0	140
		Reported cases	C1	−	8	1.5	20
		ILIs*PR	C2	−	15	1.5	26
	2022–2023	ILIs	C1	−	4	1.5	30
		Reported cases	EWMA	0.1	−	8.0	141
		ILIs*PR	EWMA	0.2	−	5.0	140
	2023–2024	ILIs	C1	−	6	1.5	14
		Reported cases	C2	−	9	2.0	14
		ILIs*PR	EWMA	0.2	−	5.0	140
Chengdu	2021–2022	ILIs	C2	−	4	1.0	10
		Reported cases	C2	−	20	1.5	58
		ILIs*PR	C1	−	9	1.0	13
	2022–2023	ILIs	C1	−	8	0.5	7
		Reported cases	C1	−	4	2.0	60
		ILIs*PR	EWMA	0.1	−	6.0	95
	2023–2024	ILIs	EWMA	0.1	−	1.0	43
		Reported cases	C2	−	20	1.5	58
		ILIs*PR	EWMA	0.5	−	3.0	137

Note: Reported cases indicate the number of reported cases from the nationwide NIDRIS; ILIs*PR indicates the number of cases of influenza-like illness multiplied by the positivity rate of the influenza virus; C1 indicates modified-CUSUM C1 model; C2 indicates modified-CUSUM C2 model.

"−" indicates that the model does not contain this parameter.

Abbreviation: NIDRIS=Notifiable Infectious Diseases Reporting Information System; ILI=influenza-like illness; PR=positivity rate; EWMA=exponentially weighted moving average; CUSUM=Cumulative Sum.