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Early warning of potential epidemics: A pilot application of an early warning tool to data from the pulmonary clinic of the university hospital of Thessaly, Greece

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A B S T R A C T

Background & methods: This paper describes a pilot application of the Epidemic Volatility Index (EVI) to data from the pulmonary clinic of the University Hospital of Thessaly, Greece, for monitoring respiratory infections, COVID-19, and flu cases. EVI, a simple and easily implemented early warning method based on the volatility of newly reported cases, exhibited consistent and stable performance in detecting new waves of epidemics. The study highlights the importance of implementing early warning tools to address the effects of epidemics, including containment of outbreaks, timely intervention strategies, and resource allocation within real-world clinical settings as part of a broader public health strategy.
Results: The results presented in the figures demonstrate the association between successive early warnings and the onset of new waves, providing valuable insights for proactive decision-making. A web-based application enabling real-time monitoring and informed decision-making by healthcare professionals, public health officials, and policymakers was developed.
Conclusions: This study emphasizes the significant role of early warning methods in managing epidemics and safeguarding public health. Future research may explore extensions and combinations of multiple warning systems for optimal outbreak interventions and application of the methods in the context of personalized medicine.

Introduction

Emerging epidemics pose a profound challenge to public health and medical infrastructures due to their potential to induce widespread morbidity, mortality, and healthcare resource strain. Epidemic Volatility Index (EVI) is considered a simple, straightforward, easily applied, warning method that was developed to identify upcoming waves in an epidemic [12]. The method is based on the volatility of newly reported cases per unit of time and issues an early warning when the volatility change rate exceeds a threshold. Originally EVI was developed for the data on the daily confirmed cases of the coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV 2) [22]. EVI's application to data from the current COVID-19 pandemic revealed a consistent and stable performance in terms of detecting new waves. It is highlighted that the application of early warning tools, like EVI, to other epidemics and syndromic surveillance tasks will alleviate the epidemics-associated effects via (i) containment of outbreaks, (ii) timely application of intervention strategy and (iii) resource allocation [12].

The potential benefits of such early warning tools extend beyond specific disease containment. Early warning tools in syndromic surveillance tasks come helpful for cases when a definite diagnosis/identification of the aetiological agent does not exist, but an increase in the reported cases of "general - non-specific" clinical conditions (e.g., respiratory infections etc.) is observed [3,9]. Key example with immense value for public health is the monitoring of respiratory infections. Firstly, many respiratory infections are highly

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transmissible, meaning they can spread rapidly among populations. By monitoring the prevalence of these infections, physicians and public health officials can detect unusual patterns or upticks in cases that might signal the beginning of an epidemic. Early epidemic detection provides more time to (i) mobilize resources, (ii) implement containment measures, and (iii) inform the public to mitigate its spread [18]. Besides COVID-19 [11] many previous epidemics and pandemics were caused by airborne pathogens (e.g., Spanish Flu [2], Severe acute respiratory syndrome (SARS) [16]) and had respiratory sytem infection as main manifestation. These illnesses have shown their capacity to cause significant morbidity and mortality on a global scale. Therefore, keeping a vigilant eye on respiratory infections can help identify the emergence of a novel, potentially dangerous pathogen before it becomes widespread [23]. Lastly, early warning allows for rapid development and distribution of relevant vaccines or treatments [20]. Scientists can start researching the pathogen sooner, and healthcare infrastructure can prepare for increased demand. It also affords government agencies and health organizations the opportunity to educate the public about the situation, possible prevention measures, and symptoms to watch for, which is crucial in managing public fear and anxiety during health crises. In essence, the value of monitoring respiratory infections as an early warning system lies in enabling a proactive rather than reactive approach to disease management, potentially saving lives and resources [21].

Many European countries, including Greece, in the last years have been affected by the financial crisis that resulted in structural challenges with declines in the number of the healthcare workforce, merging of healthcare units [13]. Thus, an outbreak will push the capabilities of the healthcare system to its limits and may compromise the health of the people. Strategy and measure implementation for mitigation of the pandemic depends on the condition of the health care system and its ability to respond to an influx of COVID-19 cases. As a respiratory disease, severely affected COVID-19 patients require intensive case and mechanical respiratory support. Furthermore, an epidemic has serious societal and economic consequences, thus initiatives from the government are needed to stimulate the affected sectors [7].

To this end, implementation of simple, easily applied, warning methods can assist experts to decide if the case augmentation is expected or not, to take further actions or not, until it is clarified what is happening. These methods as part of the syndromic surveillance scheme will aim to (i) identify illness early, before diagnoses are confirmed and reported to public health agencies, (ii) to mobilize a rapid response. The importance of reporting and monitoring of major clinical signs and laboratory indicators (e.g., lung inflammation, diarrhea, oxygen saturation etc.) was highlighted in previous influenza pandemic [19], as well as in current COVID-19 pandemic [24] This is evident from the literature where many studies highlight the significance of using real-time, often non-specific symptoms or preliminary diagnosis information collected during routine healthcare provision to supplement public health surveillance programmes [9].

This study describes an ongoing pilot application of EVI to data from the pulmonary clinic of university hospital of Thessaly (UHL), Greece as an early warning tool for respiratory infections (from October 2021), COVID-19 (February 2022) and flu (November 2022) cases. This study investigates EVI's efficacy in a clinical context and introduces an implementation of the tool in an application that facilitates automatic update of the tool and available daily output/predictions to the final user.

Materials and methods

The UHL is the largest hospital of the Thessaly region, and one of the two hospitals of Larissa, Greece. According to duty schedule, UHL received patients in 24 h-turns (i.e., on every second day) and therefore data on the variables of interest were available on every two days. Specifically, the dataset includes cases of respiratory infections, COVID–19 and flu. The project started in October 2021 monitoring respiratory infections and in February 2022 and November 2022, COVID-19, and flu, respectively, were also monitored. This is an ongoing project and the number of cases is regularly updated and reported in an online application.

Among patients admitted in the Emergency Department of university hospital of Thessaly, Greece, data are collected for those who meet at least one of the following inclusion criteria: (i) cough (productive or not), (ii) malaise and fatigue (iii) headache (iv) body temperature above 37.3 °C (v) sneezing (vi) congested nose (vii) dyspnea/shortness of breath (viii) chest tightness. Exclusion criteria of the study include: (i) known infection at another site that explains symptoms (ii) inability to cooperate (iii) denial of participation.

Polymerase Chain Reaction (PCR) or antigen-specific tests for SARS-COV2 and flu virus as well as chest X-ray are performed in all participants that fulfill the inclusion criteria. Any positive test (PCR or antigen-based test) is recorded as COVID-19 or flu infection respectively. Participants with negative tests and relative respiratory symptoms are considered as cases of respiratory infections in general.

EVI is based on the calculation of the rolling standard deviation for a time series of epidemic data (i.e., the number of new cases per two days). The number of consecutive observations used for this calculation is the rolling window size. EVI is estimated as the relative change of the standard deviation between two consecutive rolling windows and a warning signal is issued if (i) this relative change exceeds a threshold and (ii) the observed cases at the current time point are higher than the average of the reported cases in the previous week. The precision of EVI is measured by its sensitivity (correctly issuing an early warning for an upcoming epidemic wave) and specificity (not issuing an alarm in the absence of upcoming waves). At each time point sensitivity and specificity are estimated for all possible rolling window sizes and relative change thresholds. The window size and threshold values that maximize the sum of sensitivity and specificity are selected. EVI is calculated at a new time point and a decision is made on whether a warning signal is issued or not. EVI is a recently published simple early warning method and the entire estimation process is described in detail in Kostoulas et al. [12].

The model output - warning signals - is updated every two days - once a new observation is recorded. A web-based application, using the Shiny r-package [5], has been developed that automatically provides a model prediction. The shiny server is hosted by an Ubuntu virtual machine offered by ViMa (Virtual Machines) and a full guide with step-by-step instructions on how to deploy a shiny application on an Ubuntu server is available on request from the authors.

Results

Updated results, every two days, are reported in an online application (http://83.212.175.101:3838/version10/). Figs. 1–3 present observations (updated every two days), on the original and logarithmic scale, for respiratory infections, and flu cases, respectively with red dots corresponding to dates that, according to EVI, an early warning was issued, while grey dots correspond to time points without an early warning indication. Furthermore, the online application at each time point reports the number of cases, selected window size, relative change threshold, sensitivity and specificity for all monitored variables. In all variables the defined criterion for issuing an early warning (red dot), is that an increase in the mean of expected cases equal or higher to twenty percent is expected in the coming week. The result figures clearly demonstrate that successive early warnings are associated with the onset of a new wave, whereas

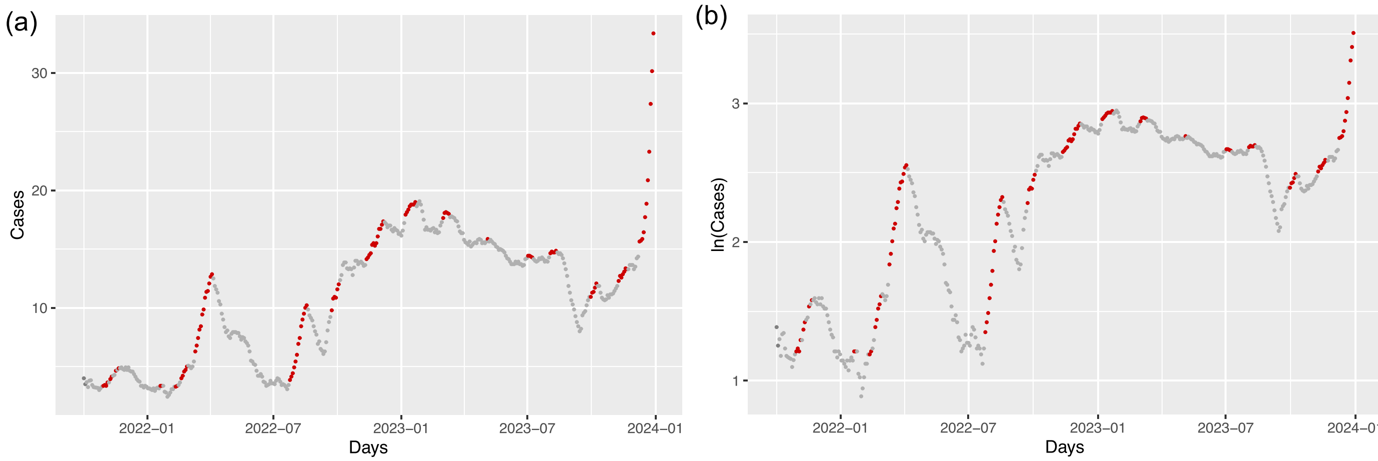

Fig. 1. a - Number of Respiratory Infections observed every two days from October 2021 - December 2023; red dots correspond to days that, according to EVI*, an early warning was issued, while grey dots correspond to days without an early warning indication. **b** - Number of Respiratory Infections observed every two days from October 2021 - December 2023 on the logarithmic scale; red dots correspond to days that, according to EVI, an early warning was issued, while grey dots correspond to days without an early warning indication.

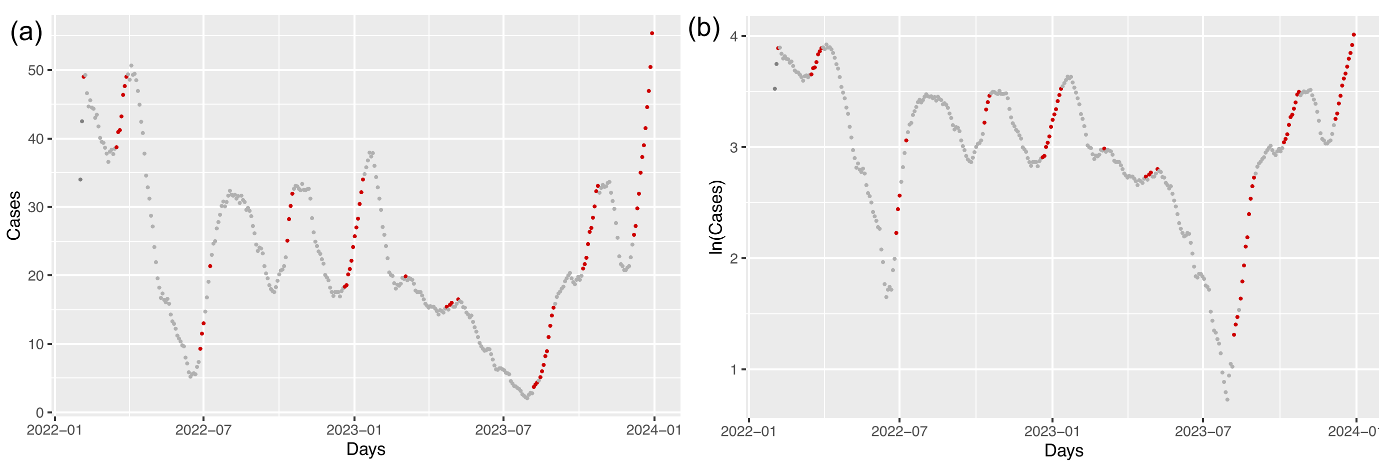

Fig. 2. a - Number of COVID-19 cases observed every two days from February 2022 - December 2023; red dots correspond to days that, according to EVI, an early warning was issued, while grey dots correspond to days without an early warning indication. **b** - Number of COVID-19 cases observed every two days from February 2022 - December 2023 on the logarithmic scale; red dots correspond to days that, according to EVI, an early warning was issued, while grey dots correspond to days without an early warning indication.

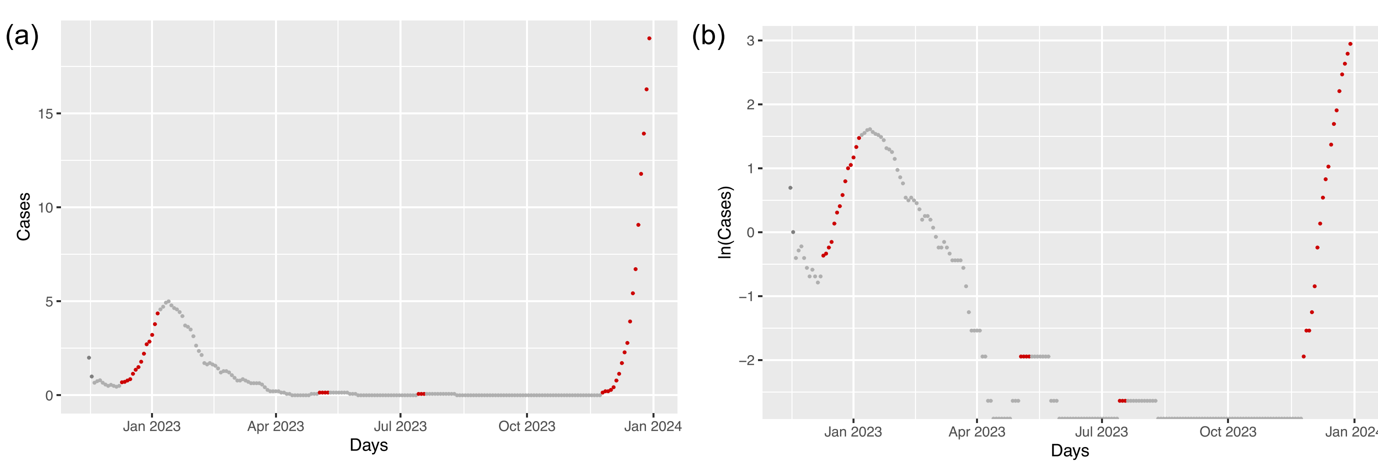

Fig. 3. a - Number of Flu cases observed every two days from November 2022 - December 2023; red dots correspond to days that, according to EVI, an early warning was issued, while grey dots correspond to days without an early warning indication. **b** - Number of Flu cases observed every two days from November 2022 - December 2023 on the logarithmic scale; red dots correspond to days that, according to EVI, an early warning was issued, while grey dots correspond to days without an early warning indication. *EVI – Epidemic Volatility Index.

the absence of warnings indicates a stable trajectory or a potential decline in the number of cases.

Discussion

This study describes a pilot application of an early warning method, called EVI that is based on the volatility of newly reported cases, to data from the pulmonary clinic of the university hospital of Thessaly, Greece. Specifically, respiratory infections, COVID-19 and flu cases between October 2021 and December 2023 were monitored. A repetition of early warnings (red dots in the figures) indicates the beginning of an epidemic wave (or similarly an absence of early warning - series of grey dots indicates that the number of cases will remain stable or drop). This is a consistent and stable finding for all the variables monitored in this study and is indicative of satisfactory model performance. For example, regarding flu cases in Fig. 3 there is a repetition of early warnings (red dots) from December 2022 until the first days of January 2023. The repetition of early warnings signals the beginning of an epidemic flu wave. However, during the first day of January 2023, the model does not issue an early warning, even though an increase in the cases of flu is observed. This phenomenon signals the reaching of the peak and a deceleration on the volatility of the new cases, since EVI is estimated based on it [12]. These situations (repetition of early warning in the beginning - absence of early warning close to the peak) is also evident in COVID-19 cases (Fig. 2 - December 2022 - January 2023). Regarding flu cases early warning signals, in the second half of April and July, are observed, while no cases are reported. These are false early warnings, isolated instances that did not occur in a consecutive series and do not pose a concern. Flu is considered a seasonal epidemic, and according to European Centre for Disease Prevention and Control (ECDC) week 17 (mid-April) indicates the end of the seasonal influenza epidemic [6].

Generally, the added value of an early warning method in public health is significant since it enables timely detection and response to potential health threats. Early warning systems provide crucial insights into emerging diseases and allow for proactive measures to be taken before an outbreak becomes widespread. The role of technology in utilizing available, easily implemented tools is crucial in assisting resource allocation and prediction in the context of epidemic management. Technological advancements enable efficient implementation of tools, real-time data collection and analysis, allowing for timely decision-making in allocating resources [4]. The availability of updated results online via a web-based application allows for continuous monitoring and informed decision-making based on the early warning indicators provided by EVI. This tool can assist healthcare professionals, public health officials, and policymakers in effectively responding to respiratory infections, COVID-19, and flu cases.

Furthermore, early warning methods can be of important value to clinical physicians as well, as a useful system for the emergency room. Physicians can be alerted to potential outbreaks or epidemics, allowing timely interventions and appropriate patient management. Plus, early warning tools can contribute to enhancing clinical decision-making by improving the accuracy of diagnoses and facilitating personalized treatment plans [8,15]. Additionally, EVI has the utility to be applied in non-infectious diseases e.g., cardiovascular diseases to monitor variations in the incidence rates. Lastly, EVI's application to data collected from the internet, e.g., news trends, could potentially offer insights into public health issues beyond traditional surveillance systems. By analyzing the variability in internet search queries, social media trends, and news reports, EVI could be adapted to serve as an early indicator of public interest for health-related topics. For instance, a sudden spike in searches or discussions about specific symptoms could precede the identification of an emerging non-infectious disease trend or a new infectious disease outbreak [14].

Respiratory infection outbreaks constitute a major public health issue as they spread widely and quickly within the community and institutions in the absence of the right precaution measures and organization. Having the recent example of COVID-19 pandemic and management of disease, the patients were not evenly treated. More specifically, treatment in hospitals in urban areas was associated with the lowest case-fatality as compared to hospitals in suburban or rural areas indicating differences in public health care services and hospital capacities [10]. Similarly, interesting challenges arise in settings such as jails and immigration removal centers, where high rates of population movement and potential contacts take place, reinforcing an outbreak and problems in management of respiratory infections [1]. To conclude, implementation of EVI in urban areas, small hospitals or prison and migration centers could be useful as a warning sign for implementation of protective measures, intensive testing for respiratory viruses and bacteria and activation of human, financial and technical resources.

Lastly, since the first description of the EVI method in 2021 [12], several extensions to the method are being developed. Recently Pateras et al. [17] introduced the convergence Epidemic Volatility Index (cEVI), a modification of EVI. Thus, a combination of multiple warning systems could potentially create a surveillance umbrella that would result in early implementation of optimal outbreak interventions.

Conclusions

In conclusion, this pilot application of EVI to data from the pulmonary clinic of the university hospital of Thessaly, Greece, for monitoring respiratory infections, COVID-19 and flu cases has emphasized the importance of implementing early warning tools for syndromic surveillance tasks in addressing the effects of epidemics and highlighted the potential of EVI within a real-world clinical setting as part of a broader public health strategy. The utilization of EVI demonstrated a consistent and stable performance in detecting new waves of epidemics. By enabling timely detection and response to potential health threats, the application of early warning methods supports healthcare professionals, public health officials, and policymakers in effectively managing epidemics and safeguarding public health.

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Declaration of Competing Interest

The authors have no competing or any other interests that might be perceived to influence the results and/or discussion reported in this paper.

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