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A framework for the early detection and prediction of dengue outbreaks in the Republic of Panama

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The dengue virus (DENV) is endemic in most tropical regions of Central and South America. It is known that when the number of mosquito vectors (*Aedes aegypti* and *Aedes albopictus)* for this disease becomes abundant, the number of infectious cases increases. DENV has been known to be continuously circulating in Panama since 1993, with an increasing number of cases reported in recent years after the COVID-19 pandemic, as well as other vector-borne diseases. Preventing dengue outbreaks by having an early detection system is of the utmost importance. To tackle this task, we propose an overall surveillance system framework tailored to the Panamanian situation but applicable to many countries suffering the same maladies. This manuscript presents a transdisciplinary vision that encompasses aspects of sample management, vector surveillance, sharing of weather information, and georeferencing of cases in a Geographic Information System and defining data-driven software solutions for prediction of possible outbreaks.

KEYWORDS

dengue virus, arbovirus, epidemiological surveillance, outbreak, one health, mosquito vectors, early detection

1 Introduction

The dengue virus (DENV) is endemic in the tropical regions of the world. Beyond the greatest scientific efforts and research, the current global dengue situation has reached unprecedented levels. More than 7 million cases worldwide have been reported to the World Health Organization (WHO) before the end of the first trimester of the year 2024 (1). Although the latest numbers have stunned the whole world, the worst is happening in the Americas, with an accumulated 4.5 million cases, that is, about 80% of the total global cases for 2023. In fact, while the four dengue serotypes (DENV-1, -2, -3, and -4) are known to be present in Asian regions and the Americas, their virulence is higher in the latter (2).

The Central and South American regions have been particularly affected by this threat. Some estimates say there is a three-fold increase compared to the same period in 2023, highlighting the acceleration of this health problem (3, 4). This situation has been noted by various authors who are pondering about it becoming a global threat (5).

Factors contributing to this increase in cases are currently unknown, but many authors point to urbanization (6), inadequate water provision (7) and waste management (8), climate change (9), changes in vector distribution and adaptation (10–12), massive population migrations (13, 14), scarce monitoring (15), and fragile health systems, mostly weakened after the COVID-19 pandemic (16).

In the specific case of Latin America, molecular and clinical information on dengue is scarce, so spatio-temporal trends are hard to determine (17). Despite the information gap in the region, there are many developments in the creation and implementation of early detection and outbreak detection systems. Some countries have developed location-based data-driven health approaches to their prediction and generation of early detection systems (18–20). Others are focusing on molecular and genomic surveillance of dengue with the creation of the Pan American Health Organization (PAHO) *VIGENDA* program for the Americas (21).

Panama only has an epidemiological guide for dengue detection and monitoring (22, 23), while in Mexico and Brazil (24, 25) clear strategies have been defined, and early detection systems have been developed or implemented for dengue. This Perspective article aims to analyze the state of the current system and provide an overview of what considerations it needs to take into account to make it a reality in the near future.

2 Brief history of dengue in Panama

According to Díaz et al. (26), DENV serotypes have been known to be re-circulating in Panama continuously since 1993. The cases have been growing steadily over the years, although it is known that some of its effects have been masked by COVID-19 and other circulating viruses (27). For example, the endemic cocirculation of other arboviruses such as chikungunya (28, 29) and Zika (30, 31), which are transmitted by the same vector. In addition, other clinically similar zoonotic diseases complicate the epidemiological approach and notification of cases (32), and the identification of the beginning of the dengue epidemic.

Figure 1 represents the laboratory detection of dengue in clinical cases reported through the surveillance of dengue and arboviral diseases during and between different outbreaks in Panama, most of them related to the reintroduction of DENV serotypes, from 1999 to the present (33). These samples are normally analyzed through the National Surveillance System of the Ministry of Health. From 1993 to 2012, dengue diagnosis and surveillance were performed at the Gorgas Memorial Institute for Health Studies (ICGES), the national public health institution and the national central laboratory that supports the Ministry of Health, and samples were analyzed using DENV-IgM or viral isolation according to the days of symptoms, and since 2013, viral isolation for acute samples has been replaced by the RT-PCR technique (26, 29).

More importantly, Figure 1 provides a view of the current state of dengue in the country. In 2024, the highest number of dengue cases was reported since its reintroduction into the country. This increase could be attributed to the introduction of serotype 4 (34, 35). Since this serotype had limited circulation in the country during 1999 and 2000, most of the population does not have a specific immune response to this serotype and can face increased transmission and a higher risk of severe dengue.

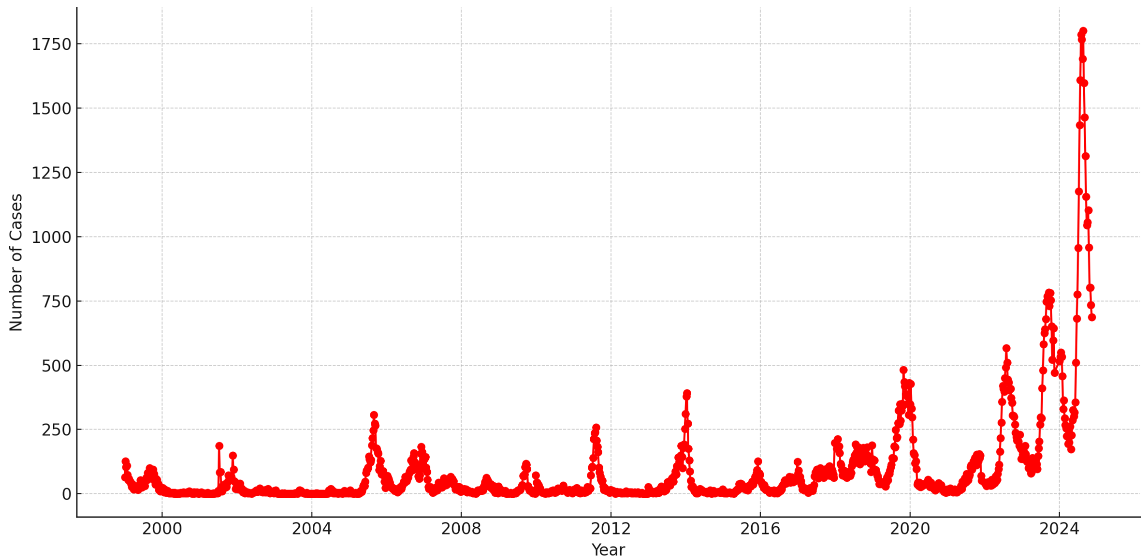

FIGURE 1
Dengue incidence in the Republic of Panama from 1999 to 2024 (epidemiological week #46). In this figure, the Y-axis represents the number of cases and the X-axis represents time, with each dot representing the total number of confirmed cases per epidemiological week.

2.1 Current Panamanian dengue monitoring and outbreak detection system

In Panama, suspected human cases are usually first detected in primary or secondary care healthcare centers, where a physician makes a diagnosis based on clinical symptoms, and laboratory diagnostics are performed *in situ* (Figure 2). Confirmed cases are reported to the National Epidemiology Department (NED) of the Ministry of Health using epidemiological nexus, the NS1 positive dengue test (<9 days of onset symptoms) or DENV-IgM (between >10 and <17 days of onset symptoms). Both suspected and confirmed cases are reported to the epidemiology department of each health region and, after the mandate, later to the NED of the Ministry of Health.

A subset of samples are sent to the Gorgas Memorial Institute of Health Studies (ICGES). Specifically, 25% DENV positive and 10% DENV negative samples are sent for further analysis using RT-qPCR DENV serotyping for acute samples (< 5 days after the onset of symptoms) or the quality control test of IgM antibodies for convalescent samples (6-21 days after the onset of symptoms). However, some healthcare centers do not have the personnel to take blood samples, do not have a laboratory, and lack laboratory resources or laboratory personnel, and thus, dengue laboratory diagnosis and surveillance are not done. In addition, it is difficult to respect the cold chain and to transport sera samples from limited access areas to the reference laboratory in the metropolitan city. This causes “silent” epidemiological regions that report suspected cases of dengue and other arboviral cases using epidemiological nexus or clinical diagnosis, without detection of a specific antigen, antibodies, or RT-qPCR test.

The dengue surveillance system in place in Panama integrates data generated from different components: 1) the clinical component is reported to the epidemiological department of each health center, this information is collected by region and then reported to the national epidemiological office; 2) the vector control component, where each region reports the larval index of the communities to the national vector office, which then reports to the national epidemiological office. The private sector also reports weekly the number of suspected and confirmed clinical cases directly to the national epidemiological office. Although there is a standard for immediately reporting dengue cases to epidemiology offices, most agencies report weekly or even monthly, and it has been a great challenge to have updated real-time epidemiological information to prevent outbreaks. This situation means that epidemiological action on dengue is about controlling the outbreak situation and not about preventing it.

Entomological surveillance and vector control are based on a systemic survey of houses infected with *Aedes* larvae (29). However, there is no automatic entomological surveillance associated with the response to the outbreak and it is not targeted to areas where human cases are highly detected. Moreover, viral molecular detection is not done as part of entomological surveillance, thus it is currently not possible to obtain viral genomic surveillance in both humans and vectors.

In addition, public health institutions are often added to the end of the sampling queue, either for human molecular sample diagnostic from healthcare institutions that do not have tests or for serotype and genomic surveillance. Finally, research projects often allow for the detailed characterization of genomic and epidemiological data of viruses retrospectively or based on outbreak responses or study-specific cohorts, and all generated data are communicated to the National Epidemiology Department.

Probably the key aspect to be noted is that in Panama there is low integration between different health systems (Ministry of Health, Social Security system, private hospitals). In addition, decisions are not taken with a multidisciplinary approach, making

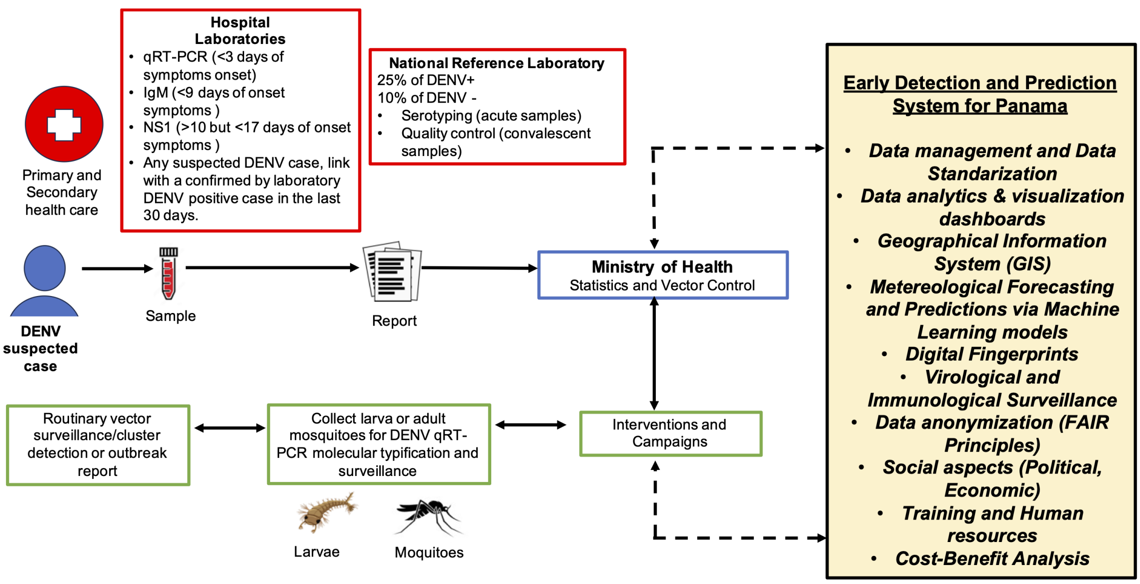

FIGURE 2
Proposed integrated system for the early detection and prediction of dengue outbreaks in Panama.

the situation more cumbersome. The implementation of a system for early detection and prediction of a dengue outbreak in Panama will challenge the traditional epidemiological format, which is currently based on the weekly and monthly collection of vector data of reported cases, to a permanent update of the epidemiological situation, including silent zones or zones that do not regularly send samples to reference laboratories due to the lack or limitation of resources to transport samples.

3 Characteristics of dengue early-warning systems

Baharom et al. (36) provide a systematic review of the use of the early warning system (EWS) as an outbreak prediction tool. More importantly, they selected 17 articles that describe EWS systems and came to conclusions on best practices and what they should encompass. The systematic analysis of the characteristics of the early warning system (EWS) revealed that they are based on an indicator-based surveillance (IBS) structure. An IBS predicts DENV + outbreaks using a set of independent variables or alarm indicators. These “alarm indicators” fall into epidemiological, meteorological, entomological, socioeconomic, and population categories. Some studies also incorporate enhanced vegetation, urbanization, and education data as alarm indicators.

In general, an EWS would use the Ministry of Health data as the primary epidemiological alarm indicator when these data are available. Meteorological data are the next most used alarm indicator for studying and predicting DENV+ outbreaks (36, 37). Temperature and rainfall are the most common variables in this alarm category. An EWS model that used these two meteorological variables in combination with epidemiological data and elevation information was able to predict 75% of the Colombian outbreaks from 2007 to 2015 (38).

After epidemiological and meteorological data, entomological or mosquito data, such as House Index (HI), Aedes Index (AI), Ovitrap Index, and infection rates for male and female mosquitoes, also have potential for developing an EWS (36, 38). Combining entomological data with meteorological factors has improved the performance of EWS models in several studies (39, 40). However, transmission is known to occur even at low vector density levels (41, 42). Finally, socioeconomic alarm indicators such as population density, socioeconomic categorization indexes, and access to water and energy can play an essential role as sources of information to predict future outbreaks (36, 43). This was tested by Zhao et al. (43) when they included the GINI index, population information, and education coverage to develop a machine learning and forecasting model to predict outbreaks on different scales in Colombia.

The prediction of a DENV+ outbreak can also be studied as a data science cycle (44), as the factors needed to predict dengue cases coincide with the alarm indicators described above. However, vital data management and data processing aspects that are required for the functioning and maintenance of an EWS are: data sources, data representation, and data preparation which are in the hands of institutions and organizations generating and recollecting the information, such as the Ministry of Health in the case of case incidence. The survey by Siriyasatien et al. (44) also addresses the models used to forecast and predict an outbreak and how to evaluate their performance using evaluation metrics. For continuous response variables, i.e., incidence, mortality, total number of cases, metrics such as mean squared error (MSE), mean absolute error (MAE), or the coefficient of determination (R^2) can be used (45). Finally, Siriyasatien et al. (44) present the challenges of deploying an EWS from a modeling point of view and managing massive amounts of data. One thing authors often add to an EWS and keep in line with health administrations is a focus on cost effectiveness, keeping in mind the financial costs of such a system (46, 47).

4 An integrated early-detection and prediction system for Panama

Here we describe the fundamental aspects and design of a dengue EWS that could then be presented to the Ministry of Health and all public and private institutions involved (such as ICGES, CSS, and private centers), as well as other organizations that could bring their expertise, such as the Panama association of epidemiology (SOEPIMO[1]) for discussion before developing a pilot study, which would allow improvement of the EWS before implementing it at the national level with constant capacity to upgrade taking into account feedback from the Ministry of Health and other users as well as its performance evaluation.

When thinking of the design of a data-based EWS for Panama, we first need to define its goals:

1. To have significant predictive power for the next outbreaks.
2. To help local authorities in their decision-making.

The system should incorporate the necessary aspects needed to prevent and control DENV+ outbreaks which have historically occurred every few years (Figure 1), but are becoming increasingly frequent.

4.1 Standardizing data management

To support the goals stated above, data management protocols must be developed. This must begin with the standardization of data from its source and end with its distribution among stakeholders and decision-makers. A nationwide effort to standardize the acquisition, preparation, and management of epidemiological data is vital for monitoring alarm indicators for future DENV+ outbreaks in Panama and could also be applied to other arboviral outbreaks. In addition to this, we foresee the development of a standard data analytics process applied to epidemiological data, incorporating software dashboards with alarm indicators. These dashboards would integrate information from active surveillance vector indexes, their dynamics, and

1 https://www.soepimo.org

incidence cases. This mimics the global dengue dashboard surveillance system launched by the WHO used to integrate reports from all regions and strengthen monitoring efforts (48, 49).

4.2 Geographic information system integration

An effective EWS for Panama should also leverage a Geographic Information System (GIS) database to support spatio-temporal analysis. For example, it should provide functions to isolate points or regions of interest and perform a specific analysis (50, 51). Time-series analysis, machine learning, and compartmental models have already been used to assess the effect of climate on the incidence of DENV+ cases in the metropolitan region of Panama (52, 53). These models should be expanded to predict outbreaks on a spatio-temporal scale, incorporating factors such as population movement, urbanization, and vegetation cover to improve predictive precision (36, 44).

4.3 Alarm indicators for early detection

A robust and effective EWS needs to include three key alarm indicators. 1) Digital fingerprint, which is needed to understand what people are searching for on social networks and querying on Internet databases and search engines. More importantly, it can be positively correlated with the onset of dengue fever (54–58). 2) Virology surveillance, focused on the surveillance of a new serotype and genotype (59, 60) of Dengue or known arboviruses. 3) Immunological surveillance, to determine the previous seroprevalence of dengue or flavivirus infection in the population (61).

4.4 Ethical and legal considerations

The use of health data for predictive models requires adherence to ethical and legal standards. Patient privacy must be protected in line with WHO guidelines (62, 63). Only de-identified clinical and demographic data should be used for real-time epidemiological analysis and predictive modeling. Governance structures involving patients, clinicians, and epidemiologists should guide the development of the model and ensure compliance with national and international regulations (64, 65). Models should operate at the neighborhood level to maintain privacy while enabling targeted interventions. Transparency in the manner of how data is collected and analyzed is critical to fostering trust among stakeholders (66).

4.5 Training and communication

The ethical use of predictive models also requires extensive training for public health professionals. Decision-making processes should balance the results of the predictive model with social, economic, and political factors (18, 67). Communicating model-based scenarios and their associated risks is key to ensuring informed decisions and public trust.

4.6 Implementation and national integration

The proposed system, illustrated in Figure 2, is based on routine data collection from human and vector samples, with rapid reporting facilitated by an integrated GIS-based platform. This system can alert healthcare facilities at both the primary and secondary levels, enabling timely responses.

This initiative represents a digital transformation project for Panama. Pilot programs in specific regions could pave the way for nationwide implementation. The project will require highly trained personnel to manage epidemiological, entomological, virological, immunological, and meteorological data, as well as to develop predictive models that capture viral dynamics and transmission intensity (68, 69).

Panamanian authorities should conduct detailed cost-benefit analyses to refine this system, drawing on regional examples from Nicaragua, Colombia, and Mexico (70–73).

5 Discussion

The general capacity of countries to respond to multiple concurrent outbreaks is limited due to global resource shortages, including inequality in the availability of diagnostic kits, silent regions for national serotype and genomic surveillance, trained staff, and community awareness (74, 75). In the context of the Latin American region, the challenges include limited access to real-time epidemiological and meteorological data and a lack of information on vector behavior. This has been highlighted in studies conducted in Peru (76), Colombia (38), Mexico, and Brazil (25). These studies use predictive models to address the lack of real-time data and other important limitations such as weak intersectoral work to coordinate response and share relevant data in response to outbreaks (25). These implementations are relevant to the Panamanian situation and their highlights were considered for our proposed integrated system.

The current increase in Panamanian cases placed the country on the path to a high-risk country under the WHO framework (49). To successfully implement a comprehensive early detection and prediction system for dengue outbreaks in Panama, it is essential to address the potential limitations and challenges specific to the country.

Panama faces technical, organizational, and data infrastructure constraints, such as limited computational resources, as there is a lack of high-performance computing (HPC) centers in the country. This is supplied through external regional computational resources (77–79). Likewise, there is a known shortage of skilled workforce capacity, especially in technological fields (80, 81). More importantly, there are limitations in the ability to collect real-time incidence data, including an uneven spatial sampling of key regions and neighboring areas (26, 52, 82). These data points are essential for public health officials to identify high-risk areas over time for current and future outbreaks (26, 82).

In addition, integrating data from various sources, including public and private health systems and agencies such as the Ministry of Health and meteorological services (83), poses logistical challenges that require detailed planning and organization. Sustainability is another crucial consideration. A cost-benefit analysis should assess the feasibility of maintaining the system over time, ensuring that adequate financial and human resources are available (84). Ethical and legal considerations are also paramount, particularly in the protection of sensitive health and geospatial data. In particular, in the Panamanian case, it should also comply with Law No. 81 on Personal Data Protection, enacted on 26 March 2019, and effective since 29 March 2021 (85),

The importance of this Perspective article is that it presents a trans-disciplinary vision encompassing aspects from sample management, tracking of cases, vector surveillance, georeferencing of cases, meteorological tracking (local and satellite), and most importantly, the use of machine learning algorithms for the prediction of possible outbreaks. These transdisciplinary monitoring and surveillance programs could have immediate potential impacts and benefits for prediction, prevention, and response systems in the country (86). As an improvement in the speed and efficiency of the public health response to dengue outbreaks and with real-time information, continuous monitoring could also allow for fast adaptation of the response to any changes or to quickly detect actions and decisions that have a greater impact and should be reinforced (87). Moreover, the fact that the system can be constantly improved by taking into account faced challenges shows that it is flexible and adaptable to different situations.

Finally, the surveillance system described in this manuscript is focused on the Panamanian scenario, but it should have a broader regional impact, as Panama could be seen as a pilot, and the system could be scaled up to other tropical countries with similar meteorological, environmental, demographic, and socioeconomic conditions facing similar mosquito vector-borne disease challenges.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

GU: Conceptualization, Writing – original draft, Writing – review & editing. YD: Conceptualization, Data curation, Methodology, Visualization, Writing – original draft, Writing – review & editing. SL-V: Conceptualization, Data curation, Methodology, Visualization, Writing – original draft, Writing – review & editing. JP: Writing – review & editing. JS-G: Conceptualization, Data curation, Funding acquisition, Methodology, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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