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Document

Unraveling the unparalleled 2024 epidemic of Dengue in the Americas

Desentrañando la incomparable epidemia de dengue de 2024 en Las Américas

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The year 2024 marked a pivotal moment in the history of public health in the Americas as the region grappled with an unprecedented surge in dengue cases[1,2]. Dengue, primarily transmitted by *Aedes aegypti* and *A. albopictus*, now also has the risk of transmission by *A. vitattus*[3], detected in Caribbean countries such as the Dominican Republic and Puerto Rico. Dengue has long been a concern in tropical and subtropical regions. However, the magnitude and severity of the outbreaks witnessed so far in 2024 surpassed anything previously recorded, posing immense challenges to healthcare systems, governments, and communities across the continent[4,5]. Further, it must be regarded as the potential role of travellers in the risk of introducing dengue into areas where mosquito vectors may be present and where there is no indigenous circulation of the virus. Therefore, there is a need to educate on preventive measures for both the population living in endemic areas and travellers from non-endemic areas. Since Latin America is one of the most frequent destinations for travellers from Europe and North America, dengue vaccination should be widely considered as a prevention tool within the scope of national dengue control programs in endemic areas and in a perspective of traveler health[6,7].

In the Americas, which reported 80% of the cases worldwide in 2023 (https://www.who.int/emergencies/disease-outbreak-news/item/2023-DON498), more than 30 countries and territories report, weekly and systematically, dengue information to the Pan American Health Organization (PAHO) (www.paho.org). Additionally, the laboratories that integrate the Dengue Laboratory Network of the Americas provide periodic information regarding the circulating serotypes in the region[8]. Nevertheless, heterogeneity in diagnosis and report may occur among some countries[9]. Just during the first 20 epidemiological weeks of 2024, a total of 8,246,951 dengue cases have been reported in the Americas (Figure 1). Of these, 3,839,613 (46.6%) were confirmed. From the total, 8,084 cases (0.09%) were classified as severe dengue, with significant variation among countries (Figure 2). In 2024, 3,666 deaths have been reported, with a case fatality rate of 0.04% (4 deaths per 10,000 cases), also with high variation among countries (Figure 3). This burden, specifically in terms of Disability-Adjusted Life Years (DALYs), represents 194,022.35 DALYs, for a rate of 32.65 DALYs per 100,000 pop. in Latin America just in 2021, according to the data of the 2021 Global Burden of Study (GBS) (https://vizhub.healthdata.org/gbd-results/) (Figure 4).

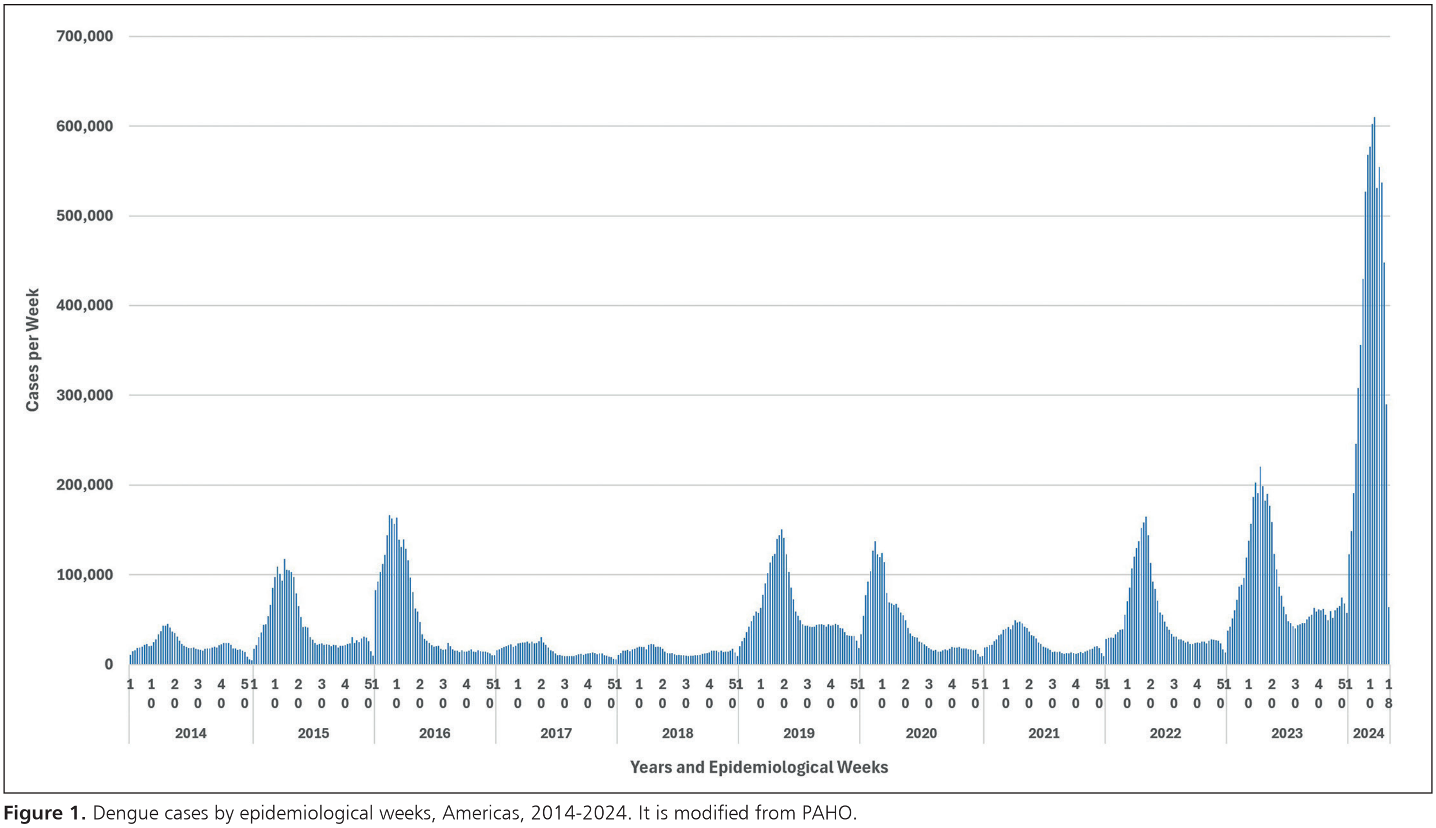

Figure 1. Dengue cases by epidemiological weeks, Americas, 2014-2024. It is modified from PAHO.

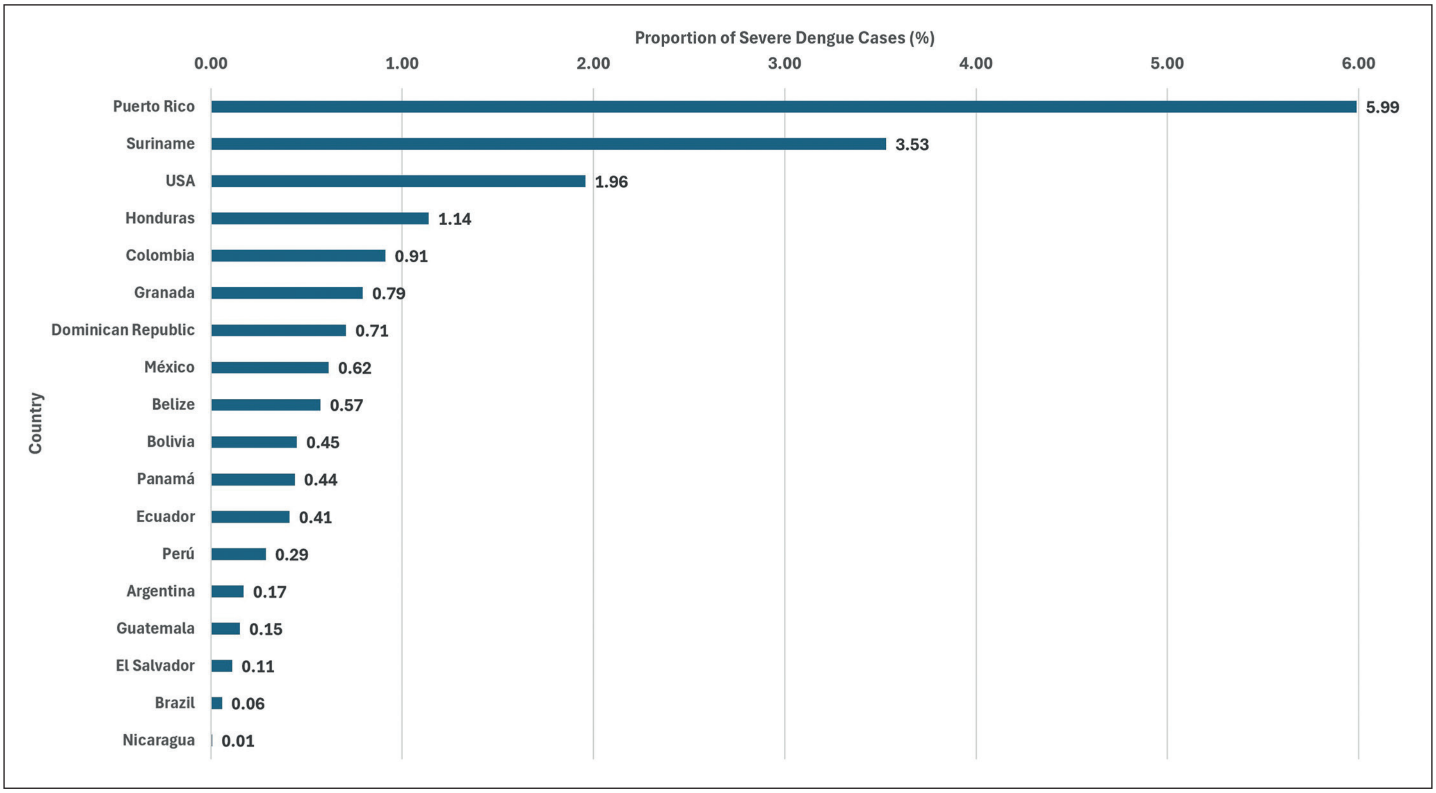

Figure 2. Proportion of Severe Dengue cases by countries, Americas, 2024. Modified from PAHO.

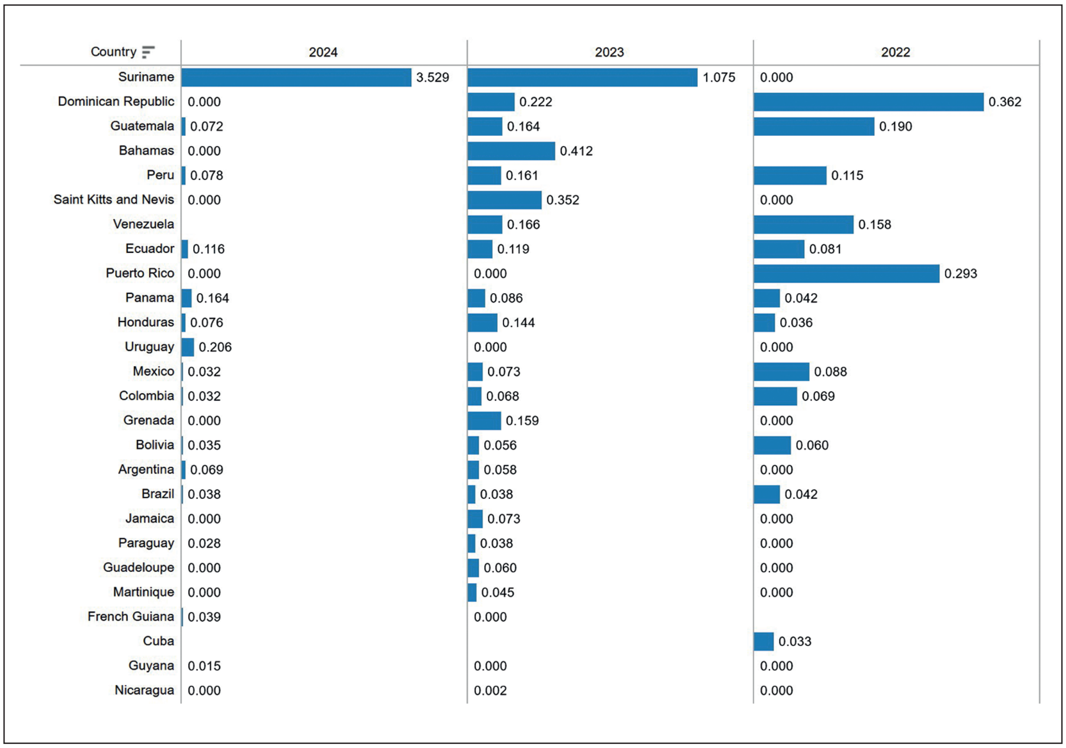

Figure 3. Case fatality rate (%CFR) associated with Dengue cases by countries, Americas, 2022-2024. From PAHO.

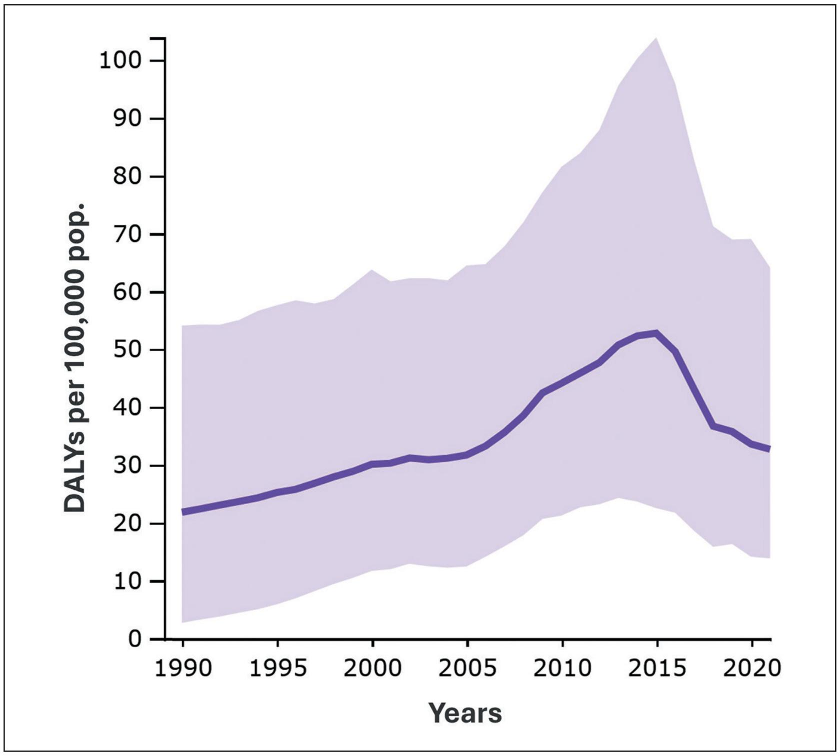

Figure 4. DALYs associated to Dengue in Latin America and the Caribbean, 1990-2021. Modified from 2021 GBS.

Regarding severe dengue, it is essential to consider the associated risk of antibody-dependent enhancement (ADE) of infection, which occurs when preexisting antibodies present in the body from a primary (first) dengue virus (DENV) infection bind to an infecting virus particle during a subsequent infection with a different dengue serotype[10,11]. Antigenic distance between primary and secondary dengue infections correlates with disease risk[12]. However, severe dengue may occur as a consequence of primary infection. Recent findings question the widely held belief that severe dengue is associated predominantly with secondary infections and emphasize the importance of developing vaccines or treatments to protect dengue-naive populations and seropositive subjects[13].

The four distinct dengue virus serotypes (DENV-1, DENV-2, DENV-3, and DENV-4), are circulating in the Americas. Several factors converged to fuel the unparalleled dengue epidemic in the Americas in 2024. Climate change, urbanization, globalization, co-circulation of different serotypes in areas with a large proportion of the population exposed in previous epidemics, and inadequate mosquito control efforts created a perfect storm for the proliferation of *Aedes* mosquitoes and the massive transmission of DENV[14,15]. Rising temperatures and changing rainfall patterns created conducive environments for mosquito breeding. At the same time, rapid urbanization led to densely populated areas with inadequate sanitation and water management systems, providing ample breeding grounds for mosquitoes[16-18]. Multiple other arboviral diseases are concurrently circulating in the Americas, especially Chikungunya and Zika, as well as Mayaro, Oropouche and Yellow Fever[19-32]. In addition, outbreaks of South American endemic hemorrhagic fever (HF) viruses such as Junin (Argentinian HF), Machupo and Chapare (Bolivian HF), Sabia (Brazilian HF), and Guanarito (Venezuelan HF)[33-37] were also reported.

Given the arboviral cocirculation, the Global Arbovirus Initiative, launched on 31 March 2022, is an essential cross-cutting effort initiated across the World Health Organization's Health Emergencies Programme, the Department of Control of Neglected Tropical Diseases, and the Immunization, Vaccines and Biologicals Department in collaboration with a growing body of multisectoral international partners. The pillars of the initiative provide a framework for objectives and priority activities to tackle emerging and re-emerging arboviruses with epidemic and pandemic potential focusing on monitoring risk, pandemic prevention, preparedness, detection and response, and building a coalition of partners (https://www.who.int/initiatives/global-arbovirus-initiative).

Globalization facilitated the rapid spread of dengue, as increased travel and trade facilitated the movement of infected individuals and vectors across borders. Moreover, the challenges posed by the COVID-19 pandemic, which strained healthcare systems and diverted resources away from mosquito control programs, further exacerbated the situation[38-42]. Hospitals and clinics were overwhelmed with patients presenting with dengue symptoms, leading to overcrowding, shortages of medical supplies, and increased pressure on healthcare workers. The dual burden of dengue and COVID-19 stretched resources to their limits, highlighting the need for robust and resilient healthcare systems capable of responding to multiple concurrent crises[43,44].

While dengue fever is endemic to many countries in the Americas, the burden of the 2024 epidemic was not evenly distributed[45,46]. Countries with weaker healthcare systems and limited resources faced disproportionate challenges in responding to the outbreak, as is probably the case for some Caribbean islands and low-income countries (Figures 2 and 3). Rural areas with limited access to healthcare and sanitation were particularly vulnerable, as were marginalized communities lacking basic infrastructure and public health services[47].

Furthermore, socioeconomic factors such as poverty, overcrowding, poor environmental management of solid waste, and inadequate housing exacerbated the risk of dengue transmission in vulnerable populations. The lack of access to mosquito repellents, proper sanitation, and healthcare services hindered prevention and control efforts, allowing the virus to spread unrestrictedly in many communities[48-50]. It should be emphasized that the One Health perspective should be included as a multidisciplinary approach to better understanding the course of emergencies and the re-emergence of dengue, which can trigger epidemics worldwide[51,52]. The pressure of climate change, global human migration, and growing interactions between wild fields and human implications in that field[1,2]. Conversely, certain regions in South America facilitate the accumulation of waste, including containers, vehicle tires, and other items that collect rainwater, thereby serving as artificial breeding grounds for mosquitoes. Compounding the challenge of dengue control, *Aedes* mosquitoes have developed resistance to repellents and insecticides[53,54].

The economic consequences of the 2024 dengue epidemic are profound, affecting individuals, communities, and entire countries. The direct and indirect costs associated with medical treatment, lost productivity, and vector control efforts burden already strained economies. Businesses suffered as employees fell ill, and tourism, a significant source of revenue for many countries in the Americas, was impacted by travel advisories and concerns about dengue transmission[55-57].

Moreover, the long-term economic impact of dengue fever[58], including its effects on workforce productivity and healthcare expenditures, threatened to exacerbate existing inequalities and hinder economic development in the region[59].

In the face of this unprecedented dengue epidemic, governments and public health authorities in the Americas implemented a range of response and mitigation efforts to contain the spread of DENV and reduce its impact. These efforts included intensified mosquito control measures, such as insecticide spraying, larval source reduction, and community mobilization campaigns to promote awareness and prevention[60-62].

Healthcare systems ramped up their capacity to diagnose and treat dengue cases. At the same time, efforts were made to improve the infrastructure for laboratory diagnosis, surveillance and reporting to understand the dengue epidemic's scope, dynamics and circulation of other arboviruses. Collaboration and coordination among countries and international organizations are crucial in sharing information, expertise, and resources to support the response efforts[63-65].

Innovations in vector control, such as Wolbachia-infected mosquitoes and novel insecticides, are promissory to control mosquito populations and reduce DENV transmission[1,66-70]. The inclusion of spatio-temporal modelling and Artificial Intelligence (AI) can be used for promising predictive purposes in the fight against dengue[1,51,52,71,72]. The integrated management strategy for preventing and controlling arboviral diseases in the Americas is key for the region (https://iris.paho.org/handle/10665.2/51787). Additionally, increase production capacity and access to the vaccine already available, in addition to research into new dengue vaccines and therapeutics continued, offering hope for future prevention and treatment strategies[73-78]. Furthermore, the role of the current introduction of a second dengue vaccine in the region, in countries such as Argentina and Brazil, needs further assessment, especially regarding effectiveness and safety in the upcoming months and years.

The unparalleled epidemic of dengue fever in the Americas in 2024 served as a stark reminder of the complex interplay of factors driving infectious disease outbreaks in an increasingly interconnected world. Climate change, urbanization of new areas without adequate planning in basic public services, globalization, and socioeconomic disparities all contributed to the emergence and spread of dengue, highlighting the need for a multifaceted and coordinated approach to disease prevention and control[79-82].

While the challenges posed by the 2024 epidemic were immense, they also spurred innovation, collaboration, and a renewed commitment to strengthening public health systems, addressing the root causes of disease transmission, and delving into innovative methods in epidemiological surveillance and vector control. As the region continues to grapple with the threat of dengue and other infectious diseases, the lessons learned from the 2024 epidemic will be invaluable in shaping future efforts to protect the health and well-being of populations across the Americas. As all these preventive measures have failed to control dengue in the region for many decades, the approval and introduction of new dengue vaccines seem to be an urgent public health intervention and probably one of the best strategies to face this disease.

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