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# The next arbovirus epidemic in Latin America and beyond: A question of when, not if – Mayaro, Oropouche, Usutu or Disease X?

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Over the past century, arboviruses have significantly shaped public health in Latin America (Fig. 1) [1–47]. Yellow fever virus (YFV) is the oldest known arbovirus in the Americas. Introduced in Africa in the 17th century, it was transmitted by *Aedes aegypti* mosquitoes until urban outbreaks were controlled, and urban YF was eliminated in Latin America [1,14,15]. Today, YF in Latin America is transmitted via sylvatic cycles involving non-human primates and Haemagogus and Sabethes forest-dwelling mosquitoes [44]. Despite the availability of an effective vaccine for over a century, YF remains a persistent threat, particularly among unvaccinated travellers and vulnerable populations [1,14,15]. The fear of the return of urban YF also persists, though, and could happen anytime.

The genetically related dengue virus (DENV), also of Old World origin, is now one of the most prevalent arboviruses in the American continent. Transmitted by *Aedes aegypti* and *Aedes albopictus*, DENV infections range from asymptomatic to severe with life-threatening complications [20]. In more than 100 countries, DENV serotypes have recently expanded into non-traditional areas, including parts of Europe, driven by climate change, travel, and migration [21,22]. In 2024, the Americas experienced the largest recorded DENV outbreak, surpassing 13 million cases [3]. Fortunately, new vaccines are crucial for mitigation.

The Chikungunya virus (CHIKV), first identified in Tanzania in 1952, emerged in the Americas in 2013. This is likely associated with human movement, causing explosive outbreaks [4,23]. Transmitted by *Aedes* mosquitoes, CHIKV leads to debilitating arthralgia that may persist for several months. In 2023, Paraguay and other South American countries experienced intense outbreaks [5]. Unlike DENV, CHIKV infection provides long-term immunity, and a newly approved vaccine is gradually becoming available.

Following CHIKV's trajectory, Zika virus (ZIKV) emerged in the Americas in 2013–2015, decades after its identification in sentinel macaques in Uganda [6]. Also transmitted by *Aedes* mosquitoes, ZIKV had devastating public health consequences during the 2014–2016 epidemic due to its teratogenic effects, including microcephaly and congenital Zika syndrome and an increased demand in mostly illegal abortion across Latin America and the Caribbean [24,25]. Additionally, ZIKV has been linked to Guillain-Barré syndrome [26,27]. Currently there are no approved vaccines [6,28]. The persistence of ZIKV in immune privileged sites and sexual transmission further contributes to high relevance in travellers, in addition to mandatory single blood donor testing across the US costing billions of US$ [45,46].

Two emerging arboviruses, Mayaro virus (MAYV) and Oropouche virus (OROV), are increasingly being recognized as potential candidates for future epidemics. The Mayaro virus (MAYV) was first isolated in Trinidad in 1954 and is primarily transmitted by *Haemagogus* mosquitoes. Although historically confined to the Amazon and other forest regions across South America, it remains under-researched [7,29]. A recent metagenomic study in the Colombian Amazon detected MAYV in febrile patients, highlighting its potential for circulation and expansion into new regions [8,48]. Immunity following MAYV infection appears to be similar to that following CHIKV infection, suggesting long-term protection after natural infection. However, the potential for urban transmission and degree of potential immune protection between the two antigenically related alphaviruses, MAYV and CHIKV, remain uncertain.

Oropouche virus (OROV) was first detected in 1955 near the Oropouche River in Trinidad, and has caused numerous outbreaks in Brazil and other South American countries [9,10,30,31]. In 2024, 16,239 cases were confirmed across Brazil, Bolivia, Peru, Cuba, Colombia, and other

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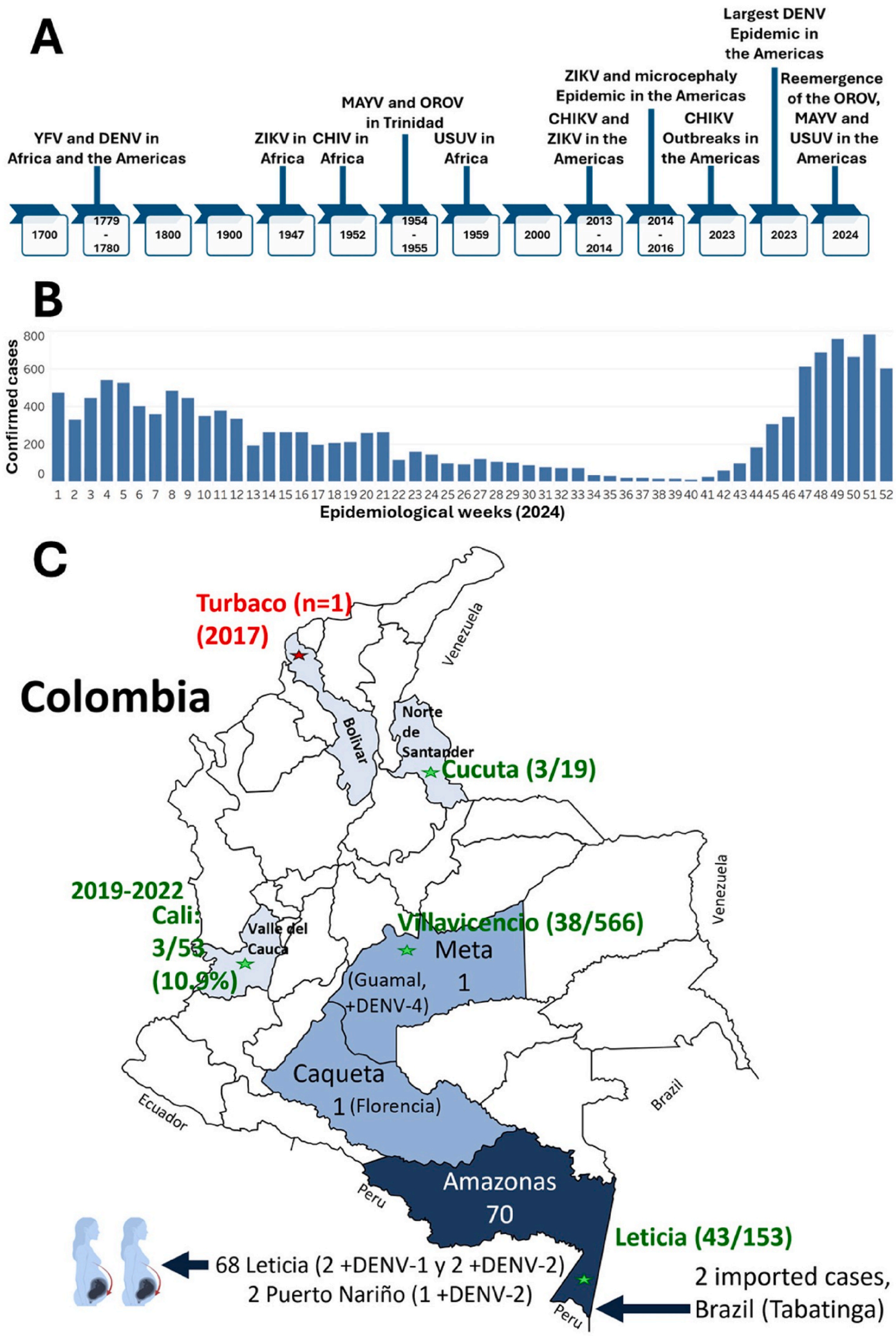


**Fig. 1.** Mosquito-borne arboviruses in the Americas. A. Timeline of the most critical events in the region. B. Evolution in the weekly number of cases of OROV in the Americas in 2024 (adapted from PAHO/WHO). C. Confirmed cases of OROV in Colombia since 2017.

countries in the Americas (Fig. 1) [11,32]. Just in the first six epidemiological weeks of 2025, six countries have confirmed 3,798 cases of OROV in the Americas, then summarizing more than 20,000 confirmed cases in 2024 and the beginning of 2025. The outbreak raised concerns about severe cases, potential vertical transmission, and even possible sexual transmission [41–43]. In addition to Latin America, imported cases have been reported in North America and Europe, highlighting the potential for global spread [33–35]. OROV is primarily transmitted by *Culicoides paraensis* (jejen), which raises concerns about urban transmission and potentia global spread given the plethora of *Culicoides* species of unknown OROV vector competence globally [12,36].

Beyond these endemic threats, global arbovirus dispersal presents additional risks, including West Nile virus (WNV) and Usutu virus (USUV). West Nile Virus has been introduced from the USA to Latin America. WNV is a growing public health concern in Latin America due to its potential impact on human and animal health. WNV can cause severe neurological diseases, including encephalitis and meningitis, especially in vulnerable populations. The region's warm climate and abundant mosquito vectors create favourable conditions for its spread. Increased surveillance, early detection, and public awareness are essential to prevent outbreaks. Additionally, WNV threatens livestock and wildlife, impacting biodiversity and economic activities. Strengthening vector control strategies and cross-border collaboration is crucial to mitigate risks and protect Latin America's human and animal populations [49,50].

Usutu virus (USUV) (Flaviviridae), first identified in South Africa in

1959, has gained attention due to outbreaks in Europe [37]. In 2024, RT-qPCR detected a fragment of the NS5 gene in febrile patients in Meta, Colombia, suggesting the possibility of the first documented human infections in the region [13]. Clinically, USUV infections resemble other South American arboviruses, and its suspected vector, *Culex pipiens*, has yet to be identified in Latin America.

Multiple converging factors have shaped the risk of arbovirus emergence in Latin America. The ongoing migration crisis involving many countries, such as Venezuela, Haiti, and large parts of Central and North America, has increased human mobility across endemic and non-endemic regions, facilitating the spread of infected vectors and viremic individuals. Climate change, particularly the El Niño Southern Oscillation (ENSO), may profoundly alter mosquito breeding patterns, vector distribution, and viral transmission dynamics [51,52]. Expanding urbanization, deforestation, and weakened public health infrastructure create ideal conditions for outbreaks.

Latin America has already seen cases of arbovirus transmission in the United States and sporadic autochthonous malaria, indicating that MAYV, OROV, and others may not remain confined to the region [53,54]. The clinical presentations of these arboviruses are often indistinguishable, complicating differential diagnosis. Molecular methods such as RT-qPCR are essential for accurate detection [38,39]. Furthermore, the potential adaptation of emerging arboviruses to *Culex* and *Aedes* vectors in urban environments increases the risk of transmission to densely populated areas. We must exclude passive uptake by viremic individuals bitten by *Culex* during outbreaks. Vector competence studies and detection of salivary glands in non-engorged female mosquitoes are urgently needed.

The patterns observed with CHIKV, ZIKV, and DENV suggest that MAYV, OROV, and others could follow a similar trajectory, transitioning from sporadic cases to widespread outbreaks. Preventive public health measures, including vector control and surveillance, are critical for mitigating the risk of future epidemics. Strengthening eco-epidemiological research and enhancing early outbreak detection efforts are essential to safeguarding Latin America from the next arboviral threat [40].

## Contributions

SM: conceptualization, writing–original draft, investigation; YL: writing, reviewing, investigation, final document; GA: writing, reviewing, editing, final document; AM: writing, reviewing, editing, fi wr document. ACB: writing, reviewing, investigation, final document.

APM: writing, reviewing, investigation, final document. JFD: writing, reviewing, investigation, final document. AJRM: writing, reviewing, investigation, final document.

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## Declaration of competing interest

AJRM has been declared a speaker/consultant in the last decade for the following industries involved in dengue and arbovirus vaccines: Sanofi Pasteur, Takeda, Abbott, MSD, Moderna, and Valneva. The rest of the authors declare no competing interests.

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Salim Mattar[a], Yesica López[a], German Arrieta[a,i], Ameth Salim Mattar[b], Antonio Carlos Bandeira[c], Alberto Paniz-Mondolfi[d], Jan Felix Drexler[e,f], Alfonso J. Rodriguez-Morales[g,h,1,*]

[a] *Instituto de Investigaciones Biologicas del Tropico, Universidad de Córdoba, Monteria, Colombia*

[b] *Faculty of Medicine, Universidad del Norte, Atlantico, Barranquilla, Colombia*

[c] *Laboratório Central de Saúde Pública da Bahia, Salvador, Brazil*

[d] *Icahn School of Medicine at Mount Sinai, New York, NY, USA*

[e] *Institute of Virology, Charité-Universitätsmedizin Berlin, Freie Universität Berlin, Humboldt-Universität zu Berlin, Berlin, Germany*

[f] *German Centre for Infection Research (DZIF), associated partner Charité-Universitätsmedizin Berlin, Berlin, Germany*

[g] *Faculty of Health Sciences, Universidad Científica del Sur, Lima, Peru*

[h] *Grupo de Investigación Biomedicina, Facultad de Medicina, Fundación Universitaria Autónoma de las Américas-Institución Universitaria Visión de las Américas, Risaralda, Pereira, 660003, Colombia*
[i] *Corporación Universitaria del Caribe -CECAR, Grupo Salud Pública y Auditoría en Salud, Sincelejo, Sucre, Colombia*

[*] Corresponding author. Faculty of Health Sciences, Universidad Científica del Sur, Lima, Peru.

*E-mail addresses:* smattar@correo.unicordoba.edu.co (S. Mattar), yesicalopezm@correo.unicordoba.edu.co (Y. López), germanarrieta@correo.unicordoba.edu.co (G. Arrieta), amethmattar@gmail.com (A.S. Mattar), antoniobandeira@gmail.com (A.C. Bandeira), Alberto.Paniz-mondolfi@mountsinai.org (A. Paniz-Mondolfi), felix.drexler@charite.de (J.F. Drexler), arodriguezmo@cientifica.edu.pe (A.J. Rodriguez-Morales).

[1] Editor-in-Chief, Travel Medicine and Infectious Disease.