Tropical Diseases, Travel Medicine and Vaccines

REVIEW

Open Access

Addressing the emerging threat of Oropouche virus: implications and public health responses for healthcare systems

Olalekan John Okesanya[1,2], Blessing Olawumi Amisu[3], Olaniyi Abideen Adigun[4], Mohamed Mustaf Ahmed[5*], Abdulmajeed Opeyemi Agboola[6], Tolga Kab[7], Gilbert Eshun[8,9], Bonaventure Michael Ukoaka[10], Tolutope Adebimpe Oso[2], Jerico Bautista Ogaya[11,12] and Don Eliseo Lucero-Prisno III[13,14,15]

Abstract

Oropouche fever is an increasingly significant health concern in tropical and subtropical areas of South and Central America, and is primarily spread by midge vectors. The Oropouche virus (OROV) was first identified in 1955 and has been responsible for numerous outbreaks, particularly in urban environments. Despite its prevalence, the disease is often under-reported, making it difficult to fully understand its impact. OROV typically causes febrile illness characterized by symptoms such as headaches, muscle pain, and, occasionally, neurological issues such as meningitis. The ability of the virus to thrive in both forested and urban areas has raised concerns regarding its potential spread to new regions, particularly in the context of climate change. This paper delves into the epidemiology, clinical features, and transmission patterns of OROV, shedding light on the difficulties in diagnosing and managing the disease. The absence of specific treatments and vaccines highlights the urgent need for continued research and development of targeted public health strategies. Advancements in molecular diagnostics and vector control strategies can mitigate Oropouche fever's impact. However, a comprehensive public health approach involving increased surveillance, public education, and cross-border collaboration is needed, especially as

Introduction

The Oropouche virus (OROV) is a zoonotic disease that impacts a range of hosts, including sloths, marsupials, primates, and birds. The presence of the virus in these diverse animal populations can pose a significant risk to human health. Emerging evidence indicates that OROV has the potential to cause febrile illness in humans, emphasizing the urgency for enhanced surveillance and public health interventions [1]. It is spread by mosquitoes like *Aedes serratus* and *Culex quinquefasciatus*. The virus is classified as an arbovirus and is part of the Peribunyaviridae family and the Orthobunyavirus genus (Fig. 1) [2]. Its primary vector is the midge *Culicoides paraensis*, which has helped the virus adapt to an urban transmission cycle involving humans (Fig. 2). The RNA genome of orthobunyaviruses, including the OROV, is made up of three distinct segments—designated as S (small), M (medium), and L (large)—that differ in nucleotide lengths (Fig. 1). These segments encode four structural proteins: RNA polymerase, two external glycoproteins, and the nucleocapsid. The OROV is classified as a Simbu serogroup, a category that comprises at least seven species complexes and 22 identified viruses [3].

Diagnosing OROV infection can be challenging due to its clinical similarities to other arboviral diseases such

*Correspondence:
Mohamed Mustaf Ahmed
momustafahmed@simad.edu.so

Full list of author information is available at the end of the article

the global climate crisis may expand vector habitats, posing risks to previously unaffected regions.

Keywords Oropouche, OROV, Oropouche virus, Oropouche fever, Arboviruses

as dengue, chikungunya, Zika, and Mayaro viruses, and other pathogens like malaria [3]. Moreover, endemic areas often lack molecular differential diagnostic techniques, further complicating the etiological diagnosis of OROV infection. As such, the OROV-caused infection is an illness with an underreported incidence [3]. In over 30 outbreaks in Central and South America over the last ten years, four distinct genotypes have been identified [4, 5]. The coexistence of certain genotypes has been demonstrated and hypothesized to result from the virus's geographic migration, as evidenced by earlier outbreak reports that followed the eastern migration of the OROV Genotype II virus [4, 5]. In addition to traditional transmission modes through vectors, air travel poses an escalating threat to the spread of the OROV. The prompt movement of individuals across regions with active virus circulation allows the virus to be transported to non-endemic areas, where it can potentially cause new outbreaks [6].

The OROV is primarily transmitted through the bite of midges (*Culicoides* spp.), which are the main carriers of the virus. The transmission cycle occurs in both forested (sylvatic) and domestic environments (urban), where the virus can infect various hosts, including mammals and birds (Fig. 2). OROV's ability to persist in these environments contributes to its widespread distribution. Recent studies have shown that the virus circulates silently in certain regions of the Amazon, making detection and control efforts more challenging. After transmission occurs, the OROV normally takes four to eight days to fully develop before causing a fever and illness. Fever, headaches, myalgia (pain in the muscles), and arthralgia (pain in the joints) are typical symptoms [3]. Additionally, gastrointestinal problems like nausea, vomiting, diarrhea, and epigastric pain may affect certain people [3]. There have been reports of a rash that resembles rubella in certain outbreaks. Although patients with OROV found in cerebrospinal fluid [7] rarely experience neurological symptoms, some patients have shown symptoms akin to meningitis. Additional symptoms could be photophobia (sensitivity to light), dizziness, retro-orbital pain, and, in rare situations, vaginal and gum bleeding [3, 8].

Silent circulation has been observed in some Amazonian locations, and the OROV possesses traits that enable prolonged transmission in endemic areas [5]. Several outbreaks of OROV have been documented in Peru, namely in Cusco, San Martin, and Cajamarca [8]. Invertebrate and vertebrate cells have different replication processes, and the Oropouche virus exemplifies the concept of genetic reassortment during replication [9]. Furthermore, genetic reassortment of the virus was found in two different strains, Iquitos and Madre de Dios, respectively. (Table 1) [10]. Because of these factors, the proliferation of OROV could eventually become a public health concern [5]. Between January and August 2024, more than 8,000 cases of Oropouche viral disease were reported across Peru, Brazil, Colombia, Bolivia, and Cuba [11]. Among these, five cases of vertical transmission were linked to fetal deaths or congenital abnormalities, and two fatalities occurred [11]. Additionally, travel-related cases were identified in Europe and the United States, indicating the potential for international spread of the virus [11]. Thus, this study aimed to provide a comprehensive analysis of the Oropouche virus epidemiology, transmission, and clinical manifestations, particularly focusing on its historical context, geographical distribution, vectors, and diagnostic challenges, and future strategies to address the potential public health concern of OROV.

Methods

We conducted a comprehensive narrative review of relevant articles from Scopus, PubMed, and Google Scholar databases to synthesize and analyze existing literature on the Oropouche virus (OROV), focusing on its epidemiology, transmission, clinical manifestations, geographical distribution, diagnostic challenges, and public health implications. The search terms included "Oropouche virus," "OROV," "OROV transmission and clinical manifestations," "arboviruses," and "public health impact of OROV" to identify relevant articles, with no limitation to publication date to capture the historical evolution of OROV, while recent articles were prioritized for the timeliness of the data. Original research, review articles, perspectives, commentaries and letters to the editor providing relevant information on the aim of the study were included. Non-peer-reviewed articles not related to OROV and not published in English were excluded. Pertinent data were extracted and succinctly narrated under appropriate sections, focusing on key themes to provide a cohesive narrative that highlights the current state of knowledge and identifies gaps in the research.

Historical and geographical spread of the OROV

The OROV was first identified in 1955 in the Trinidadian community of Vega de Oropouche, following an outbreak in which the virus was isolated from a symptomatic human case. During this outbreak, *Coquillettidia venezuelensis* mosquitoes were collected, leading to the initial isolation of the virus from human samples. In 1960, the

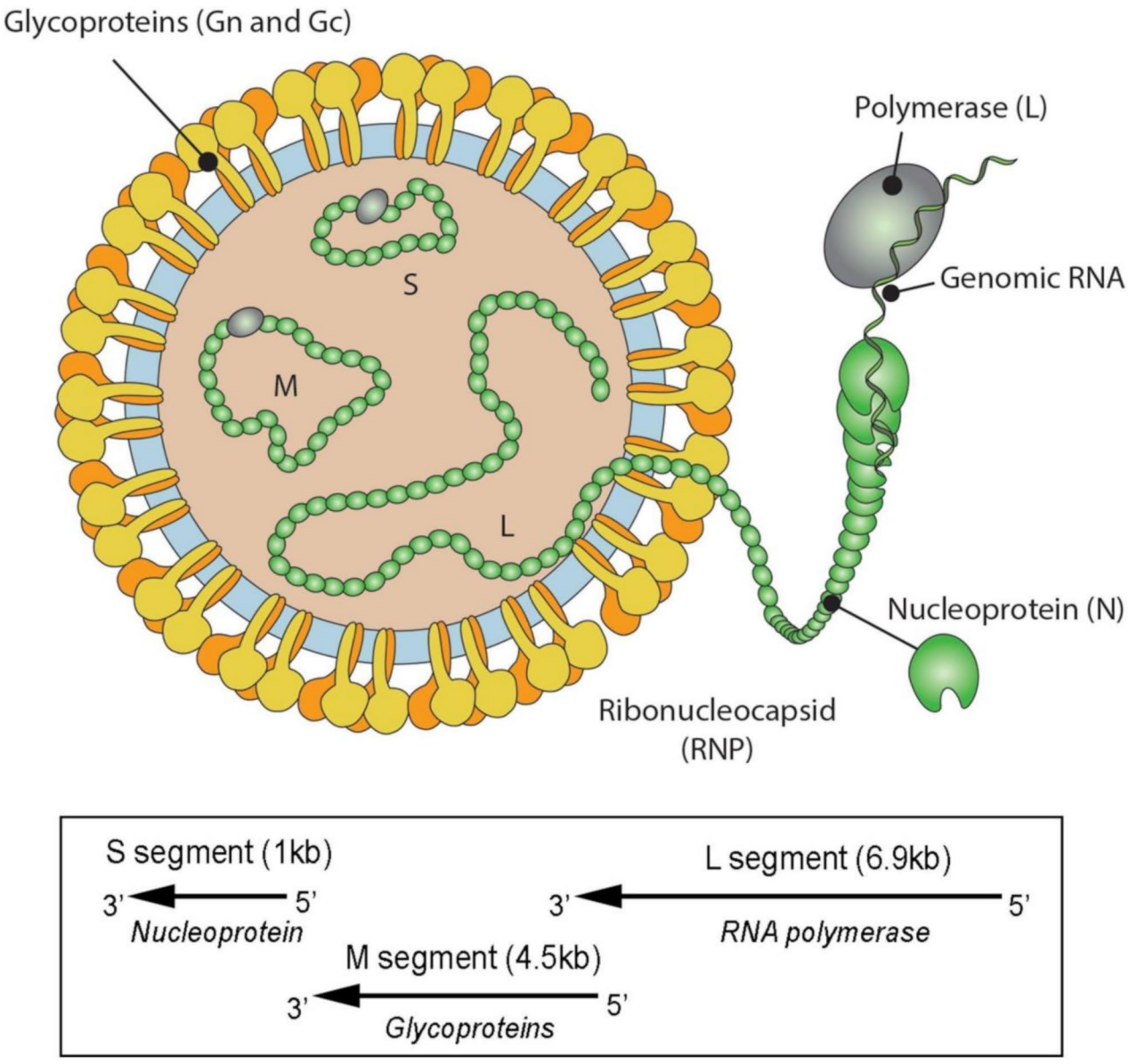

Fig. 1 A schematic illustration of the Orthobunyavirus genus. OROV belongs to the Orthobunyavirus genus, with the Bunyamwera virus serving as its prototype with similar structural characteristics, including average virion size (80–120 nm) and genome size for three fragmented RNA segments [12]. The reading frame 3′-5′ represents each RNA segment, and the corresponding codified proteins are in italics [13]

virus was detected in eastern Brazil and isolated from three-toed sloth (*Bradypus tridactylus*) and *Aedes (Ochlerotatus) serratus* mosquitoes, further highlighting its presence in both sylvatic and urban environments [14]. Around 1961, about 11,000 human cases suspected of Oropouche fever were documented in Belem City, state of Para. At the same time, the Beleme-Brasília highway was being built in the region, and it was suggested that this was a contributing factor to the outbreak [3]. The construction likely increased workers' exposure to infected vectors, highlighting the role of infrastructure in influencing infectious disease dynamics.

Over thirty epidemics of Oropouche fever were documented in Brazil between 1961 and 2000, in the states of Acre, Amapa, Amazonas, Goias, Maranhao, Para, Rondonia, and Tocantins [15]. Between 1980 and 1981, the Brazilian states of Para and Amazonas are thought to have harbored more than 100,000 cases of the disease (Table 1) [16]. A wild primate (Callithrix penicillata) in southeast Brazil was found to have OROV genotype III in 2000 [16]. Subsequently, Oropouche fever was discovered in new areas of Para in 2003 and 2004 (i.e., Parauapebas and Porto de Moz). The notion of an endemic circulation of the Oropouche virus in northwest Brazil was supported

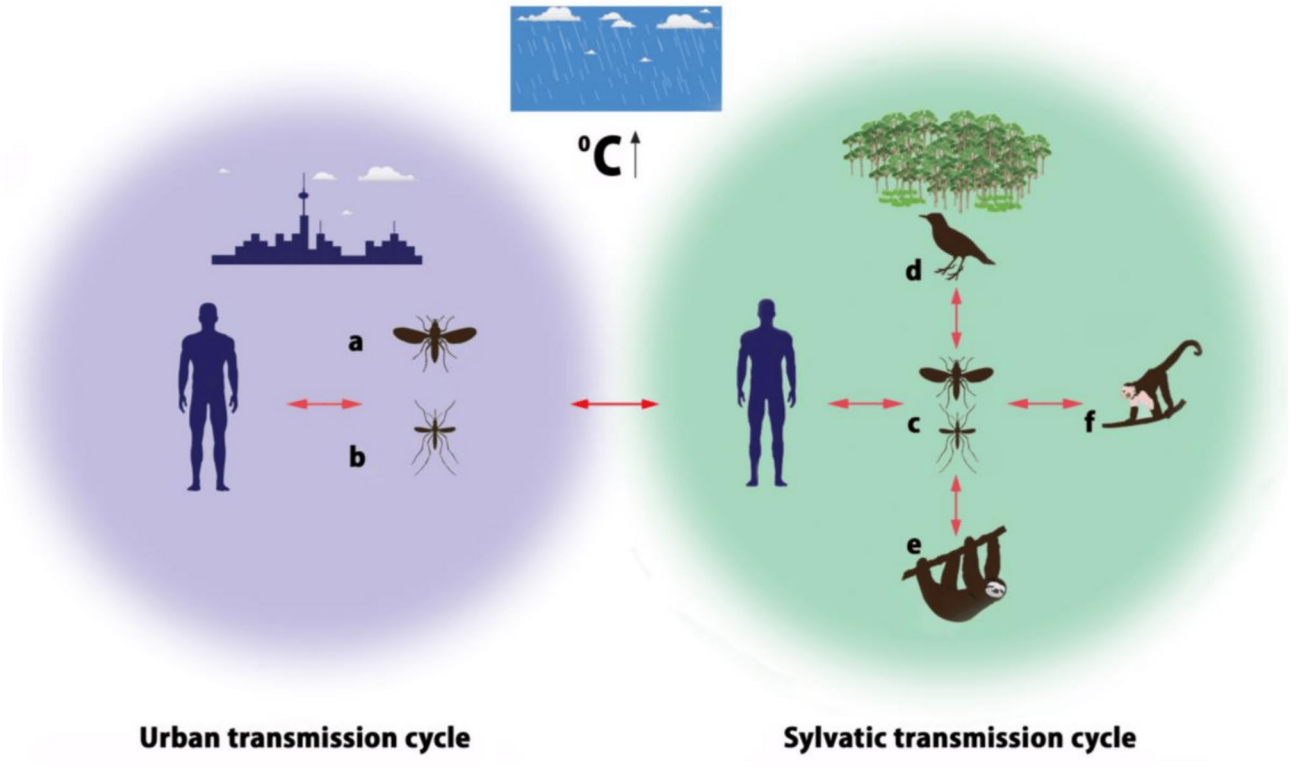

Fig. 2 Urban (U) and sylvatic (S) transmission cycles of Oropouche virus (Vectors—**a**: *C. paraensis*; **b**: *Cx. quinquefasciatus*; **c**: *Culicoides* midges, *Cq. venezuelensis*, *Ae. serratus*, *Cx. quinquefasciatus*; Hosts—d: birds; e: sloths; f: monkeys) [3]

Table 1 Oropouche Virus (OROV) isolations from different hosts, strains, and locations

Virus	Host	Strain/code	Location	Isolation	Reference
OROV	Bradypus tridactylus	BeAn19991	Brazil	Yes	[30]
OROV	Homo sapiens	BeH759024BeH759021 BeH759022BeH759025 BeH759040BeH759529 BeH759620BeH759146	Brazil	Yes	[31]
OROV	Bradypus tridactylus Homo sapiens IFNAR-/-	BeAn19991 TRVL-9760 TRVL9760	Brazil Trinidad and Tobago	Yes	[32]
OROV	Homo sapiens /	OROV/EC/Esmeraldas/057/2016 155/2016 171/2016 206/2016 210/2016 087/2016 VRL 16-SEP-2017	Ecuador	Yes	[33]
OROV	Homo sapiens	OV/Homo sapiens/Haiti-1/2014	Haiti	Yes	[34}

by the fact that by 2004, there had only been one case of Oropouche fever documented in Acrelandia (Acre State) [17]. In Guayaquil, Ecuador, and Cochabamba, Bolivia, human cases of acute febrile illnesses of unknown origin were found to have been infected with OROV, according to a multinational survey [18]. However, the identification of the origin of cases was made more difficult by the passive surveillance design and the sampling period, which spanned from 2000 to 2007. Ecuador announced the discovery of the OROV in health clinics located in the Puyo district of the Amazon over the same period, which is between 2000 and 2004. The virus has been found in Colombia in several non-human primates [19]. In 2005, fever patients in Jujuy, Argentina, were reported to have tested positive for the Oropouche virus [19].

However, following a protracted (>25 years) period of epidemiological inactivity, an Oropouche fever outbreak in northern Brazil by 2006 impacted some 18,000 people [20]. Recent reports of additional outbreaks between 2007 and 2008 came from Manaus, the previously affected city in the Amazonas state, and Trairao and Novo Progresso in Para state. In multiple municipalities in Mato Grosso, there were new outbreaks in 2011 and 2012 [21]. More significantly, the cases happened close to the nation's most populous cities. In 2016, the OROV was identified in a feverish individual in a coastal

region of Brazil for the first time (Table 1). Furthermore, according to a recent analysis, from 2011 to 2016, at least 20 localities in the state of Amazon had OROV-positive serum samples (3%), out of 306 samples that tested negative for Dengue, Zika, and Chikungunya [22]. It has been proposed that OROV entered Peruvian territory by way of human-mediated riverbank dissemination along the Amazon River. Following a dengue outbreak, a serosurvey in Iquitos, Department of Loreto, yielded the first detection of the disease in 1992 [23]. Ever since, Oropouche fever cases have been consistently found in the Iquitos region [24]. A study conducted in the municipality of Santa Clara, which is 10 km from Iquitos, discovered that going to forest regions increased the chance of contracting OROV [25].

The proposition of Oropouche being endemic in Peru has been put forth, primarily because locals are more likely than immigrants to carry antibodies [26]. Outbreaks of Oropouche fever have been documented in Puerto Maldonado, Madre de Dios Department, southeast Peru, since 1994 [27]. More recent outbreaks occurred in 2015 and 2016. Additionally, occurrences of Oropouche fever have been reported in the northern Peruvian departments of San Martín and Cajamarca in 2010 and 2011, respectively, as well as in at least ten locations in the southern Cusco Department in 2016 [28]. In 2024, several travel-associated cases of the OROV have been reported in the United States and Europe, involving individuals returning from Cuba and Brazil. Travelers from affected regions may unknowingly carry the virus during its incubation period, contributing to its silent spread. As diagnostic testing and surveillance efforts expand across the Americas, additional cases are anticipated to emerge from other regions. This health advisory emphasizes the importance of evaluating and testing travelers who have visited affected areas and present with symptoms consistent with Oropouche virus infection [29].

Epidemiology, transmission, and clinical presentation of the Oropouche virus

The true incidence of the disease in the regions probably detected is underestimated because of its clinical presentation, which is comparable to other arboviral infections, the lack of systematic surveillance of cases, and the limited dissemination of laboratory diagnosis. Retrospective population-based or laboratory epidemiological investigations have typically been used to identify outbreaks [35]. The possibility of increased OROV transmission is linked to several factors that contribute to the increased risk of the vector *C. paraensis* spreading, including increased urbanization, deforestation caused by the expansion of the agricultural frontier in the Amazon Basin Region's area of influence, and other human activities that facilitate the spread of the vector and foster vector-host interaction (Table 2) [36]. These same characteristics have a significant impact on the habitats of the reservoir hosts, driving them to proximate areas of peri-urban and urban areas where the vectors are abundant [37]. In addition to large population migrations and complicated humanitarian crises, fragile health systems in these nations should be taken into account when assessing the risk of disease transmission [37].

Table 2 Overview of epidemiology, transmission, and clinical presentation of Oropouche virus

Variable	Summary
Incidence	OROV incidence is likely underestimated due to clinical similarities with other arboviral infections, lack of systematic surveillance, and limited lab diagnostics. Outbreaks are often identified through retrospective investigations.
Factors Contributing to Spread	Urbanization, deforestation, human activity in the Amazon Basin, and population migration increase OROV risk. Vectors like *Culicoides paraensis* are more likely to spread due to increased interaction with reservoir hosts in peri-urban and urban areas.
Impact of Health Systems and Migration	Fragile health systems and complex humanitarian crises further exacerbate the spread of OROV, especially in areas with large population migrations and limited healthcare infrastructure.
Reservoir Hosts & Sylvatic Cycle	*Bradypus tridactylus* (sloths), nonhuman primates, and wild birds act as vertebrate hosts in the sylvatic cycle. The sylvatic vector remains unclear, but *Ochlerotatus serratus* and *Coquilletidia venezuelensis* were isolated in the Amazon region and Trinidad, respectively.
Urban Cycle Vectors	Humans are the only known vertebrates in the urban cycle. *Culex p. quinquefasciatus* and *Culicoides paraensis* are identified as urban vectors, though *Culex* is considered a less efficient vector based on laboratory studies.
Experimental Transmission Evidence	*Culicoides paraensis* can transmit OROV to hamsters after feeding on humans. These midges are highly aggressive and prevalent in tropical and subtropical areas. The virus can be transmitted via midge bites 3–4 days after the onset of symptoms.
Incubation and Transmission	Incubation is suspected to be 4–8 days. Viremia occurs within the first 3–4 days of symptom onset, with no evidence of direct human-to-human transmission.
Hemorrhagic Manifestations	Although they are uncommon, hemorrhagic symptoms can include petechiae, epistaxis, and gingival bleeding in certain people. The disease's clinical presentation is further complicated by these characteristics.
Clinical Manifestations	OROV infection presents as an acute febrile illness with symptoms like headache, myalgia, arthralgia, anorexia, dizziness, chills, and photophobia. Additional symptoms include nausea, vomiting, diarrhea, and conjunctival congestion. About 60% of cases experience symptom recurrence. Severe cases may involve meningitis, and there is potential CNS involvement in some cases.

The Evandro Chagas Institute's research indicates that the sylvatic and urban cycles are responsible for maintaining OROV in the natural world (Fig. 2). There is proof that nonhuman primates, certain wild birds, and pale-throated sloths (*Bradypus tridactylus*) all serve as vertebrate hosts in the sylvatic cycle (Fig. 2) [38]. The forest's OROV vector is still unknown. Two separate times in 1960, the agent was isolated from sylvatic mosquitoes. In the first isolation, *Ochlerotatus serratus* was obtained from the Brazilian Amazon region, and in the second, *Coquilletidia venezuelensis* was isolated from Trinidad [39]. Based on the exclusion of domestic animals (dogs, cats, and poultry) from research regarding their role in maintaining the urban cycle, it appears that humans are the only vertebrates implicated in the urban or epidemic cycle [40]. By invading forests, spreading diseases, and then retreating to urban areas during the viremic phase, humans are likely to also be the link between the sylvatic and urban cycles. Urban epidemics are usually associated with two vectors: the mosquito *Culex p. quinquefasciatus* (Culicidae) and the biting midge, *Culicoides paraensis* (Ceratopogonidae), which is referred to locally as "maruim." According to research conducted in lab settings, *Culex p. quinquefasciatus* is an ineffective OROV vector. Further evidence supporting *Culex* mosquitoes' likely involvement in the urban cycle of OROV comes from the detection of OROV SRNA in patients *and Culex quinquefasciatus* by Cardoso and colleagues [39].

Several experimental and epidemiological studies have provided evidence for the biting midge's role as an OROV vector [3, 38]. After feeding on the blood of people suffering from viral encephalitis for five or more days, the authors showed that *Culicoides paraensis* can transfer the virus to hamsters. These aggressive biters are drawn to humans, and they are active throughout the day, especially at dusk [41]. The tiny bug *Culicoides paraensis* is widely spread throughout the Americas' tropical and subtropical regions, where it is typically observed in large densities during epidemics. The larvae consume degrading organic materials such as accumulated garbage and the trunks of banana trees (genus Musa), coconut (*Cocos nucifera*) and cupuaçu (*Theobroma grandiflorum*) trees [21]. The low rate of viral isolation from *Culicoides paraensis* during outbreaks presents an interesting issue, though. It will take more research to ascertain if this occurrence is caused by the insect's poor susceptibility to OROV or whether a tiny portion of the *Culicoides paraensis* population is capable of spreading the virus [38].

The exact duration needed for OROV to incubate is unknown, although some observations made during significant epidemics indicate that it could take anywhere between 4 and 8 days. Two laboratory personnel unintentionally contracted OROV in 1981 and displayed symptoms of OROV three to four days later [38, 39]. The virus is believed to have spread via the respiratory system, even though the report makes no mention of the circumstances under which it was being altered. When viremia is sufficiently high to infect biting midges, the patient's blood is contagious to *Culicoides paraensis* for the first three to four days after symptoms appear [34]. An extrinsic incubation period of five or more days has been shown in experimental studies conducted on *Mesocricetus auratus* hamsters. There is no documentation of OROV being directly transferred from one individual to another [5]. An acute febrile sickness is the hallmark of OROV infections in humans, which peaks on day two and then progressively declines over a few days. Symptoms typically include headache, myalgia, arthralgia, anorexia, dizziness, chills, and photophobia. Rubella-like rashes are seen in some patients, and additional systemic symptoms such as nausea, vomiting, diarrhea, conjunctival congestion, retro-orbital pain, and epigastric pain have also been reported (Table 2) [39]. There have also been reports suggesting neurological complications [7, 42], and hemorrhagic manifestations in OROV-infected patients, which could include gingival bleeding, epistaxis, and petechiae [34], or gastrointestinal manifestations such as diarrhea, are even more infrequent, further complicating the clinical presentation of the disease [24, 34, 43]. Recurrence of symptoms is common a few days following the original feverish episode, usually with less intensity; about 60% of cases show this recurrence. A meningitis clinical presentation may occur in certain people [7]. Even in the most severe cases, recovery is complete with no obvious sequelae. The discovery of the OROV SRNA genomic sequence in the cerebral fluid of patients from the northern Brazilian state of Amazonas, however, points to the possibility that serious illness affecting the central nervous system (CNS) is happening when this virus appears in Brazil [7]. Some patients with OROV disease have been reported to have abnormal laboratory findings, such as lymphopenia, leukopenia, high c-reactive protein (CRP) and elevated liver enzymes. There have also been a few occurrences of thrombocytopenia documented. The illness usually lasts between two and seven days, but in certain cases—especially those involving the CNS—it might linger for two to four weeks and cause asthenia, or a lack of strength [34, 44].

Current epidemiological data

Brazil

An epidemiological notice concerning the identification of OROV illness cases in the state of Amazonas was released on January 6, 2024, by the Health Surveillance Foundation (FVS). The notice stated that the Central Public Health Laboratory of Amazonas (LACEN-AM) analyzed 675 clinically suitable samples between December 2023 and January 4, 2024, confirming the infection

by OROV in 199 (29.5%) of them. Out of this total, the municipality of Manaus accounts for 94.9% (189), followed by the municipality of Presidente Figueiredo (2.5%; $n=4$); Maués (1%); Tefé (1%); and Manacapuru (0.5%) [7]. There were 1,066 human cases in the state of Amazonas between 2023 and 2024 that had detectable OROV results in RT-qPCR tests. Out of these, 699 samples came from Manaus, 88 from Maués, 69 from Iranduba, 36 from Manacapuru, 32 from Presidente Figueredo, 29 from Parintins, 22 from Carauari, 21 from Itacoatiara, 17 from Rio Preto da Eva, 9 from Careiro, 8 from Borba and Coari, and 6 from Novo Airão and Tefé. A history of transmission is seen in the towns of Alvares, Autazes, Barreirinha, Benjamin Constant, Beruri, Boa Vista do Ramos, Caapiranga, Canutama, Cordeiro da Várzea, Itamarati, Lábrea, Nova Olinda do Norte, Novo Aripuanã, São Paulo de Olivença, Tabatinga and Tapauá. Furthermore, investigations are ongoing on Oropouche instances recorded in the states of Acre and Roraima [45].

Between January and July 2024, 7284 Oropouche cases were confirmed in Brazil, with the Amazon region accounting for 75.7% of the cases (Figure 3). Six states reported cases, while ten non-Amazonian states, including Bahía, Espírito Santo, Santa Catarina, Pernambuco, Minas Gerais, Rio de Janeiro, Ceará, Piauí, Maranhão, and Mato Grosso, reported autochthonous transmission. The probable place of infection is being investigated for several cases in states like Amapá, Paraná, Sergipe, and Paraíba. Over half of the cases are male, with the age group with the highest number of cases being 30-39 years [45]. Two deadly cases of OROV infection in Bahia, involving females aged 21 and 24, were reported to Brazil's IHR National Focal Point. These are the first deaths in Brazil and the Americas caused by an acute OROV infection (Table 3). The patients tested negative for other arboviruses but positive for OROV and serology, and they had no prior history of chronic illnesses. Severe coagulopathy and liver involvement were determined to be the most likely causes of the cases' quick progression from symptoms to death. Two more fatal cases linked to OROV in Paraná and Maranhão are being investigated by the Brazilian Ministry of Health [46, 47]. Recent reports from Brazil have also raised concerns about the potential risk of stillbirth and microcephaly associated with OROV infection during pregnancy [48]. These complications mirror those observed in other arbovirus infections, such as Zika virus [49, 50], and have important public health implications due to the severe impact on fetal development. In addition to the known complications like severe coagulopathy and liver involvement, these emerging risks emphasize the need for heightened surveillance and further research on OROV's effects on vulnerable populations, including pregnant women.

Fig. 3 Confirmed OROV cases in selected countries, January-July 2024

Table 3 Epidemiological data regarding Oropouche virus across the specified regions

Region/Country	Key Findings
Brazil	- **Epidemiological Notice**: 199 confirmed cases (29.5%) from 675 samples in Amazonas (Jan 6, 2024). Most cases in Manaus (94.9%). - **Total Cases (2023–2024)**: 1,066 cases in Amazonas, with 699 from Manaus. - **Deaths**: 2 reported in Bahia (first in Brazil/Americas), with severe coagulopathy as likely cause.
Plurinational State of Bolivia	- **Confirmed Cases (Jan-Jul 2024)**: 356 cases in La Paz, Beni, Pando. - **Demographics**: Half female, highest in the 30–39 age group. - **Co-infection**: 5 cases with dengue reported. No deaths recorded.
Colombia	- **Historical Cases (2019–2021)**: 87 cases in Leticia, Cúcuta, Cali, Villavicencio. - **Confirmed Cases (Jan-Jul 2024)**: 74 cases (largest in the 10–19 age group, majority female). No fatalities.
French Guiana	- **First Case Reported**: Sept 30, 2020. - **Confirmed Cases**: 7 laboratory-confirmed cases in Saül, identified through high dengue-like disease incidences.
Peru	- **Reported Cases (2016–2022)**: 94 cases in 6 departments. - **Peak Year**: 2016 with 45% of cases.
Cuba	- **Epidemic Declared**: May 27, 2024. - **Confirmed Cases**: 74 cases (Cienfuegos: 20, Santiago de Cuba: 54). Majority of cases in the 15–19 age group; no deaths recorded.

The plurinational state of Bolivia

Between January and July 2024, 356 Oropouche cases were confirmed using RT-PCR, with transmission recorded in three departments: La Paz, Beni, and Pando. The cases are reported among 16 endemic municipalities, with the highest proportion in Irupana, La Paz, followed by La Asunta, Chulumani, and Guayaramerin, Beni. Half of the cases are female, with the highest number in the 30-39-year age group. No deaths have been recorded associated with the OROV infection. Additionally, between March and April 2024, five cases of Oropouche virus disease co-infection with dengue were reported in patients from three municipalities in La Paz who presented with positive RT-PCR results for DENV-1 and DENV-2 serotypes [47].

Colombia

According to a study by the National University of Colombia that was released on December 8, 2022, there were 87 cases of OROV sickness in four cities between 2019 and 2021: Leticia (43 cases), Cúcuta (3 cases), Cali (3 cases), and Villavicencio (38 cases) (Table 3). In 2023, the National Reference Laboratory of the National Health Institute confirmed the results of the serological, molecular, and metagenomic sequencing techniques used to confirm the cases at the One Health Genomic Laboratory, Medellín Campus. The cases were identified through retrospective laboratory analysis of acute febrile illness samples [24]. There were 74 confirmed Oropouche cases recorded in three departments of Colombia between January and July 2024: the Amazonas, Caquetá, and Meta. Travelers from Tabatinga, Brazil, were found to have two instances. In 2024, the National Institute of Health of Colombia launched a retrospective laboratory case-finding approach based on febrile illness episodes and dengue surveillance. The age group of 10–19 years old accounted for the largest number of cases, with over half of them being female. There were no fatalities linked to the OROV infection [47].

French Guiana

The first case of OROV in French Guiana was reported to the Regional Health Agency of French Guiana (ARS) on September 30, 2020. The French National Reference Laboratory for Arboviruses, which includes the Institute Pasteur de Cayenne, said on September 22, 2020, that seven laboratory-confirmed instances of OROV infection had been found in the village of Saül. Clinical examinations of an abnormally high number of dengue-like diseases in this area led to the identification of these cases. In Saül, 37 cases that were clinically consistent with Oropouche virus disease were found between August 11 and September 25, 2017. Dengue, chikungunya, and Zika virus serology results were negative, whereas the reverse transcription polymerase chain reaction (RT-PCR) test revealed positive OROV results in seven out of the nine patients [45].

Peru

In six departments of Peru, namely Ayacucho, Cajamarca, Cusco, Loreto, Madre de Dios, and San Martín, 94 cases of Oropouche were documented between 2016 and 2022. The year with the greatest cumulative incidence rate (0.14 instances per 100,000 inhabitants)—2016, when outbreaks were documented in Ayacucho, Cusco, and Madre de Dios—saw 45% of all cases reported. 2022 saw the reporting of eight cases [45]. The greatest number of verified Oropouche cases to date—290—was reported in five departments in Colombia between January and July of 2024. Males made up a significant proportion of cases (52%; 150), with the biggest percentage (40%) of cases (115 instances) occurring in the 30- to 39-year-old age range.

Cuba

The Ministry of Public Health declared the first Oropouche viral illness epidemic in Cuba on May 27, 2024. The provinces of Cienfuegos (20 instances) and Santiago de Cuba (54 cases) together accounted for 74 confirmed cases. The age group with the greatest number of cases—15–19 years old—had 16% of the cases (12 instances), while women comprised half of the cases (50%; 38). There have been no documented deaths linked to the OROV infection [50].

Diagnosis, management, and challenges in treating Oropouche fever

The diagnosis of Oropouche fever is challenging due to its clinical similarity to other febrile illnesses, such as dengue and Zika [38]. OROV diagnosis involves clinical symptoms and specialized laboratory tests. Common blood tests are inconclusive [41], but significant leukopenia (as low as 2,000 leukocytes per ml) is often observed [14]. In cases of aseptic meningitis, the virus can be isolated from cerebrospinal fluid, showing pleocytosis, elevated protein levels, and normal glucose levels [7]. Confirmation relies on serological assays, which are not commercially available. Diagnosis usually begins with detecting specific antibodies (IgM and IgG) against OROV using enzyme-linked immunosorbent assay (ELISA) within five days of symptom onset [14]. However, serological cross-reactivity with other arboviruses can complicate the interpretation of OROV, which can be isolated from clinical samples using cell cultures, though this method is less commonly used due to the time and resources required [5, 51]. Other diagnostic methods include ELISA IgG seroconversion, hemagglutination inhibition, complement fixation, neutralization tests, immunofluorescence, and RT-PCR [5, 14, 43]. Recent advancements in immunofluorescence detection in peripheral blood leukocytes have shown promise for OROV identification [52]. Molecular methods such as reverse transcription polymerase chain reaction (RT-PCR) are the most reliable diagnostic tool for detecting OROV RNA in serum samples. The RT-PCR is sensitivity and specificity during the acute phase of the infection, specifically targeting the S or M segments, with the M segment being highly specific to OROV [5, 21, 41]. Given the overlap in symptoms with other tropical diseases, differential diagnosis is crucial. Healthcare providers must consider other arboviral infections, such as dengue, Zika, and chikungunya, as well as non-viral causes like leptospirosis and malaria [18].

One significant obstacle in the management of OROV is the absence of specific antiviral treatment for the fever, which limits the range of possible treatments and the efficiency of the virus's targeting, resulting in management approaches that focus on alleviating symptoms and supporting the patient through the course of the illness. The primary strategies include antipyretic medications such as acetaminophen, which can be used to manage fever and myalgia. Nonsteroidal anti-inflammatory drugs (NSAIDs) are typically avoided due to the risk of haemorrhage, similar to other arboviral infections [3, 34]. Maintaining adequate hydration is crucial, especially in patients with severe symptoms. Mild analgesics are administered to relieve joint and muscle pain, while rest is encouraged [38]. Also, patients, particularly those with severe symptoms, should be monitored for complications, including neurological manifestations, although these are rare. Hospitalization is rarely necessary unless there are complications, such as dehydration or secondary bacterial infections [38]. Furthermore, Oropouche fever is notably under-recognized by the public and medical professionals in many endemic areas. Inadequate understanding of the condition often leads to under-diagnosis and improper treatment, making it more difficult to successfully manage and treat the illness [53].

Vaccine development

The global OROV outbreak and its progression in South America have brought attention to the urgent need for effective vaccines. Potential T and B cell epitopes within the OROV M-segment polyprotein have been found in a preclinical investigation [54]. These epitopes potentially elicit an immune response against the virus, providing a viable approach for vaccine development [54]. Numerous approaches to vaccine creation are being investigated, such as protein-subunit immunization, chemical inactivation, DNA-vectoring, and live attenuated vaccination [55]. Based on the attenuated OROV strain BeAn19991, live attenuated vaccines have demonstrated efficacy in animal models and have passed safety and immunogenicity testing in a phase I clinical trial [34, 56]. All vaccinated individuals exhibit substantial levels of neutralizing antibodies, indicating that the vaccine elicits a robust immunological response. As a possible vaccine candidate, a replication-competent vesicular stomatitis virus (VSV) producing OROV glycoproteins has also been investigated [57]. The creation of a reverse genetics system for OROV is anticipated to have a major positive impact on vaccine development since it will enable genetic manipulation of the virus. A number of attenuation techniques have been investigated, including eliminating nonstructural proteins, switching untranslated regions (UTRs) between segments, trading the M segment's coding areas for related Orthobunyaviruses, and introducing mutations in the N. These strategies seek to lessen the virus's pathogenicity while maintaining its capacity to trigger an immune response [34, 58].

Efforts to create vaccines against other Simbu serogroup members, like the Akabane virus (AKAV), Aino

virus, and Schmallenberg virus (SBV), may have an impact on the development of OROV vaccines [59, 60]. Since these viruses are significant veterinary infections, the European Union has approved the use of vaccinations against them. These vaccinations have been successful in lowering or eliminating viremia in sheep and cattle. A bivalent protein-subunit containing the N-termini of the Gc proteins from both SBV and AKAV has been created as a potential vaccination against SBV-AKAV [61]. This vaccination showed no clinical signs or detectable viral RNA in blood or organs, demonstrating protection against a field strain of SBV that was passed on by cattle. In comparison to mock-vaccinated controls, two DNA-vectored vaccine candidates that encoded either N or the Gc ectodomain were demonstrated to be protective in IFNAR−/− mice, avoiding weight loss and lowering viremia [62]. The N vaccine produced large amounts of SBV-specific binding antibody, and the Gc vaccination promoted the growth of SBV-specific CD8+T cells, even though neither vaccine candidate induced detectable neutralizing antibodies [63]. Though there aren't any approved OROV vaccines at the moment, a number of them are being developed or have undergone clinical trial testing, offering a promising theoretical foundation for OROV prevention [34].

Genetic reassortment and antigenic shift in Oropouche virus

The OROV, an orthobunyavirus with a segmented RNA genome consisting of three segments: small (S), medium (M), and large (L) (Fig. 1), allows for viral reassortment, a process where two or more different strains infect the same host cell, leading to the exchange of genetic material during replication [64]. The resulting reassortment creates new viral strains with novel combinations of genetic segments from the parent strains, contributing to viral diversity and evolution [53]. Reassortment plays a critical role in the evolution of OROV, as it facilitates the generation of new viral strains with distinct antigenic and biological properties [5]. These newly formed strains may exhibit variations in virulence, transmission efficiency, or immune evasion capabilities, enabling the virus to adapt to new hosts or environments. Additionally, reassortment allows OROV to spread more efficiently by introducing novel gene combinations that enhance its ability to evade the immune responses of individuals previously exposed or vaccinated against earlier strains [34].

Reassortment is also a key driver of antigenic shift, where significant changes occur in the virus's antigenic structure due to the acquisition of new surface proteins or antigens through genetic recombination. This results in the emergence of new viral strains that may not be recognized by the immune systems of individuals previously exposed to other strains. In the case of OROV, such an antigenic shift could facilitate the emergence of a strain capable of causing new outbreaks, even in populations with pre-existing immunity to older strains [14]. In contrast, antigenic drift is a more gradual process, involving the accumulation of minor genetic mutations over time. These modifications, while altering the virus's surface proteins, are less dramatic compared to those caused by reassortment-induced antigenic shifts. Antigenic drift typically leads to incremental changes in how the immune system recognizes the virus [65]. The significance of reassortment and antigenic shift in OROV evolution is particularly concerning because these processes could enable the virus to spread to new geographic regions or hosts, including humans. The discovery of numerous OROV genotypes in different countries (Table 1) suggests that reassortment may be a contributing factor to its expanding epidemiological range [33, 34].

Public Health implications

Impact on healthcare systems

The advent and spread of Oropouche fever pose significant obstacles to healthcare systems, especially in locations that are tropical or subtropical (Table 4). Healthcare facilities could become overburdened by Oropouche fever outbreaks, particularly in places where other infectious diseases are already a problem [66, 67]. The diagnosis method adds to the complexity by placing an additional burden on limited resources in laboratories as they try to differentiate Oropouche fever from other arboviral diseases [53]. This burden is compounded by the limited availability of diagnostic tests for OROV, which often delays treatment and increases the risk of disease transmission. Furthermore, many healthcare settings may lack the infrastructure and skilled personnel required to implement rapid diagnostic techniques, contributing to delayed outbreak responses [66, 68]. To properly handle situations of severe cases, healthcare systems need to be prepared to offer specialist care, such as thorough neurological examination, for patients who exhibit severe symptoms. In addition, healthcare systems must ensure that critical care units have the capacity to manage severe cases, including those presenting with neurological complications. The need for specialized care during Oropouche fever outbreaks places a further strain on healthcare resources, particularly in under-resourced areas. The possibility of widespread epidemics emphasizes the necessity of strong monitoring networks, quick diagnostic tools, and skilled staff to guarantee efficient case handling. Enhancing these elements is necessary to lessen the effects of Oropouche fever and improve the overall preparedness of healthcare systems [38, 69]. Moreover, sustained investment in public health infrastructure and workforce training is critical to building the resilience needed to manage Oropouche fever outbreaks

Table 4 The multifaceted public health impacts of Oropouche fever

Category	Findings
Impact on Healthcare Systems	- Significant burden on healthcare facilities, especially in tropical/subtropical areas. - Diagnostic challenges add strain on limited resources. - Need for specialized care for severe cases increases resource demands. - Importance of strong monitoring networks and rapid diagnostic tools.
Strain on Healthcare Resources	- Outbreaks can delay treatment for other medical conditions. - Diversion of resources may worsen outcomes for patients needing non-urgent care. - Long-term healthcare needs post-infection add to system burden.
Impact on Public Health and Disease Control	- Expansion into new areas complicates control efforts. - Rural communities face challenges due to limited access to healthcare. - Recurrent outbreaks strain healthcare systems and exacerbate public health issues.
Socioeconomic Impact	- Direct and indirect costs affect low-income households severely. - Healthcare budgets may be depleted, compromising responses to other diseases. - High absenteeism in key industries lowers productivity and economic stability.
Social and Psychological Repercussions	- Widespread fear and anxiety during outbreaks strain mental health resources. - Increased psychological disorders complicate outbreak management. - Need for integrated care models to address both physical and mental health.

alongside other endemic diseases such as dengue, malaria, and Zika virus [70].

Strain on healthcare resources

Oropouche fever may severely strain the healthcare system, particularly during outbreaks. Due to the sudden increase in patients, treatment of various medical disorders may experience delays, disrupting usual healthcare procedures (Table 4) [71]. The provision of normal healthcare may be negatively impacted by this diversion of resources to contain the outbreak, particularly in areas where resources are scarce [53]. For instance, during peak outbreaks, healthcare systems may be forced to reprioritize emergency services, leading to the postponement of elective surgeries and non-urgent care, which can worsen health outcomes for patients with chronic conditions [72]. The majority of Oropouche fever cases resolve on their own, but some patients may have long-lasting side effects that need continued medical attention, such as persistent joint pain or neurological problems [73]. This long-term need for healthcare services, even after the acute phase of the infection, adds to the cumulative burden on healthcare systems already stretched thin [71, 74]. The ongoing management of these problems underscores the burden that outbreaks place on healthcare systems and underscores the significance of striking a balance between responding to outbreaks and maintaining basic health services [3, 53]. Ensuring that healthcare systems can both respond to Oropouche fever outbreaks and maintain essential services requires strategic planning, resource allocation, and robust public health policies. Long-term resilience in healthcare systems will depend on strengthening primary care networks and improving access to preventive measures [75].

Impact on public health and disease control in affected communities

The spread of OROV is expected to profoundly impact affected communities. Initially concentrated in urban and peri-urban areas, the disease is now spreading into forested regions. This expansion not only increases the potential population at risk but also suggests that the virus is adapting to new environmental conditions, complicating control and prevention efforts. As OROV reaches previously unaffected areas, the challenges for public health systems and the socioeconomic well-being of these communities are likely to intensify [34]. Rural communities in particular may face heightened challenges due to limited access to healthcare and diagnostic services, exacerbating the spread of the virus and complicating containment efforts [76]. Concerns are raised by this wider distribution for a variety of demographic groups, including the elderly, kids, and immunocompromised people, who are more likely to experience severe illness symptoms [3]. OROV outbreaks that recur frequently can cause significant morbidity, especially in places with high population density. These epidemics could put a further burden on healthcare systems and resources while exacerbating current public health issues [14]. Frequent outbreaks not only increase the demand for healthcare services but also strain public health surveillance systems, laboratory capacities, and supply chains, leading to potential stockouts of essential medicines and medical supplies [77, 78] The consequences of OROV are particularly severe in regions where it coexists with other medical conditions, underscoring the necessity of efficient public health plans and tools to control and lessen the illness's negative impacts on susceptible groups [5]. In regions already dealing with endemic diseases, OROV outbreaks can overwhelm healthcare providers and public health systems, which in turn can lead

to a resurgence of other diseases, worsening the overall public health situation [79].

Socioeconomic impact on public health systems

OROV has a wide-ranging, substantial socioeconomic impact on both individuals and communities. Indirect costs from the disease, such as lost wages due to the illness, add to the direct costs of medical care. For low-income homes, where the financial strain can be very acute, this burden is especially harsh [80]. The pressure on public health systems is intensified in regions where a significant portion of the population relies on government-funded healthcare. In these settings, the cost of managing recurrent Oropouche fever outbreaks and providing diagnostics, treatment, and follow-up care, can deplete already limited healthcare budgets [81]. Considerable absenteeism is a result of high Oropouche fever incidence rates, particularly in vital industries like manufacturing and agriculture. This absence from work has the potential to lower productivity and have a domino impact on overall economic production. Long-term consequences for the economic stability of impacted areas arise from the recurrent nature of epidemics and the continuous financial strain of disease management [3, 53]. Public health systems are also burdened by the need for sustained disease surveillance, particularly in areas where OROV is endemic. The constant vigilance required to monitor outbreaks strains public health personnel and infrastructure. In this context, the health systems' capacity to respond to both communicable and non-communicable diseases becomes compromised, exacerbating existing health inequities [34, 82, 83]. Oropouche fever has significant negative effects on the economy, especially in areas where it is endemic. Due to the high morbidity of Oropouche fever, a considerable number of working days are lost, which harms both individual lives and the stability of the economy as a whole [66]. The public health system bears the brunt of these economic consequences as healthcare facilities become overburdened with patients requiring both acute and long-term care. The demand for resources such as healthcare personnel, hospital beds, diagnostic equipment, and medicines often exceeds supply during outbreaks, which not only affects Oropouche fever patients but also leads to delays in treating other health conditions [71, 84, 85]. Oropouche fever epidemics can have a significant negative impact on the economy for sectors like tourism and agriculture, which rely significantly on a healthy labor force [5]. Due to the repeated nature of these outbreaks, there may be less economic growth and instability in the afflicted areas. This disturbance affects economic development in the long run in addition to impeding current economic productivity [5]. The economic strain on both individuals and the public sector can lead to increased healthcare costs for governments, which may need to import medications and testing kits due to inadequate local production. Over time, this results in a vicious cycle where the financial pressure on the healthcare system undermines the overall economic development of the region [86, 87].

Social and psychological repercussions on public health systems

OROV can have significant social and psychological repercussions, particularly in the event of widespread epidemics (Table 4). When a disease becomes a serious threat to public health, it frequently causes widespread fear and worry, especially in areas where knowledge about the sickness is scarce [14]. Public health systems face the challenge of addressing not only the physical health needs of affected individuals but also the mental health implications of widespread outbreaks. The lack of mental health resources, particularly in rural or low-income settings, exacerbates the psychological burden on affected communities. This often results in an increase in anxiety and stress-related disorders, which further exert strains on already overburdened health system. Inadequate mental health services during epidemics can lead to prolonged recovery times and reduced social cohesion, complicating outbreak containment efforts [88, 89]. The psychological effects of the disease are more severe in those who are seriously affected, which emphasizes the vital requirement of comprehensive mental health treatment in addition to physical healthcare services [5]. In many public health systems, mental health services are underfunded and understaffed, making it difficult to address the psychological trauma that results from recurring epidemics. This deficiency further highlights the need for integrated care models that combine physical and mental health services during outbreak responses. Without such integration, the long-term well-being of affected populations is jeopardized, and the ability of public health systems to foster resilience against future outbreaks is diminished [90, 91]. Oropouche fever outbreaks can cause significant disruptions to the community, making pre-existing problems worse, like poverty and poor access to healthcare [5]. The compounding effects of poverty, poor healthcare access, and recurrent outbreaks not only exacerbate social inequalities but also place additional burdens on public health systems. These systems must address both the immediate needs of outbreak management and the long-term effects on social determinants of health, such as employment, education, and housing. In marginalized communities, the lack of access to timely healthcare services means that outbreaks like Oropouche fever can rapidly spiral out of control, overwhelming local health systems and further entrenching cycles of poverty and disease [92–94].

Recommendations for public health response

The emergence of OROV as a public health threat necessitates not only a coordinated response from healthcare systems but also the development of new frameworks for outbreak management and prevention. One potential framework is the integration of One Health principles, emphasizing the interconnectedness of human, animal, and environmental health to improve early detection and response strategies [34]. Diagnostic methods must be enhanced to ensure early detection and differentiation from other arboviral infections, while clinical management protocols need to be established to guide healthcare providers in treating affected patients [51]. The public health implications of OROV, including its impact on healthcare systems, socioeconomic stability, and community well-being, require adaptive public health strategies that consider the long-term effects of the disease on affected populations. Incorporating these elements will allow for more resilient and sustainable public health responses [5].

Surveillance and monitoring

The early detection and prompt response to OROV outbreaks are crucial in mitigating the public health impact of the disease. Strengthening surveillance and monitoring systems should be guided by a multi-faceted surveillance framework, integrating community-based participatory surveillance with digital health tools to increase both accuracy and timeliness [38, 95]. Real-time data collection systems integrated with local health facilities can be enhanced through the use of machine learning algorithms to predict potential outbreak hotspots and facilitate the rapid reporting of cases, enabling swift public health interventions. Moreover, establishing sentinel surveillance sites in high-risk areas will be crucial in continuously monitoring OROV activity, providing critical data to guide response efforts [7]. Engaging communities in active surveillance by training local healthcare workers to recognize and report symptoms of Oropouche fever can further enhance these systems, making them more responsive and effective [53]. By embedding predictive analytics and AI-driven tools in these systems, health authorities can generate actionable insights to proactively manage outbreaks [96].

Strengthening surveillance systems

Building on the foundation of robust surveillance and monitoring, it is imperative to strengthen the overall surveillance infrastructure. This can be achieved through a new data integration framework to improve efficiency of response and capacity building involving training healthcare workers and equipping them with the necessary scalable technological solution tools that ensure continuous data flow to detect and respond to cases of Oropouche fever efficiently even in resource-limited settings [5, 97]. This data integration framework should be centralized and accessible to all stakeholders, allowing for the seamless integration of data from hospitals, laboratories, and community health initiatives. This will ensure that health authorities have access to comprehensive, up-to-date information, enabling a coordinated response. Furthermore, leveraging technological advancements, such as cloud-based platforms and mobile health (mHealth) technologies, can strengthen their response infrastructure and improve the overall effectiveness of surveillance systems [98].

Data collection and analysis

Accurate analysis of collected data is equally important for effective surveillance. Standardizing data gathering procedures is therefore necessary to guarantee consistent and trustworthy data from various regions [99]. A global health data-sharing approach that promotes cross-border collaboration and fosters a more thorough understanding and control measures for OROV could serve as the foundation [100]. Public health professionals will be able to recognize emerging patterns and possible outbreak hotspots owing to this uniformity, making comparisons and trend studies easier and more reliable. Furthermore, the integration of big data and artificial intelligence in real-time analytics can yield insightful information regarding the propagation, early detection, and proactive control of outbreaks [101, 102]. Thus, the framework ought to have features for automated trend analysis and real-time data visualization, which would allow national and international public health organizations to better coordinate their responses [61, 103]. It is also essential to work together to encourage data exchange between global health organizations. This comprehensive approach to data collection and analysis will help to build more efficient control techniques and improve our understanding of the disease [104].

Prevention and control measures

It is imperative to build a multi-sectoral public health framework that prioritizes vector and environmental controls. In addition to traditional techniques, this framework supports ecological interventions, including sustainable vector control through habitat change and natural predator improvement [105]. Community health education will also help the public better understand the signs, pathways of transmission, and preventative measures for OROV and encourage long-term behavioral changes if included in the prevention framework [34, 106]. Additionally, an equitable access approach should be followed while developing and delivering vaccinations to ensure that individuals in high-risk areas receive them based on need, rather than resource availability [107].

Comprehensive vector control strategies must also be put into practice, with an emphasis on reducing the populations of mosquitoes and gnats using insecticides, filling or draining water collections, and pulling weeds that could harbor mosquito larvae near breeding sites [5]. To offer long-term protection against the virus, vaccination and immunization programs should be addressed concurrently, with an emphasis on ensuring that vulnerable people have fair access to vaccines [107].

Personal protective measures

To avoid the spread of OROV, a framework for individualized protection and education should be suggested, in addition to community-wide initiatives. This entails utilizing behavioral insights in focused community engagement initiatives to promote the adoption of personal protective measures, which can dramatically lower the risk of infection. Examples of these measures include wearing protective clothing, applying insect repellents, and using bed nets [19, 108, 109]. To maximize effectiveness, these interventions should be included in current public health initiatives and tailored to local conditions [19]. Initiatives for community participation should be planned to promote broad implementation of these interventions, especially in areas where the rate of transmission is high. The overall impact of the disease can be reduced by equipping people with the necessary information and resources to safeguard themselves [110].

Policy and advocacy

The successful implementation of these strategies requires the implementation of a new supportive policy and advocacy framework at both national and international levels. This would focus on ensuring that national public health policies explicitly include Oropouche fever as a priority, ensuring that rapid response legal frameworks are in place, and adequate resources are allocated for its control and prevention [111]. At the same time, international cooperation is essential for sharing resources and expertise, particularly in regions where the healthcare infrastructure may be less developed, and the advocacy framework should emphasize cross-border health agreements for coordinated outbreak responses. Promoting legislative reforms that facilitate rapid response measures, such as quarantine and vector control, will further strengthen the ability to contain outbreaks [47, 111].

Funding and resource mobilization

A sustainable funding framework is essential to secure significant funding and resources to adequately tackle the public health impact of the OROV. This framework should involve creating a global OROV prevention fund, where international donors, public-private partnerships, and governments collaborate to pool resources for prevention, surveillance, and research efforts. The establishment of innovative financing mechanisms, such as health bonds or pandemic insurance schemes, can also be explored to provide long-term financial stability for Oropouche fever control programs [110, 112].

Future directions and long-term strategies

In the long term, research and development will be critical in overcoming the challenges posed by OROV. One of the most promising avenues of research is the development of an effective vaccine [34]. Current efforts should focus on enhancing the efficacy and safety of candidate vaccines, with an emphasis on conducting clinical trials to expedite their approval and distribution. Collaboration on a global scale is essential in this endeavor; sharing knowledge, resources, and expertise can accelerate the development process, bringing an effective vaccine to market more quickly [113]. In addition to vaccine development, there is a pressing need for innovations in diagnostic tools. The creation of rapid diagnostic tests that can accurately detect the Oropouche virus, even in remote settings, will be invaluable in controlling the spread of the disease. Point-of-care testing (POCT) should be promoted to facilitate early diagnosis and prompt treatment at the community level [56, 114]. The integration of artificial intelligence and machine learning into diagnostic processes can further improve accuracy and efficiency, making these tools more accessible and effective in diverse healthcare settings [24].

Looking beyond immediate responses, the establishment of resilient health systems is vital for managing Oropouche fever and other emerging infectious diseases. Strengthening healthcare infrastructure, particularly in regions vulnerable to outbreaks, will ensure that health systems are equipped to respond effectively to future challenges. Continuous training of healthcare workers in outbreak management and response is also crucial to maintaining a state of readiness [115]. These efforts should be underpinned by a focus on sustainability, ensuring that health system improvements are adaptable and capable of addressing evolving public health threats [116].

Finally, the importance of global collaboration cannot be overstated. Strengthening partnerships between countries, international organizations, and research institutions will enhance the global response to OROV. Information-sharing platforms should be established to facilitate the timely exchange of data, best practices, and research findings, enabling coordinated efforts to manage and control outbreaks. Joint research initiatives, aimed at addressing knowledge gaps and developing new strategies, will be essential in staying ahead of the disease and reducing its impact on global health [117].

Conclusion

OROV is becoming a significant worry in tropical and subtropical areas, especially in South and Central America, where the virus has become an important public health issue. Initially limited to urban and peri-urban areas, the virus's spread into forested regions demonstrates its potential to impact diverse populations, including those in more isolated and vulnerable communities. This expansion highlights the OROV's adaptability and the growing challenge of controlling its transmission in different environments. The disease, transmitted primarily by midge vectors, is characterized by symptoms that, while often self-limiting, can lead to severe complications, including neurological manifestations. The underreporting of Oropouche fever cases and the lack of reliable molecular diagnostic tools in many affected areas make it difficult to assess and manage the disease accurately. Additionally, the absence of specific antiviral treatments and vaccines highlights the urgent need for increased research and development. Advancements in molecular diagnostics and vector control strategies offer promising ways to reduce the impact of Oropouche fever. However, these tools must be integrated into a comprehensive public health approach. This approach should include increased surveillance, public education, and cross-border collaboration, especially as the global climate crisis may expand the habitat of the virus's vectors, posing risks to previously unaffected regions. Looking ahead, public health authorities, researchers, and policymakers must prioritize Oropouche fever within the broader context of emerging infectious diseases. By fostering innovation in diagnostics, treatment, and prevention and strengthening healthcare infrastructure in endemic areas, we can better prepare for and respond to future outbreaks. The lessons learned from Oropouche fever can serve as a model for addressing other neglected tropical diseases, ultimately contributing to improved global health outcomes.

Acknowledgements
None.

Author contributions
OJO conceptualized and designed the study. BA, MMA, AOA, TK, GE, BMU, TAO, and JBO conducted the literature review and data curation. OJO and OAA wrote the first draft of the manuscript. All the authors critically revised the manuscript for important intellectual content. DELPIII supervised the study. All authors have read and approved the final manuscript.

Funding
The authors have not received any funding for this study.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Approval from the ethics committee was not required.

Competing interests
The authors declare no competing interests.

Author details
[1]Faculty of Medicine, Department of Public Health and Maritime Transport, University of Thessaly, Volos, Greece
[2]Department of Medical Laboratory Science, Neuropsychiatric Hospital, Abeokuta, Nigeria
[3]Department of Medical Laboratory Science, State Hospital Ede, Osun, Nigeria
[4]Department of Medical Laboratory Science, Nigerian Defence Academy, Kaduna, Nigeria
[5]Faculty of Medicine and Health Sciences, SIMAD University, Mogadishu, Somalia
[6]Department of Public Health, Faculty of Health Sciences, Al-Hikmah University, Ilorin, Nigeria
[7]Faculty of Medicine, Department of Medicine, Istinye University, Istanbul, Turkey
[8]Seventh Day Adventist Hospital, Asamang, Ghana
[9]School of Veterinary Studies and the Roslin Institute, The Royal (Dick), University of Edinburgh, Midlothian, UK
[10]Community and Clinical Research Division, First On-Call Initiative, Port Harcourt, Nigeria
[11]Department of Medical Technology, Institute of Health Sciences and Nursing, Far Eastern University, Manila, Philippines
[12]Center for University Research, University of Makati, Makati City, Philippines
[13]Department of Global Health and Development, London School of Hygiene and Tropical Medicine, London, UK
[14]Research and Innovation Office, Southern Leyte State University, Leyte, Philippines
[15]Research and Development Office, Biliran Province State University, Biliran, Philippines

Received: 2 September 2024 / Accepted: 4 November 2024
Published online: 02 January 2025

References

1. Forni D, Cagliani R, Clerici M, Sironi M. Disease-causing human viruses: novelty and legacy. Trends Microbiol [Internet]. 2022;30(12):1232–42. https://linkinghub.elsevier.com/retrieve/pii/S0966842X22001755
2. McGregor BL, Connelly CR, Kenney JL. Infection, Dissemination, and Transmission Potential of North American Culex quinquefasciatus, Culex tarsalis, and Culicoides sonorensis for Oropouche Virus. Viruses [Internet]. 2021;13(2):226. https://www.mdpi.com/1999-4915/13/2/226
3. Sakkas H, Bozidis P, Franks A, Papadopoulou C, Oropouche Fever. A Review. Viruses [Internet]. 2018;10(4):175. https://www.mdpi.com/1999-4915/10/4/175
4. Amorim MT, Naveca FG, Hernández LHA, da Paz TYB et al. da Silva de Oliveira CC, da Conceição Miranda Santos A,. Detection of a Multiple Circulation Event of Dengue Virus 2 Strains in the Northern Region of Brazil. Trop Med Infect Dis [Internet]. 2024;9(1):17. https://www.mdpi.com/2414-6366/9/1/17
5. da Travassos JF, de Souza WM, Pinheiro F, de Figueiredo P, Cardoso ML, Acrani JF et al. GO,. Oropouche Virus: Clinical, Epidemiological, and Molecular Aspects of a Neglected Orthobunyavirus. Am Soc Trop Med Hyg [Internet]. 2017;96(5):1019–30. https://www.ajtmh.org/view/journals/tpmd/96/5/article-p1019.xml
6. European Centre for Disease Prevention and Control. Oropouche virus disease cases imported into the European Union Epidemiological situation Epidemiological situation in South America and the [Internet]. https://www.ecdc.europa.eu/. 2024 [cited 2024 Aug 13]. https://www.ecdc.europa.eu/en/publications-data/threat-assessment-brief-oropouche-virus-disease-cases-imported-european-union#:~:text=Epidemiological%20situation,Cuba%20and%20one%20to%20Brazil.

7. Bastos M, de Figueiredo S, Naveca LTM, Monte FG, Lessa RL, Pinto de Figueiredo N et al. RM,. Identification of Oropouche Orthobunyavirus in the Cerebrospinal Fluid of Three Patients in the Amazonas, Brazil. Am Soc Trop Med Hyg [Internet]. 2012;86(4):732–5. https://www.ajtmh.org/view/journals/tpmd/86/4/article-p732.xml
8. Vernal S, Martini CCR, da Fonseca BAL. Oropouche Virus–Associated Aseptic Meningoencephalitis, Southeastern Brazil. Emerg Infect Dis [Internet]. 2019;25(2):380–2. http://wwwnc.cdc.gov/eid/article/25/2/18-1189_article.htm
9. Bowden TA, Bitto D, McLees A, Yeromonahos C, Elliott RM, Huiskonen JT. Orthobunyavirus Ultrastructure and the Curious Tripodal Glycoprotein Spike. Pierson TC, editor. PLoS Pathog [Internet]. 2013;9(5):e1003374. https://doi.org/10.1371/journal.ppat.1003374
10. Ladner JT, Savji N, Lofts L, Travassos da Rosa A, Wiley MR, Gestole MC et al. Genomic and phylogenetic characterization of viruses included in the Manzanilla and Oropouche species complexes of the genus Orthobunyavirus, family Bunyaviridae. J Gen Virol [Internet]. 2014;95(5):1055–66. https://www.microbiologyresearch.org/content/journal/jgv/https://doi.org/10.1099/vir.0.061309-0
11. CDC. Increased Oropouche Virus Activity and Associated Risk to Travelers. 2024; [Cited 2024 Aug 13]. https://emergency.cdc.gov/han/2024/han00515.asp
12. Elliott RM. Orthobunyaviruses: recent genetic and structural insights. Nat Rev Microbiol [Internet]. 2014;12(10):673–85. https://www.nature.com/articles/nrmicro3332
13. Hulo C, de Castro E, Masson P, Bougueleret L, Bairoch A, Xenarios I et al. ViralZone: a knowledge resource to understand virus diversity. Nucleic Acids Res [Internet]. 2011;39(suppl_1):D576–82. https://academic.oup.com/nar/article-lookup/doi/https://doi.org/10.1093/nar/gkq901
14. Romero-Alvarez D, Escobar LE. Oropouche fever, an emergent disease from the Americas. Microbes Infect [Internet]. 2018;20(3):135–46. https://linkinghub.elsevier.com/retrieve/pii/S1286457917302204
15. Nunes MRT, Martins LC, Rodrigues SG, Chiang JO, Azevedo R do S da, Travassos S, da Rosa APA et al. Oropouche Virus Isolation, Southeast Brazil. Emerg Infect Dis [Internet]. 2005;11(10):1610–3. http://wwwnc.cdc.gov/eid/article/11/10/05-0464_article.htm
16. Tesh RB. The Emerging Epidemiology of Venezuelan Hemorrhagic Fever and Oropouche Fever in Tropical South Americaa. Ann N Y Acad Sci [Internet]. 1994;740(1):129–37. https://nyaspubs.onlinelibrary.wiley.com/doi/https://doi.org/10.1111/j.1749-6632.1994.tb19863.x
17. Terzian ACB, Bronzoni RV, de Drumond M, Da Silva-Nunes BP, Santos da Silva M, Ferreira N et al. MU,. Sporadic Oropouche Infection, Acre, Brazil. Emerg Infect Dis [Internet]. 2009;15(2):348–50. http://wwwnc.cdc.gov/eid/article/15/2/08-0401_article.htm
18. Ciuoderis KA, Berg MG, Perez LJ, Hadji A, Perez-Restrepo LS, Aristizabal LC et al. Oropouche virus as an emerging cause of acute febrile illness in Colombia. Emerg Microbes Infect [Internet]. 2022;11(1):2645–57. https://www.tandfonline.com/doi/full/https://doi.org/10.1080/22221751.2022.2136536
19. Pinheiro FP, Travassos da Rosa APAVP. Oropouche fever. Feigin Cherry's Textb Pediatr Infect Dis 7th ed. 2014;2537. (https://pesquisa.bvsalud.org/portal/resource/pt/dip-1921
20. Vasconcelos HB, Azevedo RSS, Casseb SM, Nunes-Neto JP, Chiang JO, Cantuária PC et al. Oropouche fever epidemic in Northern Brazil: Epidemiology and molecular characterization of isolates. Journal of Clinical Virology [Internet]. 2008;44(2):129–33. https://doi.org/10.1016/j.jcv.2008.11.006
21. Cardoso BF, Serra OP, Heinen LBdaS, Zuchi N, de Souza VC, Naveca FG et al. Detection of Oropouche virus segment S in patients and inCulex quinquefasciatus in the state of Mato Grosso, Brazil. Mem Inst Oswaldo Cruz [Internet]. 2015;110(6):745–54. http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0074-02762015000600745&lng=en&tlng=en
22. de Lima RC, Dias HG, de Souza TMA, Familiar-Macedo D, Ribeiro ED, Corrêa VCE, Pauvolid-Corrêa A, de Azeredo EL, Dos Santos FB. Oropouche Virus exposure in Febrile patients during Chikungunya Virus introduction in the state of Amapá, Amazon Region, Brazil. Pathogens. 2024;13(6):469. https://doi.org/10.3390/pathogens13060469. PMID: 38921767; PMCID: PMC11206884.
23. Phillips I, Need J, Escamilla J, Colán E, Sánchez S, Rodríguez M et al. First documented outbreak of dengue in the Peruvian Amazon region. Bull Pan Am Health Organ [Internet]. 1992;26(3):201–7. http://www.ncbi.nlm.nih.gov/pubmed/1393192
24. Alvarez-Falconi PP, Ríos Ruiz BA. [Oropuche fever outbreak in Bagazan, San Martin, Peru: epidemiological evaluation, gastrointestinal and hemorrhagic manifestations]. Rev Gastroenterol Peru [Internet]. 2010;30(4):334–40. http://www.ncbi.nlm.nih.gov/pubmed/21263761
25. Moreira HM, Sgorlon G, Queiroz JAS, Roca TP, Ribeiro J, Teixeira KS et al. Outbreak of Oropouche virus in frontier regions in western Amazon. Piantadosi A, editor. Microbiol Spectr [Internet]. 2024;12(3). https://doi.org/10.1128/spectrum.01629-23
26. Baisley KJ, Watts DM, Munstermann LE, Wilson ML. Epidemiology of endemic Oropouche virus transmission in upper Amazonian Peru. Am J Trop Med Hyg [Internet]. 1998;59(5):710–6. https://www.ajtmh.org/view/journals/tpmd/59/5/article-p710.xml
27. WHO. Oropouche Virus Disease - Peru [Internet]. https://www.who.int/. 2016 [cited 2024 Aug 11]. https://www.who.int/emergencies/disease-outbreak-news/item/03-june-2016-oropouche-peru-en
28. Romero-Alvarez D, Escobar LE. Vegetation loss and the 2016 Oropouche fever outbreak in Peru. Mem Inst Oswaldo Cruz [Internet]. 2017;112(4):292–8. http://www.ncbi.nlm.nih.gov/pubmed/28327792
29. CDC. Increased Oropouche virus activity and associated risk to travelers [Internet]. https://emergency.cdc.gov/. 2024 [cited 2024 Aug 23]. https://www.bing.com/search?q=CDC.+Increased+Oropouche+Virus+Activity+and+Associated+Risk+to+Travelers.+Emerg+Prep+Response.&cvid=660c28f5382747609a5907e94f17d3d3&gs_lcrp=EgZjaHJvbWUyBggAEEUYOdIBBzkzNGowajGoAgCwAgA&FORM=ANAB01&ucpdpc=UCPD&PC=U531&rdr=1&rdrig=D0FE7B933AA14733A90414ED28DFE1E2.
30. Aquino VH, Moreli ML, Moraes Figueiredo LT. Analysis of oropouche virus L protein amino acid sequence showed the presence of an additional conserved region that could harbour an important role for the polymerase activity. Arch Virol [Internet]. 2003;148(1):19–28. http://link.springer.com/https://doi.org/10.1007/s00705-002-0913-4
31. Tilston-Lunel NL, Acrani GO, Randall RE, Elliott RM. Generation of Recombinant Oropouche Viruses Lacking the Nonstructural Protein NSm or NSs. Williams B, editor. J Virol [Internet]. 2016;90(5):2616–27. https://doi.org/10.1128/JVI.02849-15
32. Acrani GO, Tilston-Lunel NL, Spiegel M, Weidmann M, Dilcher M, Andrade da Silva DE et al. Establishment of a minigenome system for Oropouche virus reveals the S genome segment to be significantly longer than reported previously. J Gen Virol [Internet]. 2015;96(3):513–23. https://www.microbiologyresearch.org/content/journal/jgv/https://doi.org/10.1099/jgv.0.000005
33. Gutierrez B, Wise EL, Pullan ST, Logue CH, Bowden TA, Escalera-Zamudio M et al. Evolutionary Dynamics of Oropouche Virus in South America. Parrish CR, editor. J Virol [Internet]. 2020;94(5). https://doi.org/10.1128/JVI.01127-19
34. Zhang Y, Liu X, Wu Z, Feng S, Lu K, Zhu W et al. Oropouche virus: A neglected global arboviral threat. Virus Res [Internet]. 2024;341:199318. https://linkinghub.elsevier.com/retrieve/pii/S016817022400011X
35. Girard M, Nelson CB, Picot V, Gubler DJ, Arboviruses. A global public health threat. Vaccine [Internet]. 2020;38(24):3989–94. https://linkinghub.elsevier.com/retrieve/pii/S0264410X20304709
36. Gomes BM, Rebelo CB, Alves de Sousa L. Public health, surveillance systems and preventive medicine in an interconnected world. In: One Health [Internet]. Elsevier; 2022. pp. 33–71. https://linkinghub.elsevier.com/retrieve/pii/B9780128227947000006X
37. WHO. Oropouche virus Disease. - Region of the Americas [Internet]. https://www.who.int/. 2024 [cited 2024 Oct 10]. https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON530
38. Pinheiro FP, Hoch AL, Gomes ML, Roberts DR. Oropouche virus. IV. Laboratory transmission by Culicoides paraensis. Am J Trop Med Hyg [Internet]. 1981;30(1):172–6. http://www.ncbi.nlm.nih.gov/pubmed/7212164
39. Pinheiro FP, Travassos da Rosa AP, Travassos, da Rosa JF, Ishak R, Freitas RB, Gomes ML et al. Oropouche virus. I. A review of clinicpidemiological, and ecological findings. Am J Trop Med Hyg [Internet]. 1981;30(1):149–60. http://www.ncbi.nlm.nih.gov/pubmed/6782898
40. Hassell JM, Begon M, Ward MJ, Fèvre EM. Urbanization and Disease Emergence: Dynamics at the Wildlife–Livestock–Human Interface. Trends Ecol Evol [Internet]. 2017;32(1):55–67. https://linkinghub.elsevier.com/retrieve/pii/S0169534716301847
41. Sick F, Beer M, Kampen H, Wernike K. Culicoides Biting Midges—Underestimated Vectors for Arboviruses of Public Health and Veterinary Importance. Viruses [Internet]. 2019;11(4):376. https://www.mdpi.com/1999-4915/11/4/376
42. Mourão MPG, Bastos MS, Gimaque JBL, Mota BR, Souza GS, Grimmer GHN et al. Oropouche Fever Outbreak, Manaus, Brazil, 2007–2008. Emerg Infect Dis [Internet]. 2009;15(12):2063–4. http://wwwnc.cdc.gov/eid/article/15/12/09-0917_article.htm

43. Vasconcelos HB, Azevedo RSS, Casseb SM, Nunes-Neto JP, Chiang JO, Cantuária PC et al. Oropouche fever epidemic in Northern Brazil: Epidemiology and molecular characterization of isolates. J Clin Virol [Internet]. 2009;44(2):129–33. https://linkinghub.elsevier.com/retrieve/pii/S1386653208003995
44. CDC. Clinical overview of Oropouche virus disease [Internet]. https://www.cdc.gov/. 2024 [cited 2024 July 10]. https://www.cdc.gov/oropouche/hcp/clinical-overview/index.html#:~:text=In%20June%202024%2 C%20Cuba%20reported,and%20Zika%20viruses%2 C%20and%20malaria.
45. WHO. Oropouche virus disease - Cuba [Internet]. https://www.who.int/. 2024 [cited 2024 August 10]. https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON521
46. Carlos Bandeira A, Fernandes AC, Da N, Barbosa S, Souza M, Da R et al. Clinical profile of Oropouche Fever in Bahia, Brazil: unexpected fatal cases-07-16 (version 1). 2024;16(version 1):0–17. https://doi.org/10.1590/SciELOPreprints.9342
47. WHO. Oropouche virus disease-Region of the Americas. 2024; [Cited 2024 August 13]. https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON530
48. Schwartz DA, Dashraath P, Baud D. Oropouche Virus (OROV) in Pregnancy: An Emerging Cause of Placental and Fetal Infection Associated with Stillbirth and Microcephaly following Vertical Transmission. Viruses [Internet]. 2024;16(9):1435. https://www.mdpi.com/1999-4915/16/9/1435
49. Jaenisch T, Rosenberger KD, Brito C, Brady O, Brasil P, Marques ET. Risk of microcephaly after Zika virus infection in Brazil, 2015 to 2016. Bull World Health Organ [Internet]. 2017;95(3):191–8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5328112/pdf/BLT.16.178608.pdf/
50. Elliott KC, Mattapallil JJ. Zika Virus—A Reemerging Neurotropic Arbovirus Associated with Adverse Pregnancy Outcomes and Neuropathogenesis. Pathogens [Internet]. 2024;13(2):177. https://www.mdpi.com/2076-0817/13/2/177
51. Durango-Chavez HV, Toro-Huamanchumo CJ, Silva-Caso W, Martins-Luna J, Aguilar-Luis MA, del Valle-Mendoza J et al. Oropouche virus infection in patients with acute febrile syndrome: Is a predictive model based solely on signs and symptoms useful? Sahoo MK, editor. PLoS One [Internet]. 2022;17(7):e0270294. https://doi.org/10.1371/journal.pone.0270294
52. de Souza Luna LK, Rodrigues AH, Santos RIM, Sesti-Costa R, Criado MF, Martins RB et al. Oropouche virus is detected in peripheral blood leukocytes from patients. J Med Virol [Internet]. 2017;89(6):1108–11. https://onlinelibrary.wiley.com/doi/https://doi.org/10.1002/jmv.24722
53. King AMQ, Adams MJ, Carstens EB. and E. J. Lefkowitz, Virus taxonomy: Ninth report of the international committee on taxonomy of viruses. Elsevier, 2011. Accessed: Oct. 10, 2024. [Online]. Available: http://www.sciencedirect.com:5070/book/9780123846846/virus-taxonomy
54. Barbosa NS, Concha JO, DaSilva LLP, Crump CM, Graham SC. Oropouche Virus Glycoprotein Topology and Cellular Requirements for Glycoprotein Secretion. Dutch RE, editor. J Virol [Internet]. 2023;97(1). https://doi.org/10.1128/jvi.01331-22
55. Ayers VB, Huang YJS, Dunlop JI, Kohl A, Brennan B, Higgs S et al. Replication Kinetics of a Candidate Live-Attenuated Vaccine for Cache Valley Virus in Aedes albopictus. Vector-Borne Zoonotic Dis [Internet]. 2022;22(11):553–8. https://www.liebertpub.com/doi/https://doi.org/10.1089/vbz.2022.0053
56. Tilston-Lunel NL, Hughes J, Acrani GO, da Silva DEA, Azevedo RSS, Rodrigues SG et al. Genetic analysis of members of the species Oropouche virus and identification of a novel M segment sequence. J Gen Virol [Internet]. 2015;96(7):1636–50. https://www.microbiologyresearch.org/content/journal/jgv/https://doi.org/10.1099/vir.0.000108
57. Stubbs SH, Cornejo Pontelli M, Mishra N, Zhou C, de Paula Souza J, Mendes Viana RM et al. Vesicular Stomatitis Virus Chimeras Expressing the Oropouche Virus Glycoproteins Elicit Protective Immune Responses in Mice. Desselberger U, Palese P, editors. MBio [Internet]. 2021;12(4). https://doi.org/10.1128/mBio.00463-21
58. Adhikari UK, Tayebi M, Rahman MM. Immunoinformatics Approach for Epitope-Based Peptide Vaccine Design and Active Site Prediction against Polyprotein of Emerging Oropouche Virus. J Immunol Res [Internet]. 2018;2018:1–22. https://www.hindawi.com/journals/jir/2018/6718083/
59. Afonso A, Conraths F, Editorial. Prev Vet Med [Internet]. 2014;116(4):337–8. https://linkinghub.elsevier.com/retrieve/pii/S0167587714002967
60. Yeh JY, Ga YJ. Seroepidemiology of Aino Virus in Farmed and Free-Ranging Cervids in the Republic of Korea. Front Vet Sci [Internet]. 2021;8. https://www.frontiersin.org/articles/https://doi.org/10.3389/fvets.2021.702978/full
61. Ogawa Y, Eguchi M, Shimoji Y. Two Akabane virus glycoprotein Gc domains induce neutralizing antibodies in mice. J Vet Med Sci [Internet]. 2022;84(4):21–0670. https://www.jstage.jst.go.jp/article/jvms/84/4/84_21-0670/_article
62. Kraatz F, Wernike K, Hechinger S, König P, Granzow H, Reimann I et al. Deletion Mutants of Schmallenberg Virus Are Avirulent and Protect from Virus Challenge. Doms RW, editor. J Virol [Internet]. 2015;89(3):1825–37. https://doi.org/10.1128/JVI.02729-14
63. Wernike K, Aebischer A, Roman-Sosa G, Beer M. The N-terminal domain of Schmallenberg virus envelope protein Gc is highly immunogenic and can provide protection from infection. Sci Rep [Internet]. 2017;7(1):42500. https://www.nature.com/articles/srep42500
64. Hellert J, Aebischer A, Haouz A, Guardado-Calvo P, Reiche S, Beer M et al. Structure, function, and evolution of the Orthobunyavirus membrane fusion glycoprotein. Cell Rep [Internet]. 2023;42(3):112142. https://linkinghub.elsevier.com/retrieve/pii/S2211124723001535
65. Yewdell JW. Antigenic drift: Understanding COVID-19. Immunity [Internet]. 2021;54(12):2681–7. https://linkinghub.elsevier.com/retrieve/pii/S1074761321005082
66. Romero-Alvarez D, Escobar LE, Auguste AJ, Del Valle SY, Manore CA. Transmission risk of Oropouche fever across the Americas. Infect Dis Poverty [Internet]. 2023;12(1):47. https://idpjournal.biomedcentral.com/articles/https://doi.org/10.1186/s40249-023-01091-2
67. Hassan HK, Adigun OA, Manirambona E, Olaleke NO, Abioye MS, Lucero-Prisno DE III et al. Mitigating the escalating threat of infectious diseases outbreaks in tropical Africa: a perspective examination of challenges and strategies for future preparedness. Beni-Suef Univ J Basic Appl Sci [Internet]. 2024;13(1):55. https://bjbas.springeropen.com/articles/https://doi.org/10.1186/s43088-024-00511-y
68. Yimer SA, Booij BB, Tobert G, Hebbeler A, Oloo P, Brangel P et al. Rapid diagnostic test: a critical need for outbreak preparedness and response for high priority pathogens. BMJ Glob Heal [Internet]. 2024;9(4):e014386. https://gh.bmj.com/lookup/doi/https://doi.org/10.1136/bmjgh-2023-014386
69. Kruk ME, Gage AD, Arsenault C, Jordan K, Leslie HH, Roder-DeWan S et al. High-quality health systems in the Sustainable Development Goals era: time for a revolution. Lancet Glob Heal [Internet]. 2018;6(11):e1196–252. http://www.ncbi.nlm.nih.gov/pubmed/30196093
70. Ellwanger JH, Veiga ABG da, Kaminski V, de Valverde-Villegas L, Freitas JM, de Chies AWQ. JAB. Control and prevention of infectious diseases from a One Health perspective. Genet Mol Biol [Internet]. 2021;44(1 suppl 1). http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1415-47572021000200305&tlng=en
71. Omosigho PO, Okesanya OJ, Olaleke NO, Eshun G, Lucero-Prisno DE. Multiple burden of infectious disease outbreaks: Implications for Africa healthcare system. J Taibah Univ Med Sci [Internet]. 2023;18(6):1446–8. https://linkinghub.elsevier.com/retrieve/pii/S1658361223000999
72. Chan SL, Zhang AY, Lam SSW, Rao V, Kanagalingam D, Tan HK et al. The impact of elective surgery postponement during COVID-19 on emergency bellwether procedures in a large tertiary centre in Singapore. Int J Qual Heal Care [Internet]. 2024;36(1). https://academic.oup.com/intqhc/article/doi/https://doi.org/10.1093/intqhc/mzae022/7632443
73. Chiang JO, Azevedo RS, Justino MCA, Matos HJ, Cabeça HLS, Silva SP et al. Neurological disease caused by Oropouche virus in northern Brazil: should it be included in the scope of clinical neurological diseases? J Neurovirol [Internet]. 2021;27(4):626–30. https://link.springer.com/https://doi.org/10.1007/s13365-021-00987-9
74. Valdivieso-Martínez B, Sauri I, Philibert J, Calderon JM, Gas ME, Diaz J et al. Impact of Long-COVID on Health Care Burden: A Case Control Study. J Clin Med [Internet]. 2023;12(18):5768. https://www.mdpi.com/2077-0383/12/18/5768
75. Rechel B, Doyle Y, Grundy E, Mckee M. How can health systems respond to population ageing ? WHO Europe, p. 43, 2009, Accessed: August. 10, 2024. [Online]. Available: http://www.euro.who.int/__data/assets/pdf_file/0004/64966/E92560.pdf
76. Anticona Huaynate CF, Pajuelo Travezaño MJ, Correa M, Mayta Malpartida H, Oberhelman R, Murphy LL et al. Diagnostics barriers and innovations in rural areas: insights from junior medical doctors on the frontlines of rural care in Peru. BMC Health Serv Res [Internet]. 2015;15(1):454. https://bmchealthservres.biomedcentral.com/articles/https://doi.org/10.1186/s12913-015-1114-7
77. Årdal C, Baraldi E, Beyer P, Lacotte Y, Larsson DJ, Ploy MC et al. Supply chain transparency and the availability of essential medicines. Bull World Health Organ [Internet]. 2021;99(4):319–20. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8085627/pdf/BLT.20.267724.pdf/

78. Olaniran A, Briggs J, Pradhan A, Bogue E, Schreiber B, Dini HS et al. Stock-outs of essential medicines among community health workers (CHWs) in low- and middle-income countries (LMICs): a systematic literature review of the extent, reasons, and consequences. Hum Resour Health [Internet]. 2022;20(1):58. https://human-resources-health.biomedcentral.com/articles/https://doi.org/10.1186/s12960-022-00755-8
79. Wesselmann KM, Postigo-Hidalgo I, Pezzi L, de Oliveira-Filho EF, Fischer C, de Lamballerie X et al. Emergence of Oropouche fever in Latin America: a narrative review. Lancet Infect Dis [Internet]. 2024;24(7):e439–52. https://linkinghub.elsevier.com/retrieve/pii/S1473309923007405
80. Salmon-Mulanovich G, Blazes DL, Lescano AG, Bausch DG, Montgomery JM, Pan WK. Economic Burden of Dengue Virus Infection at the Household Level Among Residents of Puerto Maldonado, Peru. Am Soc Trop Med Hyg [Internet]. 2015;93(4):684–90. https://www.ajtmh.org/view/journals/tpmd/93/4/article-p684.xml
81. Jacques O, Arpin E, Ammi M, Noël A. The political and fiscal determinants of public health and curative care expenditures: evidence from the Canadian provinces, 1980–2018. Can J Public Heal [Internet]. 2023;114(4):584–92. https://link.springer.com/https://doi.org/10.17269/s41997-023-00751-y
82. PAHO/WHO. PAHO urges countries to strengthen prevention, surveillance and diagnosis of the Oropouche virus following its geographic spread and recent clinical findings. 2024; https://www.paho.org/en/news/2-8-2024-paho-urges-countries-strengthen-prevention-surveillance-and-diagnosis-oropouche-virus
83. Aborode AT, Hasan MM, Jain S, Okereke M, Adedeji OJ, Karra-Aly A et al. Impact of poor disease surveillance system on COVID-19 response in africa: Time to rethink and rebuilt. Clin Epidemiol Glob Heal [Internet]. 2021;12:100841. https://linkinghub.elsevier.com/retrieve/pii/S2213398421001494
84. Soyemi TS, Aborode AT. Shortage of hospital bed capacity and overcrowding in emergency tertiary healthcare centers in Nigeria. Ann Med Surg (Lond). 2022;82:104675. https://doi.org/10.1016/j.amsu.2022.104675. PMID: 36268429; PMCID: PMC9577657.
85. French G, Hulse M, Nguyen D, Sobotka K, Webster K, Corman J et al. Impact of hospital strain on excess deaths during the COVID-19 pandemic—United States, july 2020–july 2021. American Journal of Transplantation [Internet]. 2022;22(2):654–7. https://doi.org/10.1111/ajt.16645
86. Yenet A, Nibret G, Tegegne BA. Challenges to the availability and affordability of essential medicines in African countries: a scoping review. ClinicoEconomics and Outcomes Research [Internet]. 2023;Volume 15:443–58. https://doi.org/10.2147/ceor.s413546
87. Faiva E, Hashim HT, Ramadhan MA, Musa SK, Bchara J, Tuama YD et al. Drug supply shortage in Nigeria during COVID – 19: efforts and challenges. J Pharm Policy Pract [Internet]. 2021;1–3. https://doi.org/10.1186/s40545-021-00302-1
88. Dzinamarira T, Iradukunda PG, Saramba E, Gashema P, Moyo E, Mangezi W et al. COVID-19 and mental health services in Sub-Saharan Africa: A critical literature review. Compr Psychiatry [Internet]. 2024;131:152465. https://linkinghub.elsevier.com/retrieve/pii/S0010440X24000166
89. Wainberg ML, Scorza P, Shultz JM, Helpman L, Mootz JJ, Johnson KA et al. Challenges and Opportunities in Global Mental Health: a Research-to-Practice Perspective. Curr Psychiatry Rep [Internet]. 2017;19(5):28. http://link.springer.com/https://doi.org/10.1007/s11920-017-0780-z
90. Mahomed F. Addressing the Problem of Severe Underinvestment in Mental Health and Well-Being from a Human Rights Perspective. Health Hum Rights [Internet]. 2020;22(1):35–49. http://www.ncbi.nlm.nih.gov/pubmed/32669787
91. Wada YH, Rajwani L, Anyam E, Karikari E, Njikizana M, Srour L et al. Mental health in Nigeria: A Neglected issue in Public Health. Public Heal Pract [Internet]. 2021;2:100166. https://linkinghub.elsevier.com/retrieve/pii/S2666535221000914
92. Green H, Fernandez R, MacPhail C. The social determinants of health and health outcomes among adults during the COVID-19 pandemic: A systematic review. Public Health Nurs [Internet]. 2021;38(6):942–52. https://onlinelibrary.wiley.com/doi/https://doi.org/10.1111/phn.12959
93. Malakoane B, Heunis JC, Chikobvu P, Kigozi NG, Kruger WH. Public health system challenges in the Free State, South Africa: a situation appraisal to inform health system strengthening. BMC Health Serv Res [Internet]. 2020;20(1):58. https://bmchealthservres.biomedcentral.com/articles/https://doi.org/10.1186/s12913-019-4862-y
94. WHO. World Bank and WHO: Half the world lacks access to essential health services, 100 million still pushed into extreme poverty because of health expenses. 2024; [Cited 2024 August 16]. https://www.who.int/news/item/13-12-2017-world-bank-and-who-half-the-world-lacks-access-to-essential-health-services-100-million-still-pushed-into-extreme-poverty-because-of-health-expenses
95. Manirambona E, Lucero-Prisno DE, Shomuyiwa DO, Denkyira SA, Okesanya OJ, Haruna UA et al. Harnessing wastewater-based surveillance (WBS) in Africa: a historic turning point towards strengthening the pandemic control. Discov Water [Internet]. 2024;4(1):9. https://link.springer.com/https://doi.org/10.1007/s43832-024-00066-0
96. Qoseem IO, Okesanya OJ, Olaleke NO, Ukoaka BM, Amisu BO, Ogaya JB et al. Digital health and health equity: How digital health can address healthcare disparities and improve access to quality care in Africa. Heal Promot Perspect [Internet]. 2024;14(1):3–8. https://hpp.tbzmed.ac.ir/Article/hpp-42822
97. Edelstein M, Lee LM, Herten-Crabb A, Heymann DL, Harper DR. Strengthening Global Public Health Surveillance through Data and Benefit Sharing. Emerg Infect Dis [Internet]. 2018;24(7):1324–30. http://wwwnc.cdc.gov/eid/article/24/7/15-1830_article.htm
98. Javaid M, Haleem A, Singh RP. Health informatics to enhance the healthcare industry's culture: An extensive analysis of its features, contributions, applications and limitations. Informatics Heal [Internet]. 2024;1(2):123–48. https://linkinghub.elsevier.com/retrieve/pii/S2949953424000092
99. Theron G, Jenkins HE, Cobelens F, Abubakar I, Khan AJ, Cohen T et al. Data for action: collection and use of local data to end tuberculosis. Lancet (London, England) [Internet]. 2015;386(10010):2324–33. http://www.ncbi.nlm.nih.gov/pubmed/26515676
100. Sharan M, Vijay D, Yadav JP, Bedi JS, Dhaka P. Surveillance and response strategies for zoonotic diseases: a comprehensive review. Sci One Heal [Internet]. 2023;2:100050. https://linkinghub.elsevier.com/retrieve/pii/S2949704323000446
101. Zhao AP, Li S, Cao Z, Hu PJH, Wang J, Xiang Y et al. AI for science: Predicting infectious diseases. J Saf Sci Resil [Internet]. 2024;5(2):130–46. https://linkinghub.elsevier.com/retrieve/pii/S266644962400015X
102. Anjaria P, Asediya V, Bhavsar P, Pathak A, Desai D, Patil V. Artificial Intelligence in Public Health: Revolutionizing Epidemiological Surveillance for Pandemic Preparedness and Equitable Vaccine Access. Vaccines [Internet]. 2023;11(7):1154. https://www.mdpi.com/2076-393X/11/7/1154
103. Al Meslamani AZ, Sobrino I, de la Fuente J. Machine learning in infectious diseases: potential applications and limitations. Ann Med [Internet]. 2024;56(1). https://www.tandfonline.com/doi/full/https://doi.org/10.1080/07853890.2024.2362869
104. Kumar S, Preetha G. Health promotion: An effective tool for global health. Indian J Community Med [Internet]. 2012;37(1):5. https://journals.lww.com/https://doi.org/10.4103/0970-0218.94009
105. World Health Organization (WHO). Multisectoral Approach to the Prevention and Control of Vector-Borne Diseases [Internet]. 2020. 19–31 p. [Cited 2024 August 18]. https://apps.who.int/iris/handle/10665/331861
106. Kruk ME, Gage AD, Arsenault C, Jordan K, Leslie HH, Roder-DeWan S et al. High-quality health systems in the Sustainable Development Goals era: time for a revolution. Lancet Glob Heal [Internet]. 2018;6(11):e1196–252. https://linkinghub.elsevier.com/retrieve/pii/S2214109X18303863
107. da Costa VG, de Rezende Féres VC, Saivish MV, de Lima Gimaque JB, Moreli ML. Silent emergence of Mayaro and Oropouche viruses in humans in Central Brazil. Int J Infect Dis [Internet]. 2017;62:84–5. http://www.ncbi.nlm.nih.gov/pubmed/28739422
108. Corbin JH, Oyene UE, Manoncourt E, Onya H, Kwamboka M, Amuyunzu-Nyamongo M et al. A health promotion approach to emergency management: effective community engagement strategies from five cases. Health Promot Int [Internet]. 2021;36(Supplement_1):i24–38. https://academic.oup.com/heapro/article/36/Supplement_1/i24/6460422
109. Ghio D, Lawes-Wickwar S, Tang MY, Epton T, Howlett N, Jenkinson E et al. What influences people's responses to public health messages for managing risks and preventing infectious diseases? A rapid systematic review of the evidence and recommendations. BMJ Open [Internet]. 2021;11(11):e048750. https://bmjopen.bmj.com/lookup/doi/https://doi.org/10.1136/bmjopen-2021-048750
110. Mashal MT, Eltayeb D, Higgins-Steele A, El Sheikh IS, Abid NS, Shukla H et al. Effective partnership and in-country resource mobilization in Sudan for cVDPV2 outbreak response amid multiple emergencies in 2020–2021. BMC Public Health [Internet]. 2024;24(1):235. https://bmcpublichealth.biomedcentral.com/articles/https://doi.org/10.1186/s12889-023-15675-y

111. WHO. Strategic framework for the prevention and control of emerging and epidemic-prone infectious diseases in the Eastern. 2019;1(October 2020). [Cited 2024 August 19]. http://apps.who.int/bookorders
112. UNFPA, World Health Organization (WHO). Invitation For Public Comment Global Action Plan For Healthy Lives And Well-Being For All Accelerator [1]. 2018;(June):1–6. https://www.who.int/docs/default-source/global-action-plan/accelerator6.pdf
113. Pujhari S. Recent Advances in Arboviral Vaccines: Emerging Platforms and Promising Innovations. Biologics [Internet]. 2023;4(1):1–16. https://www.mdpi.com/2673-8449/4/1/1
114. Yimer SA, Booij BB, Tobert G, Hebbeler A, Oloo P, Brangel P et al. Rapid diagnostic test: a critical need for outbreak preparedness and response for high priority pathogens. BMJ Glob Heal [Internet]. 2024;9(4). http://www.ncbi.nlm.nih.gov/pubmed/38688565
115. Elliott RM. Molecular biology of the Bunyaviridae. Journal of General Virology [Internet]. 1990;71(3):501–22. https://doi.org/10.1099/0022-1317-71-3-501
116. Rajapaksha RMNU, Khatri RB, Abeysena C, Wijesinghe MSD, Endalamaw A, Thomas TK et al. Success and challenges of health systems resilience-enhancing strategies for managing Public Health Emergencies of International Concerns (PHEIC): A systematic review protocol. BMJ Open [Internet]. 2022;12(11):e067829. https://bmjopen.bmj.com/lookup/doi/https://doi.org/10.1136/bmjopen-2022-067829
117. Hameed M, Najafi M, Cheeti S, Sheokand A, Mago A, Desai S. Factors influencing international collaboration on the prevention of COVID-19. Public Health [Internet]. 2022;212:95–101. https://linkinghub.elsevier.com/retrieve/pii/S0033350622002530

Publisher's note