Venezuela's humanitarian crisis, resurgence of vector-borne diseases, and implications for spillover in the region

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In the past 5–10 years, Venezuela has faced a severe economic crisis, precipitated by political instability and declining oil revenue. Public health provision has been affected particularly. In this Review, we assess the impact of Venezuela's health-care crisis on vector-borne diseases, and the spillover into neighbouring countries. Between 2000 and 2015, Venezuela witnessed a 359% increase in malaria cases, followed by a 71% increase in 2017 (411 586 cases) compared with 2016 (240 613). Neighbouring countries, such as Brazil, have reported an escalating trend of imported malaria cases from Venezuela, from 1538 in 2014 to 3129 in 2017. In Venezuela, active Chagas disease transmission has been reported, with seroprevalence in children (<10 years), estimated to be as high as 12·5% in one community tested (n=64). Dengue incidence increased by more than four times between 1990 and 2016. The estimated incidence of chikungunya during its epidemic peak is 6975 cases per 100 000 people and that of Zika virus is 2057 cases per 100 000 people. The re-emergence of many vector-borne diseases represents a public health crisis in Venezuela and has the possibility of severely undermining regional disease elimination efforts. National, regional, and global authorities must take action to address these worsening epidemics and prevent their expansion beyond Venezuelan borders.

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Introduction

Over the past two decades, Venezuela has transitioned into a deep socioeconomic and political crisis. Once recognised as a regional leader for public health and vector-control policies and programming, Venezuela's health care has collapsed, creating a severe and ongoing humanitarian crisis with no end in sight.[1,2] It is a well known fact that political and civil unrest can create conditions for the emergence and spread of infectious diseases.[3] Venezuela is no exception. With a decaying health-care infrastructure, a mass departure of trained medical personnel (a full medical professor earns <US$10 a month), and the decline of all public health programmes, the country is experiencing a surge and expansion of vector-borne diseases. The UN High Commission for Refugees estimates that in 2014–18, 1·5 million Venezuelans departed Venezuela for other countries in the Latin American and Caribbean region.[4] By March, 2018, around 40 000 Venezuelans were estimated to be living in Brazil, and at least 600 000 people have sought shelter in Colombia.[5,6] Official data are probably underestimates given the existence of informal border crossings. With these high amounts of emigration, reports of disease spillover to neighbouring countries are increasingly common.[7]

Disease surveillance and reporting have been equally affected by Venezuela's health-care crisis. Since 1938, the Venezuelan Ministry of Health uninterruptedly issued weekly and monthly epidemiological reports known as the *Boletín Epidemiológico*. However, in 2007, the reports had a 20-week interruption in publishing, regaining periodicity until November, 2014, when publication was stopped by the government; the reports have not been published since.[8] In June, 2018, the Venezuelan Center for Classification of Diseases—a part of the Division of Epidemiology and Vital Statistics of the Ministry of Health that was in charge of providing the Pan American Health Organization (PAHO) and WHO with updated morbidity and mortality indicators—was eliminated by the government after 63 years of uninterrupted activity.[9]

The return of measles and other vaccine-preventable childhood infections in Venezuela since circa 2015 has been highlighted by PAHO.[10] In this Review, we provide a comprehensive overview of the growing epidemics of the major vector-borne diseases—malaria, Chagas disease, leishmaniasis, and arboviral infections—in Venezuela and their ongoing spillover to neighbouring countries based on the scarce data available. We examine the potential effect of such spillover, and urge regional health-care authorities to declare a public health emergency of hemispheric concern.

Malaria: a regional menace

Malaria, one of the most serious parasitic diseases of the tropics, is caused by species of the genus *Plasmodium* and transmitted among humans from the bites of infected female mosquitoes of the *Anopheles* genus. WHO has established an ambitious plan for control and elimination of the disease by 2030, and Latin American countries have made substantial advances towards that goal, particularly from 2000 to 2015,[11] when symptomatic disease declined by 62% (from 1 181 095 cases in 2000 to

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451 242 in 2015), and malaria-related deaths by 61·2% (from 410 in 2000 to 159 in 2015). Nonetheless, in 2016, a considerable increase in case incidence (875 000) was reported in the region.[12] Venezuela accounted for 34·4% of the total reported cases in 2016 (240 613). The number rose to 411 586 cases in 2017 (a 71% increase). Incidence has been rising greatly since 2000 (increasing by 359% by 2015), particularly since 2010 (figure 1A).

During 2016, *Plasmodium vivax* accounted for 71% of reported cases of malaria in Venezuela, followed by *Plasmodium falciparum* (20%) and other plasmodium infections (approximately 9% of mixed and *Plasmodium malariae* cases).[12] *P vivax* cases in Venezuela increased from 62 850 in 2014, to 179 554 in 2016 (a three-fold increase). By the end of 2017, this number had increased by 76% to 316 401.[12] Since 2017, numbers of mixed malaria infections have increased, with double (*P falciparum* and *P vivax*) and triple (*P vivax, P falciparum, and P malariae*) infections exhibiting rates higher than expected based on usual occurrence for each species, reflecting high malaria transmission. Before 2003, malaria in Venezuela followed an endemoepidemic pattern.[12] Major incidence peaks occurred every 3–6 years in the two main ecological regions affected by malaria—namely, the southern lowland rainforest and savannahs of the Guayana region, and the wetlands of the northeastern coastal plains.[13] From 2003 onwards, the Guayana region, particularly the Sifontes Municipality in southeastern Bolívar State, Venezuela (figure 1B), became the highest risk area for malaria in the country.[13,14] In the Sifontes Municipality, malaria incidence is likely to be linked with an increase in illegal mining activities and forest exploitation. A complex pattern of localised, albeit persistent, hotspots of plasmodium transmission is maintained principally by *Anopheles* (soon to be *Nyssorhynchus*) *darlingi* Root (4·0%),[15] *Anopheles albitarsis* Lynch sl (5·4%), and *Anopheles nuneztovari* Gabaldon sl (0·5%),[16,17] which show high natural parasite infections.

Clearing forests for mining activities has been observed to create favourable conditions for *A darlingi* and *A albitarsis* breeding.[18] An increase in illegal mining activities is likely to be linked to the economic crisis. Highly mobile, often immunologically naive, human populations migrate from different regions of the country to mining areas in search of economic opportunities. Once people arrive, they live outdoors, constantly exposed to the risk of mosquito bites. Many internal migrants return to previous endemic malaria regions where viable anopheles vector populations exist, reintroducing malaria to areas where this infection had been previously eliminated. Additionally, financial constraints generated by the crisis in the past 5 years have severely restricted the procurement of malaria commodities (eg, insecticides, drugs, diagnostic supplies, and mosquito nets), and have hampered epidemiological surveillance, reporting activities, vector control, and disease treatment efforts.[2,19] Internal economic migration of miners and their families, combined with a deficit in provision and implementation of curative and prevention services previously provided by the state, has created ideal conditions for malaria epidemics and increases in morbidity and mortality. Since 2014, local malaria transmission has re-emerged in new areas of the country, leading to a shift in the epidemiology of this disease. Endemic malaria transmission is now beginning to propagate across the whole country, including urban and periurban foci, combined with an increase in hotspots, which persist in the Guayana Region (figure 1B). However, the numbers presented in figure 1B are likely to represent an underestimate of the situation, as *P vivax* case relapses are often not reported. Such cases are on the rise due to primaquine and chloroquine non-adherence resulting from antimalarial drugs being out of stock. Furthermore, findings have also revealed that there are four asymptomatic carriers per symptomatic case, with similar findings in Colombia and Brazil.[20]

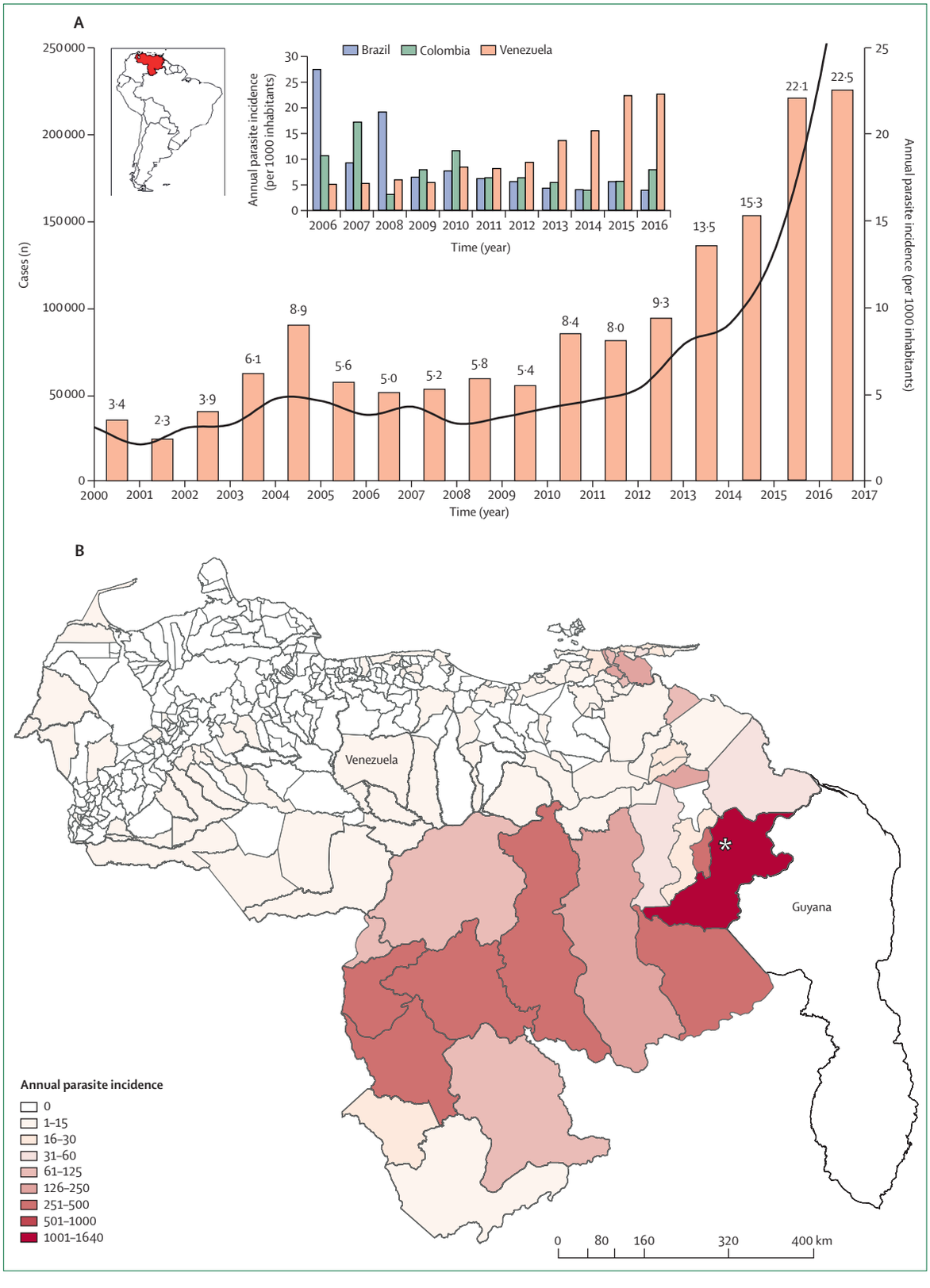
The rapidly increasing malaria burden in Venezuela and the mass departure of its citizens continues to affect neighbouring countries, particularly Brazil and Colombia. According to the Brazilian Ministry of Health, a total of 47 968 malaria cases were reported in neighbouring Roraima from 2014 to 2017 (figure 2), of which around 20% (9399) were imported from Venezuela. Numbers of such cases increased from 1538 (in 2014) to 3129 (in 2017). In 2016, 45% of reported malaria cases in the Brazilian border municipality of Pacaraima, and 86% of cases in another border municipality, Boa Vista, were attributed to Venezuelan immigration (figure 2C). The continued upsurge of malaria in Venezuela could soon become uncontrollable, jeopardising the hard-won gains of the malaria control programme in Brazil and other countries in the region. With 411 586 cases in 2017, Venezuela might now exhibit the largest malaria increase reported worldwide,[7] threatening the successful implementation of the WHO Global Technical Strategy for Malaria.[7,12]

Chagas disease: persistent endemism and resurgence

Chagas disease is caused by the kinetoplastid parasite *Trypanosoma cruzi*, which currently infects approximately 6 million people worldwide.[21] Chagas disease is a complex zoonosis involving multiple species of mammal and blood-sucking triatomine bug.[22] In approximately 30–40% of cases, human infection with *T cruzi* leads to severe, and irreversible, cardiac and intestinal pathology.[21] Chagas

Figure 1: **Annual parasite incidence and confirmed cases of malaria in Venezuela**

(A) Number of confirmed malaria cases (line) and annual parasite incidence per 1000 inhabitants (bars) in Venezuela, 2000–16. Inset left: map of Venezuela (red) in South America. Inset right: case comparison of annual parasite incidence for Colombia, Brazil, and Venezuela. (B) Annual parasite incidence for each municipality in Venezuela during 2016. *Sifontes Municipality.



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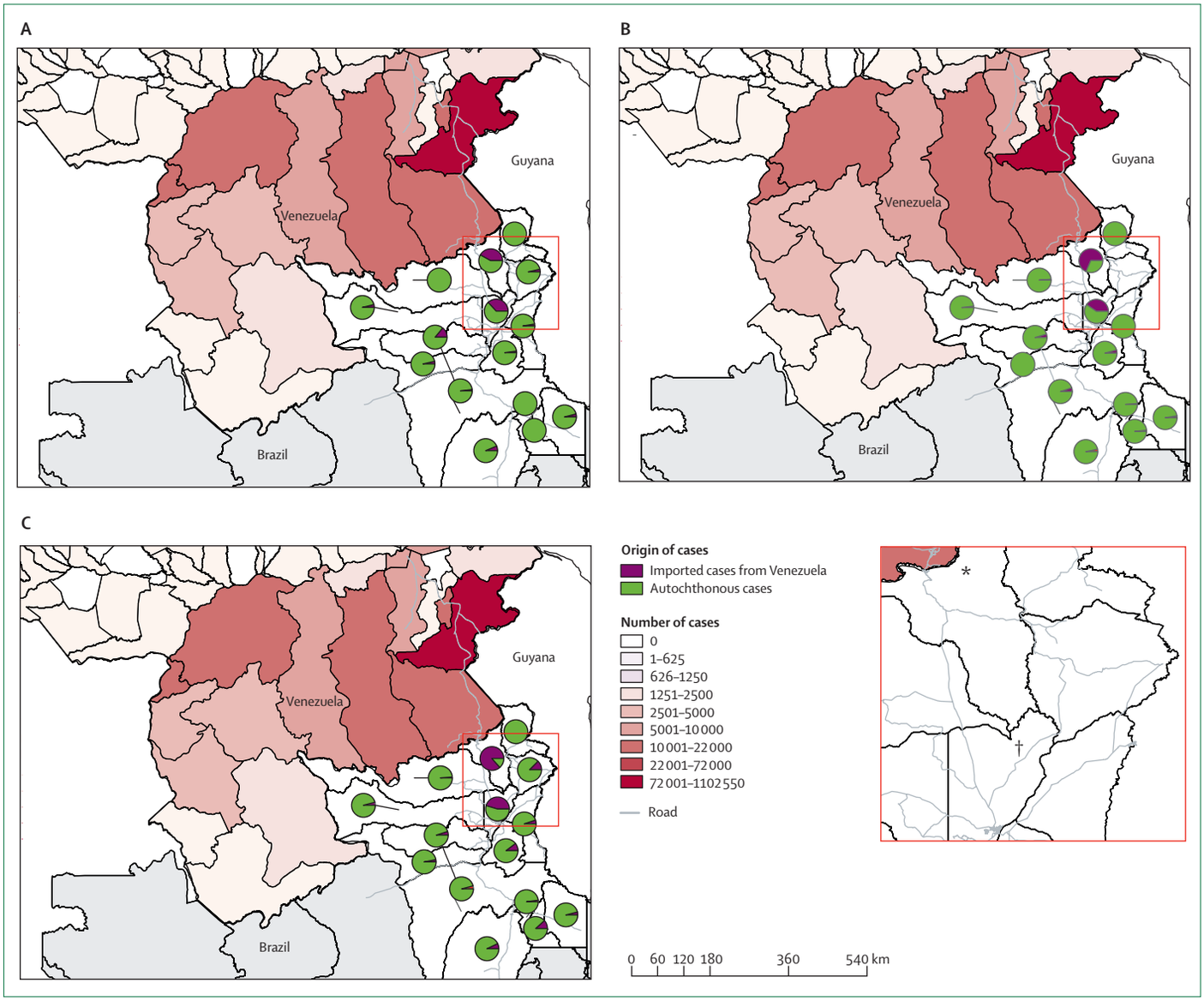

Figure 2: **Malaria cases reported in eastern Venezuela and neighbouring Roraima State, Brazil**
(A) 2014, (B) 2015, and (C) 2016. Pie charts indicate origin of cases. Inset shows the locations of Pacaraima and Boa Vista. *Pacaraima. †Boa Vista.

disease has remained endemic in Venezuela since its first description in 1919. In the 1960s and 1970s, seroprevalence was 43·9% overall, and 20·4% in young children (aged <10 years, a key indicator of active transmission).[23,24] Efforts to interrupt Chagas disease transmission, alongside widespread insecticide use against malaria vectors, succeeded in reducing seroprevalance to 9·2% and the geographical extent of transmission risk by 52%.[25] Seroprevalence among children younger than 10 years was reduced to 0·5% between 1990 and 1998.[25] Regrettably, the 1990s saw the national Chagas disease control programme reduced and decentralised.[25] Moreover, Chagas disease control in Venezuela has been hindered by the ecology of the principal vector, *Rhodnius prolixus*, which frequently invades and colonises rural houses from wild transmission cycles after insecticide spraying. Thus, even before the current economic crisis, Venezuela was at risk of resurgent Chagas disease. Since 2012, the surveillance and control of Chagas disease transmission in Venezuela have been abandoned. In this Review, we can report the multiple hotspots of new and active disease transmission by piecing together unpublished data from several sources.

See Online for appendix

In the Andes and western Venezuela, Chagas disease is present throughout many different states. Seroprevalences obtained from three endemic communities in Portuguesa State, Venezuela, between 2014 and 2016 (12·5% in those <10 years; figure 3A, appendix) show considerable active transmission. Also, house infestation

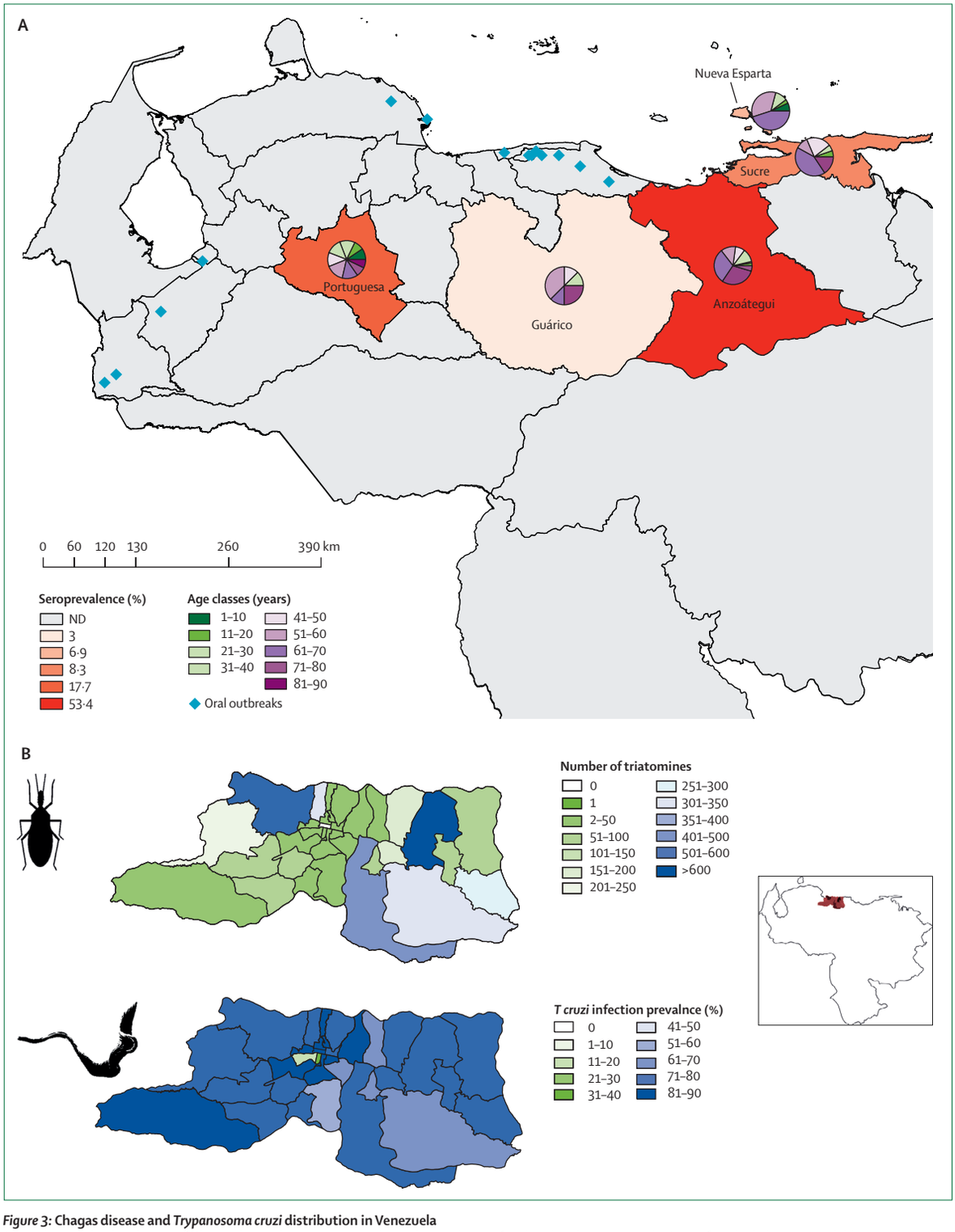

Figure 3: **Chagas disease and *Trypanosoma cruzi* distribution in Venezuela**
(A) Update on the distribution of Chagas disease human seroprevalance data and sites of oral outbreaks in Venezuela. States for which data are available are coloured by percentage overall seroprevalence. Pie charts indicate infection among different age classes. Blue diamonds indicate sites of reported oral outbreaks. (B) Distribution of peri-urban vectors and *T cruzi* infection status around Caracas. Upper map shows data for triatomines brought to the clinic at the Insituto de Medicine Tropical, Caracas, Venezuela, in 2007–16 by municipality. Lower map shows *T cruzi* infection prevalence (%) in the same vectors. Inset shows locations of sampled neighbourhoods in Venezuela. ND=no data available.

indices were estimated to be as high as 24·8% in some hotspots at the time the Chagas disease control programme was dismantled.[26] Seroprevalences observed in Lara State in 2011 (0·57% in those <10 years) also suggest some active transmission.[26,27] Seroprevalence estimates from 2011–19 for Lara State and other western states are not available; however, Chagas disease might well be resurgent, since no surveillance or preventative measures are in place. At the time of publishing, an outbreak of acute Chagas disease in Táchira State, Venezuela, reported in the Colombian media, had infected 40 people and claimed eight lives.[28] 11 cases in total of so-called spillover acute disease in Venezuelan nationals were confirmed by the Colombian authorities between October, 2017 and April, 2018. By contrast with western Venezuela, in the 2000s, studies suggested that elimination of vectorial transmission of Chagas disease in eastern Venezuela was possible.[25] However, seroprevalence data show that active transmission is present in Venezuela in Nueva Esparta State (2·5% of those aged 1–9 years in 2016; figure 3A, appendix), Anzoátegui State (8% of those aged 11–20 years in 2014; figure 3A, appendix), and Sucre State (2% of those aged 11–20 years in 2012; appendix). In Nueva Esparta State, most seropositive individuals were young or members of the older population, possibly reflecting the success of the former control programme and current resurgence of the disease (figure 3A, appendix). Overall seroprevalence among children from the data reported in the appendix and figure 3A (4·3% of those <10 years) indicates resurgent infection and resembles rate estimates from the 1970s.[25] However, our sample sizes are at least one order of magnitude lower than historical studies, although the serological approaches were similar (ELISA, indirect haemagglutination [IHA], and flow cytometry [FC]). Nationally, seroprevalences over all age groups (15·7%; appendix) exceed those in endemic provinces in Colombia (2·2% in Boyacá in 2007–09; 0·2% in Santander in 2013–14)[29] and Ecuador (3·5% in Manabí, Loja, Guayas in 2001–03)[30] by a substantial margin. Whether blood banks are still being screened for Chagas disease in Venezuela is unclear; however, in the current crisis it seems unlikely.

Oral Chagas disease transmission has also become an issue of great concern. Between 2007 and 2018, 16 outbreaks of oral Chagas disease have been recorded nationwide, and ten have been managed through the outpatient clinic of the Institute of Tropical Medicine, Caracas, Venezuela; figure 3B, appendix).[31,32] The updated data in the appendix show 321 cases and 23 deaths in 10 years. Such outbreaks have frequently been associated with consumption of artisan fruit juices contaminated with infected triatomines (especially the vector species *Panstrongylus geniculatus*) or their faeces, and show a severe clinical course and high mortality.[33] Urbanisation and deforestation of wooded areas where the triatomines are present might also be contributing to this situation.[2] Half of these outbreaks have occurred in and around Caracas, although reports from other geographical regions are increasing, with many undiagnosed cases probably remaining unreported because of the non-specific signs and symptoms as well as physicians' unfamiliarity with the acute phase of the disease. Severe drug shortages have forced patients to cross borders into neighbouring countries in search of treatment, medical care, or both. Moreover, the monitoring of these patients is essential because treatment with the only existing drugs (benznidazole and nifurtimox) is not totally effective, a situation exacerbated by the low availability of these drugs in Venezuela, and the medical personnel to administer them.[34]

Linked to several oral Chagas disease outbreaks in and around Caracas are increasing reports of peri-urban transmission of *T cruzi* in Venezuela. The presence of *T cruzi* was first reported in 2005, when 76·1% of the disease vector *P geniculatus* recovered from the capital district and the states of Miranda and Vargas were naturally infected with *T cruzi*, and that 60·2% of their gut contents gave a positive reaction to human antiserum.[35] Ongoing collections between 2007 and 2016 have continued to reveal mostly *P geniculatus* (98·96%), as well as *Triatoma nigromaculata* (0·58%), *Triatoma maculata* (0·37%), *R prolixus* (0·07%), and *Panstrongylus rufutuberculatus* (0·02%; figure 3B).[36] Vector infection rates with *T cruzi* over this period have been consistently high (75·7%; figure 3B). Intradomiciliary triatomine nymphs also present in 16 of the 32 parishes (3·42% of vectors captured) suggest active colonisation of houses by these insects. Preliminary molecular analysis of blood meals identify humans as by far the most common blood-feeding source among insects collected in 2007–16. Furthermore, molecular epidemiological analyses clearly identify parasites from these peri-urban transmission cycles as the source of local oral outbreaks.[37] To what extent vectors are also transmitting parasites directly to human populations in the metropolitan district (ie, not orally via contaminated food) is not known. However, given the high amount of feeding on humans and the high number of infected triatomines, vectoral transmission remains a possibility despite the supposed low vectoral capacity of *P geniculatus*.[36]

Leishmaniasis: an early wake-up call

Leishmaniasis refers to a spectrum of diseases caused by several trypanosomatid species belonging to the genus *Leishmania* (Old and New World) and subgenus *Viania* (New World). *Leishmania* spp are transmitted through the bite of infected phlebotomine sandflies. In Venezuela, leishmaniasis is widely distributed, with most endemic zones located throughout the valleys of the coastal mountain range, the Yaracuy River basin (west), some areas of the central plains (Los Llanos), and the Andean mountain forests. Isolated endemic foci south of the Orinoco River in the Amazon basin have also been reported, but remain to be fully characterised.[38]

As per data from the National Sanitary Dermatology Programme of the Venezuelan Minister of Health,[39] 61 576 cases of cutaneous leishmaniasis occurred between 1990 and 2016, with approximately 75% of the cases occurring in the Venezuelan states of Táchira, Mérida, Trujillo, Lara, Miranda, and Sucre (figure 4). Since 2006, regions of the leishmaniasis endemic in Venezuela have expanded substantially. This expansion is probably linked to ever-increasing trends towards urbanisation, deforestation, environmental changes, and the emergence of focal peri-urban transmission cycles as reported in several cities in the states of Lara and Trujillo.[38] Nothing in the available data suggests that the frequency of different clinical manifestations of cutaneous leishmaniasis (mucocutaneous, disseminated, and diffuse) has been affected by the crisis.

Visceral leishmaniasis is prevalent in three endemic foci across Venezuela. The central focal point includes the states of Guárico, Carabobo, Cojedes, and Aragua; the western focal point covers the states of Portuguesa, Lara, and Trujillo; and the eastern focal point, includes the states of Sucre, Anzoátegui, and the insular state of Nueva Esparta.[38] Between 1961 and 1991, reports revealed the occurrence of 675 cases nationwide; however, this might be an underestimate of the real situation. Infected dogs can develop visceral leishmaniasis and are a potential source of infection to both other dogs and humans. Sero-epidemiological surveys indicate that between 2004 and 2012, the prevalence of visceral leishmaniasis was 14·8% among 15 822 dogs evaluated, with the states of Lara and Guárico showing the highest seroprevalence, and most dogs (81%) showing no clinical signs.[40] Migratory trends might be contributing to the spread of the disease from its traditional endemic rural niches into peri-urban ecotopes where the presence of vectors (*Lutzomyia longipalpis* and *Lutzomyia evansi*) could aid the instalment of new autochthonous foci.[38]

The risk of *Leishmania* spp transmission has historically been affected by migrations, refugee crises, wars, and states of civil unrest, which can encourage cross-border movement of cases—notably observed during conflicts in Syria and Yemen since 2010.[32–37,41–43] Cross-border dispersal of *Leishmania* spp from Venezuela is already occurring, and several cases of visceral leishmaniasis and cutaneous leishmaniasis have been detected in Venezuelan migrants to Colombia in the past 6 months.[44]

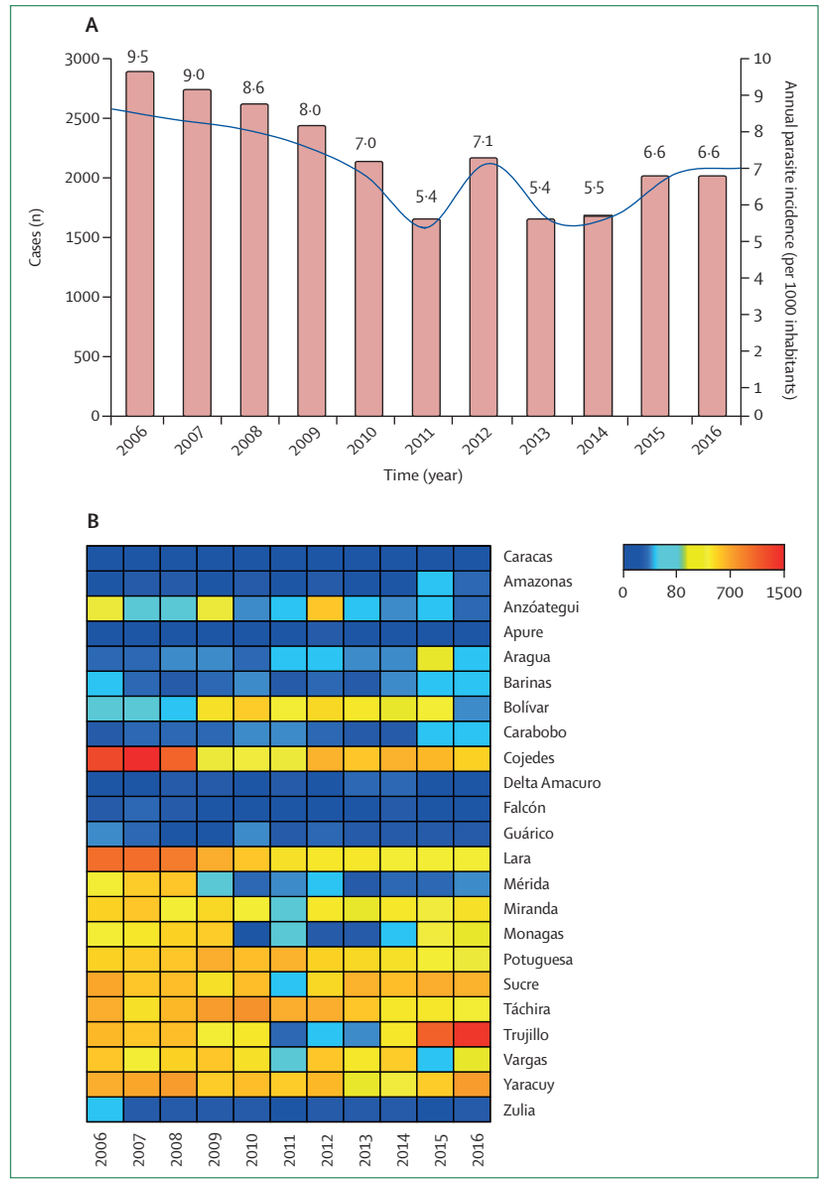

Figure 4: **Annual parasite incidence and confirmed cases of cutaneous leishmaniasis in Venezuela**
(A) Number of confirmed cases (line) and annual incidence per 100 000 inhabitants (bars) in Venezuela, 2006–16. (B) Annual parasite incidence by state per 100 000 inhabitants for 2006–16 (increasing from blue to red).

Arboviruses: an expanding threat

Viruses that are transmitted by arthropod vectors (arboviruses) have been expanding either steadily or in explosive emergent or re-emergent epidemics over the past 10 years, posing a growing threat to global public health.[45,46] In the past 4 years, the two major epidemics that swept the American continent were caused by the chikungunya and Zika arboviruses.[47] Simultaneously, dengue virus, another arboviral disease endemic in the Latin American region, is increasing its spread to previously unaffected areas. All three arboviruses are transmitted by the same mosquito, *Aedes aegypti* (L), with a potential role for the invasive species *Aedes albopictus* as well.

A member of the Flaviviridae family, dengue virus has become a major public health problem in Venezuela. Four dengue virus serotypes (DENV-1–4) co-circulate in the country, each of them capable of causing the entire range of dengue-related disease symptoms. Infected individuals can be asymptomatic or present with clinical manifestations varying from mild febrile illness, to severe disease and death.[48] Venezuela is witnessing an upswing

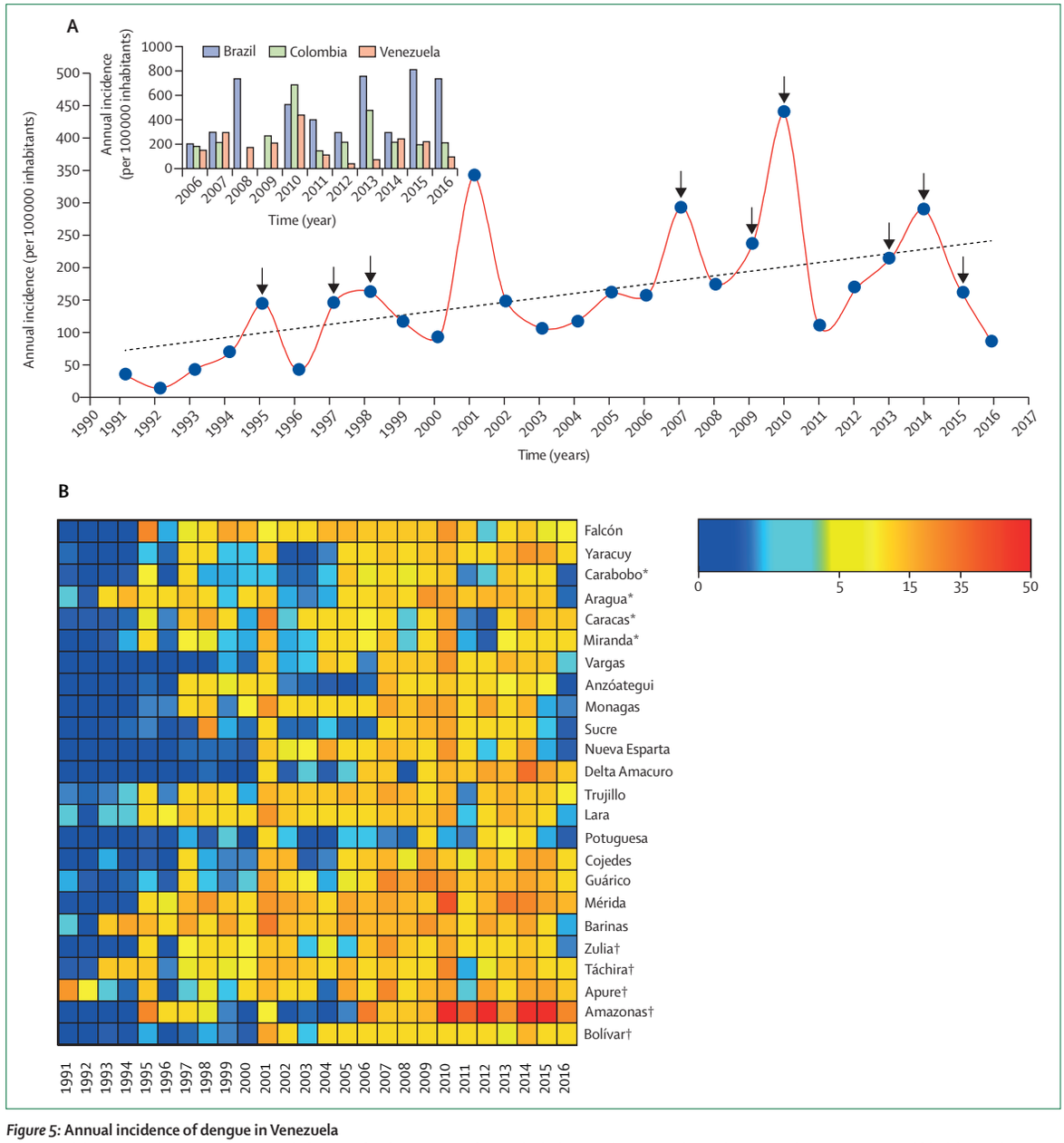

Figure 5: **Annual incidence of dengue in Venezuela**

(A) Annual dengue incidence (per 100 000 inhabitants) for the 1991–2016 period. Black vertical arrows indicate dengue epidemic years. Dotted black line indicates an increasing linear trend (R^2=0·27, t=2·99, p=0·006, n=26). Inset shows comparison of incidence data for Colombia, Brazil, and Venezuela. (B) Annual incidence by state per 100 000 inhabitants from 1991 to 2016 (increasing from blue to red). *Central region. †Border region.

in incidence, frequency, and magnitude of dengue epidemics against a background of perennial endemic transmission. Dengue incidence has increased more than five-fold. The average incidence between 2010 and 2016 was 211 cases per 100 000 population (figure 5A). Within the country, the temporal increase in cases of dengue mirrors the national dengue incidence, with regions of higher population density (central regions) and those bordering Colombia and Brazil (border regions) exhibiting a higher incidence (figure 5B). Worryingly, a total of six increasingly large epidemics were recorded nationally between 2007 and 2016, compared with four epidemics in the previous 16 years.[49] The largest epidemic occurred in 2010, when approximately 125 000 cases, including 10 300 (8·24%) with severe manifestations, were registered. During that year, Venezuela ranked third in the number of reported dengue cases in the American continent and second in the number of severe cases.[50]

The combination of poverty-related socioeconomic factors, such as increasingly crowded living conditions,

growing population density, precarious homes, and long-lasting deficits in public services including frequent and prolonged interruptions in water supply and electricity, have been linked with a greater risk of acquiring dengue virus infection in Venezuela.[51–54] These inadequacies have obliged residents to store water within households, maintaining suitable breeding conditions for *Ae aegypti* vectors during the dry season and throughout the year, driving perennial dengue transmission. Additionally, the inability of vector control programmes to do proper surveillance and timely application of vector control measures has caused the proportion of houses infested with *Ae aegypti* to surpass the WHO transmission threshold.[55] Such conditions set the stage for subsequent arboviral epidemics.

Venezuela was not spared from the havoc wrought by the epidemic of chikungunya in 2014, or the epidemic of Zika virus a year later. The effect of these epidemics was amplified by the absence of timely official information, absence of preparedness, and the worsening economic and health crisis that resulted in acute shortages of diagnostics medicines and medical supplies, and an overburdened health system. Both epidemics rapidly spread through densely inhabited regions where dengue virus transmission was high. Although nationally, the attack rate of chikungunya was estimated to be between 6·9% and 13·8%,[56] the observed attack rate in populated urban areas reached 40–50%, similar to or higher than that reported in other countries.[57,58] The total number of chikungunya cases in Venezuela reported to PAHO in 2014 (by epidemiological week 52) was 30 405, with an incidence of 112 per 100 000 population.[59] Given the paucity of official information since October, 2014, estimates based on excess fever cases not explained by another cause suggest that cases of chikungunya exceeded 2 million, resulting in an incidence of 6975 cases per 100 000 population, more than 12 times the rate reported officially by the Venezuelan Ministry of Health.[56] Moreover, an important, yet unknown, number of atypical and severe or fatal cases of chikungunya occurred[60] but were not reported by health personnel because of fear of governmental reprisal.[1,61]

In January, 2016, the Zika virus epidemic struck Venezuela at the same time as a rise in dengue virus transmission. The Zika virus outbreak evolved in a similar manner as chikungunya, rapidly affecting a high proportion of the population. Inadequate preparedness and deficiency of official communication once again was a cause for concern. The incidence of symptomatic cases during the peak of the epidemic (the first 8 weeks of 2016) was estimated at 2124 cases per 100 000 population.[62] Current estimates of serological (IgG) Zika virus positivity in pregnant women have reached roughly 80% (Tami A, unpublished). As in other countries, an increase in the number of cases of Guillain-Barré syndrome was observed during the epidemic. However, Venezuela had a rise of 877% (a 9·8-fold increase) in Guillain-Barré syndrome incidence compared with the pre-Zika virus baseline incidence—one of the highest (if not the highest) reported in the Americas.[63] The number of Guillain-Barré syndrome cases surged from a mean of 214 annual cases reported before Zika virus, to more than 700 confirmed cases since the epidemic started.[62] Cases of microcephaly and other congenital disorders related to Zika virus infections in pregnancy in Venezuela have been reported, but the incidence remains to be determined by ongoing studies.

Beyond chikungunya, Zika, and dengue viruses, other circulating arboviruses with epidemic potential exist in Venezuela. Outbreaks of Mayaro virus (often confused with chikungunya) have been reported during the past decade.[64,65] In 2010, Oropouche virus (of which there was an outbreak in Peru in 2016) was detected in the Amazonian basin in South America, outside its typical distribution zone.[66] The occurrence of epizootic strains of Venezuelan equine encephalitis virus and Madariaga virus (South American eastern equine encephalitis),[67] along with cryptic transmission cycles of these viruses, when immunisation programmes have been halted, pose a further threat. No facilities exist for rapid laboratory diagnosis of either virus in Venezuela.[68] The most common and effective Venezuelan equine encephalitis vaccine, TC-83, can no longer be bought or produced in Venezuela. The Agricultural Research Institute, with restricted production capacity, has no financial support and production has been halted. Although there are no reliable official records of equine inventories, the threat of latent outbreaks and their potential international dispersal increases with the presence of wild donkeys without owners or sanitary control and persistent circulation of epizootic Venezuelan equine encephalitis strains in interepizootic periods in different sites of the plains and the Catatumbo region, Venezuela.[69]

Disease outbreaks associated with arbovirus are increasing in frequency and magnitude throughout Latin America. Although no evidence is available to suggest that the prevalence of certain arboviruses like dengue virus is higher in Venezuela than in other countries (figure 5A), the deficiency of public health infrastructure available for diagnosis and treatment is now a disproportionate problem in Venezuela compared with other countries in the region. Furthermore, given the current situation, widespread under-reporting of cases by comparison with other countries in the region is also possible. Given previous patterns and the increase in risk factors favouring arboviral transmission, the abscence of an increase in dengue incidence from 2014 onwards suggests under-reporting.

Considering the precarious possibilities for cure of arboviral diseases in Venezuela combined with the high level of population displacement, emigrating infected individuals could be unwittingly causing a spillover of these diseases to neighbouring countries, a process that has not yet been quantified. The first major outbreak of

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For more on **Observatorio Venezolano de la Salud** see https://www.ovsalud.org

For more on the **Sistema de Vigilância** see http://200.214.130.44/sivep_malaria/

For more on the **Instituto Nacional de Salud** see http://www.ins.gov.co

Search strategy and selection criteria

For malaria, Venezuelan and Latin American data were sourced from the Pan American Health Organization (PAHO) Malaria Surveillance Indicators and Observatorio Venezolano de la Salud Documentos Oficiales. Brazilian border state data were accessed from the Brazilian Ministry of Health Sistema de Vigilância on May 5, 2018. Data for Colombian cases were accessed via the Instituto Nacional de Salud Estadísticas SIVIGILA 2017. Data on oral cases of Chagas disease in Venezuela were sourced via PubMed from literature written in English or Spanish published between Jan 1, 2007 and May 25, 2018, and patient records at the Institute de Medicine Tropical, Caracas, Venezuela. Historical serological data for Chagas disease in Venezuela and elsewhere were sourced via PubMed from literature published between Jan 1, 1950 and May 25, 2018. Serological data for 2008–16 were derived from unpublished records at the Instituto de Medicina Tropical, Universidad Central de Venezuela, Caracas, Venezuela, and the Centro de Medicina Tropical de Oriente, Universidad de Oriente Núcleo Anzoátegui, Barcelona, Venezuela. Data for vector abundance and infection rates (2014–16) were also derived from unpublished records at the Instituto de Medicina Tropical, Universidad Central de Venezuela. Data for Colombian cases were accessed from the Instituto Nacional de Salud Estadísticas SIVIGILA 2017. Human cutaneous leishmaniasis data from 1990 to 2016 were sourced from the National Sanitary Dermatology programme of the Ministry of Health, available from the Venezuelan Health Observatory (Observatorio Venezolano de la Salud). Data for Colombian cases were accessed from the Instituto Nacional de Salud Estadísticas (El Sistema de Salud Pública) 2017. For dengue virus, chikungunya, and Zika virus, we used the number of cases reported and notified by the Surveillance System of the Venezuelan Ministry of Health and Observatorio Venezolano de la Salud, at national level, the latter especially during the epidemics of chikungunya in 2014 and of Zika virus in 2015–2016. Latin American data were sourced from PAHO Dengue Surveillance Indicators.

dengue on the island of Madeira, an autonomous region of Portugal, in 2012–13 is an example of the disease export potential for Venezuela, as this outbreak was directly linked with a DENV-1 serotype from Venezuela.[70]

A call for action

For many decades, Venezuela was a leader in vector control and public health policy in Latin America, even more so after becoming the first WHO-certified country to eliminate malaria in most of its territory in 1961.[71] The interruption of malaria transmission was achieved through systematic and integrative infection and vector control, case management, preventive diagnosis, patient treatment, mass drug administration, community participation through volunteer community health workers, and sanitary engineering such as housing improvement and water management. This integrative approach differs little from current so-called best-practice prevention, control, and elimination of malaria. The success of the Venezuelan public health intervention helped to stimulate interest in global malaria elimination during the 1960s.[71]

Paradoxically, the onchocerciasis (a vector-borne helminth infection) elimination programme in Venezuela has continued to work reasonably well. The programme's success is underpinned by the commitment and resolve of its Venezuelan local health workers and indigenous health agents, and the regional support of the Onchocerciasis Elimination Program for the Americas.[2] As a result of long-term mass drug administration with ivermectin on a biannual (and four times per year) basis starting in 2000, interruption of onchocerciasis has been achieved among the northern foci located in the coastal mountain area,[72] and parasite transmission now remains in just 25% of the Venezuelan Yanomami of the southern Amazonian region.[73] This regional initiative has proven that the consensus of ministries of health, the endemic communities, non-governmental organisations, and public–private stakeholders, including WHO, is required to develop and implement effective public health programmes.[2,71]

Venezuelans have endured a decade of political, social, and economic upheaval that has left the country in crisis. In addition to the return of measles and other vaccine-preventable infectious diseases,[74] conditions are favouring the unprecedented emergence and transmission of vector-borne diseases. Underpinning the current epidemics are inadequate surveillance, education, and awareness, and a reduced capacity for effective intervention. Successful control of the emerging crisis requires regional coordination and, as we show in this Review, cross-border spillover is already ongoing, and expected to increase.

Fortunately, many solutions are possible, even with restricted resources. A good example is the successful binational strategy for the elimination of malaria on the Peru–Ecuador border. Collaboration at the operational level included strengthening surveillance and training community personnel to collect blood smears from febrile people within their border communities, which prompted effective diagnosis, case definition (indigenous, imported, introduced, induced, and cryptic), and treatment.[75] When state infrastructure does not work, however, surveillance can be achieved via the mobilisation of citizen scientists and informal networks of health-care professionals. Technological advances in low-cost sample preservation, passive sampling, and in-situ diagnostics can also contribute. Education to raise awareness among communities at risk from disease can be achieved via social media, initiatives at schools, and information campaigns at public centres. Surveillance data are powerful and must be used as an advocacy tool to raise awareness among Venezuelan and regional authorities, and ultimately to encourage them to improve their

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recognition of the growing crisis, cooperate, and accept international medical interventions. Relevant international health authorities, such as the WHO Global Outbreak Alert and Response Network, must also take action to maintain accurate disease surveillance and response systems in the region along with collaboration with other strategic partners to provide timely humanitarian assistance throughout this ongoing crisis. The wider scientific community must support this process by engaging with their Venezuelan and regional colleagues, contributing to a robust, non-partisan evidence base for such interventions. Ultimately, national and international political commitments are essential to stop a health crisis that threatens the whole region.

The emergence, or re-emergence, of vector-borne neglected diseases must be recognised as now extending beyond the borders of Venezuela. These diseases have already extended into neighbouring Brazil and Colombia, and with increasing air travel and human migration, most of the Latin American and Caribbean region (as well as some US cities hosting the Venezuelan diaspora, including Miami, FL, and Houston, TX) is at heightened risk for disease re-emergence. Accordingly, we call on the members of the Organization of American States and other international political bodies to become better and more effectively engaged in strengthening Venezuela's now-depleted health system by applying more pressure to the government to accept humanitarian assistance offered by the international community.[2] Without such international interventions, the possibility that the public health gains achieved over the past 18 years, through Millennium Development Goal 6 (to combat AIDS, malaria, and other diseases) and the new Sustainable Development Goals, could be soon reversed is real.

Contributors

All authors were involved in the writing of the Review or data analysis and figure preparations, or both.

Declaration of interests

We declare no competing interests.

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References

1 Burki T. Re-emergence of neglected tropical diseases in Venezuela. *Lancet Infect Dis* 2015; **15:** 641–42.

2 Hotez PJ, Basáñez MG, Acosta-Serrano A, Grillet ME. Venezuela and its rising vector-borne neglected diseases. *PLoS Negl Trop Dis* 2017; **11:** e0005423.

3 Du R, Stanaway J, Hotez PJ. Could violent conflict derail the London declaration on NTDs? *PLoS Negl Trop Dis* 2018; **12:** e0006136.

4 United Nations Refugee Agency. As Venezuelans flee throughout Latin America, UNHCR issues new protection guidance. 2018. http://www.unhcr.org/news/briefing/2018/3/5aa793c14/venezuelans-flee-throughout-latin-america-unhcr-issues-new-protection-guidance.html (accessed May 5, 2018).

5 United States Agency for International Development. Research and development progress report. 2018. https://www.usaid.gov/GlobalDevLab/documents/research-and-development-progress-report/fy-2015 (accessed May 5, 2018).

6 Tuite AR, Thomas-Bachli A, Acosta H, et al. Infectious disease implications of large-scale migration of Venezuelan nationals. *J Travel Med* 2018; **25:** 1–8.

7 Nebehay S. Malaria on rise in crisis-hit Venezuela, WHO says. Reuters. 2018. https://www.reuters.com/article/us-health-malaria-venezuela/malaria-on-rise-in-crisis-hit-venezuela-who-says-idUSKBN1HV1ON (accessed May 5, 2018).

8 Avilán Rovira JM. El Boletín Epidemiológico Semanal. *Gac Méd Caracas* 2008; **116:** 1.

9 El Nacional. Dejaron al país y a la OMS sin mapa de salud venezolana. 2018. http://www.el-nacional.com/noticias/sociedad/dejaron-pais-oms-sin-mapa-salud-venezolana_247285 (accessed Sept 21, 2018).

10 Pan American Health Organization. Epidemiological update—measles. WHO. 2018. https://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=44328&lang=en (accessed May 5, 2018).

11 Recht J, Siqueira AM, Monteiro WM, et al. Malaria in Brazil, Colombia, Peru and Venezuela: current challenges in malaria control and elimination. *Malar J* 2017; **16:** 273.

12 WHO. World malaria report 2018. 2018. https://www.who.int/malaria/publications/world-malaria-report-2018/report/en/ (accessed Feb 3, 2019).

13 Grillet ME, El Souki M, Laguna F, León JR. The periodicity of *Plasmodium vivax* and *Plasmodium falciparum* in Venezuela. *Acta Trop* 2014; **129:** 52–60.

14 Moreno Jorge E, Rubio-Palis Y, Martínez Ángela R, Porfirio A. Evolución espacial y temporal de la malaria en el municipio Sifontes del estado Bolívar, Venezuela. 1980–2013. *Bol Mal Salud Amb* 2014; **54:** 236–49.

15 Foster PG, de Oliveira TMP, Bergo ES, et al. Phylogeny of Anophelinae using mitochondrial protein coding genes. *R Soc Open Sci* 2017; **4:** 170758.

16 Moreno JE, Rubio-Palis Y, Páez E, Pérez E, Sánchez V. Abundance, biting behaviour and parous rate of anopheline mosquito species in relation to malaria incidence in gold-mining areas of southern Venezuela. *Med Vet Entomol* 2007; **21:** 339–49.

17 Abou Orm S, Moreno JE, Carrozza M, Acevedo P, Herrera F. *Plasmodium* spp. infection rates for some *Anopheles* spp. from Sifontes Municipality, Bolívar State, Venezuela. *Bol Mal Salud Amb* 2017; **57:** 17–25.

18 Moreno JE, Rubio-Palis Y, Sánchez V, Martínez Á. Caracterización de hábitats larvales de anofelinos en el municipio Sifontes del estado Bolívar, Venezuela. *Bol Mal Salud Amb* 2015; **55:** 117–31.

19 Grillet ME, Villegas L, Oletta JF, Tami A, Conn JE. Malaria in Venezuela requires response. *Science* 2018; **359:** 528.

20 Wide A, Pabón R, De Abreu N, et al. Prevalence of asymptomatic *Plasmodium vivax* infections in the North-Eastern focus of malaria of Venezuela. *Bol Mal Salud Amb* 2016; **56:** 160–71 (in Spanish).

21 Pérez-Molina JA, Molina I. Chagas disease. *Lancet* 2018; **391:** 82–94.

22 Yeo M, Acosta N, Llewellyn M, et al. Origins of Chagas disease: didelphis species are natural hosts of *Trypanosoma cruzi* I and armadillos hosts of *Trypanosoma cruzi* II, including hybrids. *Int J Parasitol* 2005; **35:** 225–33.

23 Añez N, Crisante G, Rojas A. Update on Chagas disease in Venezuela—a review. *Mem Inst Oswaldo Cruz* 2004; **99:** 781–87.

24 Acquatella H. Estado actual de la enfermedad de Chagas en Venezuela y de su manejo terapéutico. *Gac Méd Caracas* 2003; **111:** 136–56.

25 Aché A, Matos AJ. Interrupting Chagas disease transmission in Venezuela. *Rev Inst Med Trop Sao Paulo* 2001; **43:** 37–43.

26 Rodríguez-Bonfante C, Amaro A, García M, et al. Epidemiology of Chagas disease in Andrés Eloy Blanco, Lara, Venezuela: triatomine infestation and human seroprevalence. *Cad Saude Publica* 2007; **23:** 1133–40 (in Spanish).

27 Bonfante-Cabarcas R, Rodríguez-Bonfante C, Vielma BO, et al. Seroprevalence for *Trypanosoma cruzi* infection and associated factors in an endemic area of Venezuela. *Cad Saude Publica* 2011; **27:** 1917–29.

28 Cardozo E. Mal de Chagas deja ocho muertos y 40 infectados en Táchira. La Opinion. 2018. https://www.laopinion.com.co/venezuela/mal-de-chagas-deja-ocho-muertos-y-40-infectados-en-tachira-152365#OP (accessed May 5, 2018).

29 Cucunubá ZM, Nouvellet P, Conteh L, et al. Modelling historical changes in the force-of-infection of Chagas disease to inform control and elimination programmes: application in Colombia. *BMJ Glob Health* 2017; **2:** e000345.

30 Black CL, Ocaña-Mayorga S, Riner DK, et al. Seroprevalence of *Trypanosoma cruzi* in rural Ecuador and clustering of seropositivity within households. *Am J Trop Med Hyg* 2009; **81:** 1035–40.

31 Noya BA, Díaz-Bello Z, Colmenares C, et al. Update on oral Chagas disease outbreaks in Venezuela: epidemiological, clinical and diagnostic approaches. *Mem Inst Oswaldo Cruz* 2015; **110:** 377–86.

32 Alarcón de Noya B, Ruiz-Guevara R, Diaz-Bello Z, et al. En Venezuela la enfermedad de Chagas de transmisión oral llegó para quedarse. 2016. https://www.tribunadelinvestigador.com/ediciones/2016/2/art-7/ (accessed May 25, 2018).

33 Noya O, Ruiz-Guevara R, Diaz-Bello Z, Alarcón de Noya B. Epidemiología y clínica de la transmisión oral de *Trypanosoma cruzi*. 2015. https://issuu.com/isglobal/docs/revista_espa__ola_de_salud_publica_ (accessed May 25, 2018).

34 Alarcón de Noya B, Díaz-Bello Z, Colmenares C, et al. Eficacia terapéutica en el primer brote de transmisión oral de la enfermedad de Chagas en Venezuela. *Biomédica* 2011; **31:** 64–65.

35 Carrasco HJ, Torrellas A, García C, Segovia M, Feliciangeli MD. Risk of *Trypanosoma cruzi* I (Kinetoplastida: Trypanosomatidae) transmission by *Panstrongylus geniculatus* (Hemiptera: Reduviidae) in Caracas (Metropolitan District) and neighboring States, Venezuela. *Int J Parasitol* 2005; **35:** 1379–84.

36 Carrasco HJ, Segovia M, Londoño JC, Ortegoza J, Rodríguez M, Martínez CE. *Panstrongylus geniculatus* and four other species of triatomine bug involved in the *Trypanosoma cruzi* enzootic cycle: high risk factors for Chagas' disease transmission in the Metropolitan District of Caracas, Venezuela. *Parasit Vectors* 2014; **7:** 602.

37 Segovia M, Carrasco HJ, Martínez CE et al. Molecular epidemiologic source tracking of orally transmitted Chagas disease, Venezuela. *Emerg Infect Dis* 2013; **19:** 1098–101.

38 Incani RN. Leishmaniasis y sus vectores. In: Incani RN, ed. Parasitology. Valencia, Venezuela: Universidad de Carabobo Press, 2010: 161–76.

39 Guevara JR. Estadísticas de Leishmaniasis cútanea en Venezuela Historico / Año 1990–2016. Archives of the Ministerio de Poder Popular Para la Salud, Venezuela, Servicio Autónomo Instituto de Biomedicina. Caracas, Venezuela: Ministerio de Poder Popular Para la Salud, Venezuela official press, 2016.

40 Lugo DA, Ortega-Moreno ME, Rodriguez V, et al. Seroprevalence of canine visceral leishmaniasis by rK39-ELISA in endemic foci in Venezuela. *Rev Fac Cs Vets* 2015; **56:** 42–51.

41 Seaman J, Mercer AJ, Sondorp E. The epidemic of visceral leishmaniasis in western Upper Nile, southern Sudan: course and impact from 1984 to 1994. *Int J Epidemiol* 1996; **25:** 862–71.

42 Patino LH, Mendez C, Rodriguez O, et al. Spatial distribution, leishmania species and clinical traits of cutaneous leishmaniasis cases in the Colombian army. *PLoS Negl Trop Dis* 2017; **11:** e0005876.

43 Sharara SL, Kanj SS. War and infectious diseases: challenges of the Syrian civil war. *PLoS Pathog* 2014; **10:** e1004438.

44 Instituto Nacional de Salud. Estadísticas SIVIGILA 2017. 2017. https://www.ins.gov.co/Direcciones/Vigilancia/Lineamientosy documentos/Lineamientos%202018.pdf (accessed May 5, 2018).

45 Hotez PJ, Murray KO. Dengue, West Nile virus, chikungunya, Zika-and now Mayaro? *PLoS Negl Trop Dis* 2017; **11:** e0005462.

46 Braack L, Gouveia de Almeida AP, Cornel AJ, Swanepoel R, de Jager C. Mosquito-borne arboviruses of African origin: review of key viruses and vectors. *Parasit Vectors* 2018; **11:** 29.

47 Ferguson NM, Cucunubá ZM, Dorigatti I, Nedjati-Gilani GL, Donnelly CA, Basáñez MG. Countering the Zika epidemic in Latin America. *Science* 2016; **353:** 353–54.

48 WHO. Dengue guidelines for diagnosis, treatment, prevention and control. World Health Organization. 2009. http://www.who.int/tdr/publications/documents/dengue-diagnosis.pdf (accessed May 5, 2018).

49 Vincenti-Gonzalez MF, Tami A, Lizarazo EF, Grillet ME. ENSO-driven climate variability promotes periodic major outbreaks of dengue in Venezuela. *Sci Rep* 2018; **8:** 5727.

50 Pan American Health Organization. Reported cases of dengue fever in the Americas by country or territory. WHO. 2018. http://www.paho.org/data/index.php/en/mnu-topics/indicadores-dengue-en/dengue-nacional-en/252-dengue-pais-ano-en.html (accessed Jan 15, 2019).

51 Barrera R, Navarro JC, Mora JD, Domínguez D, González J. Public service deficiencies and *Aedes aegypti* breeding sites in Venezuela. *Bull Pan Am Health Organ* 1995; **29:** 193–205.

52 Barrera R, Delgado N, Jiménez M, Villalobos I, Romero I. Stratification of a hyperendemic city in hemorrhagic dengue. *Rev Panam Salud Publica* 2000; **8:** 225–33.

53 Velasco-Salas ZI, Sierra GM, Guzmán DM, et al. Dengue seroprevalence and risk factors for past and recent viral transmission in Venezuela: a comprehensive community-based study. *Am J Trop Med Hyg* 2014; **91:** 1039–48.

54 Vincenti-Gonzalez MF, Grillet ME, Velasco-Salas ZI, et al. Spatial analysis of dengue seroprevalence and modeling of transmission risk factors in a dengue hyperendemic city of Venezuela. *PLoS Negl Trop Dis* 2017; **11:** e0005317.

55 Grillet ME, Del Ventura. Emergencia del Zika en Latinoamerica y Control de *Aedes aegypti*. *Bol Dir Malariol Saneam Ambient* 2016; **56:** 97–102.

56 Oletta JF. Epidemia de fiebre chikungunya en Venezuela, 2014–2015. *Gac Méd Caracas* 2016; **124:** 122–37.

57 Schwartz O, Albert ML. Biology and pathogenesis of chikungunya virus. *Nat Rev Microbiol* 2010; **8:** 491–500.

58 Pimentel R, Skewes-Ramm R, Moya J. Chikungunya in the Dominican Republic: lessons learned in the first six months. *Rev Panam Salud Publica* 2014; **36:** 336–41.

59 Pan American Health Organization. Number of reported cases of chikungunya fever in the Americas, by country or territory 2013–2014. Epidemiological week 52. WHO. Dec 29, 2014. https://www.paho.org/hq/dmdocuments/2014/2014-dec-29-cha-CHIKV-cases-ew-52.pdf (accessed June 20, 2018).

60 Torres JR, Leopoldo Códova G, et al. Chikungunya fever: atypical and lethal cases in the western hemisphere: a Venezuelan experience. *IDCases* 2014; **2:** 6–10.

61 Wade L. Scientific community. For Venezuelan academics, speaking out is risky business. *Science* 2014; **346:** 287.

62 Oletta JF. 2016. Evolución de la epidemia de Zika en Venezuela, hasta el 21 de marzo de 2016. *Gac Méd Caracas* 2016; **124:** 50–56.

63 Dos Santos T, Rodriguez A, Almiron M, et al. Zika virus and the Guillain-Barré syndrome—case series from seven countries. *N Engl J Med* 2016; **375:** 1598–601.

64 Auguste AJ, Liria J, Forrester NL, et al. Evolutionary and ecological characterization of Mayaro virus strains isolated during an outbreak, Venezuela, 2010. *Emerg Infect Dis* 2015; **21:** 1742–50.

65 Muñoz M, Navarro JC. Mayaro: a re-emerging arbovirus in Venezuela and Latin America. *Biomedica* 2012; **32:** 286–302.

66 Navarro JC, Giambalvo D, Hernandez R, et al. Isolation of Madre de Dios virus (Orthobunyavirus; Bunyaviridae), an Oropouche virus species reassortant, from a monkey in Venezuela. *Am J Trop Med Hyg* 2016; **95:** 328–38.

67 Blohm GM, Lednicky JA, White SK, et al. Madariaga virus: identification of a lineage III strain in a Venezuelan child with acute undifferentiated febrile illness, in the setting of a possible equine epizootic. *Clin Infect Dis* 2018; **67:** 619–21.

68 Rodriguez-Morales AJ, Culquichicón C. The need for enhancing the message: screening for Zika, STORCH, and other agents and co-infections should be considered and assessed. *Am J Reprod Immunol* 2017; **78:** e12688.

69 Navarro JC, Medina G, Vasquez C et al. Postepizootic persistence of Venezuelan equine encephalitis virus, Venezuela. *Emerg Infect Dis* 2005; **11:** 1907–15.

70 Franco L, Pagan I, Serre Del Cor N, et al. Molecular epidemiology suggests Venezuela as the origin of the dengue outbreak in Madeira, Portugal in 2012–2013. *Clin Microbiol Infect* 2015; **21:** 713.e5–8.

71 Griffing SM, Villegas L, Udhayakumar V. Malaria control and elimination, Venezuela, 1800s–1970s. *Emerg Infect Dis* 2014; **20:** 1697–704.

72 Convit J, Schuler H, Borges R et al. Interruption of *Onchocerca volvulus* transmission in northern Venezuela. *Parasit Vectors* 2013; **6:** 289.

73 Botto C, Basañez MG, Escalona M et al. Evidence of suppression of onchocerciasis transmission in the Venezuelan Amazonian focus. *Parasit Vectors* 2016 27; **9:** 40.

74 Paniz-Mondolfi A, Tami A, Grillet ME, et al. Resurgence of vaccine-preventable diseases in Venezuela as a regional public health threat in the Americas. *Emerg Infect Dis* 2019; published online Jan 6. DOI:10.3201/eid2504.181305 (preprint).

75 Krisher LK, Krisher J, Mariano Ambulidu, et al. Successful malaria elimination in the Ecuador–Peru border region: epidemiology and lessons learned. *Malar J* 2016; **15:** 573.

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