MAJOR ARTICLE

Poverty and Arbovirus Outbreaks: When Chikungunya Virus Hits More Precarious Populations Than Dengue Virus in French Guiana

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Background. Since 2013, 3 successive arbovirus outbreaks, dengue (DENV), chikungunya (CHIKV), and Zika virus, have occurred in French Guiana (FG). The primary objective of this study was to describe the socioeconomic indicators of the first patients infected with CHIKV during the outbreak of 2014. The secondary objective was to compare those patients with patient infected by DENV and with the local population.

Methods. A monocentric, retrospective, case-control study was conducted in Cayenne hospital in FG comparing a group of patients infected with CHIKV in 2014 with a group infected with DENV in 2013. Children aged less than 15 years and pregnant women were excluded.

Results. A total of 168 CHIKV patients were compared with 168 DENV patients. Factors associated with CHIKV were living in poor neighborhoods (82% vs 44%; odds ratio [OR], 5.81; 95% confidence interval [CI], 3.35–10.2), having a precarious status (54% vs 33%; OR, 2.37; 95% CI, 1.49–3.78), and being born abroad (70% vs 35%; OR, 4.35; 95% CI, 2.69–7.06).

Conclusions. The present results suggest that early in the epidemic, the populations most at risk for CHIKV infection were the most socially vulnerable populations in the poorest neighborhoods, whereas DENV appeared to have affected a richer population and richer areas.

Keywords. chikungunya; dengue; French Guiana; poverty; precarity.

Chikungunya (CHIKV) is an arthropod-borne virus, transmitted by a mosquito of the genus *Aedes*, mainly *Aedes aegypti* and *Aedes albopictus*. Although, the first cases were described in the early 1950s, and regular outbreaks occur in Africa and South-East Asia, this arbovirus was hardly known before the massive epidemics in the Indian Ocean in 2005–2006, especially on La Reunion Island. There, one third of the population was affected, according to a seroprevalence study, and new acute and chronic clinical presentations were reported [1]. Until late 2013, no autochthonous case had been reported for more than 200 years in the Americas [2]. In December 2013, the first cases were identified in St. Martin, then in St. Barthelemy, 2 French islands in the Caribbean. The infection then spread to the rest of the West Indies and Latin America. The first cases in Latin America were described in French Guiana (FG),

a French overseas region located on the coast between Suriname and northern Brazil, in February 2017. There, the outbreak of CHIKV followed that of dengue virus (DENV) in 2013. The 4 serotypes of DENV circulate in FG in endemic-epidemic form. In the past 10 years, there has been an increase in the number of DENV outbreaks and hospitalized cases [3, 4]. Thus far, *A aegypti* mosquitoes have been the sole vector implicated in these outbreaks, and *A albopictus* have not been actually reported in FG [5].

At the beginning of the CHIKV outbreak, from April to June 2014, most of the cases were diagnosed in the Cayenne area, where approximately half of its 237 000 inhabitants lives. Attending physicians reported that the patients who sought treatment for CHIKV infection seemed to be in a more precarious situation than other patients. In fact, although the gross domestic product (GDP) is half that of mainland France, it is the highest GDP per capita in Latin America [6, 7] and thus attracts numerous immigrants in search of socioeconomic improvement, health, or education.

The hypothesis of this study is that CHIKV patients are more socially vulnerable than patients with DENV and the rest of the population. The primary objective of the study was to describe the demographic, social, and economic indicators of the first patients infected with CHIKV during the outbreak of 2014. The secondary objective was to compare them with the population with DENV and with local population.

MATERIAL AND METHODS

A monocentric, retrospective, case-control study was conducted in Cayenne hospital, the main city and the main hospital in FG.

Inclusion of Patients With Chikungunya Virus Infection

All consecutive patients who sought treatment at the hospital for CHIKV between April 1 and June 30, 2014, at the beginning of the outbreak, constituted the case group. A case of CHIKV infection was defined as a clinical presentation suggestive of arboviral infection and a microbiological confirmation of acute infection by CHIKV by reverse-transcription polymerase chain reaction (RT-PCR). All patients received a medical consultation at the hospital with an initial standard infectious biological assessment including CHIKV RT-PCR, DENV diagnostic test (NS1 antigen and immunoglobulin [Ig]M), thin and thick blood smear for malaria, and standard blood tests at the discretion of the physician. All biological tests were performed at the hospital laboratory.

Inclusion of Patients With Dengue Fever

A retrospective collection was carried out in a second step to create a control group of first patients with acute DENV infection. We exhaustively collected all of the patients with a compatible clinical picture of arbovirus infection and a positive NS1 antigen test, which is the routine diagnostic test, and not PCR, realized at the Cayenne hospital laboratory, from March to August 2013 during a DENV outbreak (mainly DENV-2). After exclusion, we selected the first patients who sought treatment in hospital until we had 1 control for each case.

Comparison With Global Population Characteristics

To study the demographic characteristics of the study population, such as the birth place, we compared it with the general population data obtained from the open access data of the National Institute for Statistics and Economic Studies (Insee).

Exclusion Criteria

The exclusion criteria were patients under 15 years and 3 months of age, ongoing pregnancy, and/or the absence of medical records. Children and pregnant women were monitored in the departments of pediatrics and gynecology-obstetrics, respectively, and thus did not allow standardized data collection.

Data Collection

We collected data for the following variables: sex, age, country of birth, health insurance status, and place of residence. Nationality, residency status, and duration of residence were not collected.

Country of Birth: Migration Status

A binary migration status was defined on the basis of the country of birth: French-born and Foreign-born. The term "French born" included patients born in FG, French West Indies, or mainland France. The terms Guianese and mainland referred to patients born in FG and born in continental France, respectively. We used nationality for the general population because data about country of birth were not available.

Health Insurance Status: Population in Precarious Social Situation

For health insurance status, we distinguished between patients in a precarious social situation and those who were not [8]. Patients without any health insurance, those benefitting from "Free universal health care" or "CMU" (which allows access to health for person who have resided legally in France for more than 3 months and who are not already covered [9]), or those benefitting from "State medical aid" or "AME" (government run insurance program specifically conceived for undocumented migrants who become eligible after 3 months of residency in a French territory [10]) were considered to be in a precarious social situation. Persons with regular social security and complementary health insurance and/or persons with "Long term illness" or "ALD" (for patients requiring prolonged treatment, reimbursing 100% of expenses related to the specific health problem [11]) were considered as not precarious.

Place of Residence: Socioeconomic Level of the Districts

A precarity score was applied to each "population group for statistical information" (IRIS), a standard geographical division unit used in French official demographic surveys. This score was previously built to determine priority areas and adjust public policy [12]. The score was computed using 7 indicators: substandard housing, overcrowded housing, unemployment rate, rate of inactive persons in the working age population, proportion of young people who dropout of school, proportion of lone-parent families, and proportion of nongraduates in the working-age population [13]. We used the previous score to define 4 categories of districts (using median and quartiles): low socioeconomic level, lower middle, upper middle, and higher levels. The score was then applied only to the capital territory and its surrounding areas: Cayenne, Rémire-Montjoly and Matoury. To understanding of the discussion, we regrouped low and lower middle socioeconomic level in poor neighborhoods and upper middle and higher level in rich neighborhoods.

Statistical Methods

The data were collected from computerized medical records: the emergency medical record (DMUnet) or the global medical record (Cora). The epidemiological characteristics of the 2 groups were compared using a χ^2 test for qualitative variables, a Student test for the normally distributed quantitative variables, or a nonparametric Mann-Whitney U test for the other continuous variables. Differences were considered significant if the P value was <.05. An analyses were performed with Stata software, version 12.0. A map was developed with MapInfo 12.0 software, to illustrate the distribution between districts and their socioeconomic level.

Ethics

The present study was monocentric and consisted of anonymized patient records (the database did not include names or any variable that could allow the precise identification of patients) as authorized by the French regulatory authorities. The database was

declared to the Commission National Informatique et des Libertés (CNIL N°TFN1490159N) following French legal requirements.

RESULTS

A total of 671 (181 CHIKV and 490 DENV) patients were eligible for the study. After applying the exclusion criteria, we included 168 patients in the CHIKV group. Therefore, 168 patients were selected in the DENV group (Figure 1). There were no CHIKV-DENV coinfections identified during the 2 epidemics.

Among these 2 groups, sex ratio was not significantly different, but the CHIKV population was older, with 67 patients (39.9%) over 50 years old versus 35 (20.8%) in the DENV group (Table 1). The proportion of foreign-born patients with CHIKV was twice that of the general population of FG (Table 2). On the contrary, the DENV group was not different from the general population (34.5% vs 34.9%; odds ratio [OR], 0.98; 95% confidence interval [CI], 0.71–1.35). Foreign patients were mainly from Haiti (64.9%) and Brazil (19.7%) in the CHIKV group. In the latter group, there was an overrepresentation of patients from Haiti compared with the global structure of the foreign population in FG (64.9% vs 25.1%; OR, 5.54; 95% CI, 3.79–8.1) and an underrepresentation of citizens from Suriname, Guyana, and Venezuela (5.6% vs 43%; OR, 0.14; 95% CI, 0.07–0.26). Sex or age were not significantly associated with the country of birth.

Among the 336 patients included in the study, 15 CHIKV patients and 8 DENV patients who lived on Cayenne Island, and 3 CHIKV and 4 DENV patients, respectively, for whom addresses could not be collected, were not represented on the map. Thus, we compared 150 CHIKV patients with 156 DENV patients. According to the score of precarity, 73.2% of patients in the CHIKV group were living in a low or lower middle socioeconomic area versus 59.2% in the global population of Cayenne and 41.1% in the DENV population (Table 1). The CHIKV epidemic began at Mount Baduel and spread to the nearest poor neighborhoods: Bonhomme, Mango, Thémire, Cabassou, and Mont Lucas. The opposite was observed during the DENV epidemic, which immediately spread throughout the island of Cayenne, targeting the richer neighborhoods in particular: Rémire, Montabo, and Montjoly (Figure 2). In the DENV group, people living in the poorest area were younger than in the richer area (mean, 31.0 vs 39.6 years old; $P < .001$), and no difference was reported in the CHIKV group (mean, 45.1 vs 45.5 years old; $P = .92$). Similarly, there were more women than men in the poorest area of DENV (56.5% vs 39.8%; OR, 0.51; 95% CI, 0.27–0.96; $P = .037$).

Concerning social status, at the beginning of the outbreak, 53.6% of patients who sought treatment for CHIKV were in a precarious social situation compared with 32.7% of DENV patients (Table 3). The health insurance coverage most significantly associated with CHIKV was "free universal health care", whereas having complementary health insurance was associated with DENV. In the DENV group, people in precarious social situations were younger (mean, 29.7 vs 38.2 years old; $P < .001$), and no difference was reported in the CHIKV group (mean, 43.7 vs 47.2 years old; $P = .20$). Sex ratios were not different between all groups. The variables significantly associated with CHIKV were as follows: being born abroad, having a precarious social situation, and living in a poor neighborhood.

DISCUSSION

Poverty and Neglected Tropical Diseases

Several studies have demonstrated connections between poverty and neglected tropical diseases (NTDs) [14–16]. In 2010, the World Health Organization emphasized the importance of poverty in the development of NTDs, including dengue, and included poverty reduction in the Millennium Development Goals (MDGs) [17]. Several studies have shown that poverty may be a risk factor for infection with CHIKV or DENV [18–20], but Mulligan et al [21] emphasize that literature investigating the arbovirus-poverty link is too scarce and methodologically is inadequate to support a definitive relationship. To this day, no
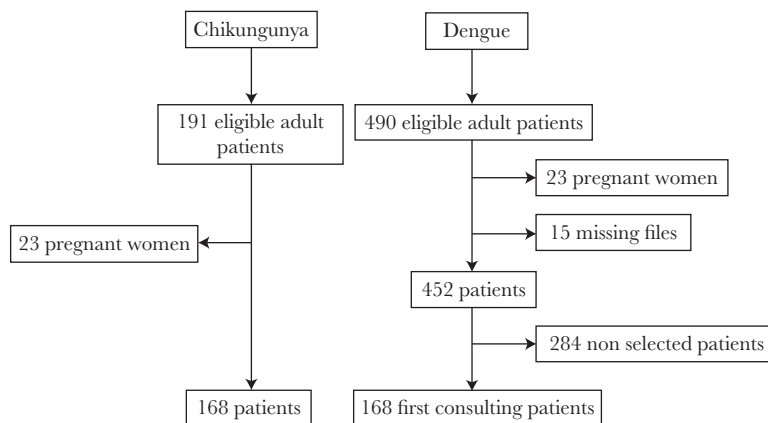

Figure 1. Flow diagram of the study.

Table 1. Univariate Analysis of the Demographic and Socioeconomic Data of CHIKV and DENV Patients

	CHIKV[a] n = 168 (%)	DENV[a] n = 168(%)	OR	95% CI	P
Born abroad[b]	117 (69.6)	58 (34.5)	4.35	2.69–7.06	<.001
No health insurance	25 (14.9)	14 (8.3)	1.92	0.92–4.16	.06
Precarious social status[c]	90 (53.6)	55 (32.7)	2.37	1.49–3.78	<.001
Poor neighborhoods[d]	123 (82.0)	69 (44.0)	5.81	3.35–10.2	<.001
Man	77 (45.8)	91 (54.2)	0.72	0.46–1.12	.13
Age (mean ± SD)	43.8 (±17.8)	35.4 (±15.5)			<.001
| Age >50 years old	67 (39.9)	35 (20.8)	2.52	1.51–4.22	<.001
| Age <18 years old	6 (3.6)	22 (13.1)	0.25	0.08–0.65	.002

Abbreviations: CHIKV, chikungunya virus; CI, confidence interval; DENV, dengue virus; OR, odds ratio; SD, standard deviation.

[a]Infection by chikungunya or dengue viruses.

[b]People who are not born in France are considered as born abroad.

[c]Patients without any health insurance, those benefitting from "Free universal health care" (CMU), or those benefitting from "State medical aid" (AME).

[d]All districts with low or lower middle socioeconomic level depending of a precarity score.

study ever compared precarity in CHIKV and DENV. As initially suspected, in the present study, social aspects of CHIKV patients differed from DENV patients.

Beyond Poverty: The Concept of Precarity

"NTDs are often referred to as diseases of poverty, but implicit in the use of the term poverty is the tight inter-relationship of poverty and inequality" [15]. Utilization of the word poverty is too simplistic to describe all interactions implicated between social status and disease development, and this is why precarity is an increasingly used term. It is a modern term to define social vulnerability, in particular employment vulnerability [22–24]. Indeed, precarity has entered English language only relatively recently, in contrast to a much longer lineage of usage in continental Europe [22]. More specifically, it can be described by 6 variables: employment, income, housing, social relations, health coverage, and residency status [25]. Presently, it is impossible to precisely know these variables in FG at the individual level.

Therefore, the aggregated precarity score was a geographical proxy to estimate the individual reality. In 2011, 87 000 persons lived in poverty in FG, a rate of 44.3% (compared with 14.3% in mainland France and approximately 19.4% in Guadeloupe and 21.1% in Martinique). Over the 2001–2011 period, the household poverty rate increased by 9.7% in FG [26]. Although the health system is quite accessible, there are marked social inequalities that affect the determinants of health and the distribution of diseases among the population of FG.

Chikungunya Virus Was Associated With Poorest Areas Compared With Dengue Virus

The present results suggest that early in the epidemic, the populations most at risk for CHIKV infection were the most socially vulnerable populations in the poorest neighborhoods; however, in 2013, DENV appeared to have affected a richer population and richer areas than CHIKV, but also than the general population. The main explanation for the relationship between

Table 2. Comparison of the Distribution of Countries of Birth in the Population of the DENV and CHIKV Groups to That of the General Population of Guyana (Insee 2011)

Countries of Birth		CHIKV[a] n (%)		DENV[a] n (%)		Population of French Guiana[b] n (%)	
Born in France	French West Indies	8 (5)	51 (30)	5 (3)	110 (66)		154 562 (65)
	French Guiana	39 (23)		51 (31)			
	Mainland France	4 (2)		54 (32)			
Born abroad[c]	Brazil	23 (14)	117 (70)	22 (13)	58 (34)	20 254 (8)	82 987 (35)
	Guyana/Suriname/Venezuela	11 (7)		8 (5)		35 723 (15)	
	Haiti	76 (45)		2 (1)		20 813 (9)	
	Other Latin America	5 (3)		9 (5)		2 839 (1)	
	Other out of Latin America	2 (1)		17 (10)		3 358 (2)	
Total		168		168		237 549	

Abbreviations: CHIKV, chikungunya virus; DENV, dengue virus.

[a]Infection by CHIKV or DENV.

[b]According to Insee 2011. We used nationality; however, data about country of birth was not available.

[c]People who are not born in France are considered as born abroad.
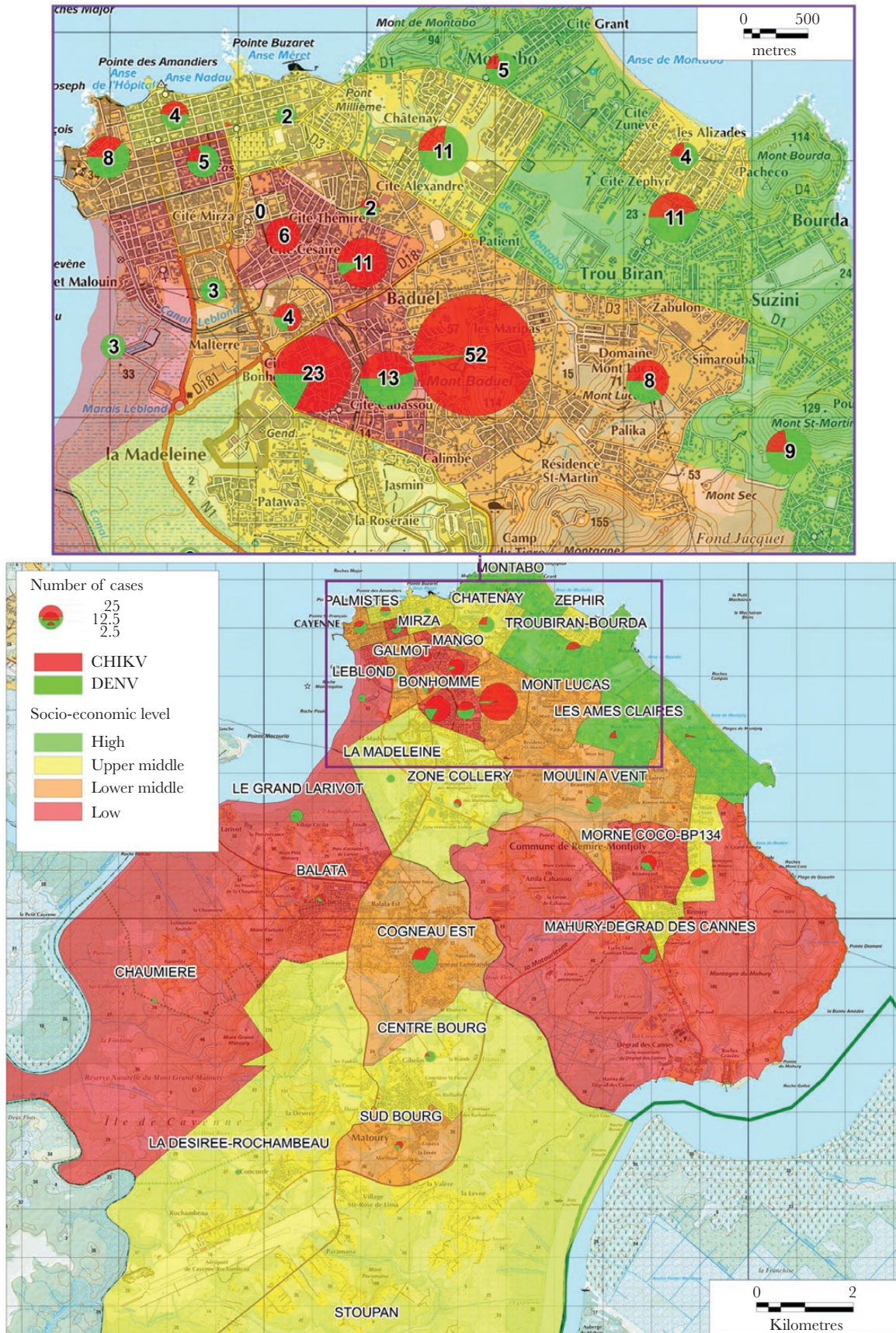
Figure 2. Map of the island of Cayenne showing the distribution of the first 168 cases of chikungunya virus (CHIKV) and dengue virus (DENV) according to the socioeconomic level of the districts.

Table 3. Univariate Analysis of the Social Coverage of Patients in the CHIKV and DENV Groups

Health Insurance Status		CHIKV n = 168 (%)		DENV n = 168 (%)		OR (95% CI)	P
Precarious Social Status[a]	None	25 (14.9)	90 (54)	14 (8.3)	55 (33)	1.92 (0.92–4.16)	.06
	AME	11 (6.6)		6 (3.6)		1.89 (0.62–6.37)	.21
	CMU	54 (32.1)		35 (20.8)		1.8 (1.07–3.05)	.02
No Precarious Social Status[b]	Social security only	46 (27.4)	78 (46)	18 (10.7)	113 (67)	3.14 (1.68–6.04)	.001
	ALD	10 (6.0)		7 (4.2)		1.46 (0.49–4.62)	.45
	Complementary health insurance	22 (13.1)		88 (52.4)		0.14 (0.08–0.24)	<.001

Abbreviations: CHIKV, chikungunya virus; CI, confidence interval; DENV, dengue virus; OR, odds ratio.

[a]Precarious social status included those without any health insurance, those benefitting from "Free universal health care" (CMU), or those benefitting from "State medical aid" (AME).

[b]No precarious status were those with regular social security and complementary health insurance (mutual) and/or persons with "Long term illness" (ALD).

vectorborne disease and poverty is environmental because vector breeding places are more prevalent in the poorest neighborhoods. *Aedes aegypti*, an urban mosquito, preferentially breeds around human dwellings, in outdoor water storage containers, flower pots, and in any recipient containing stagnant rain water. *Aedes albopictus* has never been reported in FG. These conditions are particularly frequent in the poorest areas, especially illegal neighborhoods where organization of waste collection fails or running water is not systematically available [27]. Thus, the emergence of *A aegypti*-transmitted viruses is known to be linked to unplanned urbanization [28]. Several studies confirmed these results but did not compare different arboviruses to determine whether it applies across all agents [18–20, 29]. Counterintuitively, CHIKV and DENV, transmitted by the same vector, did not follow the same geographical distribution in Cayenne. There may be several explanations for this result. First, the CHIKV outbreak followed that of DENV very closely, and richer districts may have had a better vector control that was more difficult to establish in the poorest neighborhoods. It is noteworthy that municipal elections took place in the middle of the CHIKV epidemic, and thus being proactive in rich neighborhoods inhabited by potential voters may have led to prioritize vector control efforts in the more "politically interesting" areas. Altered mosquito control measures were also questioned. One difference for vector control between both epidemics was the use of deltamethrin in 2013 during DENV outbreak and malathion in 2014 during CHIKV outbreak. Another possibility is that there were some foci of CHIKV occurring in illegally built neighborhoods, and the antivectorial teams may have had greater difficulties in reaching those areas. Second, differences in herd immunity must be considered. Thus, in poor neighborhoods, most persons originate from FG or other endemic areas, vector proliferation is a problem, and infections by different DENVs could lead to a higher degree of herd immunity. In contrast, in richer neighborhoods, persons are more likely to have recently arrived from nonendemic areas, predominantly mainland France (a great proportion of the administrative workforce comes for a period

of a few years), hence herd immunity is more likely to be low, and thus epidemics may spread despite better vector control. It is possible that when DENV first surfaced in FG in the past, the poorest areas were the areas where DENV was most active, and successive epidemics may have change ecological dynamism. Unfortunately, we were not able to evaluate the prior dengue exposure because of the following: (1) anti-DENV IgG was not performed in our study; and (2) patients were asked questions regarding previous DENV infections, but anamnesis alone is not very reliable because of potential differential diagnoses. Another factor probably affected dynamism of DENV infection. Thus, some studies describe different levels of infection at various key locations of the city related to the diurnal activity of *A aegypti* and local patterns of human activities [29–31]. Socioeconomic differences in human populations' movements may also affect DENV and CHIKV epidemiological dynamics and guide strategic vector management efforts.

Study Limitations

The selected populations have particularities that can help data interpretation. Because all persons were living on the coastal area, the study patients were not exposed to malaria, and, at the time of the study, Zika virus was not yet circulating in America, which reduces the number of differential diagnoses. Studies are in progress to compare DENV and leptospirosis infection. In addition, yellow fever vaccination is required in FG, and the impact of the immunization against yellow fever, which is a flavivirus, on the occurrence and incidence of arbovirus infections may be different among genuses because DENV belongs to the flavivirus genus and CHIKV belongs to the alphavirus genus. There are potential biases to the study and interpretations. As a retrospective collection, missing data are person-dependent. Our study was hospital based, but because of the lack of private practitioners and unique access to emergency, the study population seemed representative of the general population of Cayenne. There may have been an immunization bias: some studies found that detection rate is higher in acute primary than in acute secondary infections with a NS1 diagnostic and may have selected a less immune DENV population

[32, 33]. No DENV coinfection was reported during the CHIKV outbreak, and most coinfections described in the literature are serology-based studies. The circulation of DENV was low during this period, and only few cases were reported, and even fewer viruses were isolated [34]. In addition, poverty, precarity, or vulnerability are terms to describe the socioeconomic status of people but are difficult to standardize. Several scales exist, such as the "EPICES score" [25], but they are not usable everywhere. To remedy this, studies used several variables to describe standards of living and to characterize populations, for example, education, income, presence of house walls, wall gaps, or water sources [20, 27]. Although these variables are explicit, the absence of standardization may lead researchers to generalize a lot of different social situations by using the term poverty.

A Neglected Population at Risk for Arboviruses

At the beginning of outbreaks in FG, CHIKV targeted people born abroad with precarious social status and those living in poor neighborhoods. These observations are not trivial and may reflect the specific living conditions in FG and its particular social inequalities [35]. Naturally, these results should not be interpreted as blaming the poor or foreign populations, and the findings point more towards the sobering reality of health inequalities and the notion of neglected populations. Recently, other publications in FG pointed out the existence of neglected populations, eg, the illegal gold miners, who live in poor sanitary conditions and are at risk for various infectious and noninfectious diseases such as malaria, leptospirosis, leishmaniasis, helmenthiasis, ankylostomiasis, or thiamine deficiency [36–40]. In FG, precarity seemed to be a risk factor for CHIKV and, to a lesser degree, DENV infection. Several reasons were suggested for these findings, and policy and decision makers should pay closer attention to more specific risk factors, including those faced by nonpoor communities, in combating this rapidly spreading disease [21].

CONCLUSIONS

Despite France's broad social benefits, social inequalities still remain a major determinant of poor health outcomes, for chronic, occupational, and infectious diseases of various transmission mechanisms [41]. To reduce health inequalities, in addition to improving access to care and access to rights, health promotion should be extended to environments where the poorest populations live. Coordinated efforts are required to improve sanitation, access to water and electricity, garbage collection, and wastewater treatment, particularly in illegal neighborhoods. This should be a priority even if these populations are often not electors of the local officials in charge of the infrastructure and services that ensure tropical hygiene.

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