

The Epidemiology and Transmissibility of Zika Virus in Girardot and San Andres Island, Colombia

Diana Patricia Rojas MD^a, Natalie E. Dean PhD^{*b}, Yang Yang PhD^{*b}, Eben Kenah PhD^b, Juliana Quintero MD^c, Simon Tomasi^c, Erika L. Ramirez^d, Yendi Kelly^e, Carolina Castro^f, Gabriel Carrasquilla DrPH^c, M. Elizabeth Halloran DSc^{g,h}, Ira M. Longini, Jr PhD^b

^a*Department of Epidemiology, University of Florida, Gainesville, FL, USA*

^b*Department of Biostatistics, University of Florida, Gainesville, FL, USA*

^c*Centro de Estudios e Investigación en Salud, Fundación Santa Fé de Bogotá, Bogotá, Colombia*

^d*Secretaria Municipal de Salud, Girardot, Colombia*

^e*IPS Universitaria, San Andrés, Colombia*

^f*Secretaria Departamental de Salud, San Andrés, Colombia*

^g*Department of Biostatistics, University of Washington, Seattle, WA, USA*

^h*Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA*

Abstract

Background:

Zika virus (ZIKV) is an arbovirus in the same genus as dengue virus and yellow fever virus. ZIKV transmission was first detected in Colombia in September 2015. The virus has spread rapidly across the country in areas infested with the vector *Aedes aegypti*. As of March 2016, Colombia has reported over 50,000 cases of Zika virus disease (ZVD).

Methods:

We analyzed surveillance data of ZVD cases reported to the local health authorities of San Andres, Colombia, and Girardot, Colombia, between September 2015 and January 2016. Standardized case definitions used in both areas were determined by the Ministry of Health and Colombian National Institute of Health at the beginning of the ZIKV epidemic. ZVD was laboratory-confirmed by a finding of Zika virus RNA in the serum of acute cases. We

*These authors contributed equally.

report epidemiological summaries of the two outbreaks. We also use daily incidence data to estimate the basic reproductive number R_0 in each population.

Findings:

We identified 928 and 1,936 laboratory or clinically confirmed cases in San Andres and Girardot, respectively. The overall attack rate for reported ZVD detected by healthcare local surveillance was 12.13 cases per 1,000 residents of San Andres and 18.43 cases per 1,000 residents of Girardot. Attack rates were significantly higher in females in both municipalities. Cases occurred in all age groups but the most affected group was 20 to 49 year olds. The estimated R_0 for the Zika outbreak in San Andres was 1.41 (95% CI 1.15 to 1.74), and in Girardot was 4.61 (95% CI 4.11 to 5.16).

Interpretation:

Transmission of ZIKV is ongoing and spreading throughout the Americas rapidly. The observed rapid spread is supported by the relatively high basic reproductive numbers calculated from these two outbreaks in Colombia.

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Keywords: Zika virus, outbreak, epidemiology, Basic reproductive number

Research in Context

Evidence before this study

The ongoing outbreak of Zika virus disease in the Americas is the largest ever recorded. Since its first detection in April 2015 in Brazil, around 500,000 cases have been estimated, and the virus is spreading rapidly in the Americas region. There are many unanswered questions about the transmissibility and pathogenicity of the virus. Limited data are available from recent outbreaks occurring in islands in the Pacific, and little epidemiological data is available on the current outbreak.

We searched PubMed on March 12, 2016, for epidemiological reports on Zika virus outbreaks using the search terms “Zika” AND “Basic reproductive number”. We applied no date or language restrictions. Our search identified one previous paper assessing the basic reproductive number, R_0 of Zika virus in Yap Island, Federal State of Micronesia and in French Polynesia, but no papers estimating R_0 using data from the Latin American Zika outbreak. Because of the sparsity of the data, we could not do a detailed systematic review at this point in time.

Added value of this study

We report detailed epidemiological data on outbreaks in San Andres and Girardot, Colombia. Because such reports are currently unavailable, we provide early information on age and gender effects and the functioning of local and national surveillance in the second-most affected country in this epidemic. We provide early estimates of R_0 . Our results can be used by mathematical modelers to understand the future impact of the disease and potential spread.

Implications of all the available evidence

We report attack rates similar to those reported in the Yap Island outbreak. We find that Zika impacts individuals of all ages, though the most affected age group is 20 to 49 years of age. The surveillance system detected more cases among women in both areas, though this finding may be attributable to reporting bias. Our estimates of R_0 imply that Zika has the capacity for widespread transmission in areas with the vector.

1. Introduction

1 First isolated in the Zika Forest of Uganda in 1947, Zika virus (ZIKV)
 2 is an arbovirus primarily transmitted by *Aedes aegypti* mosquitoes [1]. Al-
 3 though ZIKV has circulated in Africa and Asia since the 1950s, little is known
 4 about its transmission dynamics [2]. Recent outbreaks in Yap Island in the
 5 Federated States of Micronesia (2007), French Polynesia (2013), and other
 6 Pacific islands, including Cook Islands, Easter Island, and New Caledonia
 7 (2014), indicate that ZIKV has spread beyond its former geographic range
 8 [3, 4, 5, 6]. In April 2015 ZIKV was isolated in the Northeast of Brazil [7].
 9 As of March 11, 2016, around 500,000 Zika virus disease (ZVD) cases have
 10 been estimated in Brazil, and autochthonous circulation has been observed

in 31 countries in the Americas region. Further spread to countries within the geographical range of *Ae. aegypti* mosquitoes is considered likely [8].

ZIKV is a flavivirus in the same genus as dengue virus and yellow fever virus. Infection typically causes a self-limited dengue-like illness characterized by exanthema, low-grade fever, conjunctivitis, and arthralgia [9]. While illness is believed to be mild or asymptomatic in approximately 80% of the infections [10], an increase in rates of Guillain-Barré syndrome (GBS) has been observed during ZIKV outbreaks [8, 11, 12]. Furthermore, in October 2015, the Brazilian Ministry of Health reported a dramatic increase in cases of microcephaly in Northeast Brazil where ZIKV had been circulating [13]. On the basis of the possible link between ZIKV, GBS and microcephaly, the World Health Organization declared a public health emergency on February 1, 2016 [14].

The virus was first detected in Colombia in mid-September 2015 in a municipality called Turbaco on the Caribbean coast. Turbaco is located approximately 20 minutes from Cartagena, a well known commercial and tourist hub (Figure 1). In October 2015, ZIKV spread through the central region of the country, appearing in areas with endemic dengue and ongoing circulation of chikungunya (CHIKV) since 2014. Through March 2016, Colombia has reported over 50,000 cases of ZVD, making it the second-most affected country in this outbreak, after Brazil. There were 2,090 laboratory-confirmed cases with the rest being suspected cases or confirmed by clinical findings [15]. Up to March 2016, 280 cases of neurological complications including Guillain-Barré syndrome (GBS) and three deaths possibly associated with ZVD have been reported in Colombia [16]. As of March 2016, there have been several suspected but no confirmed cases of ZIKV-associated microcephaly in Colombia [15].

In this paper we describe local ZIKV outbreaks in Girardot and San Andres Island between September 2015 and January 2016 for which detailed epidemiological data are available. We conduct an investigation to define the epidemiological features of these outbreaks and to estimate corresponding transmission parameters.

2. Methods

San Andres

San Andres is the largest island in a Colombian archipelago in the Caribbean sea located about 750 km north of mainland Colombia and 230 km east of

45 Nicaragua (Figure 1). The island has an area of 27 km², a population of
 46 54,513 inhabitants across 13,652 households, and a population density of
 47 2,932 habitants per km² in 2010 [17, 18]. The average temperature is 27.3°C,
 48 and 80% of the total annual rainfall of 1,700 mm occurs during the heavy
 49 rainy season between October and December. The weather is humid subtrop-
 50 ical with occasional tropical cyclones and hurricanes. The population in San
 51 Andres has two main ethnic groups: Afro-Colombians (17.5%) and Raizal (an
 52 ethnic group of mixed Afro-Caribbean and British descent) (39.2%) [18]. The
 53 most productive breeding sites of *Ae. aegypti* in San Andres are unprotected
 54 water containers located in the households. San Andres has experienced low
 55 dengue transmission since 1983. Since 1995, the frequency of dengue out-
 56 breaks increased to every two to five years with a mean annual incidence
 57 of 43.6 cases per 100,000 inhabitants between 1999 and 2010 [17]. In 2014,
 58 CHIKV began circulating in San Andres, reaching an annual incidence of
 59 365.1 cases per 100,000 inhabitants [19].



Figure 1: Map of Colombia

Girardot

60 The city of Girardot is located 134 km (2 hours drive) from the capi-
61 tal city of Bogota (Figure 1). Girardot has 102,225 inhabitants across ap-
62 proximately 23,000 households based on the most recent census from the
63 National Statistics Department (NSD) [20], though the population triples
64 during weekends and holidays. Girardot is 289 meters above sea level. The
65 average temperature is 33.3°C, and the relative humidity is 66%. The mean
66 annual precipitation is 1,220 mm with a rainy season extending from May
67 through October [21]. The most productive breeding sites of *Ae. aegypti*
68 in Girardot are unprotected private water containers, such as water storage
69 tanks used in the households during the dry and rainy seasons, while public
70 spaces provide more breeding sites during the rainy season [22]. Girardot has
71 experienced hyperendemic transmission of dengue since 1990 with simulta-
72 neous circulation of all four serotypes; the mean annual incidence was 572.2
73 per 100,000 inhabitants between 1999 and 2010 [17]. In late 2014, CHIKV
74 began circulating in Girardot reaching an annual incidence of 394 per 100,000
75 inhabitants in 2014 and 8,416 per 100,000 inhabitants in 2015.

Case definition and laboratory analysis

76 We analyzed surveillance data from nine local health care sites in San
77 Andres and twenty-two local health care sites in Girardot. Standardized
78 case definitions used in both areas were defined by the Ministry of Health
79 (MoH) and Colombian National Institute of Health (C-NIH) at the beginning
80 of the ZIKV epidemic. A suspected ZVD case is defined as a person who
81 lived or traveled in an area below 2,000 meters above sea level who presents
82 with maculopapular exanthema, temperature higher than 37.2°C, and one
83 or more of the following: non-purulent conjunctivitis, arthralgia, myalgia,
84 headache, or malaise. A laboratory confirmed case is a suspected case with
85 a ZIKV positive reverse-transcriptase-polymerase-chain-reaction (RT-PCR)
86 result as determined by the C-NIH virology reference laboratory. A clinically
87 confirmed case is a suspected case that lived or traveled in an area with
88 laboratory confirmed ZIKV circulation prior to onset of symptoms [23].

89 At the start of the outbreak, all suspected cases were reported based
90 on the suspected case definition to the Colombian national surveillance sys-
91 tem. Once laboratory confirmation from C-NIH was performed for cases in
92 Girardot and San Andres, the new suspected ZIKV cases were laboratory
93 confirmed if they fell into the risk groups defined by the C-NIH: newborns,
94 age <1 year, age >65 years, and cases with co-morbidities [23]. After ZIKV

95 circulation was confirmed in the regions, all suspected cases were reclassified
96 as clinically confirmed.

Data collection

97 The data was collected using the C-NIH standard report form for Zika
98 surveillance. The form includes socio-demographic variables. We analyzed
99 a deidentified data set with the following variables: gender, age, pregnancy
100 status, date of symptom onset, date the case visited the health care facility,
101 date the case was reported to the national surveillance system, and case type
102 (suspected, laboratory confirmed, clinically confirmed) [24].

Statistical analysis

103 We calculated overall and age/gender-specific attack rates using popula-
104 tion census data from NSD [20]. Surveillance data were analyzed using R ver-
105 sion 3.2.0 [25]. For descriptive results, categorical variables are presented as
106 proportions and continuous variables by the median and interquartile range
107 (IQR) or range. The impact of age and gender on attack rates was tested
108 using log-linear models for case counts with age category, gender, and an
109 interaction as independent variables with population size as an offset.

110 To estimate the basic reproductive number R_0 in each population, we
111 used maximum likelihood methods to fit a chain-binomial model to daily
112 incidence data [26]. R_0 is the median effective reproductive number during
113 the growth phase of the epidemic, after accounting for early under-reporting.
114 (See Supplementary Online Materials for additional details on the model.)

3. Results

115 In San Andres, we identified 928 reported ZVD cases (Table 1). Of these
116 cases, 52 (5.6%) were laboratory confirmed by RT-PCR on acute phase sam-
117 ples collected within five days of symptom onset, and 876 (94.4%) cases were
118 clinically confirmed.

119 The dates of symptom onset among cases in San Andres ranged from
120 September 6, 2015, to January 30, 2016 (Figure 2). Though the earliest
121 case reported symptom onset on September, 6, 2015, the local health care
122 authorities did not receive laboratory confirmation of ZIKV until October 22,
123 2015. The number of cases peaked in epidemiological week 45 (November 8
124 to 14) and subsided in the last week of December. The median time between
125 symptom onset and visiting a health care facility was 4 days (IQR 1 to 16).

Table 1: Characteristics of reported cases of Zika Virus Disease

Region	San Andres	Girardot
Total number of cases	928	1936
Laboratory confirmed cases	52 (5.6%)	32 (1.7%)
Clinically confirmed cases	876 (94.4%)	1904 (98.3%)
Female	589 (63.5%)	1138 (58.8%)
Median age, years (IQR)	31 (15, 47)	34 (24, 46)
Median time, days, to visit healthcare facility from symptom onset (IQR)	4 (1, 16)	1 (1, 2)

126 79% of cases were reported to the national surveillance system on the same
 127 day they visited the health care facility. The median age of reported ZVD
 128 cases in San Andres was 31 years old (IQR 15 to 47; range 12 days to 82
 129 years). 589 (63.5%) of the reported cases occurred in females. During this
 130 time period 70 dengue cases and 10 CHIKV cases were confirmed in San
 131 Andres.

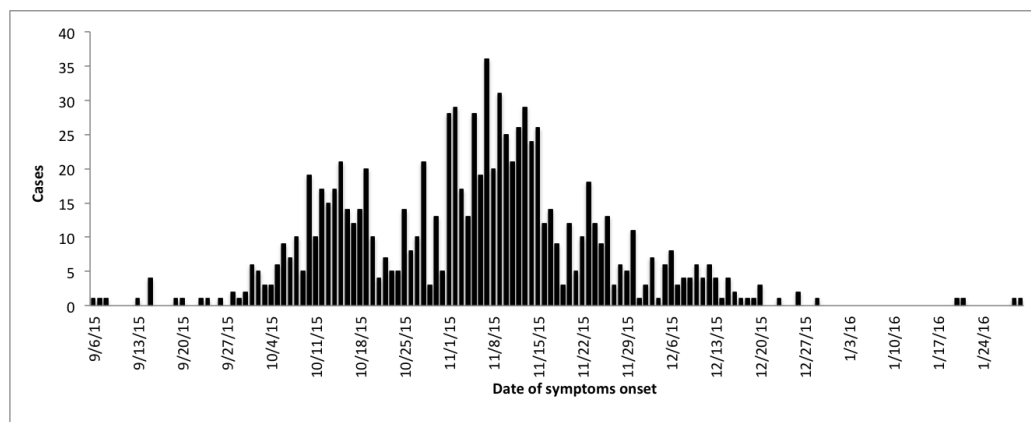


Figure 2: Daily ZVD incidence for San Andres, Colombia

132 The overall attack rate for ZVD reported by local surveillance was 12.13
 133 per 1,000 San Andres residents. The gender-specific attack rates were 15.34
 134 per 1,000 females and 8.91 per 1,000 males; the difference was significant
 135 adjusting for age ($p < 0.001$). Cases occurred among all age groups, but the
 136 incidence of ZVD detected by local surveillance was highest among persons
 137 20 to 49 years old (Figure 3); there was significant heterogeneity across the

age groups ($p < 0.001$). Attack rates were higher in females across all age groups 10 years old and above; there was a significant interaction between age and gender ($p < 0.001$).

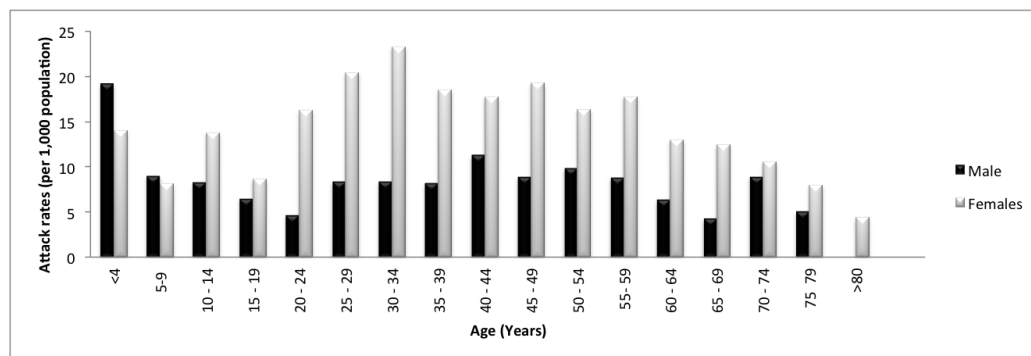


Figure 3: Age- and gender-specific ZVD attack rates for San Andres, Colombia

Thirty two pregnant women with ZVD were reported in San Andres and are being followed according to national guidelines. By March 2016, fourteen of them had given birth with no microcephaly reported. There were eight neurological syndromes reported in San Andres, including GBS and meningoencephalitis attributed to ZIKV and among them one death was reported. The incidence rate of neurological syndromes among ZVD cases in San Andres is 8.6 per 1,000 cases.

Girardot

In Girardot, we identified 1,936 reported ZVD cases (Table 1). Of these cases, 32 (1.7%) were laboratory confirmed by RT-PCR on acute phase samples collected within five days of symptom onset and 1,904 (98.3%) were clinically confirmed. During this time period were confirmed 67 dengue cases and 37 CHIKV cases in Girardot.

The date of symptom onset among cases in Girardot ranged from October 19, 2015, to January 22, 2016 (Figure 4). The first suspected case was reported on October 23, 2015, with laboratory confirmation obtained on January 27, 2016. The number of cases peaked in epidemiological week 48 (November 29 to December 5) and subsided in early January. The median time between symptom onset and visiting a health care facility was 1 day (IQR 1 to 2 days). 89% of cases were reported to the national surveillance system on the same day they visited the health care facility. The median age

161 of confirmed ZVD cases was 34 years old (IQR 24 to 46; range 15 days to 92
162 years). 1138 (58.8%) of the cases occurred in females.

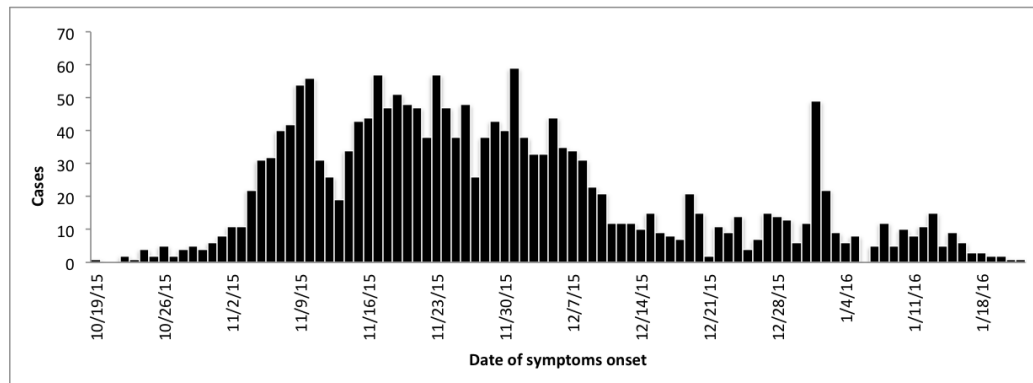


Figure 4: **Daily ZVD incidence for Girardot, Colombia**

163 The overall attack rate for confirmed ZVD detected by local surveillance
164 was 18.43 per 1,000 Girardot residents. The gender-specific attack rates
165 were 20.53 per 1,000 females and 16.07 per 1,000 males; the difference was
166 significant adjusting for age ($p < 0.001$). Cases occurred among all age groups,
167 but the incidence of ZVD detected by local surveillance was highest among
168 persons 20 to 49 years old (Figure 5); there was significant heterogeneity
169 across the age groups ($p < 0.001$). Attack rates were higher in females in all
170 age groups except in those 10 to 14 and 65 to 69 years old; there was no
171 significant interaction between age and gender.

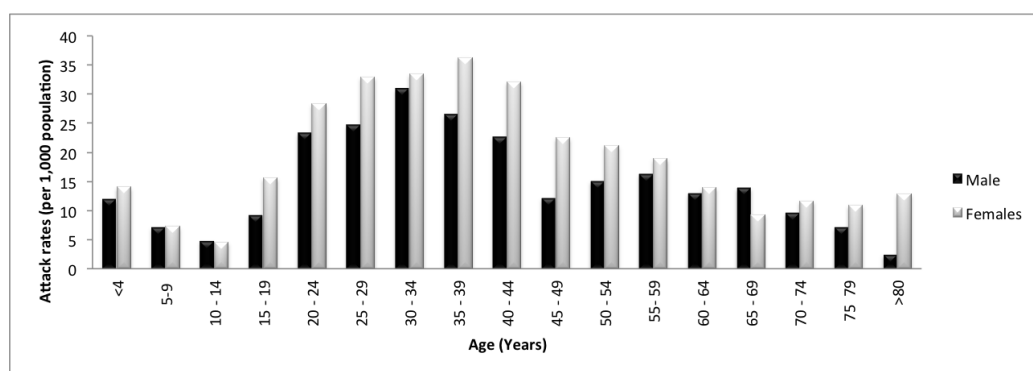


Figure 5: **Age- and gender-specific ZVD attack rates for Girardot, Colombia**

172 Sixteen pregnant women with ZVD were reported in Girardot and are
173 being followed according to national guidelines. By March 2016, seven of
174 them had given birth with no complications or microcephaly reported. Nine
175 cases with GBS have been reported after an initial suspected ZIKV infection;
176 laboratory-confirmation of ZIKV is pending. There were no deaths attributed
177 to ZIKV. The incidence rate of neurological syndromes among ZVD cases in
178 Girardot is 4.6 per 1,000 cases.

Basic reproductive number calculations

179 The basic reproductive number (R_0) was estimated using daily incidence
180 data. The model assumes a mean serial interval (time between successive
181 cases in a chain of transmission) of 22 days, based on a mean incubation
182 period in humans of 5 days, an extrinsic latent period (time from infection
183 to infectiousness within the mosquito) of 10 days, and a mean infectious
184 period in mosquitoes of 10 days. Under-reporting is assumed to be high
185 (only 10% of cases reported) at the start of the outbreak and full reporting
186 is assumed to be achieved in four weeks after the outbreak begins to grow.
187 The estimated R_0 for the Zika outbreak in San Andres was 1.41 (95% CI 1.15
188 to 1.74), and the R_0 in Girardot was 4.61 (95% CI 4.11 to 5.16) (Table 2
189 and Figure 6). Odds ratios for gender and age effects were obtained from the
190 likelihood model, indicating increased odds of transmission among females
191 and adults aged 20 to 49 years old in both San Andres and Girardot (Table 2).

192 The estimation procedure was also applied to daily incidence data from
193 a published outbreak in Salvador, Brazil, that occurred between February
194 15, 2015, and June 25, 2015; 14,835 cases were reported with an overall
195 attack rate of 5.5 cases per 1,000 Salvador residents [7]. The estimated R_0
196 of the Zika outbreak in Salvador, Brazil was 1.42 (95% CI 1.35 to 1.49).
197 Sensitivity analyses are reported in the Supplementary Online Materials,
198 including varying the incubation period in humans, the infectious period in
199 humans, the infectious period in mosquitoes, the duration of under-reporting,
200 and the level of under-reporting at the start of the outbreak.

4. Discussion

201 We report surveillance data on ZIKV outbreaks in two regions in Colom-
202 bia between September 2015 and January 2016. The first region, San Andres,
203 is a small, densely-populated island that is relatively isolated from continen-
204 tal Colombia. The second region, Girardot, is a typical moderately sized

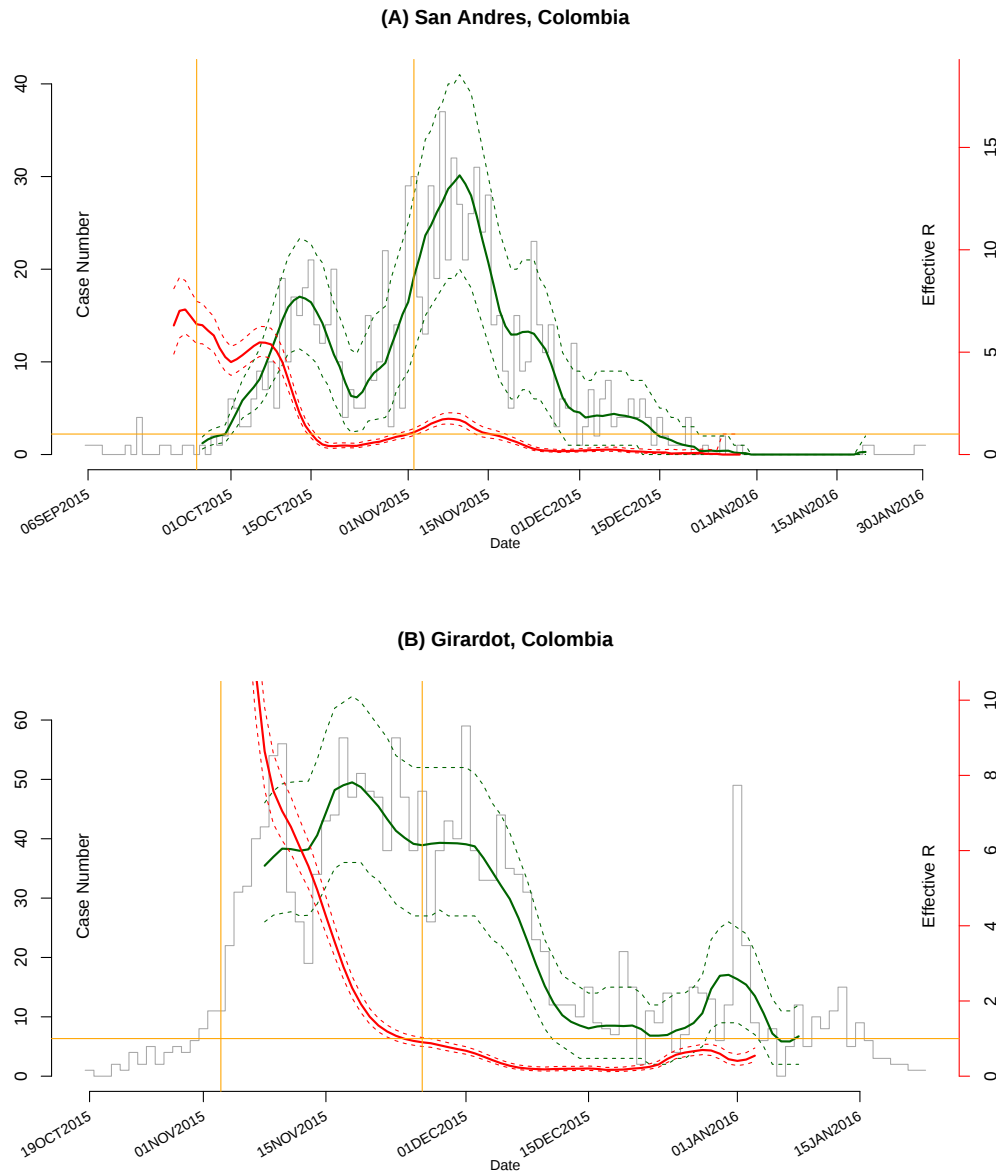


Figure 6: (a) Estimates of effective R (red) and model-fitted daily case numbers (green) for the outbreak of ZVD in San Andres, Colombia. The reporting ratio is assumed to increase linearly from 10% on and before September 30, 2015, to 100% in 4 weeks. Dashed curves (both red and green) are conservative 95% CIs. Histogram in grey shows the epidemic curve. The horizontal orange line indicates the reference value of 1. The two vertical orange lines indicate the time interval used for the estimation of R_0 . (b) As (a) for Girardot, Colombia. The reporting ratio increases on October 19, 2015.

Table 2: Estimates of R_0 , gender-specific odds ratios for transmission, and age-specific odds ratios for transmission for ZVD in San Andres and Girardot, Colombia.

Parameter	Level	San Andres		Girardot	
		Est.	95% CI	Est.	95% CI
R_0		1.41	(1.15, 1.74)	4.61	(4.11, 5.16)
OR_{gender}	Male	-	-	-	-
	Female	1.71	(1.50, 1.95)	1.28	(1.17, 1.40)
OR_{age}	20-49	-	-	-	-
	0-19	0.86	(0.74, 0.99)	0.37	(0.33, 0.42)
	≥ 50	0.74	(0.63, 0.88)	0.46	(0.41, 0.52)

Colombian municipality. Both regions have endemic transmission of dengue and experienced recent outbreaks of CHIKV. We describe key epidemiological features of the Zika outbreaks and estimate the R_0 from daily incidence data.

The overall attack rates for ZVD as detected by local surveillance were 12.13 cases per 1,000 residents of San Andres and 18.43 cases per 1,000 residents of Girardot. These attack rates are similar to those reported from Yap Island (14.3 per 1,000) [3] but higher than those reported in Salvador, Brazil (5.5 per 1,000) [7]. In both areas, significantly higher attack rates are observed among women, especially those of child-bearing age. The Colombian government issued an epidemiological alert on December 2015 to actively search for pregnant women with Zika-like symptoms in areas with active transmission [27, 28]. This effort may partially explain the findings, though differences in gender-specific attack rates persist when only cases occurring prior to December are considered. Cases occurred in all age groups, but the most affected age group was 20 to 49 year of age, similar to previously published outbreaks in Yap Island, Federated States of Micronesia, and in Salvador, Brazil [3, 7]. As the population was fully susceptible to Zika transmission before the outbreaks, it is reasonable that all age groups would be affected.

Forty-eight pregnant women with ZVD were reported from San Andres and Girardot. These women are being followed according to national guidelines [27, 28] with no confirmed cases of microcephaly observed yet. Seventeen neurological syndromes, including GBS and ZIKV-associated meningoencephalitis, were identified, similar to reports from French Polynesia and

230 Brazil [12, 29]. Laboratory-confirmation of these cases is challenging because
 231 neurological symptoms generally appear two weeks after acute symptoms [30]
 232 at which time ZIKV diagnosis by RT-PCR is not possible and serological tests
 233 are unreliable because of cross-reactivity with dengue [31, 32]. As ZIKV can
 234 be detected in urine longer than in blood [33], using urine samples to confirm
 235 ZIKV in GBS cases may be an alternative [34]. These challenges underscore
 236 the need for reliable diagnostic tests that can detect ZIKV after the viremic
 237 period.

238 The basic reproductive number (R_0) was estimated in each area using
 239 daily incidence data. Our estimated R_0 for the Zika outbreak in San Andres
 240 was 1.41 (95% CI 1.15 to 1.74), and the R_0 for Girardot was 4.61 (95%
 241 CI 4.11 to 5.16). Applying the same methods with previously published
 242 data, we estimated that the R_0 for Zika virus in Salvador, Brazil, was 1.42
 243 (95% CI 1.35 to 1.49) [7]. We consider the estimate from San Andres to
 244 be the most reliable because it is a small, densely populated island, while
 245 Girardot has a higher risk of importation because the population fluctuates
 246 during weekends and holidays. The relative magnitudes of R_0 are consistent
 247 with the higher dengue transmission observed in Girardot versus San Andres.
 248 Estimates of R_0 in Zika are not widely available, though reports suggest an
 249 R_0 of 4.3 to 5.8 in Yap Island and R_0 of 1.8 to 2.0 in French Polynesia [35].
 250 A recent manuscript considering the French Polynesian outbreak reported a
 251 range from 1.9 to 3.1 [36].

252 Relatively few cases were laboratory confirmed. The majority of cases
 253 were clinically confirmed, and the symptoms could be caused by other eti-
 254 ologies such as dengue. This report only includes symptomatic cases who
 255 attended a health care facility and were captured by the surveillance sys-
 256 tems. ZIKV usually causes relatively mild illness lasting several days, and
 257 around 80% of infections are currently believed to be asymptomatic, so we
 258 are likely missing many mild or asymptomatic cases [10]. We also do not have
 259 a reliable estimate of under-reporting at these sites. Early under-reporting
 260 appeared to be especially apparent in the Girardot outbreak, and the sharp
 261 increase in cases observed may be due to increased public awareness of the
 262 disease. This phenomenon can result in an overestimate of R_0 .

263 Well-designed studies can provide valuable insight. Phylogenetic anal-
 264 yses of circulating ZIKV strains will be critical for understanding whether
 265 mutations in the viral genome are associated with an increased severity of
 266 disease, as manifested by microcephaly and GBS in this outbreak. House-
 267 hold studies can allow for more accurate estimation of transmission dynamics

268 and enhance understanding of asymptomatic infection. Studies are required
269 to understand the interactions between ZIKV, dengue, CHIKV, and other
270 co-circulating arboviruses and their impact on disease. It is also necessary
271 to increase surveillance of neurological syndromes associated with ZVD, like
272 GBS and encephalitis.

273 The evidence for a causal relationship between ZIKV and microcephaly
274 is strengthening [37, 38, 39]. Recent evidence from the French Polynesia out-
275 break suggests an estimated number of microcephaly cases associated with
276 ZIKV is around one per 100 women infected in the first trimester[40]. Cur-
277 rently the Colombian Government is following a cohort of pregnant women
278 that reported Zika-like symptoms anytime during their pregnancy. Those
279 who are detected during the acute phase are being diagnosed with ZIKV
280 RT-PCR. All women will be followed until the end of pregnancy, and the
281 fetus will be evaluated during pregnancy and post-natally for twelve months.
282 The prospective collection of data through this and other similar national
283 cohorts will be essential for assessing causality, determining risk factors, and
284 estimating rates of birth defects.

285 The results of this and other reports concludes that transmission of ZIKV
286 may be widespread. Vector control has had limited success in controlling
287 other arboviruses, such as dengue. A safe and efficacious vaccine, especially
288 for women of child-bearing age, may be needed to reduce the disease burden.

Declaration of interests

All authors have completed the unified competing interest form. None of the authors declared conflicts of interest.

Role of the funding source

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References

- [1] J. E. Staples, E. J. Dziuban, M. Fischer, J. D. Cragan, Interim guidelines for the evaluation and testing of infants with possible congenital Zika virus infection — United States, 2016, *MMWR Morb Mortal Wkly Rep* 65 (2016) 63–67.
- [2] A. D. Haddow, A. J. Schuh, C. Y. Yasuda, M. R. Kasper, V. Heang, R. Huy, H. Guzman, R. B. Tesh, S. C. Weaver, Genetic characterization of Zika virus strains: Geographic expansion of the Asian lineage, *PLoS Negl Trop Dis* 6 (2012) e1477.
- [3] M. R. Duffy, T.-H. Chen, W. T. Hancock, A. M. Powers, J. L. Kool, R. S. Lanciotti, M. Pretrick, M. Marfel, S. Holzbauer, C. Dubray, L. Guillamot, A. Griggs, M. Bel, A. J. Lambert, J. Laven, O. Kosoy, A. Panella, B. J. Biggerstaff, M. Fischer, E. B. Hayes, Zika virus outbreak on Yap Island, Federated States of Micronesia, *N Engl J Med* 360 (2009) 2536–2543. PMID: 19516034.
- [4] E. B. Hayes, Zika virus outside Africa 15 (2009) 1347.
- [5] S. Ios, H.-P. Mallet, I. L. Goffart, V. Gauthier, T. Cardoso, M. Herida, Current Zika virus epidemiology and recent epidemics, *Medecine et Maladies Infectieuses* 44 (2014) 302 – 307.
- [6] J. Tognarelli, S. Ulloa, E. Villagra, J. Lagos, C. Aguayo, R. Fasce, B. Parra, J. Mora, N. Becerra, N. Lagos, L. Vera, B. Olivares, M. Vilches, J. Fernández, A report on the outbreak of Zika virus on Easter Island, South Pacific, 2014, *Archives of Virology* (2015) 1–4.
- [7] C. W. Cardoso, I. A. Paploski, M. Kikuti, M. S. Rodrigues, M. M. Silva, G. S. Campos, S. I. Sardi, U. Kitron, M. G. Reis, G. S. Ribeiro, Outbreak of exanthematous illness associated with Zika, Chikungunya, and dengue viruses, Salvador, Brazil, *Emerging Infectious Diseases* 21 (2015) 2274–2276.
- [8] Pan-American Health Organization, World Health Organization, Geographic distribution of confirmed cases of Zika virus (locally acquired) in countries and territories of the Americas, 2015-2016, 2016.

- [9] European Centre for Disease Prevention and Control, Rapid risk assessment: Zika virus infection outbreak, French Polynesia, 2016.
- [10] E. E. Petersen, J. E. Staples, D. Meaney-Delman, M. Fischer, S. R. Ellington, W. M. Callaghan, D. J. Jamieson., Interim guidelines for pregnant women during a Zika virus outbreak — United States, 2016, *Morb Mortal Wkly Rep* 65 (2016) 30–33.
- [11] D. Musso, Zika virus transmission from French polynesia to Brazil, *Emerging Infectious Diseases* 21 (2015).
- [12] V.-M. Cao-Lormeau, A. Blake, S. Mons, S. Lastère, C. Roche, J. Vanhomwegen, T. Dub, L. Baudouin, A. Teissier, P. Larre, A.-L. Vial, C. Decam, V. Choumet, S. K. Halstead, H. J. Willison, L. Musset, J.-C. Manuguerra, P. Despres, E. Fournier, H.-P. Mallet, D. Musso, A. Fontanet, J. Neil, F. Ghawché, Guillain-Barre syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study, *The Lancet* (2016).
- [13] L. Schuler-Faccini, E. M. Ribeiro, I. M. Feitosa, D. D. Horovitz, D. P. Cavalcanti, A. Pessoa, M. J. R. Doriqui, J. I. Neri, J. M. de Pina Neto, H. Y. Wanderley, M. Cernach, A. S. El-Husny, M. V. Pone, C. L. Sero, M. T. V. Sanseverino, Possible association between Zika virus infection and microcephaly - Brazil, 2015, *MMWR Morb Mortal Wkly Rep* 65 (2016) 59–62.
- [14] H. Lazear, E. Stringer, A. de Silva, The emerging Zika virus epidemic in the Americas: Research priorities, *JAMA* (2016).
- [15] Instituto Nacional de Salud, Boletín epidemiológico semanal - semana epidemiológica 08 de 2016, 2016.
- [16] Instituto Nacional de Salud, Vigilancia intensificada de síndromes neurológicos, (Guillain-Barre, polineuropatías ascendentes, entre otras afecciones neurológicas similares), en la fase epidémica de la infección por virus Zika en Colombia, 2015 – 2016, 2016.
- [17] J. C. Padilla, D. P. Rojas, R. Saenz-Gomez, Dengue en Colombia: Epidemiología de la reemergencia a la hiperendemia, *Guías de Impresión*, first edition edition, 2012.

- [18] Ministerio de Salud, Analisis de situacion de salud (ASIS) Archipielago de San Andres, 2011.
- [19] D. Salas, Informe final del evento Chikungunya, Colombia 2014, 2014.
- [20] Departamento Administrativo Nacional de Estadística, Estimación y proyección de población Nacional, Departamental y Municipal total por área 1985-2020, 2016.
- [21] T. García-Betancourt, D. R. Higuera-Mendieta, C. González-Uribe, S. Cortés, J. Quintero, Understanding water storage practices of urban residents of an endemic dengue area in Colombia: Perceptions, rationale and socio-demographic characteristics, PLoS ONE 10 (2015) 1–19.
- [22] L. Alcala, J. Quintero, C. Gomez-Uribe, H. Brochero, Productividad de *Aedes aegypti* (l.) (Diptera: Culicidae) en viviendas y espacios públicos en una ciudad end éndemica para dengue en colombia, Biomedica 35 (2015).
- [23] Ministerio de Salud , Instituto Nacional de Salud, Circular conjunta externa no. 061 de 2015, 2015.
- [24] Instituto Nacional de Salud, Report form Zika illness- Colombia, 2015.
- [25] R Core Team, R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria, 2015.
- [26] Y. Yang, J. D. Sugimoto, M. E. Halloran, N. E. Basta, D. L. Chao, L. Matrajt, G. Potter, E. Kenah, I. M. Longini, The transmissibility and control of pandemic Influenza A (H1N1)virus, Science (2009).
- [27] Ministerio de Salud , Instituto Nacional de Salud, Circular externa 004 de 2016, 2016.
- [28] Instituto Nacional de Salud, Circular 007 de 2016, 2016.
- [29] World Health Organization, Guillain-Barré syndrome - Brazil, 2016.
- [30] N. Yuki, H.-P. Hartung, Guillain-Barré syndrome, New England Journal of Medicine 366 (2012) 2294–2304. PMID: 22694000.

- [31] G. S. Campos, A. C. Bandeira, S. I. Sardi, Zika virus outbreak, Bahia, Brazil, *Emerging Infectious Diseases* 21 (2015) 1885–1886.
- [32] W. E. Villamil-Gómez, O. González-Camargo, J. Rodriguez-Ayubi, D. Zapata-Serpa, A. J. Rodriguez-Morales, Dengue, chikungunya and Zika co-infection in a patient from Colombia, *Journal of Infection and Public Health* (2016).
- [33] A.-C. Gourinat, O. O'Connor, E. Calvez, C. Goarant, M. Dupont-Rouzeyrol, Detection of Zika virus in urine, *Emerging Infectious Diseases* 21 (2015).
- [34] B. Rozé, F. Najioullah, J. Ferge, K. Apetse, Y. Brouste, R. Cesaire, C. Fagour, L. Fagour, P. Hochedez, S. Jeannin, J. Joux, H. Mehdaoui, R. Valentino, A. Signate, A. Cabie, Zika virus detection in urine from patients with Guillain-Barré syndrome on Martinique, January 2016, *Euro Surveillance* 21 (2016).
- [35] H. Nishiura, R. Kinoshita, K. Mizumoto, Y. Yasuda, K. Nah, Transmission potential of zika virus infection in the south pacific, *International Journal of Infectious Diseases* (2016) –.
- [36] A. J. Kucharski, S. Funk, R. M. M. Eggo, H.-P. Mallet, J. Edmunds, E. J. Nilles, Transmission dynamics of Zika virus in island populations: a modelling analysis of the 2013-14 French Polynesia outbreak, *bioRxiv* (2016).
- [37] J. Mlakar, M. Korva, N. Tul, M. Popović, M. Poljšak-Prijatelj, J. Mraz, M. Kolenc, K. Resman Rus, T. Vesnaver Vipotnik, V. Fabjan Vodusek, A. Vizjak, J. Pižem, M. Petrovec, T. Avšič Županc, Zika virus associated with microcephaly, *New England Journal of Medicine* 374 (2016) 951–958. PMID: 26862926.
- [38] World Health Organization, Zika situation report, 2016.
- [39] P. Brasil, J. P. Pereira, Jr., C. Raja Gabaglia, L. Damasceno, M. Wakimoto, R. M. Ribeiro Nogueira, P. Carvalho de Sequeira, A. Machado Siqueira, L. M. Abreu de Carvalho, D. Cotrim da Cunha, G. A. Calvet, E. S. Neves, M. E. Moreira, A. E. Rodrigues Baião, P. R. Nassar de Carvalho, C. Janzen, S. G. Valderramos, J. D. Cherry, A. M.

Bispo de Filippis, K. Nielsen-Saines, Zika virus infection in pregnant women in Rio de Janeiro — preliminary report, *New England Journal of Medicine* 0 (2016) null. PMID: 26943629.

- [40] S. Cauchemez, B. P. Besnard, Marianne AND, T. Dub, P. Guillemette-Artur, D. Eyrolle-Guignot, et al., Association between zika virus and microcephaly in french polynesia, 2013–15: a retrospective study, *The Lancet* 0 (2016) DOI: [http://dx.doi.org/10.1016/S0140-6736\(16\)00651-6](http://dx.doi.org/10.1016/S0140-6736(16)00651-6).