The malaria burden of Amerindian groups of three Venezuelan states: A descriptive study based on programmatic data

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Abstract

Background: Fifty-three percent of all cases of malaria in the Americas in 2019 came from Venezuela, where the epidemic is heavily focused south of the Orinoco river, and where most of the country's Amerindian groups live. Despite the disease is known to represent a significant public health problem among these populations, little epidemiological data exists on the subject. This study aims to provide information on malaria incidence, geospatial clustering, and risk factors associated to *Plasmodium falciparum* infection among these groups.

Methods: This is a descriptive study based on the analysis of published and unpublished programmatic data collected by Venezuelan health authorities and non-government organizations between 2014 and 2018. The Annual Parasite Index among indigenous groups (API-i) in municipalities of three states: Amazonas, Bolivar and Sucre was calculated and compared using the Kruskal Wallis test, risk factors for *P. falciparum* infection were identified via binomial logistic regression and maps were constructed to identify clusters of malaria cases among indigenous patients via Moran's I and Getis-Ord's hot spot analysis.

Results: 116,097 cases of malaria in Amerindian groups were registered during the study period. An increasing trend was observed between 2014 and 2016 but reverted in 2018. Malaria incidence remains higher than in 2014 and hot spots were identified in the three states, although more importantly south of Bolivar. Most cases (73.3%) were caused by *P. vivax*, but the Hoti and Yanomami indigenous groups presented higher odds for infection with *P. falciparum.*

Conclusion: Malaria cases among Amerindian populations increased between 2014 and 2018 and seem to have a different geographic distribution as those among the general population. Our findings suggest that tailored, cost-effective interventions will be needed to curb the negative impact of malaria transmission in these groups. Attention to the Hoti and Yanomami should be prioritized.

Background

Malaria is a major public health concern in the Americas, where 889,000 cases and 550 deaths were estimated to have occurred in 2019. Fifty-three percent of these cases, and 73% of all deaths came from Venezuela, where incidence has increased in over 1,000% in the last two decades, amidst a context of economic crisis and political unrest.[1] The disease disproportionally affects regions south of the Orinoco River, where cases are clustered in the Sifontes municipality, of the Bolivar state[2]. There is a significantly lesser burden in the northeast coast of the country.[3] By 2016, the last year with detailed public epidemiological data, only three states: Bolívar, Amazonas (south of the country) and Sucre (northeast), accounted for 90% of all registered cases[4]. *Plasmodium vivax* causes 77% of all registered cases, followed by *P. falciparum*, with 16%, and mixed infections (6.5%). *P. malariae* is rare and underdiagnosed.[1]

The total Amerindian population in Venezuela was estimated to surpass 720,000 people in 2011, [5] most of which are concentrated in malaria-endemic regions. These indigenous groups are particularly vulnerable, given a historically poor access to healthcare services and antimalarial medication, as well as the expansion of illegal mining across their territories.[6, 7] Epidemiological studies in other endemic regions of South America have demonstrated that malaria transmission in indigenous communities responds to epidemiological factors different to those in the general population.[8] Moreover, the increasingly important influence of illegal mining in said transmission dynamics has not been studied in detail and has been traditionally limited to a few settlements along the Caura River basin.[7, 9, 10].

This work analyses published, and unpublished epidemiological records collected by Venezuelan health authorities and Non-Government Organizations (NGOs), between 2014 and 2018. The aim is to provide information on the general burden of malaria among the indigenous people of Amazonas, Bolivar, and Sucre states, describe differences in regional incidence, spatial clustering, risk factors for infection with *P. falciparum,* and transmission seasonality.

Materials And Methods

This is a descriptive study based on the analysis of programmatic data collected by Venezuelan health authorities and NGOs in three Venezuelan states. Morbidity data from 2014 until 2017 was obtained from publicly available sources,[4, 11-13] while data from 2018 was retrieved from raw datasets and reports collected by local volunteers (Unpublished datasets, Venezuelan Ministry of Health). All data sources are part of a national passive malaria surveillance program. As per national guidelines, only symptomatic patients seeking care at a public health facility are tested, either with thin and thick blood films, or a rapid diagnostic test (RDT). Only new cases are included in registries, and are defined by the Venezuelan Health Ministry as any symptomatic infection with a positive test occurring 90 days or more since the completion of a treatment scheme. [14] Nonetheless, parasites are not regularly genotyped, which hampers differentiation of true new cases from relapses, given the high prevalence of *P. vivax*.

Malaria incidence among indigenous groups at different locations was estimated calculating the Annual Parasite Index (API-i) at the municipality level (administrative level 3) and compared using a Kruskal-Wallis test. The indigenous population of municipalities was estimated based on data from the last available census and using a geometric growth method, based on the following formula [15].

$$P_n = P_0(1 + R_G)^n$$

$$R_G = \frac{\ln\left(\frac{P_0}{P_{0-1}}\right)}{T}$$

Where P_n represents the estimated population at any time, n is the time in years between the last available census and the time of estimation, P_0 the size of the population in the last available census, P_{0-1} the population size at the second last available census, R_G is the estimated rate of growth and T represents the time between the last two available censuses.

Incidence trends were plotted fitting a local regression (LOESS) curve with an α smoothing factor of 0.8 into monthly time series of cases. Incidence among indigenous and non-indigenous inhabitants of each state and municipality was compared using relative risk (RR), and significance tested using a z- score.

Spatial autocorrelation of cases was determined using the global Moran's I, with positive *I* values indicating clustering. This test fails to identify individual clusters, and it is of limited value when the spatial pattern is not homogenously distributed. Thus, we also mapped individual clusters of high (hot spots) and low (cold spots) burden, applying the Getis-Ord's Gi* statistic to individual parishes (administrative level 4), except in Amazonas, where it was applied to municipalities (administrative level 3), due to the lack of adequate parish-level data. Large positive z values and small *p* values indicate a significant hot spot, while large negative z values and small *p* values suggest a significant cold spot.[16, 17]

The significance of clustering was determined with a z-score and parishes were classified based on it: Confidence 90% ($0.1 > p > 0.05$), confidence 95% ($0.05 > p > 0.01$) and confidence 99% ($p < 0.01$), as done in similar studies. [17, 18].

The proportion of malaria cases caused by different *Plasmodium* species was compared using the Chi-square test. Odds ratios in univariate and multivariable models for *P. falciparum* vs *P. vivax* infection were calculated via binomial logistic regression and *p* values determined via Wald's test.

Data analysis and processing was performed using Excel 2016 (Microsoft, Richmond, Virginia), SPSS 25 (IBM, Armonk, New York) and RStudio V 1.3.1093 (RStudio Team, Boston, Massachusetts). ArcGIS Pro 24 (Esri, Redlands, California) was used to construct maps and perform spatial analysis. Significance was set at 0.05.

Results

Malaria incidence among indigenous communities in Amazonas, Bolivar and Sucre

A total of 116,097 new cases of malaria were registered in the 2014-2018 period among Amerindians. Of these, 62,267 (53.6%) were male and 53,830 (46.4%), female. Median age was 19 years (IQR: IQR: 9-31 years, additional file 1).

Studied patients belonged to 41 different ethnic groups. However, only nine accounted for 91% of cases. These are: Pemon (27.3%), Jivi (25%), Piaroa/Wotjuja (16.1%), Yekuana (8.9%), Kurripaco (3.9%), Eñepa (2.9%), Piapoko (2.9%), Yanomami (2.8%) and Baré (1.3%). For a full list, see additional file 1.

Most cases were registered in Amazonas (56.6%) followed by Bolivar (43.2%) and Sucre (0.25%). The year with the highest number of new malaria cases was 2017 with 30,976.

Amazonas state

Most patients belonged to ethnic groups located north of the state, namely, Jivi (39.8%), Wotjuja (25%) and Yekuana (9.1%). The number of new malaria cases in indigenous communities in 2018 (21,530), was 174.2% higher than compared to the 2014 baseline (7,852). An increasing trend in the number of monthly cases was observed between January 2016 and January 2018, when cases started to decrease (Figure 1A). Despite this, the relative malaria risk for indigenous people compared to the non-indigenous population fell from 2.44 in 2014 (p<0.01), to 0.89 (p<0.01) in 2018 (table 1). Cases in Amazonas were typically higher between January and June, but a clear seasonal pattern was not observed (Figure1B), and no significant differences were seen in the median number of monthly cases during the study period (p=0.57, additional file 5).

At municipal level, the Atures Municipality accounted for most cases during the five-year study period (55,28%). There was a significant difference in the median incidence of municipalities (p<0.01), with the highest median API-i registered in Manapiare: 249.05 (IQR:151.25-301.64, Figure 2, additional file 2).

Bolivar state

The Pemon, the most numerous ethnic group in the state, accounted for 63.2% of all cases in Bolivar, followed by the Yekuana (8.7%) and the Eñepa (6.6%). As in Amazonas, malaria cases increased during the study period, compared to the 2014 baseline (7,854), but particularly in 2016 (15,676). From this point on, incidence reduced, reaching 8,565 cases in 2018, 9.05% more than in 2014 (Figure 1C). Compared to that in the rest of the population, malaria risk for indigenous people was consistently higher in Bolivar: RR: 3.39 in 2014 (p<0.01), 2.47 in 2015 (p<0.01), 2.80 in 2016 (p<0.01), 1.11 in 2017 (p<0.01) and 1.02 in 2018 (p=0.04, table 1). A seasonal pattern seems more patent in this state, as cases peak between February and April, and start declining from June onwards (Figure 1C-D). There was a significant difference in the median number of monthly cases throughout the five-year period (p<0.01).

At municipal level, almost a quarter of all cases originated in the Gran Sabana municipality (24.2%), followed by Angostura (formerly known and noted in maps as Raul Leoni, 23.3%) and Cedeño (20.4%) municipalities. Incidence in the study period was significantly different between municipalities (p=0.012), with the highest median API-i registered in El Callao: 575.76 cases per 1,000 indigenous people (IQR: 457.14-1205.88). This however, is probably a result of the extremely small projected indigenous population in the municipality (additional file 3). Angostura had the highest median API-i of all municipalities with 100 indigenous inhabitants or more (310.84, IQR: 207.81-334.57, Figure 2, additional file 2).

Sucre state

The Warao ethnic group accounted for 228 cases (78.4%), followed by the Uruak (10%), and the Puinave (7.2%). Although the number of cases remained considerably lower than in Amazonas and Bolivar, it increased from zero in 2014 and 2015 to 140 in 2017, followed by a 72% reduction in 2018 (39 cases). Annual incidence peaked in 2017 (5.75 cases per 1,000 indigenous people), and then reduced to 1.58 in 2018 (Figure 1E, table 1).

At municipal level, Benítez registered the highest API-I of the state (174.52, IQR: 0-174.52), however, this difference was not significant (p=0.06) when municipalities with an indigenous population below 100 were excluded from the analysis. There is no evident seasonal pattern in Sucre (Figure 1F).

Table 1: Incidence of malaria among indigenous and non-indigenous groups in Amazonas, Bolivar and Sucre states, Venezuela, 2014-2018.

Amazonas							
Year	Cases-i	Est. Pop-i	API-i	Cases non-i	Est. Pop non-i	API non-i	RR
2014	7852	82800	94.83	3512	90344	38.87	*2.44
2015	7164	85082	84.20	11477	92921	123.51	*0.68
2016	7942	87427	90.84	17009	95481	178.14	*0.51
2017	21187	89837	235.84	45113	98015	460.27	*0.51
2018	21530	92313	233.23	26283	100522	261.47	*0.89
Bolivar							
2014	7854	57451	136.71	67089	1665910	40.27	*3.39
2015	8387	58404	143.60	98466	1693846	58.13	*2.47
2016	15676	59372	264.03	161943	1721527	94.07	*2.81
2017	9649	60357	159.87	251673	1748949	143.90	*1.11
2018	8565	61357	139.59	242801	1776128	136.70	*1.02
Sucre							
2014	0	23256	0.00	922	988415	0.93	0
2015	0	23615	0.00	3208	1003939	3.20	0
2016	112	23978	4.67	20821	1019515	20.42	*0.23
2017	140	24348	5.75	61747	1035140	59.65	*0.10
2018	39	24723	1.58	67992	1050722	64.70	*0.02

Est. Pop: *Estimated population.* ***API:*** *Annual parasite index.* ***i****: Indigenous people.* ***Non-i****: Non-Indigenous people (cases per 1,000 people).* ***RR****: Risk ratio indigenous/non-indigenous. Z test for significance: * p <0.05*

Spatial autocorrelation and clustering

The origin of malaria cases registered in 2014 (2016 for Sucre) and 2018 was mapped to compare changes in geographic clustering. Maps were constructed to the parish level (fourth administrative level) in Bolivar and Sucre, and to the municipality level (third administrative level) in Amazonas, due to the lack of adequate parish-level data in this state.

The Atures municipality accounted for most cases in Amazonas (44.1% in 2014, and 67.5% in 2018). Yet, Moran's I showed no significant clustering either year. The Getis-Ord analysis, however, revealed a low-significance hot spot (confidence 90%) in Atures (Figures 3A, and 3B).

In Bolivar, the Moran's I was positive and statistically significant in 2014 (I=0.19, p=0.006) and 2018 (I=0.17, p=0.006) indicating stable clustering of cases. This was reflected in the hot spot analysis: In 2014, two highly significant (confidence 99%) hot spots were seen in Aripao (Sucre municipality) and Barceloneta (Angostura municipality). Lower significance ones (confidence 90%) were seen in Guaniamo (Cedeño), Gran Sabana and Ikabaru (Gran Sabana municipality, figure 3C and 3D). New high-significance clusters appeared in the entire Gran Sabana municipality in 2018. The central northern region of the state remained a high-significance cold spot during the entire study period.

The situation in Sucre state was only compared to 2016, due to the absence of cases the two previous years. No significant clusters were identified via Moran's I analysis. The Getis-Ord's Gi* revealed highly significant hot spots in Union in 2016 and 2018 (Benitez municipality), and Romulo Gallegos (Andrés Eloy Blanco municipality) in 2018.

The full results of the Getis-Ord's analysis can be found in additional file 4.

Proportion of Plasmodium species and risk factors associated to P. falciparum infection

Most infections were caused by *P. vivax*: 85,124 (73.3%), *P. falciparum*: 25,201 (21.7%), or both: 5,726 (4.9%). *P. malariae* was only identified in 46 patients (0.04%), from eight ethnic groups, all of them from Amazonas, and mostly infected in Alto Orinoco (31 cases), and Manapiare (8 cases). The Yanomami accounted for 58.7% of all *P. malariae* cases. While *P. vivax* was the dominant species in all the states, the proportion of *P. falciparum* cases in Amazonas and Bolivar (22% and 21.4%, respectively) was more than twice as that in Sucre state (8.6%, X^2= 35.82 df=2, p<0.01).

The proportion of patients with *P. falciparum* or mixed infection was also higher in two ethnic groups: the Hoti (42.9%) and the Yanomami (41.5.%), compared to the rest of the indigenous population (26.1%, X^2=128.30, df=1, p<0.01 and X^2=380.83, df=1, p<0.01, respectively).

To evaluate possible reasons behind this difference, the odds ratios (OR) for *P. falciparum* vs. *P. vivax* infection were calculated considering ethnic group, and other available variables such as occupation, gender, age group, and state of origin of patients, results are summarised in table 2. *P. malariae* and mixed infections were excluded from the analysis.

Table 2: Univariate and multivariable analysis of the odds ratios for P. falciparum infection among indigenous groups of Amazonas, Bolivar and Sucre states, Venezuela, 2014-2018

			Univariate				Multivariable			
Occupation	*Pv*	*Pf*	**OR (Pf/Pv)**	**CI**		***p* value**	**OR (Pf/Pv)**	**CI**		***p* value**
Mining	7763	2656	1.44	1.35	1.54	<0.01	1.09	1.01	1.18	0.03
Agriculture	2951	886	1.26	1.15	1.39	<0.01	0.82	0.74	0.91	<0.01
Commerce	8371	2873	1.45	1.35	1.55	<0.01				
Student	8391	2257	1.13	1.06	1.21	<0.01				
Others	7268	1726	1.00							
Age group										
5-14	23101	5619	1.02	0.97	1.07	0.50	1.08	1.02	1.15	0.01
15-29	28739	8893	1.30	1.23	1.36	<0.01	1.47	1.39	1.56	<0.01
30-64	21127	7565	1.50	1.43	1.58	<0.01	1.75	1.64	1.85	<0.01
65+	1307	550	1.76	1.58	1.96	<0.01	2.07	1.85	2.32	<0.01
0-4	10424	2489	1.00							
Gender										
Female	39443	11876	1.03	1.00	1.06	0.03	1.04	1.01	1.08	0.01
Male	45681	13325	1.00							
Ethnic group										
Pemon	22002	6633	1.19	1.12	1.26	<0.01	1.17	1.09	1.25	<0.01
Jivi	21332	6701	1.24	1.17	1.32	<0.01	1.29	1.22	1.37	<0.01
Yekuana	7804	2328	1.18	1.10	1.26	<0.01	1.21	1.13	1.30	<0.01
Wotjuja	14640	3429	0.93	0.87	0.99	0.02				
Kurripaco	3591	812	0.89	0.82	0.98	0.02	0.87	0.79	0.96	<0.01
Eñepa	2335	946	1.60	1.46	1.75	<0.01	1.76	1.59	1.94	<0.01
Piapoko	2500	712	1.13	1.02	1.24	0.02	1.20	1.09	1.33	<0.01
Yanomami	1875	1248	2.63	2.41	2.87	<0.01	3.08	2.81	3.38	<0.01
Hoti	538	389	2.86	2.48	3.29	<0.01	3.33	2.89	3.84	<0.01
Kubeo	25	3	0.47	0.14	1.57	0.22				
Warao	325	48	0.58	0.43	0.79	<0.01				
Warekena	255	44	0.68	0.49	0.94	0.02	0.67	0.48	0.93	0.02
Akawayo	791	108	0.54	0.44	0.66	<0.01	0.46	0.38	0.57	<0.01

Other	7111	1800	1.00							
State										
Amazonas	48894	14452	2.92	1.93	4.41	<0.01	2.52	1.49	4.29	<0.01
Bolivar	35983	10724	2.94	1.95	4.45	<0.01	2.31	1.38	3.87	<0.01
Sucre	247	25	1.00							

P.f: Plasmodium falciparum, P.v: Plasmodium vivax. OR: Odd ratios calculated via binomial logistic regression, CI: 95% confidence intervals, p values calculated via Fisher's exact test

Discussion

Reported malaria cases among Amerindian groups in Venezuela increased between 2014 and 2018. However, this was particularly marked between 2014 and 2017, with a clear inversion of the trend in all the states during 2018. This matches a slight reduction in overall cases in the country that year, [13] and probably responds to efforts carried out by local and international actors in highly endemic areas. Despite this, table 1 and figure 2 show that total malaria cases and population-adjusted incidence remain higher than in 2014 across the three states.

However, the municipal API-Is should be interpreted carefully, as the malaria burden of communities with a small projected indigenous population is likely overestimated. Our population estimates are entirely based on census data, which does not include transient inhabitants who are living and working in the study area. This is a major limitation of this study, as the actual at-risk population in these places is certainly larger than estimated. Places like El Callao (Bolívar), where registered malaria cases exceed the projected indigenous population, leading to abnormally large API-Is, are a good example of this.

A full list of the estimated indigenous populations of individual municipalities can be found in the additional file 3.

To address this issue and prioritise areas for eventual interventions, the cluster analysis was carried out with individual cases, rather than calculated incidence.

In Amazonas state, despite most cases originated in Atures (where the only large town in the state is located), the Getis-Ord's Gi* statistic revealed only low-significance hotspots there in 2014 and 2018. This suggests that cases are more evenly distributed north of the state. Although the lack of parish-level data in Amazonas limits the interpretation of these results, this might be partially influenced by the Orinoco Mining Arc, a large-scale mining project involving areas in the border between Bolivar and Amazonas. Importantly, the relative risk of indigenous patients reduced, this indicates that incidence among the non-indigenous population increased more importantly than among Amerindians and might respond to an increase in domestic migration due to mining.

In Bolivar state, clustering was consistently identified south of the State. This region comprises the historical location of the Pemon, the largest single ethnic group identified in this study. Illegal mining by this and other groups in protected areas of Canaima National Park, mostly located in the Gran Sabana municipality, as well as in the Upper Caura River basin (Aripao) has been widely reported [19, 20] and likely influences the local clustering of malaria among Amerindian communities in this region. The highly significant cold spots identified north of the state, respond to the small proportion of indigenous population in the area.

Surprisingly, the Sifontes municipality, recently identified as the most important cluster of malaria transmission in the Americas [2], was not found to be a significant hot spot for Amerindian groups, while this might reflect a predominance of mining activity by the Pemon in other areas of the state, as discussed above, further research is needed to confirm this finding and understand the reasons behind it.

If malaria among Amerindian groups indeed presents a different geographic pattern, interventions in locations apart from Sifontes will be necessary to curb the impact of the epidemic. Hot spots in Sucre matched areas of known high-incidence [13], where indigenous patients have probably benefited more from interventions currently in place, explaining the sharp reduction in cases seen in 2018.

Seasonality was only observed in Bolivar, but this has not been described in the general population. [21] However, these studies date from 2010, and malaria cases in Bolivar are highly influenced by the El Niño Southern Oscillation (ENSO) phenomenon, [21] which was particularly intense in the 2015-2016 period [22] and might have influenced the large peak of cases in the early months of 2016 and 2017. The exposure of the indigenous population to infectious bites might also change more markedly during the year due to specific cultural or economic factors. Further studies are needed before making conclusions regarding these patterns.

The presence of *P. malariae* exclusively in patients from Amazonas, and mostly among the Yanomami, matches previous reports that link this species to remote areas of the state. [23] The Hoti and the Yanomami were also found to have significantly higher odds for *P. falciparum* infection. Similar to *P. malariae, P. falciparum* is known to be more prevalent in the rainforest of Amazonas than in the rest of the country. [24] Previous works suggest that the higher prevalence of *P. falciparum* and *P. malariae* in the Alto Orinoco region might be explained by a longer life expectancy of local *Anopheles darlingi* mosquitos. [24] This might in turn reflect flaws in local vector control strategies, and the lack of targeted measures that adapt to the particular living conditions of the Yanomami and the Hoti, such as their nomadic habits, and housing materials that render IRS and bed nets ineffective.[24] Insecticide treated hammocks have proven to be an useful alternative in this context.[25]

Although miners presented higher odds for *P. falciparum* infection too, the difference was very small and might be more related to their increased exposure to infectious bites, than to a higher *P. falciparum* prevalence in Venezuelan mines, which has not been described. [26] Furthermore, occupation data was only available for 45,142 patients (40.9% of the total analysed). Increased exposition to infectious bites is probably also the reason for higher odds in older age groups.

Conclusion

Malaria incidence among Amerindian groups has increased since 2014, although the trend has partly reversed in the last two years. Clustering of malaria cases is particularly clear in Bolivar, where a wider deployment of cost-effective interventions is needed. Access to antimalarial medication, as well as specifically targeted interventions should be guaranteed to all groups, but prioritized to the Hoti and Yanomami, due to their increased risk of *P. falciparum* infection.

Abbreviations

API-i: Annual Parasite index among Amerindian groups (number of cases of malaria reported in Amerindian patients per 1,000 Amerindian people).

ENSO: El Niño Southern Oscillation.

NGO: Non-government organization.

Declarations

Ethics approval: This project was approved by the independent ethics committee of the Venezuelan National Bioethics Center (Reference number: CIBI-CENABI-04/2020), and the MSc Research Ethics Committee at the London School of Hygiene and Tropical Medicine (Reference number: 21868).

Consent for publication: Not applicable

Availability of data and materials: The datasets are available from the corresponding author on reasonable request.

Competing interests: The authors declare no conflict of interest.

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Figures

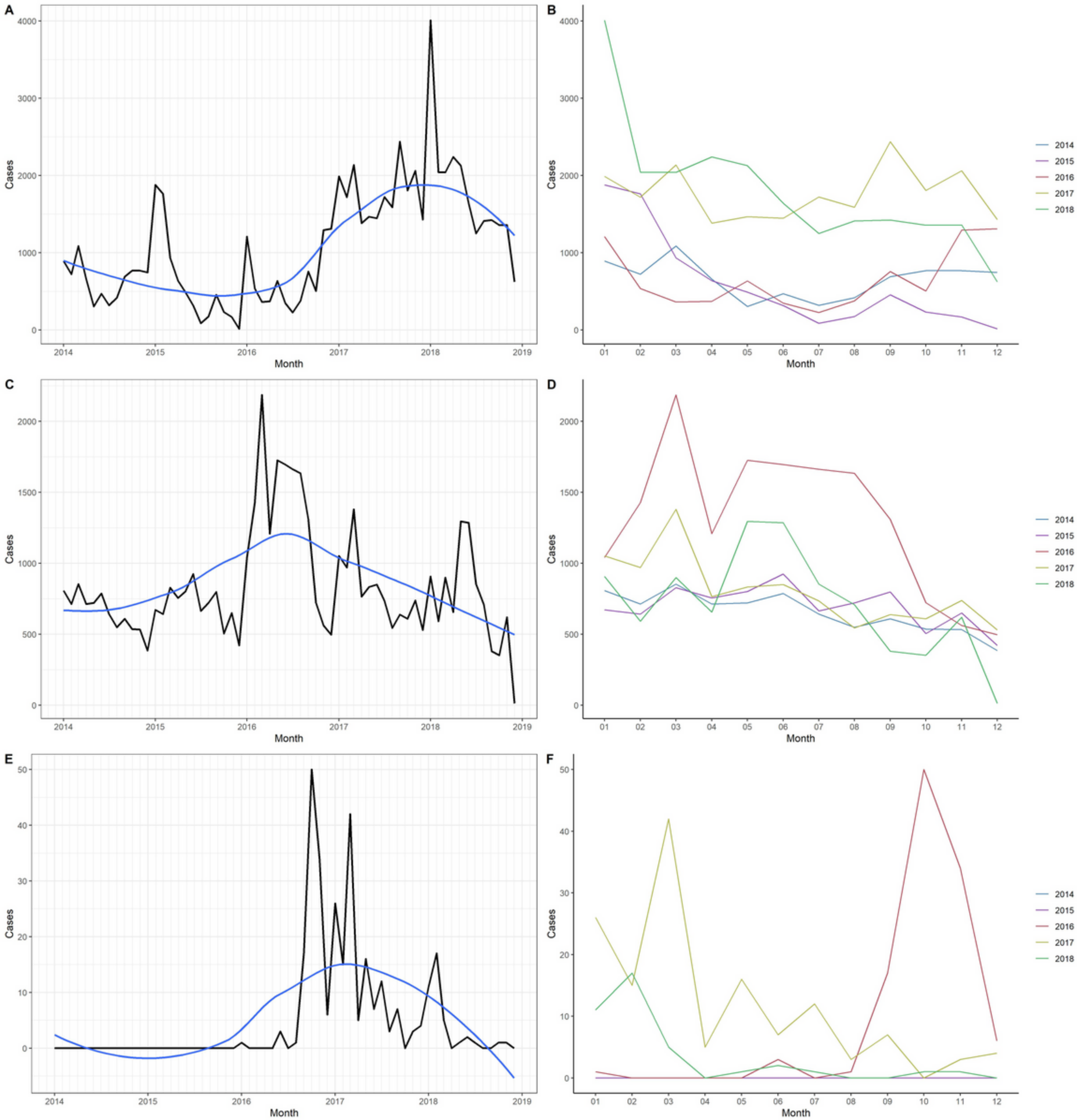

Figure 1

Monthly malaria cases registered in Amerindian groups of Amazonas, Bolivar and Sucre states, Venezuela, 2014-2018. Monthly cases registered between 2014 and 2018 in Amazonas (A), Bolívar (C) and Sucre (E), and aggregated cases per month and year in the three states (B, D, and F, respectively). The blue line in the panels on the left represents the LOESS curve.

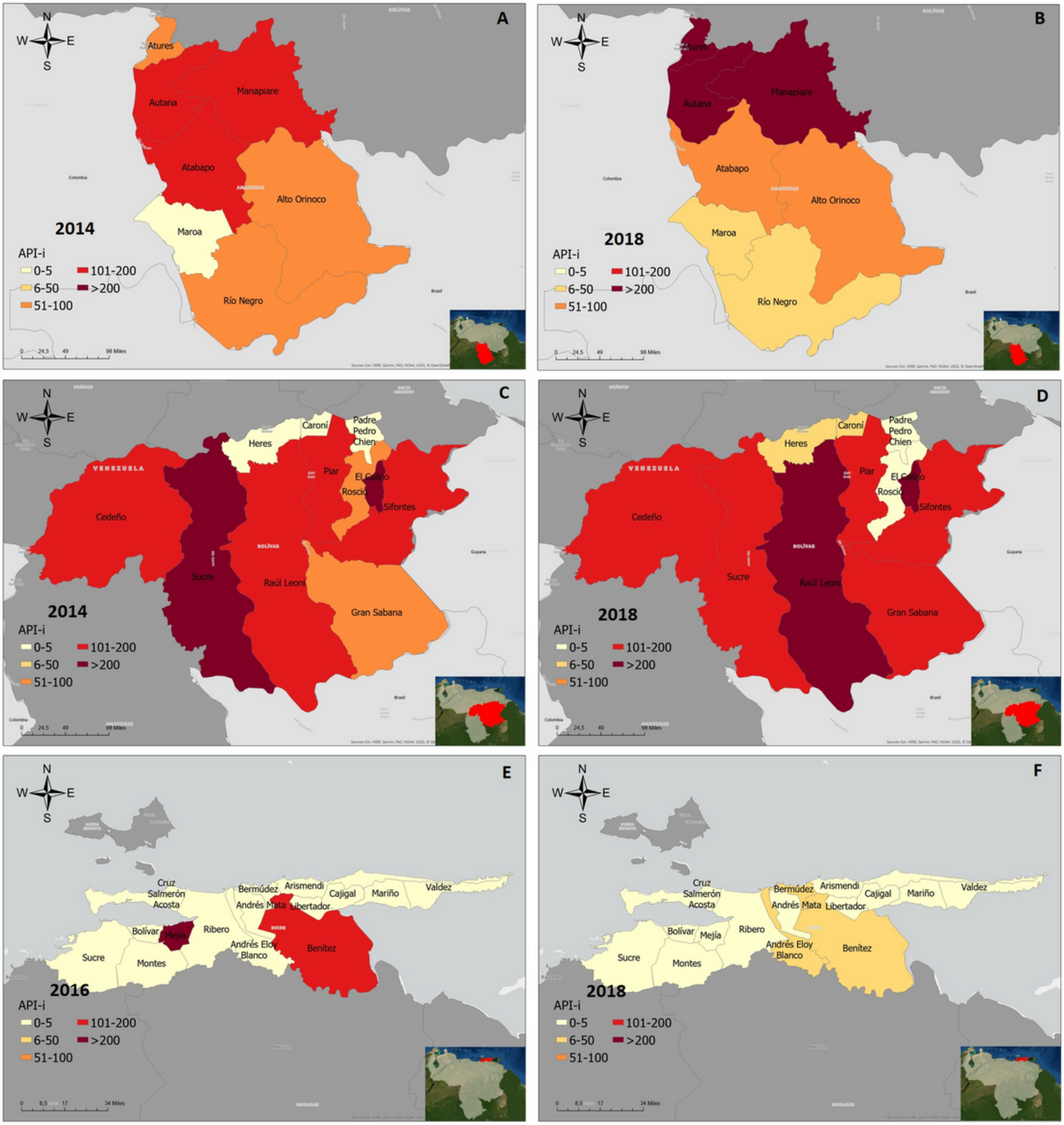

Figure 2

Evolution of malaria incidence in Amerindian groups of Amazonas, Bolivar and Sucre states, Venezuela, 2016 and 2018. Annual Parasite Index among indigenous patients (API-i) in Amazonas (A, B), Bolivar (C, D), and Sucre (E, F). Panels on the left represent 2014 data (except Sucre), panels on the right, 2018. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area o bbnhjr of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

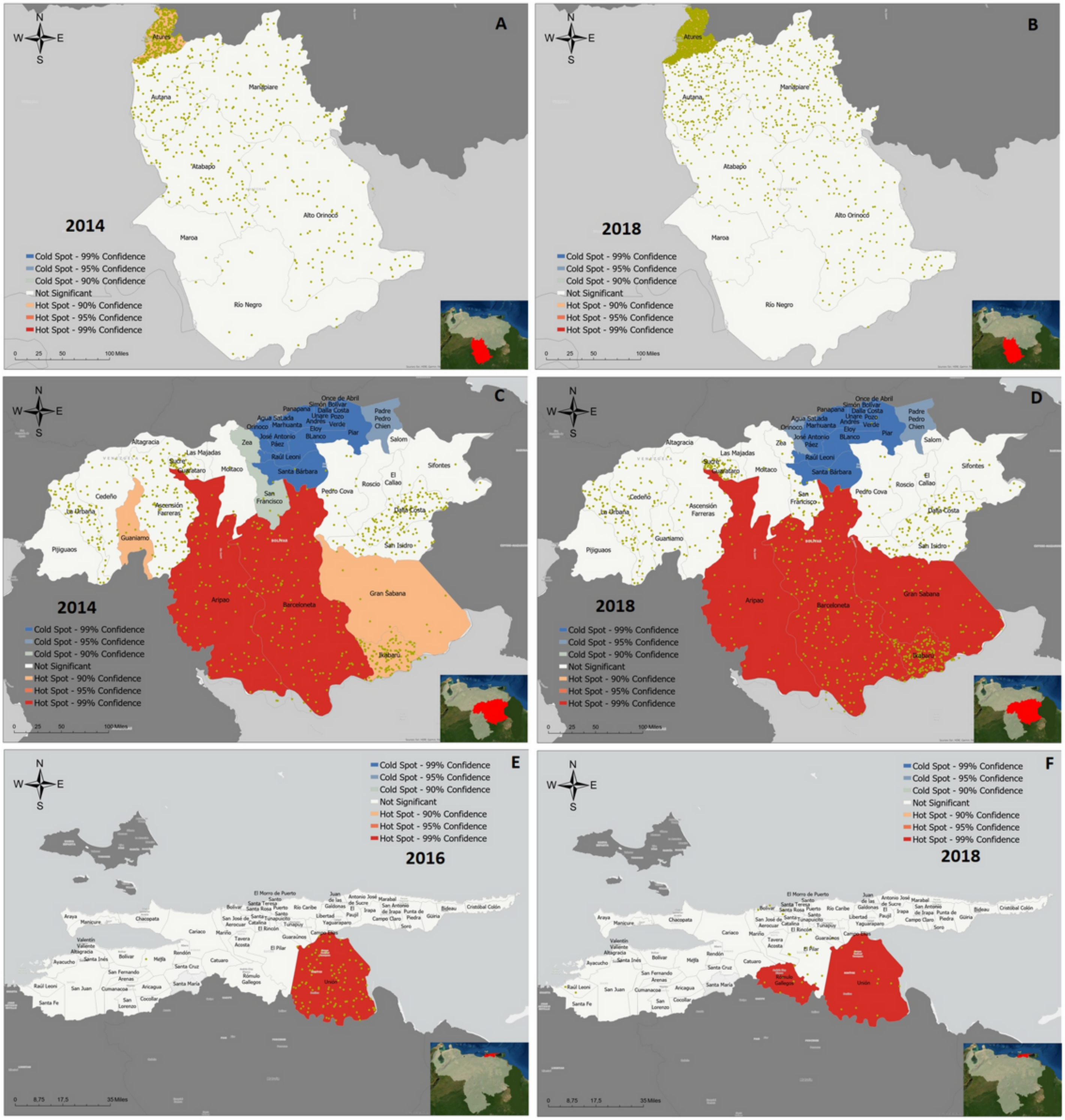

Figure 3

Evolution of clustering of malaria cases diagnosed among indigenous groups of Amazonas, Bolivar, and Sucre states, Venezuela, 2014-2018. Burden hot and cold spots detected in Amazonas (A, B), Bolivar (C, D) and Sucre (E, F). Panels on the left represent 2014 data, panels on the right, 2018. Data of 2016 is not shown, except for Sucre, where no cases were registered in 2014. Each dot represents 10 cases of malaria in indigenous people (Amazonas and Bolivar) or 1 case (Sucre). Confidence: 99% ($p < 0.01$), 95% ($0.05 > p > 0.01$), 90% ($0.1 > p > 0.05$). Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area o bbnhjr of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

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