

Updates on malaria epidemiology and profile in Cabo Verde from 2010 to 2019: The goal of Elimination

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Research

Keywords: surveillance, imported infections, prevention of reintroduction

Posted Date: July 21st, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-41864/v1>

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Version of Record: A version of this preprint was published on October 23rd, 2020. See the published version at <https://doi.org/10.1186/s12936-020-03455-7>.

Abstract

Background

Cabo Verde is one of the E-2020 Initiative, a group of 21 countries identified by World Health Organization (WHO) in 2016 as having the potential to eliminate malaria by 2020. Located in west Africa, Cabo Verde is an archipelago consisting of nine inhabited islands. Malaria has been endemic since the settlement of the islands during the during the 16th century and is poised to achieve malaria elimination in January 2021. The aim of this research is to characterise the trends in malaria cases from 2010 to 2019 as the country transitions from endemic transmission to elimination and prevention of reintroduction phases.

Methods

All confirmed malaria cases reported to the Ministry of Health between 2010 and 2019 were extracted and secondary analysis was conducted. Variables collected as part of the routine reporting for each confirmed case included age, sex, municipality of residence, and if classified as imported, the reported country of travel within the past 30 days, providing the presumed origin of infection. Trends in reported cases were visualised and logistic regression used to identify risk factors associated with imported malaria.

Results

A total of 819 malaria cases were reported in the country between 2010 and 2019, the majority of which were *Plasmodium falciparum*. Overall, 554 (67.6%) and 263 (32.1%) of cases were reported as locally acquired and imported, respectively, with the last locally acquired case reported in January 2018. Only two (0.20%) of the cases were classified as introduced, a single case in each of 2018 and 2019. Of the locally acquired cases, 80.5% (446/554) were reported during the outbreak in 2017. The majority of malaria cases were identified in males (766; 73.3%) or those aged 20 years or older (658; 79.7%). The adjusted odds ratio (AOR) of cases being imported was 3.73 (95% CI: 2.47–4.99) in the post epidemic period compared with the pre-epidemic period and reported on Sao Vicente island (AOR = 6.96, 95% CI = 4.40–9.53, $p < 0.0001$) compared to Boa Vista.

Conclusions

Cabo Verde has made substantial gains in reducing malaria burden in the country over the past decade and are poised to achieve elimination in 2020. However, the high mobility between the islands and continental Africa where malaria is still highly endemic, means there is a constant risk of malaria reintroduction. Characterisation of imported cases provides useful insight for program and enables better evidence-based decision-making to ensure malaria elimination can be sustained.

Background

Malaria elimination means, a country or territory, has had at least three consecutive years without any indigenous case of malaria, and can apply for certification from the World Health Organization (WHO) to be listed amongst the "malaria-free countries" [1]. To achieve malaria elimination, it requires an unremitting political commitment, substantial and predictable financing and increased regional collaboration [2]. To fuel the drive for malaria elimination, the WHO identified 21 countries in five regions, which could overcome malaria by 2020, a process that accounted for both technical, operational, and biological factors [2]. Since 2016, 49 countries reported fewer than 10,000 cases (2018), five countries have reported no infections since 2017, placing them on track for certification, and five countries have received malaria elimination certification [3–8].

Cabo Verde is one of 21 countries identified with the potential to achieve malaria elimination by 2020 [2]. Located off the coast of West Africa, malaria has been endemic since it was imported during the colonization period [9]. Historically, malaria transmission was associated with low levels of transmission, with sporadic epidemics linked with unseasonably high rainfall [10]. Malaria transmission has been interrupted twice in the country's history but has not been sustained, likely due to a high degree of population movement between the islands and endemic countries [11]. In recent years, malaria transmission in Cabo Verde has been low and unstable, with sporadic and seasonal transmission associated with the rainy season and increasing vector densities [12–14].

Cabo Verde is again in a position where endemic malaria transmission in the country has been interrupted and will be eligible for applying for WHO certification in January 2021. To ensure elimination can be sustained and to support the prevention to reintroduction phase, the malaria case data collected as part of routine surveillance from the decade before interruption can be valuable for characterizing the malaria epidemiology and identify risk factors for improved surveillance activities. Therefore, this research extends previous research about malaria cases in the country [13, 14] and characterizes both individual and spatial risk factors for endemic and introduced malaria infections.

Methods

Study area

Cabo Verde is an archipelago of volcanic origin located approximately 450 km from the West African coast, west of Dakar, Senegal with approximately 550,000 residents (2019 estimates) [15] (Fig. 1A). It occupies an area of 4033 km² and is composed of ten islands, nine of which are inhabited, divided into two groups called Barlavento (northern) and Sotavento (southern). The islands are composed of a hilly terrain, with only about 10% of the land available for farming. The temperature in the country ranges from a maximum of 25°C to 30°C from August to October, with the lowest temperatures around 19°C to 25°C, typically from January to February. Like all Sahelian zones, the archipelago has a contrasting wet and dry season. The rain is irregular and the archipelago undergoes periodic droughts. The average annual

precipitation ranges between 300 mm and 700 mm in the low-lying and high-altitude areas, respectively [16].

Figure 1: The location of Cabo Verde (A) highlighted in the red box with respect to West Africa is shown in the inset map. Total number of (B) locally acquired and (C) imported malaria cases in Cabo Verde between 2010 and 2019.

Administratively, the country has 22 municipalities, 24 cities, each with at least one hospital and lower level facilities. Access to healthcare is free for all residents and malaria is a notifiable disease, an essential component of the elimination programme. All suspected malaria cases are tested by rapid diagnostic test and confirmed by microscopy (see Table 1 for case definition applied in Cabo Verde [17, 18]). All confirmed cases are treated as inpatients and reported to the National Malaria Control Programme (NMCP) and the Integrated Surveillance and Response to Epidemics (SVIRE) program within 24 hours, prompting an immediate foci investigation. Age, gender, test result, residential address and travel history to enable the classification of the case as indigenous or imported (table 1) is recorded for each confirmed case.

Table 1 - Case definition and classification for malaria used in Cabo Verde and consistent with the WHO definitions [17, 18].

The individual-level malaria case data reported from January 2010 to December 2019 was obtained from the Ministry of Health and used for this analysis. All data are anonymous and collected as part of routine public health activities so ethical approvals or individual consent were not sought. However, permission for use of this data obtained by the Malaria Elimination Program.

Data analysis

First, descriptive statistics and visualisation were used to show the variation of malaria cases during the period, stratified by indigenous and imported, reporting year, age, sex, and island. Annual incidence per 1,000 and mortality per 100,000 rates were calculated using the annual population estimate for Cabo Verde per year [15]. The Case Fatality Rate (CFR) was also determined according to the number of deaths and confirmed cases reported per year.

Logistic regression was applied to assess risk factors associated with being an imported compared to a locally acquired case. Analysis was conducted in R statistical software (V 3.6.1). Covariables available for the risk factor analysis included time period, categorized as pre-epidemic (2010–2016), epidemic (2017) and post-epidemic (2018–2019) period, the island where the case was reported aggregated based on the number of reported cases (Boa Vista, Santiago, Sao Vicente, and Other), age, sex, and the population size residing on the island. The annual estimate of the basic reproductive number (R_0) was calculated according to the ratio of local to imported infections using methods developed by Churcher et al. [19].

Results

Number of malaria cases

Over the ten year period between 2010 and 2019, 833 confirmed malaria cases were reported in Cabo Verde, of which 570 (68.4%) were classified as indigenous, 263 (31.5%) as imported, and two as introduced, one each in 2018 and 2019 (Table 2). However, 423 (74.2%) of the locally acquired cases occurred during the outbreak between July to October, 2017. Indegeneous cases have been reported from almost all municipalities, with the last reported locally acuiired case in January 2018 (Fig. 1B, Fig. 2A). Imported infections consisted of 58.1% of all confirmed cases in the pre-epidemic, and 93.4% of cases in the post-epidemic period and occur in the majority of municipalities (Fig. 1C; Fig. 2B). Malaria incidence per 1,000 population was estimated to be less than 0.09 for all years except for during the 2017 epidemic (0.80/1,000 people). Malaria mortality was very low throughout the study period, with a total of nine deaths (range 0 to 3; the maximum case fatality rate was 8.33%) and a corresponding mortality rate ranging from 0 to 0.60 per 100,000 population at risk (Fig. 2C).

Figure 2: The total number of malaria cases (A), imported infections (B) and deaths (C) per year reported in Cabo Verde between 2010 and 2019. The different colours in the stacked bar chart represents the location the case was reported

Demographic characteristics of malaria cases

Overall, there was good routine reporting of demographic information with only two individuals missing the sex classification and 16 missing age. Across the ten-year period, 74.1% of cases were male, and was consistent across time and according to the case classification (Table 2). Similarly, the median age of cases was 33 years (IQR = 20–43 years). However, individuals with imported malaria were older compared to locally acquired infections with a median age of 35 and 24, respectively. Only 2.6% and 6.0% of reported cases were under 5 years, and 6–19 years old, respectively. Locally acquired cases were consistently reported between August and October (75.4%) whereas imported infections were reported throughout the year, ranging from 3.4% in February to 13.3% of infections in October. However, the highest risk period for imported infections was between August (9.5%) and January (8.4%), coinciding with the main transmission period in west African countries.

Table 2: Demographic characteristics of confirmed malaria infections reported in Cabo Verde between 2010 and 2019, stratified by pre-epidemic, epidemic, and post-epidemic years as well as locally acquired and imported infections as classified by routine malaria programs. The total (N), percentages and corresponding 95 Confidence Intervals (95% CI) are included.

Malaria cases were reported from the majority of municipalities in the country (14/22) at some point during the study period (Fig. 1A). The majority of cases were reported in Praia, on Santiago Island, the capital of the country (686; 83.4%), followed by São Vicente (33; 4.0%), Assomada (22; 2.7%), Sal (20; 2.4%) and Boa Vista (17; 2.1%). The municipalities reporting the greatest proportion of imported

infections were Praia (163; 62.0%), São Vicente (34; 12.9%), and Santa Caterina (21; 8.0%) (Fig. 1B). The likely origin of imported infections based on travel history spanned 22 countries including Brazil (the single case of *P. vivax*), Philippines, and multiple African countries (Fig. 3). The majority of imported malaria infections had reported travel to Portuguese speaking countries, including 24.3% and 22.4% of cases recently travelling to Guinea Bissau and Angola, respectively. Other main countries where imported infections reported traveling to include Senegal (30; 11.4%), Equatorial Guinea (20; 7.6%), Nigeria and Guinea Conakry (both with 15; 5.7%) and Cote d'Ivoire (10; 3.8). The ratio of imported to locally acquired infections suggests that the estimated R_0 was likely below 1 in 6 of the 10 years of analysis (Fig. 4A). According to the specific estimates for Santiago, where there was sufficient cases to determine the island specific estimates, the pattern was similar, except in 2018 where it lingered around 1 for that year (Fig. 4B).

Figure 3: Global map showing the likely origin of imported infections that were reported in Cabo Verde between 2010 and 2019. The size of the circle is scaled according to the number of cases likely originating in that country, with the different colors to differentiate the different countries for visualisation. The location of Cabo Verde is shown as the black circles and connector lines shown in light grey.

Figure 4: Estimated annual R_0 according to the ratio of imported to local cases reported for Cabo Verde (A) and Santiago Island only (B) where there were sufficient cases (min 10 cases required for models) per year to obtain estimates. The y-axis presents the maximum estimate of R_0 that is plausible based on the data with year presented on the x-axis. The red dashed line shows where R_0 equals 1 whereby above this line transmission is increasing and below, transmission is expected to die out.

Discussion

The last indigenous malaria case in Cabo Verde was reported in January 2018, and if maintained, puts the country in the position where they can apply for malaria elimination certification in early 2021. Here, we describe the malaria cases reported in Cabo Verde over the previous 10 years to characterise the transition to successfully eliminating transmission. This work highlights two, non-mutually exclusive challenges for elimination countries to sustain their gains: the risk of epidemics and continued importation. Reported locally acquired malaria cases prior to the 2017 epidemic were generally low, ranging from 0 to 33 cases per month and the estimated R_0 being less than 1 for most years. In contrast, infections are consistently imported in Cabo Verde over time and present in almost all municipalities. Understanding these trends, where and when imported infections are most likely to occur, and their potential to lead to onward transmission will be essential to sustain elimination and avoid future malaria epidemics.

To achieve malaria elimination in Cabo Verde, there has been a strong political commitment and investment in the health system [20–22]: there is good coverage of the health system across the country and is freely accessible to all residents. Malaria has been considered a notifiable disease for some time, to ensure that all cases are confirmed, offered supervised treatment with an effective antimalarial drug,

and investigated within 24 hours of reporting. The surveillance data available for this analysis was largely complete with few missing data points. The investment to ensure complete, high-quality surveillance data will enable evidence-based targeting of resources and rapid responses to eliminate and monitor for any future epidemics [23]. Similarly, as part of strengthening the surveillance system, intensive training on classifying imported infections was conducted. It is possible that transmission had been eliminated in the country earlier, but misclassification of imported as locally acquired would not have enabled that success to be measured. Effective classification of the like origin of infection also ensure that surveillance and intervention activities can be targeted to those individuals and/or areas most at risk [24–27]. The frequent travel from Cabo Verde to endemic countries in continental Africa may be the most important risk for re-introduction of malaria, putting the island’s malaria-free status at risk in the future [28, 29].

Over the ten years examined in this analysis, the capital city, Praia, experienced the highest burden of malaria cases in the country, including locally acquired (largely driven by the epidemic), imported, and also the two introduced infections. Praia is the largest urban area in the country, has the highest population of people traveling, including both nationals and immigrant workers, and has frequent flight connections to endemic countries [28, 30]. Combined with the presence of semi-permanent breeding sites, which allow the persistence of *Anopheles arabiensis* in several neighbourhoods of the city, conditions in the city are highly conducive to malaria transmission [31–33]. Maintaining accessibility to health facilities, clinical management capacity for malaria and continued vector control will be important factors to prevent reestablishment of malaria transmission in the city, as well as other municipalities with a high degree of importation.

Conclusions

Cabo Verde has interrupted malaria transmission, however, for this achievement to be sustained, understanding where the country may be vulnerable to reinitiation of transmission will be critical for evidence-based decision-making. The sustained low levels of transmission, strong public health system and active malaria programs in the country indicate that the archipelago is a good candidate to achieve elimination in the African sub-region. [12, 17] Although the epidemic that occurred in Praia in 2017 resulted in 423 locally acquired cases, there were no deaths and showed that the country is able to effectively contain transmission [14]. Given the likelihood of continued malaria importation from continental African countries the risk profiles of imported identified here will be helpful in prioritizing resources. Other countries currently working to achieve and sustain malaria elimination may benefit from the insights presented here. Ultimately, to prevent reintroduction, the malaria program in Cabo Verde must remain diligent and monitor malaria importation, seasonality of receptivity and vulnerability for transmission, and ensure a sustained investment in the healthcare system to ensure the achievement can be maintained.

Abbreviations

CFR: Case Fatality Rate; ED-SEV:Ecole Doctorale des Sciences de la Vie, de la Santé et de l'Environnement; NMCP:National Malaria Control Programme; SVIRE:Integrated Surveillance and Response to Epidemics; UCAD:Université Cheikh Anta Diop; WHO:World Health Organization;

Declarations

Ethics approval and consent to participate

Not applicable. No consent taken from patient since this is a secondary data review of all diagnosed and reported malaria confirmed cases.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

“Sir Henry Wellcome Fellowship (204693/Z/16/Z) from the Wellcome Trust, UK and the Freedom From Infection project funded by the Bill & Melinda Gates Foundation (OPP1177272) awarded to GS provided her salary support and dedicated time for research and facilitated the collaborative work.” Part of the AJD salary is supported by the Program Investing to achieve elimination for Malaria and impact against TB and HIV in Cape Verde, Grant CPZ-Z-CCSSIDA, by The Global Fund to Fight AIDS, Tuberculosis and Malaria, implemented by the Comitê de Coordenação e Combate ao VIH-SIDA (CCS-SIDA), Ministério da Saúde e da Segurança Social (MSSS) in Cabo Verde.

Author's contributions

AJD, HSBB and ALM design of study; AJD, GS analysis and interpretation of data and draft the manuscript; AJD, GS, AKD, EHAN revised the final manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors thank the National Malaria team for the for making the data available and program staff at the local level working on data reporting.

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Tables

Table 1 - Case definition and classification for malaria used in Cabo Verde and consistent with the WHO definitions [17, 18].

Case Definition

Malaria case, confirmed Malaria case (or infection) in which the parasite has been detected in a diagnostic test, i.e., microscopy, a rapid test or a molecular diagnostic test.

Malaria, all cases All malaria cases irrespective of Plasmodium species (including imported case)

Malaria case, imported Malaria case or infection in which the infection was acquired outside the area in which it is diagnosed (get infected outsider from Cabo Verde)

Malaria case, indigenous A case contracted locally with no evidence of importation and no direct link to transmission from an imported case (get infected in Cabo Verde).

Malaria elimination Interruption of local transmission (reduction to zero incidence of indigenous case) of a specified malaria parasite in a defined geographical area as a result of deliberate activities. Continued measures to prevent re-establishment of transmission are required.

Case Classification

Imported case Malaria case or infection in which the infection was acquired outside the area in which it is diagnosed. Infection from a country outside of Cabo Verde.

Indigenous case A case contracted locally with no evidence of importation and no direct link to transmission from an imported case.

Introduced case A case contracted locally, with strong epidemiological evidence linking it directly to a known imported case (first-generation local transmission).

Recrudescent case Malaria case attributed to the recurrence of asexual parasitemia after antimalarial treatment, due to incomplete clearance of asexual parasitemia of the same genotype(s) that caused the original illness.

Table 2: Demographic characteristics of confirmed malaria infections reported in Cabe Verde between 2010 and 2019, stratified by pre-epidemic, epidemic, and post-epidemic years as well as locally acquired and imported infections as classified by routine malaria programs. The total (N), percentages and corresponding 95 Confidence Intervals (95% CI) are included.

	Pre-Epidemic Years (2010-16)		Epidemic (2017)		Post-Epidemic (2018-19)	
	Malaria Cases (N=315)	95 CI	Malaria Cases (N = 457)	95 CI	Malaria Cases (N = 61)	95 CI
Imported Infections - % (n)	58.09 (n=183)	52.64- 63.55	5.03 (n=23)	3.03 - 7.04	93.44 (57)	87.18 - 99.71
Island - % imported (n)						
Boa Vista	40.0 (6)	14.34 - 65.66	0	-	100 (4)	-
Santiago	54.13 (144)	48.13- 60.13	3.12 (14)	1.15- 4.73	90.48 (38)	81.49 - 99.46
Sao Vicente	95.45 (21)	86.54- 100	100 (7)	-	100 (6)	-
Other	100 (12)	-	100 (2)	-	100 (9)	-
Sex (M=1)	78.52	73.98 - 83.07	70.38	66.20 - 74.58	78.69	68.33 - 89.05
Locally Acquired	73.48 (n=132)	65.92 - 81.04	69.98 (n=434)	65.66 - 74.29	75.0 (n=4)	26.0 - 100
Imported	82.22 (n=183)	76.67 - 87.78	78.26 (n=23)	61.02 - 95.50	78.95 (n=57)	68.27 - 89.62
Median Age (IQR)	33.0 (25.0- 42.0)	-	30.0 (20.0- 43.0)	-	35.5 (27.0- 41.25)	-
Locally Acquired	28.0 (17.25- 40.75)	-	30.0 (20.0- 43.0)	-	14.5 (8.75- 25.0)	-

Imported	35.0 (28.0-46.0)	-	33.0 (31.0-39.5)	-	36.0 (28.0 - 41.75)	-
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Table 3: Results of the univariable and multivariable logistic regression analysis to identify risk factors associated with imported infections compared to indigenous. The odds ratios (OR) and adjusted odds ratios (AOR) are presented, respectively, with the corresponding 95% Confidence Intervals (CI) and p-value.

	Univariable Analysis			Multivariable Analysis		
	OR	95% CI	P-value	AOR	95% CI	P-value
Epidemic Period						
Pre-Epidemic	1	-	-	1.0	-	-
Epidemic Year	-3.26	-3.74 - -2.79	<0.0001	-2.57	-3.31 - -1.84	<0.0001
Post-Epidemic	2.33	1.29 - 3.37	<0.0001	3.73	2.47 - 4.99	<0.0001
Year	-0.32	-0.39 - -0.26	<0.0001	-0.24	-0.37 - -0.12	<0.0001
Island						
Boa Vista	1.0	-	-	1.0	-	-
Santiago	-1.15	-2.07 - -0.24	0.01	1.89	0.32 - 3.46	0.0182
Sao Vicente	3.42	1.24 - 5.60	0.0021	6.96	4.40 - 9.53	<0.0001
Other	16.46	-964.19 - 997.11	0.9737	19.11	-1266.64 - 1304.86	0.9768
Sex (M)	0.57	0.21 - 0.93	0.0018			
Age	0.02	0.01 - 0.03	<0.0001	0.03	0.02 - 0.05	<0.0001
Log10(Pop Size)	-3.35	-4.11 - -2.58	<0.0001	-1.34	-2.51 - -0.18	0.0236
Epidemic period (July-Oct 2017)	-3.84	-4.42 - -3.25	<0.0001			

Figures

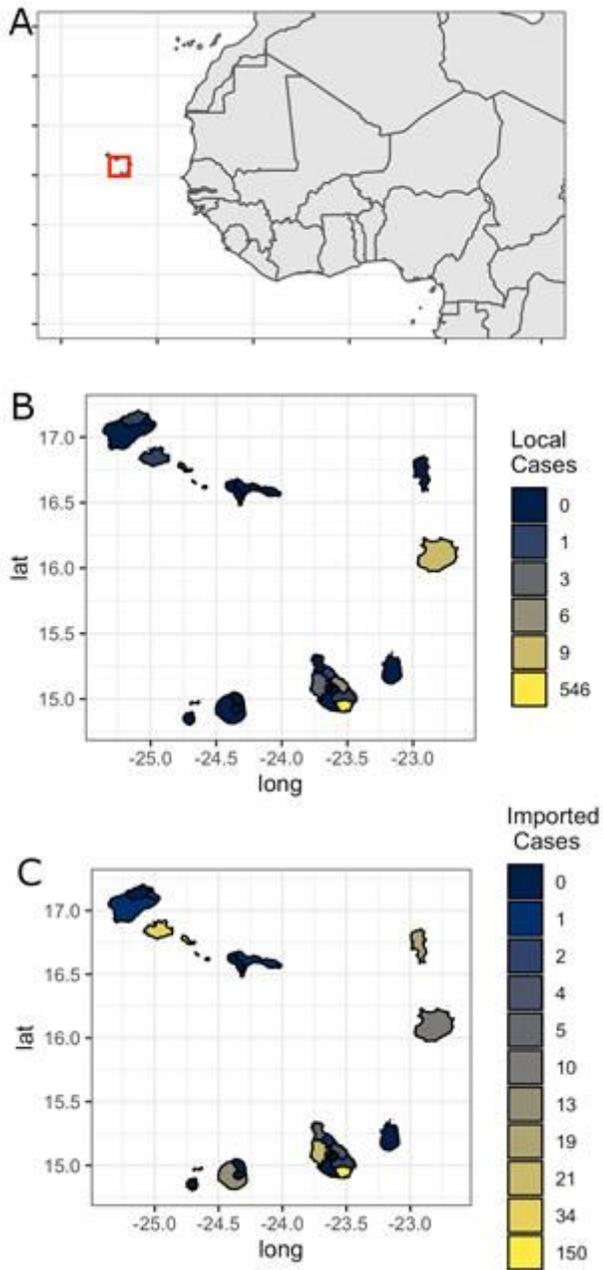


Figure 1

The location of Cabo Verde (A) shown in red off the coast of Senegal, in reference to continental Africa. Total number of locally acquired (B) and imported malaria cases (C) in Cabo Verde between 2010 and 2019 by municipality.

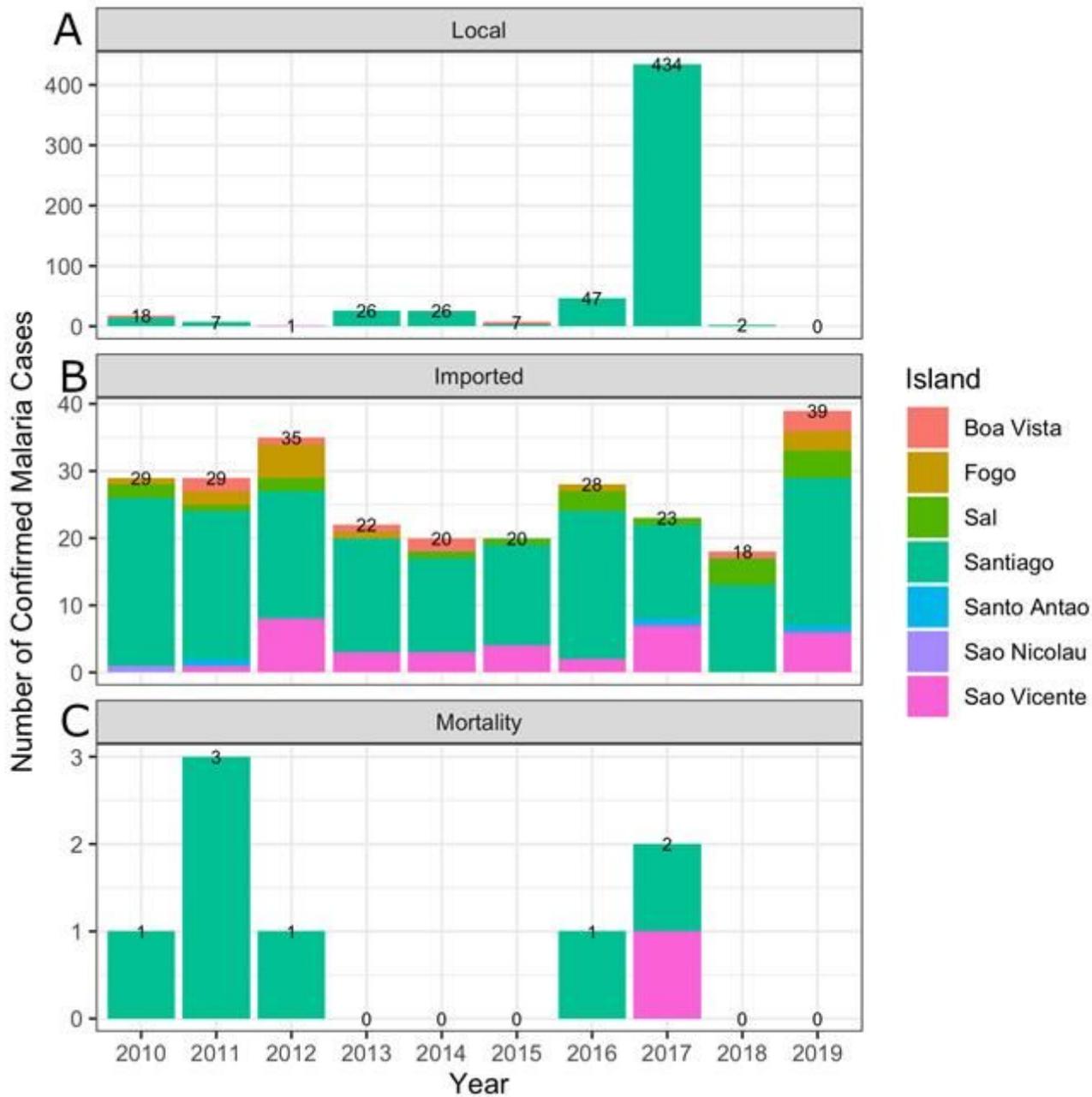


Figure 2

The total number of malaria cases (A), imported infections (B) and deaths (C) per year. The different colours within each bar represent the number of events reported by each island, with each bar labelled with the total number of cases per year.

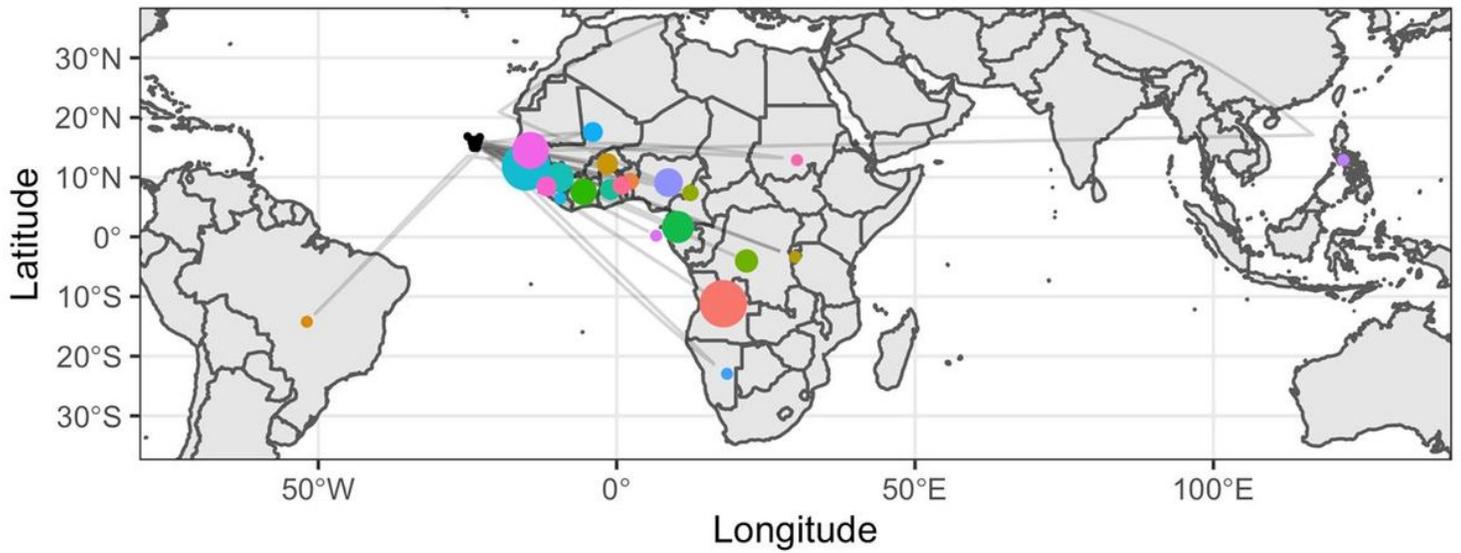


Figure 3

Global map showing the likely origin of imported infections that were reported in Cabo Verde between 2010 and 2019. The size of the circle is scaled according to the number of cases likely originating in that country, with the different colors shown to differentiate the different countries. The location of Cabo Verde is shown as the black circles and connector lines shown in light grey. 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 or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

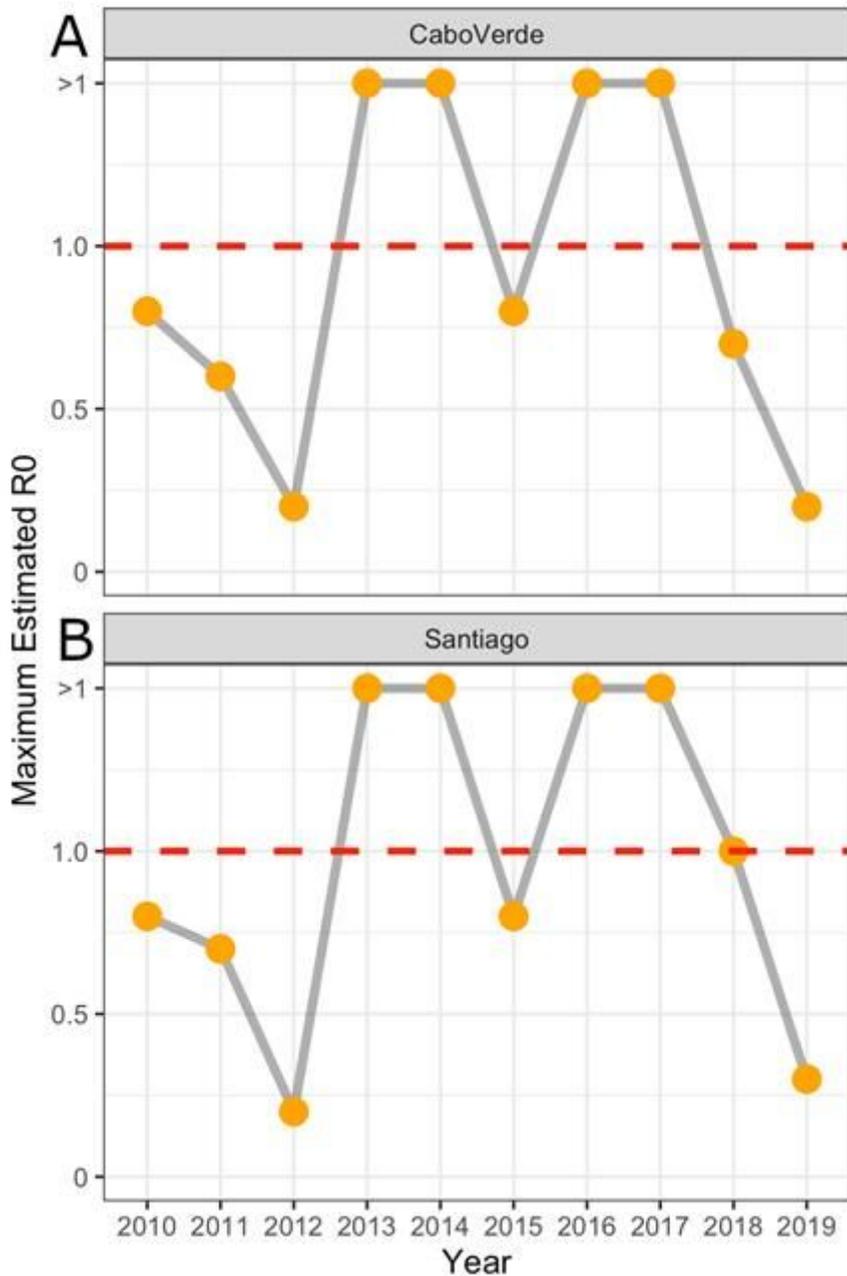


Figure 4

Estimated annual R0 according to the ratio of imported to local cases reported for Cabo Verde (A) and Santiago Island only (B) where there were sufficient cases (min 10 cases required for models) per year to obtain estimates. The y-axis presents the maximum estimate of R0 that is plausible based on the data with year presented on the x-axis. The red dashed line shows where R0 equals 1 whereby above this line transmission is increasing and below, transmission is expected to die out.