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**When local phytotherapies meet biomedicine. Cross-sectional study of knowledge and intercultural practices against malaria in Eastern French Guiana.**

1 G. Odonne<sup>1</sup>, L. Musset<sup>2</sup>, C. Cropet<sup>3</sup>, B. Philogene<sup>4</sup>, M. Gaillet<sup>5</sup>, M.-A. Tareau<sup>1</sup>, M. Douine<sup>3,6</sup>, C.  
2 Michaud<sup>5</sup>, D. Davy<sup>1</sup>, L. Epelboin<sup>3,7</sup>, Y. Lazrek<sup>2</sup>, P. Brousse<sup>5</sup>, P. Travers<sup>5</sup>, F. Djossou<sup>7</sup>, E.  
3 Mosnier<sup>7,8</sup>

4

5 **Authors affiliations:**

6 <sup>1</sup> UMR 3456 LEEISA (Laboratoire Ecologie, Evolution, Interactions des Systèmes Amazoniens),  
7 CNRS, Université de Guyane, IFREMER, Cayenne, French Guiana

8 <sup>2</sup> Laboratoire de parasitologie, Centre National de Référence du Paludisme, Pôle Zones  
9 Endémiques, WHO Collaborating Center for Surveillance of Antimalarial Drug Resistance,  
10 Institut Pasteur de la Guyane, 23 avenue Pasteur, Cayenne, French Guiana.

11 <sup>3</sup> Centre d'Investigation Clinique Antilles Guyane – Inserm 1424, Centre Hospitalier de  
12 Cayenne Andrée Rosemon, rue des flamboyants, Cayenne, French Guiana.

13 <sup>4</sup> DAAC NGO, Saint Georges de l'Oyapock, French Guiana

14 <sup>5</sup> Pôle santé publique Recherche, Coordination des Centres délocalisés de prévention et de  
15 soin, Centre hospitalier de Cayenne Andrée Rosemon, Cayenne, French Guiana

16 <sup>6</sup> TBIP, U1019-UMR9017-CIIL (Centre d'Infection et d'Immunité de Lille), Université de  
17 Guyane, Université de Lille, CNRS, Inserm, Institut Pasteur de Lille, Cayenne, French Guiana

18 <sup>7</sup> Unité de Maladies Infectieuses et Tropicales, Centre Hospitalier de Cayenne Andrée  
19 Rosemon, Cayenne, French Guiana

20 <sup>8</sup> SESSTIM (Sciences Economiques & Sociales de la Santé & Traitement de l'Information  
21 Médicale), Aix Marseille University, INSERM, IRD, Marseille, France

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23

24

25 **\*Corresponding Author:**

26 Guillaume Odonne: guillaume.odonne@cirs.fr

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28 **Keywords:** medicinal plants, traditional phytotherapies, Amazonia, integrated community  
29 survey, medical pluralism, knowledge attitudes and practices

30

31 **Abstract**

32 **Ethnopharmacological relevance**

33 In French Guiana, traditional phytotherapies are an important part of self-healthcare,  
34 however, a precise understanding of the interactions between local phytotherapies and  
35 biomedicine is lacking. Malaria is still endemic in the transition area between French Guiana  
36 and Brazil, and practices of self-treatment, although difficult to detect, have possible  
37 consequences on the outcome of public health policies.

38 **Aim of the study**

39 The objectives of this research were 1) to document occurrences of co-medication  
40 (interactions between biomedicine and local phytotherapies) against malaria around Saint-  
41 Georges de l'Oyapock (SGO), 2) to quantify and to qualify plant uses against malaria, 3) and  
42 to discuss potential effects of such co-medications, in order to improve synergy between  
43 community efforts and public health programs in SGO particularly, and in Amazonia more  
44 broadly.

45 **Materials and methods**

46 This cross-sectional study was conducted in 2017 in SGO. Inhabitants of any age and  
47 nationality were interviewed using a questionnaire (122 questions) about their knowledge  
48 and habits regarding malaria, and their use of plants to prevent and treat it. They were  
49 invited to show their potential responses on a poster illustrating the most common  
50 antimalarial plants used in the area. In order to correlate plant uses and malaria  
51 epidemiology, all participants subsequently received a medical examination, and malaria  
52 detection was performed by Rapid Diagnostic Test (RDT) and Polymerase Chain Reaction  
53 (PCR).

54 **Results**

55 A total of 1,566 inhabitants were included in the study. Forty-six percent of them declared  
56 that they had been infected by malaria at least once, and this rate increased with age. Every  
57 person who reported that they had had malaria also indicated that they had taken  
58 antimalarial drugs (at least for the last episode), and self-medication against malaria with  
59 pharmaceuticals was reported in 142 cases. A total of 550 plant users was recorded (35.1%  
60 of the interviewed population). Among them 95.5% associated pharmaceuticals to plants. All  
61 plants reported to treat malaria were shared by every cultural group around SGO, but three  
62 plants were primarily used by the Palikur: *Cymbopogon citratus*, *Citrus aurantifolia* and  
63 *Siparuna guianensis*. Two plants stand out among those used by Creoles: *Eryngium foetidum*  
64 and *Quassia amara*, although the latter is used by all groups and is by far the most cited  
65 plant by every cultural group. Cultivated species accounts for 91.3% of the use reports, while  
66 wild taxa account for only 18.4%.

67

68 **Conclusions**

69 This study showed that residents of SGO in French Guiana are relying on both traditional  
70 phytotherapies and pharmaceutical drugs to treat malaria. This medical pluralism is to be  
71 understood as a form of pragmatism: people are collecting or cultivating plants for medicinal  
72 purposes, which is probably more congruent with their respective cultures and highlights the  
73 wish for a certain independence of the care process. A better consideration of these  
74 practices is thus necessary to improve public health response to malaria.

75

76 **1. Introduction**

77 In French Guiana, as elsewhere in Amazonia and more widely in Latin America, traditional  
78 phytotherapies are still an important part of self-healthcare (Fleury, 2007, 2017; Grenand et  
79 al., 2004; Odonne et al., 2011; Tareau et al., 2017; Vigneron et al., 2005). However, a precise  
80 understanding of the articulations between local phytotherapies and biomedicine is lacking  
81 in this area. This question has not been much addressed in Latin America in general (Calvet-  
82 Mir et al., 2008; Vandebroek et al., 2004), and is beginning to emerge as an important  
83 research question even in Europe (Djuv et al., 2013; Welz et al., 2018). Given that local  
84 practices appear to be continuing among young, urban people in French Guiana (Tareau et  
85 al., 2017), a better understanding of these entanglements and their integration with  
86 community behaviors is thus necessary in order to foster global health.

87 French Guiana is a persistent malaria endemic area. The regional control program promotes  
88 the use of insecticide-treated bed nets and provides free and accessible bed nets for  
89 pregnant women, malaria testing and treatment at local health centers (Nathalie, 2015).  
90 Saint-Georges de l'Oyapock (SGO) is particularly affected by malaria (Mosnier et al., 2017;  
91 Musset et al., 2014), and *Plasmodium vivax* is responsible for the large majority of diagnosed  
92 cases over the last 10 years (Mosnier et al., 2020a; Saldanha et al., 2020). This small  
93 multicultural municipality is located along the Oyapock river, the border between French  
94 Guiana and Brazil (Davy et al., 2011; Grenand, 2012). Mostly populated by Amerindians (the  
95 majority Palikur, and a few Kari'puna and Galibi-Marworno), Creole and Brazilian people, it is  
96 the meeting point of the lower Oyapock basin. There, interculturality leads to a discrete,  
97 highly prevalent but not yet documented, medical pluralism. This piece of the European  
98 Union in South America thus experiences singular patterns of medical hybridization. In SGO  
99 it is typical for Amerindian, Brazilian and Creole people to treat with herbal remedies while  
100 also using biomedicine, as has been documented among many other groups in French  
101 Guiana (Grenand et al., 2004; Tareau et al., 2017; Tareau et al., 2019). However, despite the  
102 WHO report on traditional medicine, initiatives aiming to integrate collective and local  
103 knowledge of communities living in malaria endemic areas are very scarce to date (WHO,  
104 2013), and particularly in French Guiana.

105 Hidden use of self-treatment has nevertheless possible consequences on the outcome of  
106 public health policies and might hamper the relationships between the different medical  
107 cultures. When efficient, such treatments might lower the rate of consultation at health  
108 centers, possibly leading to a misunderstanding of the real epidemic situation by  
109 epidemiologists. When partially efficient, they might lead to the persistence of  
110 asymptomatic infections in the less supervised self-medicated population (Okwundu et al.,  
111 2013; Howes et al., 2016). Lastly, when inefficient, they may delay the care of sick patients  
112 or increase the transmission of malaria.

113 This study is part of a broader project, Palustop, aiming at understanding the malaria  
114 epidemics in Eastern French Guiana and at preventing the emergence of resistance to  
115 antimalarial treatments (Mosnier et al., 2019, 2020a; Saldanha et al., 2020).

116 Consequently, the objectives of the work were 1) to document the reality of co-medications  
117 (interactions between biomedicine and local phytotherapies and concomitant use of these  
118 two systems), 2) to quantify and to qualify plant uses against malaria, and 3) to discuss  
119 potential effects of such co-medications, in order to improve synergy between community  
120 efforts and public health programs in Saint-Georges de l'Oyapock, and in Amazonia more  
121 broadly.

## 122 **2. Materials and methods**

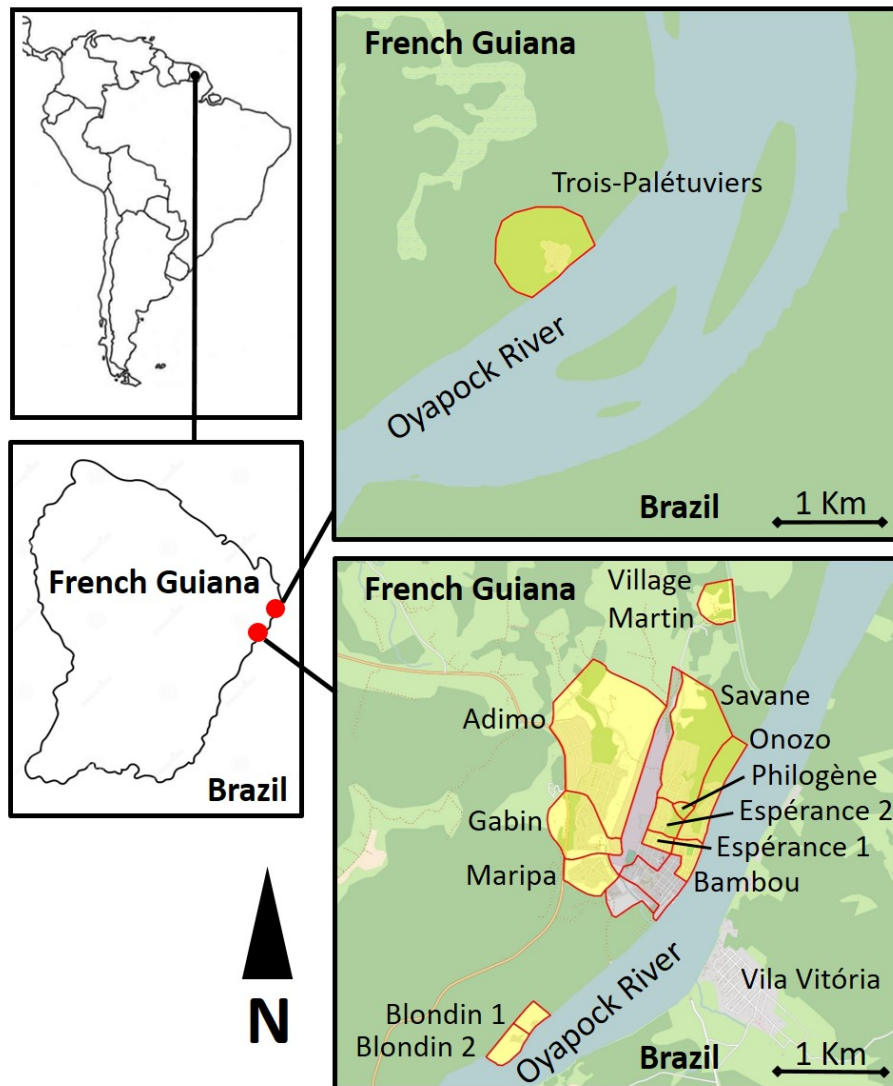
### 123 **2.1. Survey and study area**

124 Saint-Georges de l'Oyapock (Figure 1) is a small French overseas municipality located along  
125 the left bank of the Oyapock River, which forms the border between French Guiana and the  
126 Brazilian state of Amapá. It is inhabited by almost 4,076 people (INSEE, 2020), living mainly  
127 in the city center. The population stems from a great diversity of cultural groups:  
128 Amerindians (mostly Palikur, Wayãpi and Teko from the upper-Oyapock, and a minority of  
129 Karipuna and Galibi-Marworno from Brazil), French Guianese Creoles, a mixed Franco-  
130 Brazilian population, and Brazilian migrants. As discussed in previous works (Tareau et al.,  
131 2020), defining ethnicity in these mixed-populations is difficult, as cultural groups may be  
132 built upon ethnic specificities as much as upon nationalities. We thus adopted the most  
133 common self-denominations (for example Palikur or Creole), and considered the broad  
134 "Brazilian" group, understood as "non-Amerindian Portuguese speaking people". Therefore,  
135 local habits such as agricultural practices or housing types (Ogeron et al., 2018) can vary  
136 widely from one area to another and lifestyles range from swidden cultivators practicing  
137 hunting and fishing in nearby forests and living in open wooden stilt houses in the riverine  
138 areas, to occidental lifestyles with concrete houses. From the biomedical point of view,  
139 people from SGO looking for healthcare can choose between the public (and free) health  
140 center, depending on the general hospital of Cayenne, the main city of French Guiana, and a  
141 unique general practitioner. Health workers from the health center also visit the Trois-  
142 Palétuviers village (a part of SGO municipality further North along the Oyapock River) twice a  
143 month.

144 On the opposite bank of the Oyapock River stands the Brazilian city of Oiapoque, a city of  
145 about 27,270 inhabitants (IBGE, 2020), of which a minority is Palikur, Galibi-Marworno and  
146 Karipuna Amerindians. For medical care, people there can choose between the malaria  
147 health center of Taparabo (a small village facing Trois-Palétuviers on the Brazilian riverbank),  
148 health centers in the indigenous areas (*Casa de Saúde do Índio-CASAI*), and the public  
149 hospital or the public neighborhood health centers (*Unidade Básica de Saúde-UBS*) in  
150 Oiapoque.

151 For the purpose of the study, the village of Saint-Georges de l'Oyapock was divided into 16  
152 areas according to informal geographic and demographic parameters (Figure 1). Thirteen out  
153 of these 16 areas were visited during this study. Three of them were not included in the  
154 study (in grey on Figure 1) for the following reasons: the town center because inhabitants  
155 are rarely affected by malaria, the airport area which is uninhabited and the military camp

156 where soldiers, mainly from mainland France, stay only for short journeys, take preventative  
157 treatment against malaria delivered by the French Armed Forces Health Service in French  
158 Guiana, and thus hardly consult the public health center. Three areas were accessible only  
159 by boat: Blondin 1, Blondin 2 (10 minutes) and Trois-Palétuviers (one hour). The areas  
160 surveyed account for 2,663 people, according to the SGO health center's census.



161  
162 **Figure 1:** Study area, top right: the village of Trois-Palétuviers, bottom right: the village of  
163 Saint-Georges de l'Oyapock showing in yellow the 13 neighborhoods where the study took  
164 place.  
165

## 166 2.2. Interviews

167 This cross-sectional study was conducted between October and December 2017. Inhabitants  
168 of any age and any nationality from the selected areas were invited to participate, with the  
169 aim of approaching a comprehensive census (cf. Mosnier et al., 2019). Community  
170 awareness interventions were conducted during the study to secure the commitment and  
171 participation of a majority of inhabitants. Community engagement started from meetings

172 with the Amerindian community leaders and the village mayor as well as the healthcare  
173 workers and the members of local associations related to health. Stakeholders were  
174 informed of the study objectives, interventions and expected role of the community  
175 (Mosnier et al., 2020b). Meetings were held in neighborhoods in their local language with  
176 trained cultural mediators. Additional mobilization strategies included video clips and  
177 WhatsApp messages.

178 People were interviewed using a questionnaire (122 questions, supplementary data 1)  
179 designed to gather multiple information on risk factors for malaria infection, knowledge of  
180 the disease, and practices in case of fever or malaria (due to a possible overlap between  
181 fever and malaria in vernacular perceptions), with a special focus on remedies (including  
182 plants) and therapeutic itineraries.

183 Questionnaires were administered in either French, Portuguese or Creole by trained cultural  
184 mediators from a NGO (*Développement Accompagnement Animation Coopération Guyane-*  
185 *DAAC*), by nurses or by physicians of the study depending on the questions. Due to the  
186 length and multiple foci of the questionnaire, the results published here are only a selection  
187 of those gathered during this extensive work. Parental agreement was asked for children,  
188 and parents were interviewed on behalf of the child. For some questions (such as knowledge  
189 of the disease and its signs, or those involving food-producing activities), answers were only  
190 taken into account if the interviewee was 15 years of age or older, which corresponds to the  
191 perceived age of adulthood. Therefore, the term 'adult' here indicates people over 15 years  
192 of age unless otherwise specified.

### 193 **2.3. Plant selection**

194 Interviewees were asked whether they used plants to prevent or treat fever or malaria. Due  
195 to multiple correspondences between vernacular and botanical names, they were invited to  
196 point out their potential responses on a poster (supplementary data 2) representing a  
197 selection of 17 medicinal plants potentially used in this area, compiled from available  
198 literature (Cetout and Weniger, 2016; Grenand et al., 2004; Vigneron et al., 2005) and  
199 presenting Portuguese, Palikur, French Guianese Creole and French names when available.

200 The absence of voucher specimens (although uncommon in ethnobotanical studies) is here  
201 justified by the large number of people interviewed (> 1500) and the fact that all the plants  
202 selected were widely known in the area and were clearly displayed in the form of detailed  
203 pictures with accompanying names. Botanical plant names were updated from references  
204 according to *The Plant List* (<http://www.theplantlist.org/>).

### 205 **2.4. Medical attention and malaria detection**

206 In order to correlate plant uses and malaria epidemiology, all participants subsequently  
207 received a medical examination. Temperatures were taken with an ear thermometer to  
208 estimate fever, which was defined as a temperature of  $\geq 38^{\circ}\text{C}$  according to Oyakhirome et al.,  
209 2010. Malaria detection was performed by Rapid Diagnostic Test (RDT) and Polymerase  
210 Chain Reaction (PCR). The RDT used was the SD BIOLINE Malaria Ag Pf/Pan test



211 (pfHRP2/pLDH), as used in all French Guianese health centers and Malaria PCR detection was  
212 performed as previously described in Mosnier et al. (2019). This allowed the formation of  
213 *Plasmodium* positive (*Plasmodium*+) and *Plasmodium* negative (*Plasmodium*-) study groups.  
214 If RDT or PCR results were positive, voluntary participants were treated for free with a  
215 combination of arthemeter and lumefantrine (*P. falciparum* infection) or chloroquine and  
216 primaquine, according to the standard therapeutic scheme used in French Guiana (for *P.*  
217 *vivax* infection).

## 218 **2.5. Data analysis**

219 Data analysis was conducted with STATA 13. Basic social and demographic characteristics  
220 were presented as percentage and frequencies. Continuous variables were described with  
221 median and interquartile groupings. Chi-square tests were employed to assess any  
222 significant difference in knowledge and practices between participants who used local  
223 phytotherapies versus those who did not.

224 Maps were created using QGIS 2.3.

## 225 **2.6. Ethics statement**

226 The study was approved by the *Comité de Protection des Personnes du Sud-Ouest et Outre-*  
227 *Mer 4* N° AM-36/1/ CPP15-024. The database was anonymized and declared to the  
228 *Commission Nationale Informatique et Libertés* (n°917186).

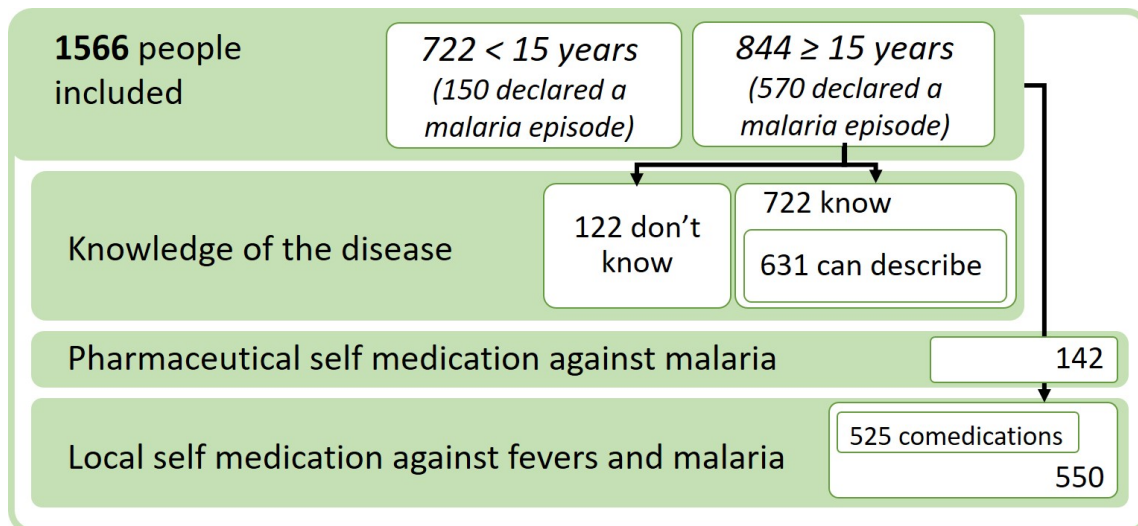
229 Before commencing fieldwork, the study was presented to and approved by the leaders of  
230 Amerindian communities and by the municipality of SGO according to the Nagoya protocol.

231 As the plants presented to the interviewees were selected from bibliographical sources and  
232 are widely known and their knowledge shared among many communities, legal  
233 authorization from the French Ministry of Environment was not necessary (according to  
234 French law N° 2016-1087 of the 8<sup>th</sup> of August 2016).

## 235 **3. Results**

### 236 **3.1. Sociodemographic and practices details of participants**

237 A total of 1,566 inhabitants were included in the study (figure 2). Median age was 23.3 years  
238 [22.1-24.1], and 36.7 [35.6-37.8] for only those over 15 years old. Sex ratio of males to  
239 females was 0.88, or 0.75 for those over 15. More than a half of the participants had French  
240 nationality (56.7% 888/1,566), 42.7% (668/1,566) had Brazilian nationality and 0.6%  
241 (10/1,566) reported to have another nationality. A third (32.6%; 513/1,566) of participants  
242 declared themselves to belong to the Brazilian community. People from Amerindian  
243 communities represented 31.7% (498/1,566) of whom a majority was Palikur (74.7%;  
244 372/498) followed by Karipuna (14.5%; 72/498), Teko (7.8%; 39/498) and Wayãpi (3%;  
245 15/498). Lastly, 23.7% (n=371) and 6% (n=98) were French Guianese Creoles and French  
246 from mainland France, respectively.



247

248 **Figure 2:** Flowchart of the study

249

250 A majority (78.2%; 1,225/1,566) of participants had an effective health insurance (French  
 251 universal health coverage or Brazilian social coverage or French social security), and 21.8%  
 252 (n=341) had none or had a precarious coverage (no social coverage or unknown status or  
 253 French state medical assistance (AME), which is a social coverage for migrants without a  
 254 residency permit). The large majority of inhabitants (88.7%; 1,385/1,566) live in households  
 255 counting less than ten people.

256 Many of the interviewees were under 15 (46.1%; 722/1,566) of which 79.2% (572/722)  
 257 declared themselves to be pupils. Others were too young to be in school. Among the 844  
 258 people over 15 years old (53.9%; 844/1,566), a large proportion reported that they work at  
 259 home (39.5%; 333/844). People working outdoor (as single occupation workers, excluding  
 260 informal multiple activities) as farmers, hunters, fishermen or pirogue drivers accounted for  
 261 12.8% (108/844), 4.4% (37/844), 3.3% (28/844) and 0.5% (4/844) respectively. Very few  
 262 participants reported to be employed in the center of SGO or in Oiapoque city (11.0%;  
 263 93/844).

### 264 **3.2. Knowledge of malaria disease**

265 Out of the 844 people over 15 years old at the date of the interview, 722 knew the malaria  
 266 disease, at least conceptually (85.5%), and 631 were able to describe at least one sign  
 267 related to the disease (74.8%) from a restricted list of symptoms (figure 2). The symptoms  
 268 most cited by the interviewees, in decreasing order, are: headache (75.9%; 479/631), fever  
 269 (62.9%; 397/631), aching muscles (48.0%; 303/631), chills (40.6%; 256/631), tiredness  
 270 (27.6%; 174/631) and abdominal pain (23.0%; 145/631).

271 Out of the 722 people who know the disease, most are aware of its transmission by  
 272 mosquitos (83.4%; 602/722), while 12.7% (92/722) are unaware of the transmission mode of  
 273 the disease.

274 Regarding preventive practices, use of mosquito nets is the most frequently cited (57.8%;  
275 417/722), followed by the emptying of water containers for 19.8% of participants (143/722).  
276 Use of repellent sprays (19.7%; 142/722) and of indoor insecticides (13.3%; 96/722) follows.  
277 Use of long clothes is reported by 8.0% (58/722). Those citing the use of preventive  
278 pharmaceutical tablets or medicinal plants are 7.1% (51/722) and 6.8% (49/722) of the  
279 sample respectively. Lastly, outdoor spraying seems not to appear as a common practice,  
280 with only 2.9% (21/722) of people citing it. People who had no response to this question are  
281 nevertheless numerous, 163 respondents (22.6%).

### 282 **3.3. Cases of malaria among the population**

283 Forty-six percent (720/1,566) of participants declared that they had been infected by malaria  
284 at least once, and this rate increased with age: from 20.7% (150/722) among persons under  
285 15 years old to 67.4% (570/844) among participants older than 15. Experience of previous  
286 malaria infections is highly variable from one locality to another, ranging from 96% already  
287 affected at Martin village to 27.9% at Adimo (supplementary data 3). Other data relative to  
288 local epidemiology are available in Mosnier et al. (2019).

### 289 **3.4. Fever and malaria diagnostic and treatment perspectives**

290 When people experience fever in general or malaria in particular, they reported *often* trying  
291 to consult an official health practitioner (58.4%; 915/1,566), while 36.9% (578/1,566) and  
292 4.7% (73/1,566) declared that they *rarely* or *never* go to the health center, respectively.

293 Among the 651 people that *rarely* or *never* go to the health center, the reasons cited are: the  
294 short length of the fever (46.9%; 305/651), followed by the absence of other symptoms  
295 (26.3%; 171/651), then by the remoteness of the dispensary (6.5%; 42/651). Lastly, 133  
296 people (20.4%) did not answer or answered with other unspecified reasons. Spatial  
297 opportunistic strategies regarding the access to health facilities seems limited. For example,  
298 in the Trois-Palétuviers area, only 10% (18/181) of the participants reported a visit in the  
299 Brazilian health centers of Taparabo or Oiapoque. In case of health management in  
300 Oiapoque, 43.3% (26/60) of participants of the study reported having been at the hospital of  
301 the city, 25% (15/60) at an indigenous health center (CASAI), 20% (12/60) at public  
302 neighborhood health centers (UBS), 6.7% (4/60) at a malaria health center and only 5%  
303 (3/60) in non-institutional health centers or a traditional practitioner's office.

### 304 **3.5. Malaria and fever treatments**

305 People over 15 years old who are aware of malaria (n=722), when asked what kind of  
306 treatment is able to treat malaria specifically, responded both biomedical treatments  
307 (86.3%; 623/722) and traditional practices, which encompass medicinal plants (19.3%;  
308 139/722) and spiritual healing (1.2%; 9/722). One hundred people answered both  
309 pharmaceuticals and plants/spiritual healing (13.9%; 100/722).

310

311 **3.5.1. Biomedical treatments against malaria**

312 Every person among the 720 who declared that they had had a confirmed case reported that  
313 they took antimalarial drugs (at least for the last episode) mainly provided by the health  
314 center or the pharmacy of Saint Georges (57.2%; 412/720 and 15.4%; 111/720, respectively)  
315 or from another institution in French Guiana for 8.7% (63/720), while 18.6% of participants  
316 reported to have consumed Brazilian drugs from the city of Oiapoque (12.4%; 89/720) or  
317 from another place in Brazil (6.2%; 45/720).

318 Self-medication against malaria with pharmaceuticals was reported in 142 cases. However,  
319 the large majority mentioned taking symptomatic medications such as  
320 acetaminophen/paracetamol (71.1%; 101/142). The use of an anti-malarial in self-  
321 medication was reported by 16.2% of the patients (23/142), and was mostly chloroquine  
322 (10.6%; 15/142), then primaquine (2.8%; 4/142), atovaquone-proguanil in 2 cases (1.4%) and  
323 Artecom® (dihydroartemisinin-piperazine-trimethoprim) or doxycycline in 1 case each  
324 (0.7%). Eighteen participants (12.4%) reported self-medication with other medications, of  
325 which 11 were unknown treatments.

326 **3.5.2. Phytotherapies to prevent and/or treat fever and malaria symptoms**

327 Questions related to plants were widened to malaria and fevers in general, as many plant  
328 users cannot confirm that the disease was malaria due to the absence of a diagnostic test.  
329 These questions concerned the whole sample (both adults and children), because parents  
330 reported which plants they gave to their children. A total of 550 plant users were counted,  
331 which represented 35.1% of the interviewed population. Among them, 79.5% and 20.5%  
332 (437/550 and 113/550) reported that they *sometimes* or *often* use traditional herbal  
333 medicine, respectively. The majority (60.4%; 335/550) declared that they use only one plant,  
334 25.8% (142/550) and 13.8% (73/550) reported the use of up to two and three plants at the  
335 same time, respectively.

336 **3.5.3. Complex therapeutic itineraries**

337 Out of all the participants (children and parents included) who reported that they took  
338 plants in case of fever or malaria, a large majority utilized pharmaceuticals as well (95.5%;  
339 525/550). More precisely, 40.5% (223/550) took herbal drugs after pharmaceuticals when  
340 they thought the pharmaceuticals were not effective enough. Some people, 25.6%  
341 (141/550), took plants and pharmaceuticals simultaneously, and 20.4% (112/550) took  
342 plants first and switched to pharmaceuticals afterward because the plants were found not to  
343 be effective enough. Finally, 8.9% (49/550) used both without describing modalities, and  
344 4.5% (25/550) decided to use plants only.

345

346 **3.6. Medicinal plant uses**347 **3.6.1. Factors associated with the use of plants**

348 It appeared from the interviews that medicinal plant uses were not homogeneous across the  
 349 population of SGO (Table 1). People using plants were older than those not using them, 28 vs  
 350 20.7 years old ( $p < 0.005$ ), and gender did not affect the use of medicinal plants ( $p = 0.4$ ).

351

352 Table 1: Main factors associated with the use of medicinal plants against fever and malaria in  
 353 Saint-Georges de l'Oyapock

	Not using plants N=1016	Using plants N=550	p-value	Not Using plants / $\geq 15$ years old N=497	Using plants / $\geq 15$ years old N=347	p-value
<b>Age (Median) [IQR]*</b>	20.7 [19.6-21.8]	28.0 [26.3-29.8]	<0.005	34.5 [33.1-36.0]	39.8 [38.1-41.5]	<0.005
<b>Gender of participants</b>			0.40			0.17
Female	65.8% (547)	34.2% (284)		60.9% (293)	39.1% (188)	
Male	63.8% (469)	36.2% (266)		56.2% (204)	43.8% (159)	
<b>Nationality</b>			0.005			0.41
French	68.2% (606)	31.8% (282)		61.1% (215)	38.9% (137)	
Brazilian	60.3% (403)	39.7% (265)		57.1% (277)	42.9% (208)	
Other	70.0% (7)	30.0% (3)		71.4% (5)	28.6% (2)	
<b>Cultural group</b>			<0.001			<0.001
Amerindians	51.8% (258)	48.2% (240)		45.1% (133)	54.9% (162)	
French Guianese Creoles	61.5% (228)	38.5% (143)		58.8% (100)	41.2% (70)	
French from mainland France	85.7% (84)	14.3% (14)		77.8% (28)	22.2% (8)	
Brazilians	75.8% (389)	24.2% (124)		69.8% (213)	30.2% (92)	
Other	66.3% (57)	33.7% (29)		60.5% (23)	39.5% (15)	
<b>Health insurance</b>			0.003			0.37
No or AME**	58.8% (234)	41.2% (164)		56.6% (146)	43.4% (112)	
Standart social coverage	67.0% (782)	33.0% (386)		59.9% (351)	40.1% (235)	
<b>Level of education</b>						<0.001
$\leq$ primary school				41.9% (109)	58.1% (151)	
> primary school				66.4% (388)	33.6% (196)	
<b>Number of people in household</b>	6.4 [6.2-6.6]	6.6 [6.3-6.9]	0.8			
<b>Neighborhood</b>			<0.001			<0.001
Trois-Palétuviers	44.3% (81)	55.7% (102)		42.2% (35)	57.8% (48)	
Adimo	64.0% (71)	36.0% (40)		51.6% (32)	48.4% (30)	

Bambou	77.8% (35)	22.2% (10)		63.6% (14)	36.4% (8)	
Blondin 1	90.9% (10)	10.1% (1)		100.0% (8)	0% (0)	
Blondin 2	65.9% (29)	34.1% (15)		40.9% (9)	59.1% (13)	
Espérance 1	69.6% (55)	30.4% (24)		64.7% (33)	35.3% (18)	
Espérance 2	68.6% (94)	31.4% (43)		61.3% (46)	38.7% (29)	
Gabin	72.6% (82)	27.4% (31)		73.7% (42)	26.3% (15)	
Maripa	77.8% (42)	22.2% (12)		74.1% (20)	25.9% (7)	
Onozo	70.2% (177)	29.8% (75)		61.8% (89)	38.2% (55)	
Philogène	41.6% (32)	58.4% (45)		38.1% (16)	61.2% (26)	
Savane	68.2% (290)	31.8% (135)		61.7% (142)	38.3% (88)	
Village Martin	51.4% (18)	48.6% (17)		52.4% (11)	47.6% (10)	
<b>Swidden agriculture</b>						<0.001
Yes				47.3% (202)	52.7% (225)	
no				70.7% (295)	29.3% (122)	
<b>Fishing</b>						<0.001
Yes				46.9% (143)	53.1% (162)	
No				65.7% (354)	34.3% (185)	
<b>Hunting</b>						<0.001
Yes				44.0% (92)	56.0% (117)	
No				63.8% (405)	36.2% (230)	
<b>Occupation</b>			<0.001			
Farmer	42.3% (47)	57.7% (64)				
Hunter	55.3% (21)	44.7% (17)				
Work at home	61.0% (203)	39.0% (130)				
Student/Pupil	71.0% (406)	29.0% (166)				
Goldminer	0% (0)	100% (1)				
Fisherman	39.3% (11)	60.7% (17)				
Canoe driver	25.0% (1)	75.0% (3)				
Pensioner	64.9% (24)	35.1% (13)				
Employee in SGO village	71.0% (66)	29.0% (27)				
Others	67.9% (237)	32.1% (112)				
<b>Previous medical history of malaria</b>			<0.001			<0.001
Yes	52.8% (380)	47.2% (340)		52.3% (298)	47.7% (272)	
No	75.2% (636)	24.8% (210)		72.6% (199)	27.4% (75)	
<b>Number of previous malaria infections Median [IQR] *</b>	2.8 [2.5-3.2]	3.6 [2.9-4.3]	0.007	3.1 [2.7-3.6]	4.0 [3.2-4.9]	0.015
<b>Using bed nets</b>			<0.001			<0.001
Yes	60.5% (701)	39.5% (457)		55.4% (347)	44.6% (279)	
No	77.2% (315)	22.8% (93)		68.8% (150)	31.2% (68)	

<b>Plasmodium RDT carriage</b>			0.42			0.68
Yes	53.8% (7)	46.2% (6)		66.7% (4)	33.3% (2)	
No	64.7% (988)	35.3% (539)		58.4% (485)	41.6% (345)	
<b>Plasmodium PCR carriage</b>			0.004			0.03
Yes	51.0% (51)	49.0% (49)		46.5% (33)	53.5% (38)	
No	65.2% (913)	34.8% (488)		59.7% (455)	40.3% (307)	
*IQR: interquartile intervals **AME: State Medical Assistance - Social coverage for immigrants without a residency permit or a document proving that immigrant have begun the application process for legal residency						

354

355 Among people over 15 years old, education level seems to have an influence on plant use, as  
356 those who have a lower than primary level of schooling are 21.9% among the non-users,  
357 while they are 43.5% among the plant users (109/497 vs 151/347;  $p < 0.001$ ).

358 A trend appears in relation to social insurance, as 41.2% of people with no insurance or AME  
359 use plants, while 33.0% of people with standard health insurance do (164/398 vs 386/1168;  
360  $p = 0.003$ ). Nevertheless, when considering only the adults, there is no significance at all  
361 ( $p = 0.37$ ).

362 Interestingly, adults engaged in nature based activities are more prone to be medicinal plant  
363 users. As an example, 52.7% of people practicing swidden agriculture are plant users, while  
364 they are only 29.3% among those who don't practice local agriculture (225/427 vs 122/417;  
365  $p < 0.001$ ). The same statement applies to fishers, with 53.1% of fishers that use plants  
366 (162/305) vs 34.3% of non-fishers (185/539) ( $p < 0.001$ ) or hunters with respectively 56.0% of  
367 users among hunters (117/209) vs 36.2% (230/635) ( $p < 0.001$ ). These values might also  
368 reflect the large proportion of Amerindians in medicinal plant users. Indeed, the distribution  
369 among maternal language (with both adults and children) shows a neat pattern ( $p < 0.001$ ), as  
370 48.2% of Amerindian native speakers (mostly Palikur and Karipuna) are using plants  
371 (240/498), while Creoles are only 38.5% (144/371), Brazilian 24.2% (124/513) and French  
372 14.3% (14/98). This observation is further supported by the relative heterogeneity of plant  
373 use frequency in the different areas of Saint Georges (supplementary data 4 & 5). For  
374 example, inhabitants from Trois-Palétuviers, Philogène and Village Martin, where the Palikur  
375 population is largely predominant, are more prone to use medicinal plants.

376 Lastly, adults who already experienced malaria were more prone to use medicinal plants,  
377 (47.7%; 272/570) than those who hadn't (27.4%; 75/274);  $p < 0.001$ ).

### 378 **3.6.2. Most used plants**

379 A total of 694 use reports (URs) were counted, including 582 citations for the plants of the  
380 poster and 112 for other non-identified species. Table 2 presents the result of the most cited  
381 plants organized by citation frequency.  
382

383 **Table 2:** Citation frequency of plants against fevers and malaria

<i>Species names (Botanical family)</i>	<b>Use reports</b> N=694	<b>Citation frequency</b>	<b>Agricultural status</b>
<i>Quassia amara</i> L. ( <b>Simaroubaceae</b> )	226	32.6%	C*
<i>Cymbopogon citratus</i> (DC.) Stapf ( <b>Poaceae</b> )	92	32.6%	C
<i>Eryngium foetidum</i> L. ( <b>Apiaceae</b> )	68	9.8%	C
<i>Citrus aurantiifolia</i> (Christm.) Swingle ( <b>Rutaceae</b> )	49	7.1%	C
<i>Bryophyllum pinnatum</i> (Lam.) Oken ( <b>Crassulaceae</b> )	26	3.7%	C
<i>Siparuna guianensis</i> Aubl. ( <b>Siparunaceae</b> )	22	3.2%	W**
<i>Petiveria alliacea</i> L. ( <b>Phytolaccaceae</b> )	20	2.9%	C
<i>Solanum leuocarpon</i> Dunal ( <b>Solanaceae</b> )	13	1.9%	W
<i>Eupatorium triplinerve</i> Vahl ( <b>Asteraceae</b> )	12	1.7%	C/W
<i>Geissospermum</i> spp. ( <b>Apocynaceae</b> ) <i>G. argenteum</i> Woodson, <i>G. sericeum</i> Miers, <i>G. laeve</i> (Vell.) Miers	12	1.7%	W
<i>Phyllanthus</i> spp. ( <b>Phyllanthaceae</b> ) <i>P. amarus</i> Schumach. & Thonn.; <i>P. niruri</i> L.	12	1.7%	W
<i>Picrolemma sprucei</i> Hook f. ( <b>Simaroubaceae</b> )	10	1.4%	W
<i>Aristolochia</i> spp. ( <b>Aristolochiaceae</b> ) <i>A. stahelii</i> O.C. Schmidt, <i>A. mossii</i> S.Moore, <i>A. trilobata</i> L.	9	1.3%	C/W
<i>Zanthoxylum rhoifolium</i> Lam. ( <b>Rutaceae</b> )	7	1.0%	W
<i>Mikania micrantha</i> Kunth ( <b>Asteraceae</b> )	4	0.6%	W
Other non-identified species	112	16.1%	-
*C: cultivated; **W: wild			

384

385 The number of taxa collected wild or cultivated is relatively similar (9 cultivated vs 10 wild),  
 386 but interestingly, cultivated species accounts for 91.3% of the use reports of identified  
 387 species (502/550), while wild taxa account for only 18.4% (101/550) (total >100% due to  
 388 species found both wild or cultivated). This trend is similar for women and men.

389 Concerning the uses of the plants, there are no significant differences between plants  
 390 considering gender or ethnicity at the global level, although some trends are interesting to  
 391 discuss.

392 All the plant listed are commonly used by every cultural groups around SGO, but three plants  
 393 are used mostly by the Palikur. They are *Cymbopogon citratus* (44.6% of the total of its use  
 394 reports; 41/92; p=0.1), *Citrus aurantifolia* (48.9%; 24/49; p=0.03) and *Siparuna guianensis*  
 395 (40.1%; 9/22; non-significant). Two plants stand out as used mostly by the Creoles: *Eryngium*  
 396 *foetidum* (39.7%; 27/68; p=0.03) and *Quassia amara* (35.8%; 81/226; p<0.0001), although  
 397 the latter is by far the most cited plant by every cultural group.

398



399 **3.6.3. Modes of preparation and administration of herbal remedies**

400 A total of 662 recipes are described, among which infusions/decoctions stand out (93.5%;  
401 619/662), followed by fresh crushed plants (4.7%; 31/662), alcoholic macerations (1.2%;  
402 8/662) and dry crushed plants (0.6%; 4/662).

403 Leaves are the most frequently used plant part, with 67.6% of the URs for *E. foetidum*  
404 (46/68), 95.6% for *Q. amara* (216/226), 94.6% for *C. citratus* (87/92) and 53.1% for *C.*  
405 *aurantiifolia* (26/49), along with fruit for *C. aurantiifolia* (34.7%, 17/49).

406 Concerning these plants, the main administration route is unequivocally oral, with 97.1%  
407 (66/68), 83.6% (189/226), 77.2% (71/92) and 91.8% (45/49) of the citations, respectively. *C.*  
408 *citratus* is nevertheless also used as a bath (18.5%; 17/92).

409 **3.6.4. Influence of plant uses on parasitaemia**

410 This section aims to establish a correlation between medicinal plant use and biological  
411 results. Considering *Plasmodium* spp. carriage detected with a rapid diagnostic test (RDT), it  
412 is impossible to conclude ( $p=0.42$ ) due to a very low proportion of positive results (13).

413 When considering *Plasmodium* spp. carriage detected by PCR, it appears that infection is  
414 correlated to medicinal plant use in general ( $p=0.004$ ), which is probably the result of several  
415 confounding factors hampering a proper interpretation of these results.

416 **4. Discussion**

417 This study offers insight into the complex processes of intercultural therapeutic practices  
418 that are too often under-evaluated. The prevalence of medical pluralism demonstrated here  
419 is of utmost importance for public health in French Guiana and in Latin America in general.

420 **4.1. Limitations**

421 One of the major limitations of this study is the self-reported nature of the data collected.  
422 Despite the participation of professional cultural mediators, who helped interviewees to  
423 understand the questions, uncertainty remains about the accuracy of some responses, for  
424 example when more people answer they had a test for malaria than those which answered  
425 that they knew malaria. This is a common challenge which is difficult to overcome in large  
426 scale studies, especially in field sites as complex and multicultural as SGO.

427 The fact that the project was conducted in association with biomedical professional probably  
428 influenced some answers, particularly those dealing with topics often disregarded by the  
429 biomedical system.

430 Due to the length of the questionnaire (122 questions) and the various aspects it dealt with,  
431 several themes were not as detailed as they would have been if the work had focused on a  
432 single topic. This led to somehow fragmented data. For example, questions related to the  
433 reasons of the choice of a treatment would have been insightful and deserve new in depth  
434 studies.

435 No information was collected regarding side effects of antimalarial pharmaceuticals, which  
436 could be a factor favoring the consumption of herbal remedies, either to lower them or to  
437 replace pharmaceuticals.

438 The localization of the pictures on the poster (two of the most commonly used plants are at  
439 the top) might have influenced respondent's perceptions, as well as the fact that some  
440 species had two pictures to show more details, although probably in a minor way.

441 Finally, the choice to switch from malaria to fever in general, justified by the impossibility to  
442 ensure that people were effectively having malaria when they self-treated, might have led to  
443 confusion, so the data in response to these questions must be analyzed carefully.

#### 444 **4.2. Sociodemographic and practices details of participants**

445 To our knowledge, this is one of the most extensive epidemiological study addressing the  
446 question of co-medication between biomedical and traditional treatments associated with  
447 an active *Plasmodium* spp. diagnosis in Latin America (Lipowsky et al., 1992). It is somewhat  
448 similar to the one conducted by Vigneron et al. (2005), although they interviewed only 117  
449 people, in the center and eastern part of French Guiana, and did not performed *Plasmodium*  
450 spp. detection. Their results are nevertheless used with care on a comparative basis to  
451 indicate possibly evolution in practices.

452 The sampled population represents 38.4% of SGO's population in 2017 (1,566/4,076), but  
453 excluding the town center probably shifted the sampling towards a higher Amerindian  
454 representation.

455 The very low average age is representative of the young population of SGO, with 40.6%  
456 under 14 years old (INSEE, 2020).

#### 457 **4.3. Knowledge of malaria disease**

458 Malaria description among the interviewees is well correlated to its biomedical definition,  
459 although this correlation seems less evident than what was observed 14 years earlier  
460 (Vigneron et al., 2005). The difference comes probably from our wider recruitment, as they  
461 questioned preferentially more knowledgeable persons. Fever is interestingly not given as  
462 the most commonly reported symptom in our study, although it was observed as the most  
463 commonly reported symptom by both Vigneron et al., 2005 and by Forero et al. (2014) in  
464 three communities in Colombia. By using a closed list of symptoms more or less related to  
465 the biomedical definition of malaria, a certain bias was introduced, making it difficult to  
466 define more accurately the equivalency between local perception and biomedical definition  
467 of malaria.

468 The question related to transmission included various possibilities such as "*air, contact with*  
469 *an infected person, food...*", and the high rate of response for insect transmission reflects  
470 local perception. The same result was observed in Colombia (Forero et al., 2014) and 15  
471 years ago in French Guiana (Vigneron et al., 2005).

472 Preventive practices cited also show the impact of recurrent prevention messages against  
473 vector-borne diseases. Interestingly, medicinal plants, although some are said to be taken

474 preventively, are rarely cited in this section (although they were included in the answer  
475 sheet), which indicates a clear difference between biomedical and traditional  
476 representations.

#### 477 **4.4. Fever and malaria diagnostic and treatment perspectives**

478 The relatively balanced ratio of people going *often* to the health center vs. those going *rarely*  
479 or *never* (58.4% vs 41.6%) is also interesting. Resorting to the health center seemed to be  
480 associated with the relative severity of the illness. At the scale of the SGO population,  
481 distance seems not to be a major factor deterring people from visiting the health center,  
482 probably due to the high mobility of the local population. Nevertheless, the 133 people who  
483 did not wish to answer this question probably had other reasons. A degree of mistrust  
484 toward biomedicine in general, or toward the health center in particular should not be  
485 ignored as a factor influencing choices about treatment (Tareau, 2019), and it might be due  
486 to cultural insecurity, the sometimes long queues at the health center, or to previous  
487 negative experiences (Valmy et al., 2016). Nevertheless, due to the wide array of options  
488 available, access to biomedical antimalarial facilities seems easy, on both the Brazilian and  
489 French sides of the border.

490 Concerning the use of plant medicine in general in French Guiana, access to plants is largely  
491 informal, but easy. Plants are often locally collected in gardens or around villages, either by  
492 patients themselves or by their relatives (Grenand et al., 2004; Tareau et al., 2017) although  
493 important exchange networks have also been documented in the region (Tareau et al.,  
494 2019a, 2019b).

#### 495 **4.5. Malaria and fever treatments**

##### 496 **4.5.1. Biomedical treatments against malaria**

497 It appears that the distinction between symptomatic and antiplasmodial treatments is not  
498 evident, which is a common trend. Pharmaceutical medicines come from official distributors,  
499 although 23 people reported self-medication with antimalarials (mainly chloroquine and  
500 primaquine). This matches with the local epidemiology of SGO, where a majority of *P. vivax*  
501 infection is reported (Mosnier et al., 2019). However, self-medication with artemisinin  
502 derivatives is also reported for one patient, which must be considered carefully to prevent  
503 the emergence of resistance to artemisinin-based drugs. Even if antimalarial drugs are free  
504 in French Guiana and the study was conducted on the French Guianese side of the border, it  
505 is interesting to note that Brazilian antimalarials are imported into French Guiana.

##### 506 **4.5.2. Phytotherapies to prevent and/or treat fever and malaria**

507 There is an interesting discrepancy between the 19.3% of interviewees who stated that  
508 phytotherapies are able to treat malaria, and the number of people who actually reported  
509 using plants in case of fever at large (35.1%; 550/1566).

510 This important use of medicinal plants against malaria was already highlighted in previous  
511 studies, such as Vigneron et al. (2005), or in a rapid assessment of the plants used to treat  
512 malaria by patients consulting at the Saint Laurent du Maroni general hospital (at the

513 Western side of French Guiana, at the border with Suriname) performed in 2016 (Cetout and  
514 Weniger, 2016). Regarding other diseases, such as leishmaniasis, a similar trend was  
515 observed in the close Upper Oyapock valley (Odonne et al., 2011), and Tareau et al. (2017)  
516 encountered a similar pattern of use along the littoral of French Guiana.

517 Along the Pacific Coast of Colombia, values range from 25.2% (urban areas) to 10.7% (rural  
518 areas) for plant use against malaria (Lipowsky et al., 1992), and similar values were observed  
519 in Assam (India), where 39.2% of the population refers to *Vaidya* (traditional healers) when  
520 experiencing malaria symptoms (Chaturvedi et al., 2009), and approximately one fifth of the  
521 people use *Jamu* medicine for this condition in Indonesia (Suswardany et al., 2017).

## 522 **4.6. Medicinal plant uses**

### 523 **4.6.1. Factors associated with the use of plants**

524 First, medicinal plant users are older than non-users. This trend is common in South America,  
525 as exemplified by several studies (Figueiredo et al., 1993; Phillips and Gentry, 1993; Quinlan  
526 and Quinlan, 2007; Voeks, 2007; Voeks and Leony, 2004). The observed correlation between  
527 use of medicinal plants and past history of malaria in the patient's life has also been  
528 reported by Vigneron et al. (2005). It remains unclear to us if this correlation is a  
529 consequence of aging, of being more exposed, of a better accessibility to pharmaceuticals in  
530 recent times, or other factors. According to Soldati et al. (2015), illness triggers local learning  
531 regarding medicinal plant uses.

532 Factors such as low education level or absence of health insurance, in this case, were not  
533 associated with an increased use of medicinal plants. This has already been observed in  
534 other situations, for example among Haitian migrants in Cayenne (Tareau et al., 2019a), and  
535 seems thus not reproduced here. Even if the renouncement of biomedical health care is a  
536 reality in French Guiana among poor populations (Valmy et al., 2016), SGO is another  
537 context, and the elevated rate of medicinal plant use seems more related to cultural  
538 attachment than to a difficulty of accessing biomedicine.

539 Moreover, the largest proportion of plant users being among hunters, fishermen and  
540 farmers is probably related to their cultural background favoring ethnomedicines more than  
541 to their proximity to wild vegetation, since cultivated plants in home gardens are more often  
542 used than wild plants (91.3% vs 18.4% of the URs).

543 Ultimately, distinguishing cultural from socio-economic factors is difficult, but it seems likely  
544 that in this case cultural aspects outweigh economical ones. An example comes from the  
545 difference between Blondin 1 and Blondin 2, which, despite their geographic proximity (and  
546 thus the sharing of common urban patterns), are inhabited by different populations. Thus  
547 one is mainly protestant and more averse to medicinal plant uses.

548 *Q. amara* is the most cited species. In keeping with Hurrell and Pochettino (2014) and Leonti,  
549 (2011), the use of this plant has probably increased due to its prominence in local media.  
550 This species of widespread use (Odonne et al., 2020) was in recent years the center of a  
551 polemic related to a biopiracy issue (Bourdy et al., 2017) that has certainly added a kind of

552 scientific dressing to its already widespread fame. It is also interesting to note that this  
553 species is the most cited in SGO regarding all kind of diseases (Tareau et al., 2019b).

554 Some seemingly highly cited plants from Eastern French Guiana in 2005, such as *Mikania*  
555 *micrantha*, *Coutoubea* spp., and *Plectranthus* spp., are not or only rarely cited in our study, a  
556 testament to the ongoing cultural dynamics in the region, as already discussed by Odonne et  
557 al. (2011) and Tareau et al. (2019b). It is likely that some other species would have appeared  
558 with an open questionnaire.

559 As most of the citations refer to widespread plants cultivated in home gardens, it is likely  
560 that the utilization of medicinal plants is before all linked to the availability of the resource,  
561 and thus is a question of pragmatism and proximity, as much as a question of cultural safety.  
562 Moreover, medicinal plants are often perceived to be less toxic than pharmaceuticals, and  
563 phytotherapeutic remedies benefit by the way of a positive feeling people associate with  
564 them (Tareau, 2019; van Andel et al., 2013).

#### 565 **4.6.2. Complex therapeutic itineraries**

566 As highlighted by Benoist (1996), medical pluralism is a fact in French Guiana. As shown by  
567 Vigneron et al. (2005) on the scale of Eastern French Guiana, people normally co-medicate.  
568 They observed in 2004 that 58.3% (42/72) of the interviewees who had experienced malaria  
569 used both ethnomedical and biomedical therapies to treat malaria, 37.5% (27/72) used only  
570 pharmaceuticals and 4.2% (3/72) used only medicinal plants. A slightly different pattern has  
571 been observed for leishmaniasis among the Wayãpi and the Teko Amerindians of the Upper  
572 Oyapock (Odonne et al., 2011) with respectively 36.8% (25/68) using both therapies, 48.5%  
573 (33/68) using pharmaceuticals only and 14.7% (10/68) using traditional therapy only.

574 Due to the construction of our questionnaire (regarding malaria only or fever and malaria  
575 together), it was not possible to determine such ratios. We might nevertheless compare the  
576 525 persons that used both medicinal plants and pharmaceuticals in case of fever to the 720  
577 persons that were treated with biomedicine in case of malaria, and suppose that nearly a  
578 quarter would have used only pharmaceuticals.

579 Cultural differences certainly play a key role in these variations, but it is interesting to note  
580 that the most remote Amerindian populations (Wayãpi and Teko) relied more confidently on  
581 pharmaceuticals exclusively for leishmaniasis than mixed populations of SGO for malaria.  
582 Regardless, such co-medications are undoubtedly an important aspect to be taken into  
583 account in further public health projects. Such a high proportion of co-medication also raises  
584 questions about the general acceptance of biomedical therapies, a question that would best  
585 be investigated by other means (such as qualitative interviews). One study among native  
586 Amazonian in Bolivia suggested organizing training workshop between doctors and local  
587 practitioners in order to improve collaboration between them, but also to achieve the  
588 revalorization of local medicinal knowledge (Vandebroek et al., 2004).

589 Moreover, these behaviors are thought to possibly delay patients care, possibly resulting in  
590 severe cases, the persistence of the parasite in the population, or the creation of reservoirs,

591 notably in *P. vivax* infections. These infections are characterized by an early parasitemia with  
592 gametocytes carriage which can contribute to local transmission in case of a delay of  
593 efficient antimalarial treatment (Howes et al., 2016).

#### 594 **4.6.3. Influence of plant uses on parasitaemia**

595 Due to several confounding biases, it is impossible to be affirmative regarding a possible  
596 causality. As the use of medicinal plants was not related to a specific recent episode of  
597 malaria, it might not explain the presence of parasites. Further studies in that field are  
598 urgently needed.

#### 599 **4.6.4. Ethnopharmacology of cited species**

600 Uses of plants against malaria are numerous in Latin America (Milliken et al., 2021).  
601 Ethnopharmacological works highlighting the therapeutic potential of some of these plants  
602 have already been realized *in vitro* and *in vivo*. Among all the species presented on the  
603 poster, *Q. amara* has been the most widely and successfully studied, which has led to the  
604 isolation of some interesting compounds (Bertani et al., 2007, 2006; Cachet et al., 2009;  
605 Houël et al., 2009). *C. citratus* is also a well-studied species and its essential oil has moderate  
606 activity against *P. falciparum* (IC<sub>50</sub>: 48µg/mL) (Kpoviessi et al., 2014; Oladeji et al., 2019). *E.*  
607 *foetidum* seems to have a weak antimalarial potential according to the literature (IC<sub>50</sub>  
608 undetermined but >25 µg/mL) (Paul et al., 2011; Roumy et al., 2007). *C. aurantiifolia*, despite  
609 its wide distribution and widespread use as a medicinal species, has not been much studied  
610 against malaria. Nevertheless, an interesting clinical study highlighted a higher parasite  
611 clearance in children when combining lime juice and ACT vs. ACT alone (Adegoke et al.,  
612 2011). *B. pinnatum* is well described from the phytochemical point of view (Fernandes et al.,  
613 2019) and a leaf EtOH extract had an IC<sub>50</sub> *in vitro* ranging between 11–20 µg/mL (Singh et al.,  
614 2015). *S. guianensis* EtOH extract was found active *in vitro* against two strains of *P.*  
615 *falciparum* with activities of 6.7 and 14.7 µg/mL (Fischer et al., 2004), but it was considered  
616 inactive in another *in vitro* assay (Bertani et al., 2005). Two Peruvian species, *S. aspera* (Ruiz  
617 & Pav.) A. DC. and *S. radiata* (Poepp. & Endl.) A. DC. exhibited *in vitro* IC<sub>50</sub> of respectively 6.4  
618 and 21.7 µg/mL (Valadeau et al., 2009). *P. alliacea* displayed *in vitro* an excellent activity  
619 (99% inhibition at 10 µg/mL) but a weak one *in vivo* (41% inhibition at 1 g/kg) (Muñoz et al.,  
620 2000a). *S. leucocarpon* seems not to have been tested for antimalarial/antiplasmodial  
621 activities. No toxicity has been observed in an *Artemia* assay (Correa et al., 2011), nor on  
622 *Aedes aegypti* (Falkowski et al., 2019). An *E. triplinerve* MeOH extract displayed an IC<sub>50</sub> of  
623 36µg/mL *in vitro* on *P. falciparum* and no toxicity on A-549 cell lines (Jonville et al., 2011),  
624 although it was considered inactive (same solvent, IC<sub>50</sub>>50µg/mL) a few years ago (Jonville et  
625 al., 2008). *G. laevis* and *G. argenteum* were considered inactive *in vitro* and exhibited  
626 respectively 35% inhibition (23mg/kg) and 44.3% inhibition (324mg/kg) on *P. yoelii* rodent  
627 malaria *in vivo*. The later exhibited 83% inhibition on the hepatic stage at the same dose  
628 (Bertani et al., 2005). An EtOH extract of *G. laevis* also displayed a good activity *in vitro* (IC<sub>50</sub>  
629 around 3.1µg/mL). It was found active against *P. vinckei* rodent malaria, inactive against *P.*  
630 *berghei* rodent malaria, and highly toxic at 100 mg/kg (Muñoz et al., 2000a). *P. amarus* water

631 and EtOH extracts showed prophylactic and curative effects on *P. yoelii*. For example, water  
632 extract inhibited 68% of the parasite growth at 400mg/kg *in vivo* (Ajala et al., 2011),  
633 although this species is reported to show a kidney toxicity (Patel et al., 2011). *P. sprucei* (ex.  
634 *P. pseudocoffea* Ducke) is the most active species both *in vitro* and *in vivo* against *P.*  
635 *falciparum* studied by Bertani et al. (2005) (IC<sub>50</sub>=1.4µg/mL; 77.5% inhibition at 95mg/kg),  
636 which is probably due to the quassinoid sergeolide that exhibited an IC<sub>50</sub> of 0.002µg/mL but  
637 was also highly toxic (Fandeur et al., 1985; Lemma et al., 2017). No results are available on  
638 activities of the *Aristolochia* spp. used against malaria in French Guiana. However, the  
639 Bolivian *A. prostrata* Duch. showed a weak *in vivo* activity (10% growth inhibition at  
640 880mg/kg) (Muñoz et al., 2000b). The African *A. elegans* Mast. exhibited no activity  
641 (>50µg/mL) *in vitro* (Muganga et al., 2010) while the Indian *A. indica* L. suppressed 52.3% of  
642 *P. berghei* *in vivo* at a dose of 300mg/kg (Gandhi et al., 2019). Nevertheless, kidney toxicity  
643 of aristolochic acids encountered in these species raise a concern regarding their use  
644 (Debelle et al., 2008). *Z. rhoifolium* was found active *in vivo* (*P. yoelii*), but at a relatively high  
645 dose (78% inhibition at 715 mg/kg) (Bertani et al., 2005). This was notably due to  
646 benzophenanthridine alkaloids, among which one of the most active, the nitidine, is a well-  
647 known cytotoxic molecule (Jullian et al., 2006). It seems that *M. micrantha* had not been  
648 tested against *Plasmodium*. *M. congesta* DC. and an undetermined *Mikania* sp. were both  
649 found inactive *in vitro* (Muñoz et al., 2000a; Roumy et al., 2007).

## 650 5. Conclusion

651 This study showed *in extenso* that residents of SGO in French Guiana are relying on both  
652 traditional plant medicine and biomedicine to treat malaria. This medical pluralism is to be  
653 understood as a form of pragmatism, and it is highly probable that local populations do not  
654 oppose such therapeutics. Nevertheless, qualitative anthropological research is needed to  
655 understand more clearly to what extent these coexisting systems are able to merge.

656 Plants are indeed a continuing, vibrant tool for local health care along the French Guiana-  
657 Brazil frontier. This study shows that, despite the presence of biomedical health facilities,  
658 people are collecting, cultivating and utilizing plants for medicinal purposes, which is  
659 probably more congruent with their respective cultures and highlights the wish for a certain  
660 independence in relation to the care process.

661 Research should also be conducted, with the support of the communities, to improve our  
662 understanding of the functioning of these medicinal plants through an  
663 ethnopharmacological approach. As preliminary pharmacological results exist for most of  
664 the cited species, further studies should be focused on investigating the synergies between  
665 local phytotherapies and pharmaceuticals in order to improve the effectiveness of malaria  
666 treatment and avoid negative drug/plant interactions. *Solanum leucocarpon* would also  
667 benefit of further pharmacochemical studies due to the overall lack of data concerning this  
668 species.

669 There is a real need for more integrated approaches which target not only generic best  
670 practices in malaria prevention and control communication but also adapt these efforts to

671 local practices and knowledge, such as phytotherapies, in order to improve the pragmatic  
672 uptake of prevention messages. New collective and participatory approaches between local  
673 communities and health workers are needed to co-generate messages of prevention  
674 compatible with local cultural safety.

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## 691 **8. Author Contributions**

692 Designed the study: GO, LM, EM. Performed field study: BP, MG, CM, LE, EM. Performed  
693 statistical analysis: CC, GO, EM. Wrote the manuscript: GO, EM. Every author corrected and  
694 commented the manuscript.

## 695 **9. Availability of data and materials**

696 The datasets generated and analyzed during the present study are not publicly available due  
697 to the requirement of special authorization to transfer databases provided by the CNIL.  
698 Upon prior CNIL authorization, the datasets can be made available from the corresponding  
699 author upon reasonable request.

## 700 **10. Competing interests**

701 The authors declare that they have no competing interests.

## 702 **11. References**

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- 951

952 **Supplementary data**

953

954 **Supplementary data 1:**

955 Questionnaire

956

957 **Supplementary data 2:** poster presented during the interviews



958

9591. *Eryngium foetidum* L. (Apiaceae)

9602. *Quassia amara* L. (Simaroubaceae)  
 9613. *Geissospermum argenteum* woodson, *Geissospermum sericeum* Benth. and Hook. f. ex Miers  
 962 (Apocynaceae)  
 9634. *Phyllanthus amarus* Schumach. & Thonn., *Phyllanthus niruri* L. (Phyllanthaceae)  
 9645. *Aristolochia trilobata* L., *Aristolochia stahelii* O.C. Schmidt, *Aristolochia leprieurii* Duch.  
 965 (Aristolochiaceae)  
 9666. *Cymbopogon citratus* Stapf. (Poaceae)  
 9677. *Coutoubea spicata* Aublet, *Coutoubea ramosa* Aublet (Gentianaceae)  
 9688. *Citrus aurantiifolia* (Christm.) Swingle (Rutaceae)  
 9699. *Picrolemma sprucei* Hook. f. (Simaroubaceae)  
 97010. *Siparuna guianensis* Aublet (Siparunaceae)  
 97111. *Plectranthus barbatus* Andrews, *Plectranthus neochilus* Schltr. (Lamiaceae)  
 97212. *Solanum leucocarpon* Dunal (Solanaceae)  
 97313. *Petiveria aliacea* L. (Petiveriaceae)  
 97414. *Eupatorium triplinerve* Vahl (Asteraceae)  
 97515. *Mikania micrantha* Kunth. (Asteraceae)  
 97616. *Zanthoxylum rhoifolium* Lam. (Rutaceae)

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979 **Supplementary data 3:** number of participants who experienced malaria prior to the  
 980 interview according to their residence

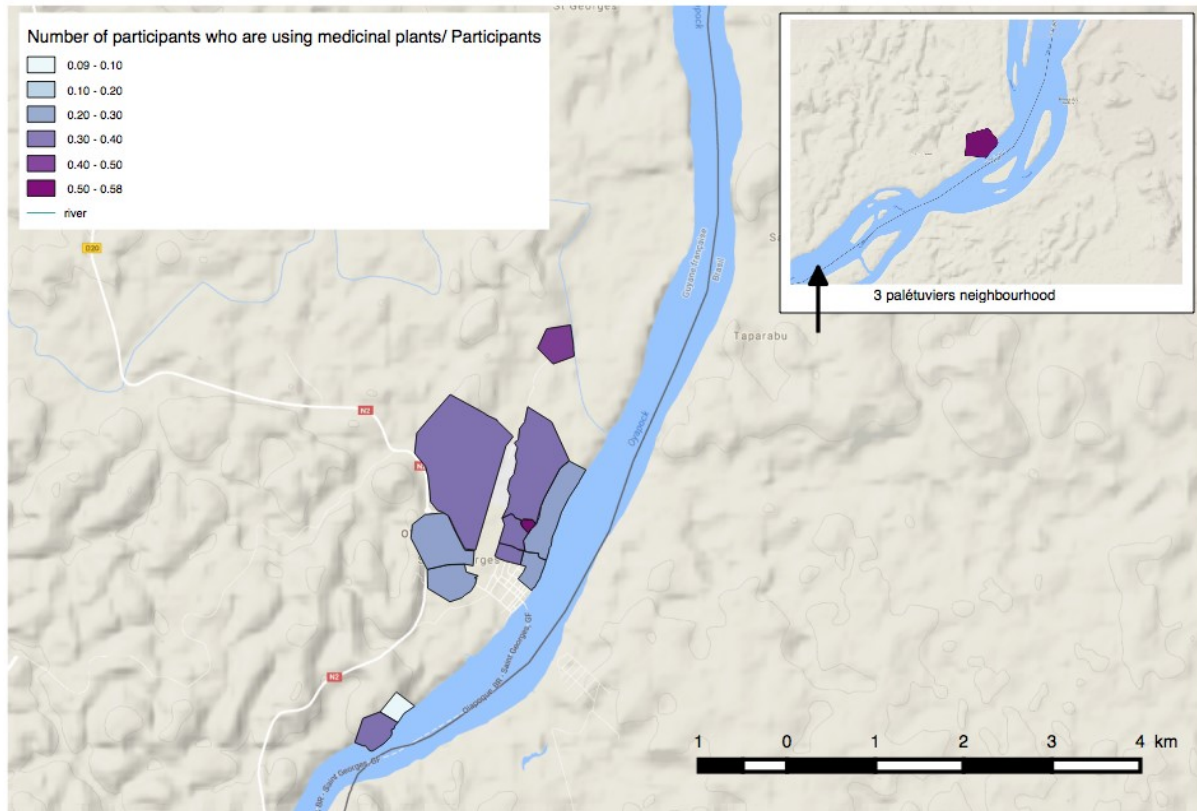
Neighborhood	Participants who experienced malaria prior to the interview (and %)	Participants ≥15 years old who experienced malaria prior to the interview (and %)
Trois-Palétuviers	123/183 (67.2%)	63/83 (75.9%)
Adimo	31/111 (27.9%)	45/62 (72.6%)
Bambou	15/45 (33.3%)	13/22 (59.1%)
Blondin 1	9/11 (81.8%)	8/8 (100%)
Blondin2	28/44 (63.6%)	18/22 (81.8%)
Espérance 1	34/79 (43%)	33/51 (64.7%)
Espérance 2	51/137 (37.2%)	44/75 (58.7%)
Gabin	42/113 (37.2%)	33/57 (57.9%)
Maripa	26/54 (48.1%)	21/27 (77.8%)
Onozo	104/252 (41.3%)	95/144 (66%)
Philogène	33/77 (42.9%)	24/42 (57.1%)
Savane	184/425 (43.3%)	159/230 (69.1%)
Village Martin	24/25 (96%)	20/21 (95.2%)

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983 **Supplementary data 4:** Spatial distribution of participants who reported the use of medicinal  
 984 plant against fevers and malaria



985  
 986

987 **Supplementary data 5:** percentage of the population using plants according to their  
 988 residence

Neighborhood name	% of the population using plants (p<0.005)	Use reports	Use ≥15 years old
Philogène	58.4%	45/77	26/42
Trois-Palétuviers	55.7%	81/183	48/83
Village martin	48.6%	17/35	10/21
Adimo	36.0%	40/111	30/62
Blondin 2	34.1%	15/44	13/22
Savane	31.8%	135/425	88/230
Espérance 2	31.4%	43/137	29/75
Espérance 1	30.4%	24/79	18/51
Onozo	29.8%	75/252	55/144
Gabin	27.4%	31/113	15/57
Bambou	22.2%	10/45	8/22
Maripa	22.2%	12/54	7/27
Blondin 1	9.1%	1/11	0/8

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