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Predictors of antimalarial self-medication in illegal gold miners in French Guiana: a pathway towards artemisinin resistance.

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27

28 **Abstract** (255 words)

29 **Background**

30 Malaria is endemic in French Guiana (FG), South America. Despite the decrease of cases in the
31 local population, illegal gold miners are very affected by malaria (22.3% of them carried
32 *Plasmodium spp*). Self-medication seems to be very common but its modalities and associated
33 factors have not been studied. The aim of this study was to evaluate parasite susceptibility to
34 drugs and to document behaviours that could contribute to resistance selection.

35 **Method**

36 This multicentric cross-sectional study was conducted in resting sites along the Surinamese
37 border. Participating gold miners working in French Guiana completed a questionnaire and
38 provided a blood sample.

39 **Results**

40 From January to June 2015, 421 illegal gold miners were included. Most were Brazilian (93.8%),
41 70.5% were male. During the most recent malaria attack, 45.5% reported having been tested for
42 malaria and 52.4% self-medicated, mainly with artemisinin derivatives (90%). Being in FG
43 during the last malaria attack was the main factor associated with self-medication (AOR=22.1).
44 This suggests that access to malaria diagnosis in FG is particularly difficult for Brazilian illegal
45 gold miners. Treatment adherence was better for persons who reported being tested. None of the
46 32 samples with *P. falciparum* presented any mutation on the pfK13 gene, but one isolate showed
47 a resistance profile to artemisinin derivatives *in vitro*.

48 **Conclusion**

49 The risk factors for the selection of resistance are well known and this study showed that they are
50 present in French Guiana with persons who self-medicated with poor adherence. Interventions
51 should be implemented among this specific population to avoid the emergence of artemisinin
52 resistance.

53

54

55 **Text words count:** 3658 words

56 **Background**

57 Malaria is a major parasitic illness, with 198 million cases and 584,000 deaths in 2014,
58 worldwide.¹ In French Guiana (FG), a French overseas territory located on the Guiana Shield in
59 South America, malaria is endemic.² Great efforts have been deployed to control malaria in the
60 region. In Suriname as in local villages in French Guiana, the number of cases decreased
61 drastically.^{3,4} But in this territory, mainly covered by Amazonian forest, the soil is rich in gold. In
62 addition to the legal mining industry, 8 to 10 thousand illegal gold miners, mainly Brazilian,
63 work in the forest.⁵ They have difficult life conditions with poor hygiene and exhausting work
64 which lead to poor health. Deforestation and still water pools favor mosquito proliferation,
65 notably *Anopheles darlingi*, the main malaria vector. In 2015, in western French Guiana,
66 molecular malaria diagnosis showed 22.3% of illegal gold miners carried *Plasmodium spp.*, 84%
67 of whom were asymptomatic.⁶ In 2014, in a gold mining site near Maripa Soula, 48.5% of gold
68 miners were *Plasmodium spp.* positive by PCR.⁷ This indicated that although malaria in local
69 populations keeps decreasing, it remains hyperendemic in this specific population in French
70 Guiana. Medical care is free in Health Centers but the remoteness of the mines and the fear of
71 law enforcement hamper effective access to care for miners. A first study in this population in
72 Suriname and French Guiana has shown that self-medication with artemisinin derivatives seemed
73 to be very common, with poor treatment adherence.⁸ But self-medication modes and factors
74 associated with it have not been studied specifically in French Guiana despite access to care
75 differences between those two countries. This frequent self-medication threatens the efficacy of
76 artemisinin derivatives. In fact, the main known factors contributing to antimalarial drug
77 resistance are: poor treatment adherence (quantity or treatment duration), poor quality of drugs
78 and drug pressure with monotherapy.^{9,10} Historically, antimalarial drug resistance emerged
79 independently, in South-East Asia and in the Amazon region, as it happened for chloroquine

80 resistance in the 1960's.^{11,12} The decrease of sensitivity to artemisinin derivatives appeared about
81 10 years ago in South East Asia and now concerns five countries in the Mekong Region.¹³⁻¹⁵ .
82 The transborder context between Suriname, Brazil and French Guiana, with movements of
83 precarious populations in remote areas, challenges malaria control in this area and is similar to
84 the transborder context of the Mekong region.¹⁶ Several parameters are used to characterize
85 artemisinin resistance. *In vivo*, the persistence of parasites in the blood more than three days after
86 treatment or a delayed parasite clearance time are indicators.¹⁷ *In vitro*, the survival rate of ring-
87 stage parasites that have been exposed for six hours to dihydroartemisinin is the best phenotyping
88 method to identify a decreased parasite sensitivity to dihydroartemisinin.¹⁸ Finally in 2013,
89 certain mutations in the *pfk13* gene were shown to be associated with an increased parasite
90 clearance time in isolates from South-East Asia.¹⁹

91
92 The objectives of this study were to describe the behaviours of illegal gold miners working in
93 French Guiana when they had a malaria attack; to evaluate factors associated with self-
94 medication and with poor treatment adherence; and to characterize artemisinin sensitivity of the
95 associated parasites.

96

97 **Methods**

98 A multicentric cross-sectional observational study was conducted in 2015 between January 1st and
99 June 30th. As no sampling frame exists, illegal gold miners were recruited using convenience and
100 snow-ball sampling on « resting sites », areas where they go for rest, supplies or medical care.
101 These sites were spread along the Suriname-French Guiana border on the Maroni river.

102 Inclusion criteria were: working on a gold mining site in FG; being at the resting site for less than
103 seven days; being over 18 years of age; and giving informed consent. A questionnaire collected
104 socio-demographic data, knowledge, attitudes and practices (KAP) in gold miners concerning
105 malaria. Poor adherence was considered if the person declared that there were remaining pills at
106 the end of the last malaria treatment. Behaviour when having malaria referred to the last malaria
107 episode only, to avoid memory bias. A rapid diagnostic test was performed on the field and
108 malaria treatment was given if the test was positive. A 5 ml-blood sample was taken from each
109 participant for further analysis and sent to the National Reference Center for Malaria for
110 biological investigations. If the thin smear was positive for *Plasmodium falciparum*, parasites
111 were phenotyped using the standard isotopic method and the ring survival assay (RSA).¹⁸⁻²⁰ DNA
112 was extracted from 200µL of whole blood with the QIA amp[®] DNA kit (Qiagen). The *pfK13*
113 gene was amplified and sequenced using the Sanger method.¹⁹ Study size and bias assessment are
114 described in reference⁶.

115 **Statistical analyses**

116 Data were analysed with Stata12 software (StataCorp[®] College Station, Texas). Data from the
117 KAP study were analysed using Multiple Correspondence Analyses (MCA) in order to reduce the
118 dimension of the variables. Ascending Hierarchical Classification (AHC) was used to define
119 clusters with similar characteristics; individuals were grouped in clusters using variables selected
120 from the MCA, namely those with higher weights on MCA. Bivariate analyses was done using
121 Chi-Square tests or Student's t-test depending on the type of variable. Variables with a p-value <
122 0.20 in bivariate analyses were included in a multivariate logistic regression to identify factors
123 associated with self-medication and poor treatment adherence. A backward selection method was
124 used to retain variables significant at a 0.05 level in the final multivariate model. The goodness of

125 fit of the logistical regression model was tested with the Hosmer and Lemeshow test. All
126 statistical analyses used a 5% significance level.

127 **Ethics**

128 The study was approved by the Comité d'Evaluation Ethique de l'Inserm, Process n°14-187
129 (IRB00003888 FWA00005831). The database was anonymized and declared to the Commission
130 Nationale Informatique et Libertés. Patients were included after recording informed consent.

131

132 **Results**

133 **Study population**

134 From January to June 2015, 421 illegal gold miners were included in the study with a
135 participation rate of 90.5%.⁶ The mean age was 37.7 years (min-max=18-62) and 70.5% of
136 participants were men. Most of them (93.8%) were born in Brazil and they worked in 67 different
137 mining sites.

138 **Malaria knowledge and protection**

139 Malaria was mentioned in the top three health problems at mining sites by 84.8% of interviewed
140 people. The mode of transmission was well known: 91.4% mentioned the mosquito but 3.3%
141 mentioned living near dirty water or 3.3% in a dirty environment, or 1.6% drinking dirty water.

142 One hundred twenty eight (30.4%) considered that it was better to take treatment even if the
143 malaria test was negative, 11.2% that treatment could be stopped when feeling better and 8.5%
144 that malaria could be cured without treatment. Most (95.7%) thought that malaria kills. French
145 malaria treatment was considered better than Surinamese treatment for 93% of them, and better

146 than Brazilian treatment for 84%. However, the three treatments are in fact the same: artemether-
147 lumefantrine, labelled as Riamet® in France and Coartem® in Brazil or Suriname. The majority
148 of interviewed people (85.5%) could mention three or more malaria symptoms.

149 Considering malaria protection, 18% declared protecting themselves from malaria always or
150 often, but 54.8% never. The modes of protection were: mosquito nets (29%), mosquito repellents
151 (21.6%), wearing long clothes (2.1%) and living far from dirty water (1.2%). However, only
152 15.7% declared having slept under a mosquito net the last night at the mining camp, of which
153 only 19.7% were insecticide-treated nets. The main reasons for not using a mosquito net were:
154 did not have any (63.4%), uncomfortable (19.1%), destroyed by French Army (10.4%) (military
155 operations against illegal gold mining aim at destroying all logistical supplies on mining camps),
156 too constraining (7.9%), useless (5.6%) and would hamper flight in the event of a military raid in
157 the camp (3.4%). Malaria chemoprophylaxis was used by 6.4% of people, mainly with Artecom®
158 (dihydroartemisinin/piperazine/trimethoprim + primaquine single dose).

159 **Past malaria history and behaviours**

160 The flow chart is presented figure 1. Forty five persons (10.7%) declared never having had
161 malaria. They differed from the 376 people who declared a past history of malaria for sex (51%
162 of male in persons who never had malaria versus 73% in person with a past history of malaria,
163 $p=0.002$), age (31% more than 37 years versus 52%, $p=0.009$) but the place of birth did not
164 differ. Most participants (66.2%) declared having had more than seven malaria attacks, and
165 24.2% three or less. The median time since the last malaria attack was two years [Interquartile
166 range: 6 months - 6 years]. During the last malaria attack, 52.4% (N=197) self-medicated with
167 antimalarial drugs, 45.5% (N=171) got tested for malaria, 1.3% (N=5) used medicinal plants and

168 0.8% (N=3) declared having done nothing, without statistical difference between groups for
169 socio-demographic variables. When only considering people having had their last malaria attack
170 less than two years ago, 66% took the whole treatment and 66.5% self-medicated, compared to
171 86.7% and 39.3% for those who had malaria more than two years ago, respectively ($p<0.001$ for
172 both). Behaviour also varied with the place of the last malaria attack: 66% of self-medication if in
173 French Guiana, 28% if in Suriname and 7% if in Brazil ($p<0.001$).

174 **Malaria testing**

175 For persons who got tested for malaria (N=171), the testing location depended on the country
176 where the malaria attack occurred. If malaria occurred in Brazil (N=56) or Suriname (N=18),
177 people got tested in these countries. But if malaria occurred in French Guiana (N=86), 47.7%
178 went to Suriname to get tested (33 persons to a health center, 8 to Malaria Service Deliverers
179 (MSD)), 37.2% to a French health center, and 12.8% went back to Brazil. The two other persons
180 (2.3%) declared having been tested by Surinamese malaria service deliverers at a mining site in
181 French Guiana. Easy accessibility was the main reason declared for choosing a place for malaria
182 diagnosis and treatment (85.9%). Care was free for 87.7% of the surveyed miners. Treatment
183 effectiveness was perceived to be good for 93.6% persons, and 90% declared having taken the
184 complete treatment course.

185 **Self-medication**

186 A majority of those who reported self-medication (N=197) bought antimalarial drugs directly on
187 the mining site (80.7%), or got it from friends or family (6.1%). Ninety percent (178/197) of
188 antimalarial drugs contained artemisinin derivatives, of which 93.8% were Artecom®. Most of
189 the time (85.1%), the treatment was paid in gold, 1 to 3 grams, which is worth 30 to 90 USD.

190 Treatment effectiveness was considered to be good for 68% of the persons but insufficient for
191 23.9%. One hundred and twenty persons (60.9%) declared having taken the whole treatment. The
192 majority (93.4%) declared that self-medication was related to the distance of malaria testing
193 structures. After multivariate analyses, the main variables significantly associated with self-
194 medication were being in FG during the last malaria attack (adjusted odds-ratio (AOR)=22.1) and
195 being born in Brazil (AOR=10.74) (Table 1).

196 **Factors associated with poor adherence**

197 Treatment adherence was statistically different between persons who got tested (N=154/171,
198 90.1%) and those who self-medicated (N=120/197, 60.9%) ($p<0.001$). The main factors
199 associated with poor adherence were self-medication (AOR=6.03) and thinking that it is better to
200 take a treatment even if the malaria test is negative (AOR=2) (Table 2).

201 **Multiple correspondence analyses**

202 Two-dimensional projection of the correspondence analyses showed malaria behaviours on the
203 first axis, with the opposition between self-medication and malaria testing. The second axis
204 describes malaria knowledge with on the positive coordinate inadequate malaria knowledge.
205 Dimension 1 plus 2 displayed 81% of the variance. The smaller the distance between points, the
206 stronger was their association. Thus, self-medication, poor adherence, more than four malaria
207 attacks, and the last malaria attack in the past two years were associated, as well as the opposite
208 modalities(Figure2).

209 Based on significant variables in the correspondence analyses, two clusters of persons were
210 defined with ascending hierarchical classification. The first one regrouped people declaring a past
211 history of three or less malaria attacks, the last one occurring more than two years ago, for which

212 they got tested and treated with a good adherence. They did not consider malaria as a major
213 health problem. The second opposite cluster regrouped people declaring four or more malaria
214 attacks, the last one more recently (less than two years ago), for which they self-medicated with a
215 poor adherence. They considered malaria as a major health problem. Sociodemographic data did
216 not differ between the two clusters (Table 3).

217 **The state of parasite sensitivity to artemisinin derivatives in French Guiana**

218 Among the 421 miners included, 94 were diagnosed positive by PCR for *Plasmodium spp*
219 carriage including 55 *P. falciparum* cases (10 coinfecting with *P. vivax*). The other PCR were
220 positive for *P. vivax* only (35/94), *P. malariae* (3/94) and *P. vivax* + *P. malariae* (1/94). Among
221 these *P. falciparum* samples, the parasite density was sufficient for successful amplification and
222 sequencing of the *pfk13* gene in 32 samples (58%). None of them revealed any mutation in the
223 propeller part of the gene.

224 Six *P. falciparum* samples were successfully phenotyped using the RSA method. Five out of six
225 exhibited a 0% survival rate. The last one exhibited a survival rate of 2.70% which is above the
226 decreased sensitivity threshold of 1%. This result has not been confirmed by a second analyses
227 (survival rate at 0%). However this isolate was also associated with an *in vitro* susceptibility
228 (IC₅₀) to artemether of 14.18 nM whereas the other values were between 1.35nM and 5.42nM.
229 This value is considered to be higher than the decreased susceptibility threshold of 12 nM.
230 Therefore, those two methods suggest at least a transient resistance profile for these parasites to
231 artemisinin derivatives. These parasites were isolated from a 28 years old Brazilian man who
232 took one pill of Artecom® four days before the sampling for malaria symptoms.

233

234 **Discussion**

235 **Study limitations**

236 Because sampling did not use probabilistic methods we cannot exclude recruitment biases.

237 Behaviour in case of malaria symptoms and adherence were analysed with a questionnaire, which
238 may lead to declaration bias (« correct answer » given to health professional) and memory bias.

239 Missing data (8 for adherence for example) could also contribute to bias the results.

240 **Frequent self-medication linked to difficult access to care in French Guiana**

241 This study showed that self-medication is very common in illegal gold miners working in FG:
242 53.7% resorted to self-medication for the last malaria episode. These results confirm previous
243 observations in a specific mining site in FG.⁷

244 The multivariate analyses shows that health-seeking behaviour depends on which country gold
245 miners worked in: being in FG during the last malaria attack was the main factor associated with
246 self-medication. This suggests that access to malaria diagnosis in FG is particularly difficult for
247 Brazilian gold miners compared to Brazil or Suriname. The main reason given by gold miners
248 was the remoteness of the mine from the health care centers (93.4% versus 64% in the
249 Surinamese survey) and we could also add the illegality of their activities and residency in
250 France. Currently, in Suriname, Malaria Service Deliverers procure free malaria diagnostic tests
251 and treatment everywhere on the Surinamese territory, even in gold mining areas, with the
252 program “Looking for Gold, Finding Malaria”.^{3,21} In Suriname, 50% of gold miners declared
253 having used self-medication during the past 18 months in 2013, but these results included people
254 working in Suriname and in FG, without differentiation. Therefore, it was not representative of
255 the specific behaviour of gold miners in Suriname.⁸ Thus, even if healthcare is free for everyone

256 in FG, in practice it is difficult to reach these healthcare structures for illegal gold miners who
257 often live days away.

258 Self-medication was also linked to personal malaria history: the more people had experienced
259 malaria, the more they were likely to self-treat themselves. This link could also be explained by a
260 general behaviour which associates: disregarding health issues, not protecting themselves from
261 malaria and not seeking medical care. We could assume that the acquired knowledge about
262 treatment after the first malaria attack could facilitate self-medication for future malaria episodes.
263 Malaria treatment misconceptions were also associated with self-medication. This emphasizes the
264 necessity to reinforce public health messages for this specific population.

265 **Self-medication is quasi-exclusively associated with ACT intake**

266 The majority of the drugs used in self-medication are artemisinin based combination therapies
267 (ACT) (90%). This is concordant with what was observed in Suriname (96.1%).⁸ Treatment was
268 mainly Artecom®, produced by a Chinese firm, Tonghe Pharmaceutical Co.Ltd (Chongqing,
269 China). This drug had good efficacy and tolerance in Africa and Asia.^{22,23} However, Artecom®
270 has some weaknesses: the dihydroartemisinin dose may vary; and there is no information on
271 the dose of primaquine included on the Guiana Shield.^{24,25} The information leaflet in a package of
272 Artecom® bought in the forest during the study mentioned the regimen in English and French
273 (two pills twice a day for two days), which is not understandable for most Brazilian miners.
274 Finally, the package indicated “protect from light and keep in a dry and cool place”, which is
275 probably not feasible in illegal gold mining sites in the Amazonian forest.

276 **Malaria treatment adherence is better when it is cheap and delivered by health workers**

277 It is difficult to really evaluate adherence, generally based on self-reports or pill counts.^{26,27} In
278 this study, the question “did pills remain when you have stopped the treatment?” was used to
279 allow comparison with the results from the Surinamese anthropological study⁸ and because the
280 packaging of drugs used in our region (in legal or illegal market) contains one complete
281 treatment. A Brazilian study in the Amazon basin found a difference between self-reported non-
282 adherence and pill counts (12.2% versus 21.8%).²⁸ But in Tanzania, the comparison of declared
283 adherence with adherence estimated through “smart blister packs” (Coartem® tablets with
284 microchip recording pills push out date and time) showed very similar results (64% of complete
285 adherence versus 67%).²⁹ Studies assessing adherence refer to a current malaria attack. But in this
286 study, the behaviour concerned the last malaria attack which occurred at a median of two years
287 before. When the last malaria attack occurred long before, people were more likely to have
288 declared getting tested and having taken the complete malaria treatment. This may reflect a
289 memory bias the embellishment of reality towards the socially desirable answer. Malaria
290 diagnosis and treatment adherence might have been overestimated. Self-medication and poor
291 adherence could therefore be even more frequent than reported.³⁰

292 Treatment adherence was significantly better when treatment was given after getting a malaria
293 test (90.1% versus 60.9% if self-medication). This suggests that there was a real impact of getting
294 tested and having malaria treatment with explanations from health workers. In the Surinamese
295 study, the same results were found with 78.9% of the miners who declared having completed the
296 treatment when given by a health worker compared to 40.2% when self-medicated.⁸ In 2015, a
297 meta-analyses observed a higher level of adherence to ACT in the public sector than in the retail
298 sector (76% versus 45%).²⁶ This could be explained by the fact that in the public sector, ACTs
299 are given for free with instructions by the health workers whereas informal drug stores dispense a
300 presumptive malaria treatment without clear instructions. A study in Uganda in 2016 reinforced

301 this idea as it found no association between testing and treatment adherence as long as the
302 treatment sent by shop vendors was associated with treatment information.³¹ Beside the lack of
303 treatment information, the high cost of the treatment on the black market is another factor leading
304 to poor adherence. In fact, ACTs cost 1 to 3 grams of gold (25 to 90 USD), when miners gain
305 about 10 to 15 grams per week.³² Therefore, most people declared interrupting the treatment as
306 soon as they felt better, and kept pills for the next malaria episode. Thus, the easy availability (for
307 free or at a low price) and explanation from health workers might explain the association between
308 malaria test and adherence.

309

310 **Putative emergence of artemisinin resistance in the parasite population of French Guiana**

311 This high level of self-medication raises the concern of selection for drug resistant parasites. In
312 Guyana (formerly English Guiana), 5% of the isolates collected in 2010 carried the C580Y *pfK13*
313 mutation.³³ Since then, no other mutations associated with artemisinin resistance in South East
314 Asia have been observed on the Guiana Shield.³⁴ Phenotyping methods identified one putative
315 resistant isolate with a survival rate above the threshold. However, this result was not confirmed
316 despite the conformity of the quality control (Cambodian strains). Therefore we could speculate
317 that these parasites exhibited a transient stage of resistance/tolerance that is not stable through
318 time and not necessarily associated with mutations on the *pfK13* gene. This phenotype could have
319 been lost during *in vitro* multiplication.³⁵ Therefore, resistance parameters to characterize parasite
320 resistance to artemisinin in South America still need to be validated.

321 **Whether artemisinin resistance has already emerged or not, there is an urgent need for**
322 **actions**

323 Malaria resistance is a threat for global health throughout the world.³⁶ The risk factors for
324 selection of resistance are well known and this study showed that they are present in French
325 Guiana with people who self-medicated themselves with poor adherence. In addition, the quality
326 of the drug could be altered by living conditions and poor storage conditions. Parasite
327 phenotyping suggested that the first step of resistance selection was reached with some parasites
328 exhibiting transient stage on the path of resistance.

329 Therefore, it is urgent to address the problem based on the data provided by the scientific
330 evidence (the present study as well as references 6–8). To limit self-medication and poor
331 adherence, improving the access to diagnosis and free, or even cheap, medication delivered with
332 instructions for use are required. Countering false beliefs is also required: one third of
333 interviewed people thought that it was better to take a treatment even if the malaria test was
334 negative and 6.4% used ACT as chemoprophylaxis. Beside treatment improvement, individual
335 protection from vectors in these areas of high transmission is crucial and the distribution of
336 insecticide-treated nets should be improved. Gold miners are easily accessible on resting sites and
337 are concerned about their health. Public health interventions in cooperation with Suriname and
338 Brazil should be considered to reduce malaria transmission and limit the risk of emergence of
339 artemisinin resistance, which would have disastrous health and economic consequences well
340 beyond French Guiana.³⁶

341

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353 **Transparency declarations**

354 The authors declare that they have no competing interests.

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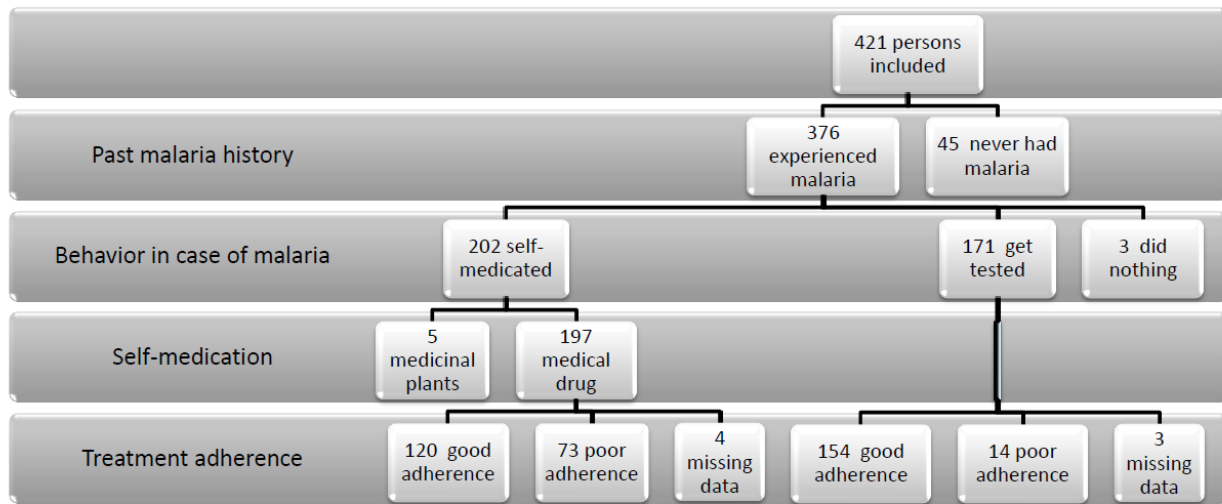
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- 446

447 **Figure 1: Flow chart of the study***

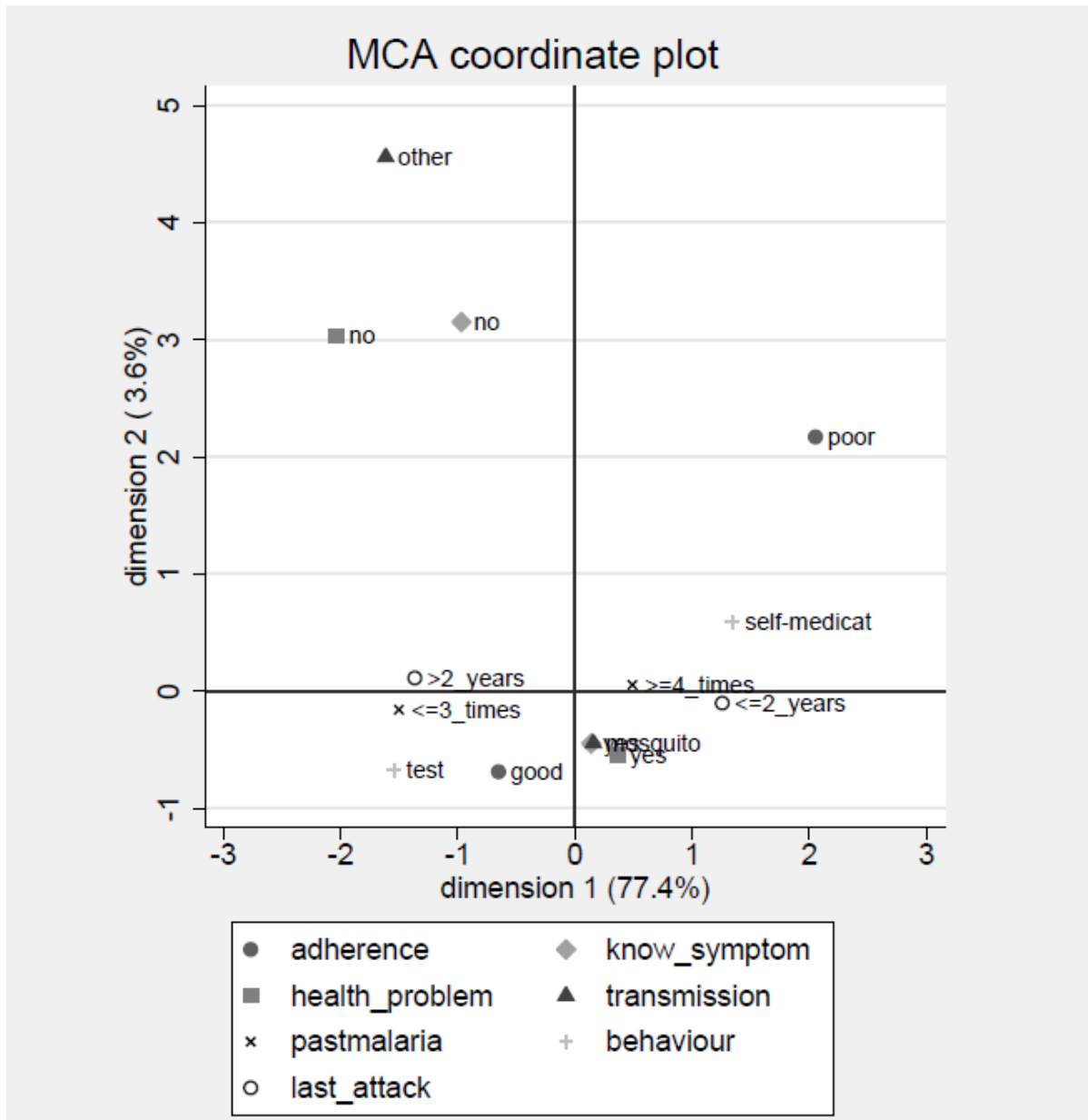


448

449 * In our region, free medication is given to all persons who are tested positive for malaria so getting tested
450 for malaria and self-medication are mutually exclusive categories

451

452 Figure 2: Illegal gold miners behaviours towards malaria in French Guiana, analysed with Multiple
453 Correspondence analyses



454

455 **Table 1: Logistic regression model for factors associated with self-medication in illegal gold miners working in French Guiana, 2015**
 456 (n=202/N=373)

	Self-medication n/N (%)	Univariate analyses		Multivariate analyses ^a	
		OR [CI 95%]	<i>p</i> ^b	AOR [CI 95%]	<i>p</i> ^b
Socio-demographic characteristics					
age^c					
<= 38 years	98/178 (55.06)	1	0.739	1	0.384
> 38 years	104/195 (53.33)	0.99 [0.98-1.01]		0.99 [0.97-1.01]	
sex^c					
female	57/101 (56.44)	1	0.59	1	0.770
male	145/272 (53.31)	0.88 [0.56-1.40]		1.09 [0.61-1.96]	
country of birth					
other than Brazil	3/21 (14.29)	1	<0.001	1	<0.001
Brazil	199/352 (56.53)	7.8 [2.26-26.98]		10.74 [2.82-40.82]	
countries of work the last three years^d					
FG ^e and others	47/115 (40.87)	1	<0.001	1	0.016
FG ^e only	155/258 (60.08)	2.18 [1.39-3.41]		2 [1.14-3.55]	
Attitude and knowledge					
malaria is a major health problem^f					
no	19/55 (34.55)	1	0.001		
yes	183/318 (57.55)	2.57 (1.41-4.67)			
better to treat even if test negative^g					
no	133/263 (50.57)	1	0.031	1	0.039
yes	69/110 (62.73)	1.64 [1.04-2.59]		1.82 [1.03-3.22]	
malaria stays all life^h					
no	148/287 (51.57)	1	0.065		
yes	54/86 (62.79)	1.58 [0.97-2.60]			
cure without treatmentⁱ					
no	180/342 (52.63)	1	0.046	1	0.036
yes	22/31 (70.97)	2.2 [0.98-4.92]		3.19 [1.08-9.46]	
protection against mosquitoes					
sometimes/never	177/315 (56.19)	1	0.066		
always/often	25/58 (43.10)	0.59 [0.34-1.04]			
Clinical data					
past history of malaria					
<=3 malaria attacks	30/91 (32.97)	1	<0.001	1	0.005
>= 4 malaria attacks	172/282 (60.99)	3.18 [1.93-5.23]		2.47 [1.31-4.64]	
date of last malaria attack					
<=2 years	130/194 (67.01)	1	<0.001	1	0.028
> 2 years	72/179 (40.22)	0.97 [0.96-0.98]		0.98 [0.97-1)	
place when last malaria attack					

Brazil	4/60 (6.67)	1	<0.001	1	
French Guiana	188/274 (68.61)	30.60 [10.75-87.11]		22.1 [7.39-66.04]	<0.001
other	10/39 (25.64)	4.82 [1.39-16.74]		6.11 [1.60-23.4]	0.008
<i>Plasmodium spp. PCR</i>					
negative	162/286 (56.64)	1	0.081	1	0.002
positive	40/87 (45.98)	0.65 [0.40-1.05]		0.37 [0.20-0.68]	

a Hosmer-Lemeshow test: p=0,507

b obtained from the likelihood ratio test

c age and sex were forced

d countries were people worked for gold mining the last three years

e French Guiana (FG)

f considering malaria as a major health problem on mining sites

^g thinking that it is better to take a malaria treatment even if the malaria test is negative, just to be sure

h thinking that malaria stay the all life in the body

i thinking that malaria can be cure without treatment

458 Table 2: Factors associated with poor malaria treatment adherence in illegal gold miners working in French Guiana, 2015 (N=87/361)

	Poor adherence	Univariate analyses		Multivariate analyses ^a	
	n/N (%)	OR [CI 95%]	p ^b	AOR [CI 95%]	p ^b
Socio-demographic characteristics					
sex^c					
female	29/98 (29.59)	1	0.142	1	0.184
male	58/263 (22.05)	0.67 [0.40-1.14]		0.67 [0.37-1.21]	
age^c					
<= 38 years	52/172 (30.23)	1	0.009	1	0.005
> 38 years	35/189 (18.52)	0.52 [0.32-0.86]		0.97 [0.95-0.99]	
work time in gold mining					
<= 10 years	56/202 (27.72)	1	0.068		
> 10 years	31/159 (19.50)	0.99 [0.98-1.01]			
Attitude and knowledge					
better treat even if test negative^d					
no	51/256 (19.92)	1	0.004	1	0.016
yes	36/105 (34.29)	2.10 [1.26-3.48]		2 [1.14-3.51]	
malaria kills^e					
no	86/347 (24.78)	1	0.089		
yes	1/14 (7.14)	0.23 [0.03-1.81]			
protection against mosquitos					
sometimes/never	78/304 (25.66)	1	0.097		
always/often	9/57 (15.79)	0.54 [0.25-1.16]			
Clinical data					
past history of malaria					
<=3 malaria attack	16/89 (17.98]	1	0.112		
>= 4 malaria attack	71/272 (26.10)	1.61 [0.88-2.95]			
date of last malaria attack					

<=2 years	64/188 (34.04)	1	<0,001	1	0.003
> 2 years	23/173 (13.29)	0.96 [0.96-0.98]		0.98 [0.96-0.99]	
health-seeking behaviour^f					
get tested	14/168 (8.33)	1	<0.001	1	<0.001
self-medication	73/193 (37.82)	6.69 [3.60-12.43]		6.03 [3.15-11.54]	
place when last malaria attack					
Brazil	4/59 (6.78)	1	<0.001		
French Guiana	75/263 (28.52)	5.48 [1.92-15.67]			
other	8/39 (20.51)	3.54 [0.99-12.74]			

a Hosmer-Lemeshow test: p=0,799

b obtained from the likelihood ratio test

c age and sexe were forced

^d thinking that it is better to take a malaria treatment even if the malaria test is negative, just to be sure

e thinking that malaria can kill

f for the last malaria attack

460 Table 3: Two clusters of persons in Ascending Hierarchical Classification (N=361)*

	Cluster 1 N=213 n (%)	Cluster 2 N=148 n (%)	p
Variables included in ACH			
health-seeking behaviour			
get tested	161 (75.6)	7 (4.7)	
self-medication	52 (24.4)	141 (95.3)	<0,001
treatment adherence			
good	206 (96.7)	68 (45.9)	
poor	7 (3.3)	80 (54.1)	<0,001
date of last malaria attack			
<=2 years	56 (26.3)	132 (89.2)	
> 2 years	157 (73.7)	16 (10.8)	<0,001
malaria is a major health problem			
no	44 (20.7)	11 (7.4)	<0,001
yes	169 (79.3)	137 (92.6)	
transmission pathway			
other	21 (9.9)	11 (7.4)	
mosquito	192 (90.1)	137 (92.6)	0,425
past history of malaria			
<=3 malaria attack	67 (31.5)	22 (14.9)	
>= 4 malaria attack	146 (68.5)	126 (85.1)	<0,001
symptoms knowledge			
no	28 (13.2)	17 (11.5)	
yes	185 (86.8)	131 (88.5)	0,639
Socio-demographical data			
sex			
female	50 (23.5)	48 (32.4)	
male	163 (76.5)	100 (67.6)	0,059
age			
<= 38 years	96 (45.1)	76 (51.4)	
> 38 years	117 (54.9)	72 (48.6)	0,239
education			
none/primary	113 (53.1)	69 (46.6)	
secondary/university	100 (46.9)	79 (53.4)	0,229
time in gold mining			
<=10 years	112 (52.6)	90 (60.8)	
> 10 years	101 (47.4)	58 (39.2)	0,121

461 *N=120+73+154+14=361