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Malaria overdiagnosis and subsequent overconsumption of antimalarial drugs in Angola: Consequences and effects on human health

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ABSTRACT

Microscopic blood smear examinations done in health centers of Angola demonstrated a large overdiagnosis of malaria cases with an average rate of errors as high as 85%. Overall 83% of patients who received Coartem® had an inappropriate treatment. Overestimated malaria diagnosis was noticed even when specific symptoms were part of the clinical observation, antimalarial treatments being subsequently given. Then, malaria overdiagnosis has three main consequences, (i) the lack of data reliability is of great concern, impeding epidemiological records and evaluation of the actual influence of operations as scheduled by the National Malaria Control Programme; (ii) the large misuse of antimalarial drug can increase the selective pressure for resistant strain and can make a false consideration of drug resistant *P. falciparum* crisis; and (iii) the need of strengthening national health centers in term of human, with training in microscopy, and equipment resources to improve malaria diagnosis with a large scale use of rapid diagnostic tests associated with thick blood smears, backed up by a "quality control" developed by the national health authorities.

Monitoring of malaria cases was done in three Angolan health centers of Alto Liro (Lobito town) and neighbor villages of Cambambi and Asseque (Benguéla Province) to evaluate the real burden of malaria. Carriers of *Plasmodium* among patients of newly-borne to 14 years old, with or without fever, were analyzed and compared to presumptive malaria cases diagnosed in these health centers. Presumptive malaria cases were diagnosed six times more than the positive thick blood smears done on the same children. In Alto Liro health center, the percentage of diagnosis error reached 98%, while in Cambambi and Asseque it was of 79% and 78% respectively. The percentage of confirmed malaria cases was significantly higher during the dry (20.2%) than the rainy (13.2%) season. These observations in three peripheral health centers confirmed what has already been noticed in other malaria endemic regions, and highlight the need for an accurate evaluation of the Malaria control programme implemented in Angola.

1. Introduction

Angola is currently facing an outbreak of malaria and in the last bi-annual letter (June 24, 2016) of the Chief of the Global Malaria Programme, Dr P. Alonso stated that "According to government reports, there has been a significant increase in the number of malaria cases and deaths in Luanda since late 2015. Hospital reports showed very high case fatality rates, mainly among older children and adults. Across the country, weak data collection systems are hampering a timely and effective response to malaria. The epidemic in Angola offers a stark reminder of the importance of strong surveillance to measure the extent of increases in disease burden and to ensure targeted interventions for those most in need".

It is well recognized that malaria cases reported from national surveillance systems vary in quality and quantity (Besnard et al., 2006; Besnard et al., 2009). This may have limited value in understanding the actual malaria burden, but may be useful for understanding trends in the relative burden of malaria in the public health sector.

One of the key point is the actual reliability of data reported from health centers in a passive detection method due to 3 main points moreover the bias in recruitment:

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1) There is no pathognomonic symptoms of malaria "simple crisis" and the lack of reliability of clinical diagnosis (even if and when a clinical examination is done) has been long ago underlined (Baudon et al., 1988; Baudon et al., 1986);
2) There is a lack of technical equipment such as microscope which is critical to diagnose malaria (Baudon et al., 1988; Besnard et al., 2006; Rogier et al., 2001) and in countries where 50% or more children are asymptomatic carriers, parasite density could be of great help even with its limitations (Bouvier et al., 1997; Delley et al., 2000). To overcome this issue, WHO recommended a large scale use of Rapid Detection Tests (RDT) and actually "The WHO African Region has had the largest increase in levels of malaria diagnostic testing, from 36% of suspected malaria cases tested in 2005, to 41% in 2010 and 65% in 2014" (World Health Organization, 2015). But RDT has some well-known drawbacks and limitations such as false negative, no detection of low densities, no estimation of parasite densities, etc. Nevertheless they can be considered as interesting tools for malaria diagnosis at Peripheral Health Centre (PHC). Immunological method based on PCR are scientifically the best to detect parasite (Fancony et al., 2013) even at a very low density but they required some skills and equipment which can be implemented only at the Central level and not at the Peripheral one.
3) There is a usual behavior in several PHC to consider any fever as malaria and to implement Artemisinin-based combination therapy (ACT) without going any further. This attitude has 3 main consequences: (1) lack of reliability of malaria diagnosis ("overdiagnosis") and therefore of data dealing with actual malaria; (2) lack of diagnosis of other diseases that do not receive needed appropriate treatment and are not quoted in official statistics such as diseases that could blow up (recent dengue epidemics); (3) increase of selective pressure due to over scale use of ACT.

Although the Angolan Ministry of Health has put efforts these past 12 years to rebuild the health-care infrastructure, child (167/1,000) and maternal (460/100,000) mortality rates remain among the highest in the world (Luckett et al., 2016). Recent reports have shown that in Angola the available statistics for the burden of malaria are not reliable because of the poor case reporting system and the scarcity of nationally representative malaria surveys (Gosoniu et al., 2010; Luckett et al., 2016). For 2002, official numbers reported 1,4 million malaria cases with 11,344 deaths; in 2004, 3,2 million cases and two-thirds occurred in children > 5 years old (UNICEF, 2008). Then, in 2006–2007, a large scale Angola Malaria Indicator Survey was implemented at the national level to assess the prevalence of malaria and anemia among children > 5 years old. For 2013, a total of 2,3 million cases were officially reported with 5,714 deaths. According to recent surveys in Angola, malaria is by far the highest cause of morbidity and mortality and has an epidemic potential in five provinces (Gosoniu et al., 2010).

In the framework of the National Malaria Control Programme, which implemented several integrated measures, including case management based upon ACT and large scale distribution of long lasting impregnated nets (LLIN), a cross sectional study was done to monitor three public health centers and to compare their malaria diagnosis with crosscheck microscopy done in the laboratory of the Medical Department (MD) of the private SONAMET® Company.

2. Materials and methods

2.1. Study setting and design

Between July 2010 and March 2011, at the request of the National Malaria Control Programme (NMCP), the Sonamet MCP team implemented a classical case-control study during the dry and rainy seasons in three health centers, one in Alto Liro (district of Lobito town) and two in neighboring villages, Cambambi and Asseque, located in the Benguela Province. Carriers of *Plasmodium*, among 724 patients of newly-born to 14 years old, with or without fever, were analyzed (Table 1). Information on age, gender and temperature (front) were taken. Thick blood smears were systematically processed in order to estimate their parasite load by classical microscopy. Parasitological data were compared to the malaria diagnosis done in the health center according to clinical symptoms, and eventually parasitological observations, which was considered as "presumptive malaria". In these cases, antimalarial drugs were systematically given, free of charge, by the nurse of these health centers. Initially, the aim of the study was to evaluate the proportion of malaria cases among feverish patients, then to use this information for other health centers and improve the statistical data on malaria procured by Peripheral Health Centre. However, it quickly appeared that even the notion of "fever" was not reliable and could not be used as good discriminant factor of "cases" and "control" because we noticed records of "fever" with body temperature of 35 °C–36 °C (Carnevale, unpublished observation). Therefore, we changed and considered clinically diagnosed malaria (or "presumptive malaria") as cases and "other pathologies" as controls.

Table 1
Number of patients, presumptive and confirmed malaria cases with their proportions (%), and diagnosis error rate per health center.

Health Centers	Alto Liro	Cambambi	Asseque	Total
Patients	227	152	345	724
Presumptive cases	156	78	339	573
%	68.7%	51.3%	98.3%	79.1%
Confirmed cases[a]	3	13	74	90
% per Presumptive cases	1.9%	16.7%	21.8%	15.7%
% per Patients	1.3%	8.6%	21.4%	12.4%
Rate of error (%)	98.1%	83.3%	78.2%	**84.3%**

[a] Thick blood smears.

2.2. Location

Three health centers were chosen for our study. One is in Alto Liro (12°21′S; 13°32′E) located on the upper part of Lobito, a town of 200,000 inhabitants. Vegetation is scarce and the landscape is dry. Until 2007, domestic water was kept permanently in tanks close to habitations, which were suitable breeding sites for *Anopheles gambiae* (Carnevale et al., 2015; Toto et al., 2011). The Alto Liro health center was selected by the NMCP for monitoring data, as it is well equipped with biological service and microscopes. Asseque (12°39′S; 13°27E) is a village of 8,000 inhabitants, close to Benguela town, in an agricultural area with numerous irrigation canals. The health center is well equipped with microscopes and solar panels given by Sonamet. Cambambi village (12°33′S; 13°32′E) is close to Asseque although located in a dryer area with fewer plantations and the health center has no microscope. In addition, some classical cross-sectional malaria surveys were done by MCP team among asymptomatic children of the same three locations to evaluate their *P. falciparum* prevalence for a comparison with the plasmodial prevalence and parasite load among patients of the health centers.

2.3. Ethics statement

This study was conducted in accordance with the Edinburgh revision of the Helsinki Declaration and was approved by the National Malaria Control Program of the Ministry of Health of Angola, the ethical authority in charge of approving studies on malaria research in Angola.

Table 2
Number of patients, presumptive and confirmed malaria cases with their proportions (%), and diagnosis error rate during the dry and rainy seasons according to the health center.

Health Centers (Number of patients)	Alto Liro (n = 227)		Cambambi (n = 152)		Asseque (n = 345)		Total (n = 724)	
Season	Dry	Rainy	Dry	Rainy	Dry	Rainy	Dry	Rainy
Patients	62	165	49	103	143	202	254	470
Presumptive cases	42	114	29	49	137	202	208	365
%	67.7%	69.1%	59.2%	47.6%	95.8%	100%	81.9%	77.7%
Confirmed cases	1	2	11	2	30	44	42	48
%	2.4%	1.8%	37.9%	4.1%	21.9%	21.8%	20.2%	13.2%
Rate of errors (%)	97.6%	98.2%	62.1%	95.9%	78.1%	78.2%	79.8%	86.8%

3. Results

Presumptive malaria was diagnosed for 573 cases of the 724 children selected for the study (79.1%), while only 90 (15.7%) of them were confirmed malaria cases with positive thick blood smears giving thus an overall error rate of 84.3% (Table 1). Presumptive malaria cases were diagnosed 6 times more than the confirmed cases with positive thick blood smears done on the same children. Therefore, the official percentage of presumptive malaria cases constituted nearly 80% of the patients, while reliable parasitological diagnosis showed that 12.4% of the patients were actually parasite carriers and 15.7% of clinically diagnosed malaria were *Plasmodium* positive (Table 1).

3.1. Variations according to season

The comparison of "presumptive" and "confirmed" malaria cases according to dry and rainy seasons and health centers is shown in Table 2. It is worth noticing that the number of presumptive malaria cases diagnosed during the dry and the rainy seasons was not significantly different (respectively 81.9% and 77.7%) ($\chi^2 = 1.79$; $p = 0.091$) and the rate of diagnosis error was around 80% for both seasons (Table 2).

For the confirmed cases of *Plasmodium,* with positive thick smears, the percentage was significantly higher during the dry season than the rainy one, respectively 20.2% and 13.2% ($\chi^2 = 6.05$; $p = 0.008$).

3.2. Variations according to health center

The Alto Liro health center had a similarly elevated rate of diagnosis errors with 97.6% and 98.2% for the dry and rainy seasons respectively (Table 2). The overall of 68.4% of patients (n = 227) were clinically diagnosed as malaria cases, while only three (2%) were confirmed cases with positive blood smear. All 98% of presumptive malaria cases received an ACT treatment in spite of the presence of a microscope and a laboratory unit. The percentage of "presumptive clinical malaria cases" among patients was similar during the dry (67.7%) and the rainy (69.1%) seasons ($\chi^2 = 0.038$; $p = 0.42$). In random cross-sectional surveys done by the MCP team, among 428 symptomless children of the Alto Liro community, the result showed that during the dry season, 12.9% (n = 18) of the 140 children tested had positive blood smears, while during the rainy season, 13.5% (n = 39) were positive among 288 children. Thus, the plasmodial prevalence (PP) was significantly higher among symptomless children (PP = 13.3%; n = 428) than in patients of the Alto Liro health center (PP = 1.3%; n = 227), even if the official declaration of presumptive malaria cases in this health center was very high with two thirds of the patients diagnosed with malaria. The reliability of data from such health center is matter of great concern.

In the Cambambi health center, a total of 78 out of 152 patients were clinically diagnosed with malaria, while only 13 of them (16.7%) were confirmed positive, representing 8.6% of the total patients instead of 51.3% of officially reported cases by the health center, with an overdiagnosis rate of malaria cases reaching 83.3% (Table 2).

The percentage of presumptive malaria cases among patients was similar during the dry (59.2%; n = 49) and the rainy (47.6%; n = 103) seasons ($\chi^2 = 1.79$; $p = 0.09$). The percentage of positive thick smears confirmed as malaria cases was much higher in the dry compared to the rainy season (37.9% and 4.1% respectively) and the overdiagnosis of malaria is therefore significantly higher in the rainy season, reaching nearly 96%, than in the dry season (62.1%) ($\chi^2 = 12.69$; $p = 0.0001$) (Table 2). When compared to Alto Liro, it is interesting to notice that the percentage of positive thick smears among presumptive malaria cases is significantly higher in Cambambi (16.7%; n = 78) without microscope, than in Alto Liro with microscope (1.9%; n = 156) ($\chi^2 = 15.5$; $p < 0.05$) where clearly this tool is not correctly used.

In the Asseque health center, close to Cambambi and well equipped in microscopes and solar panels, presumptive malaria was diagnosed in 339 out of 345 patients (98.3%), while *Plasmodium* confirmed cases were actually reported in 74 thick blood smears (21.8%) giving a diagnosis error rate of 78.2% (Table 2). When Asseque health center reported 98.3% malaria cases among all patients, there were actually 21.4% of confirmed cases. There is an obvious high rate of overdiagnosis of malaria in patients (100%) during the rainy season, while 22% only had confirmed *Plasmodium* parasites on their thick blood smears (Table 2). The percentage of positive blood smears among presumptive malaria cases were similar during the dry and rainy seasons (21.9% and 21.8%; ($\chi^2 = 0.0006$; $p = 0.49$). The prevalence of *Plasmodium* confirmed cases in Asseque was similar to Cambambi, respectively 21.8% (n = 339) with microscopes available and 16.7% (n = 78) ($\chi^2 = 1.02$; $p = 0.31$), in the latter case where no microscope (Table 1). Cross-sectional surveys done by MCP team among the Asseque community covered by this health center showed an overall plasmodial prevalence of 31.1% among the 363 asymptomatic children less than 14 years examined. This plasmodic index appeared significantly higher than the prevalence of *Plasmodium* among the 345 patients of Asseque in our study (21.4%) ($\chi^2 = 7.76$; $p < 0.05$). Plasmodial prevalence was also significantly higher during the dry season (43.2%; n = 132) than the rainy season (24.2%; n = 231) ($\chi^2 = 14.05$; $p < 0.05$), while this prevalence during both seasons was the same (21.8%) in our study (Table 2).

The densities of parasites in thick blood smears of patients and asymptomatic children were analyzed with arithmetic mean of respectively 93,535 [± 148,343] and 1,665 [± 3,176] parasites/µl during the dry season and 47,878 [± 50,353] and 2,695 [± 5,825] parasites/µl during the rainy season (Table 3). Parasitaemia of malaria patients was 56 times higher than in asymptomatic children during the dry season and 18 times during the rainy season. However, the standard deviation is high with overlapping values and no conclusion could be statistically drawn. Therefore, in this epidemiological situation, even parasitaemia by itself could not be the ultimate criteria at individual level for clinical diagnosis. On the other hand, the median of parasitaemia appeared as an interesting parasitological criterion (Table 3) that could be discriminate at a collective level.

Table 3
Parasitaemia, arithmetic mean and median (parasites/μl) for patients and symptomless children according to season.

Season	Patients (parasites/μl)			Asymptomatic children (parasites/μl)		
	Parasitemia (mini-maxi)	Mean (sd)[a]	Median	Parasitemia (mini-maxi)	Mean (sd)[a]	Median
Dry	185–480,000	93,535 [± 148,343]	14,169	32–16,320	1,665 [± 3,176]	533
Rainy	31–192,471	47,878 [± 50,353]	34,376	32–34,933	2,695 [± 5,825]	889

[a] sd, standard deviation.

Table 4
Antimalarial drugs misused for the treatment of presumptive malaria patients according to the respective health center and number of patients.

Drug	Presumptive malaria cases treated/total presumptive malaria cases				
		Alto Liro (n = 156)	Cambambi (n = 78)	Asseque (n = 339)	TOTAL (n = 573)
Coartem®	N (%)	142/145 (97.9%)	52/64 (81.3%)	235/309 (76.1%)	429/518 (82.8%)
Quinine	N	1/1	1/1	24/24	26/26
Amodiaquine	N	1/1	0	5/5	6/6
Arsucam®	N	0	2/2	0	2/2
Arinate®	N	0	5/5	0	5/5
Arthemeter®	N	3/3	1/1	0	4/4
Unspecified drug	N	0	1/1	0	1/1
No antimalarial drug	N (%)	4/4	3/4 (75%)	0	7/8 (87.5%)
Unknown	N	2/2	0	1/1	2/2

3.3. Misusage of antimalarial drugs

Among the 573 presumptive malaria cases that received antimalarial drugs, 90 only were parasitological confirmed cases, meaning that 84.3% of the patients (n = 483) received useless antimalarial drugs that were inadequately recommended (Tables 1 and 4). Such misdiagnosis induced not only a large misusage of antimalarial drug, but also 83% of patients who received Coartem® had an inappropriate treatment, such as, to a lesser extent, those who had other antimalarial drugs including Quinine, Amodiaquine, Arsucam®, Arinate®, or Arthemeter® (Table 4).

4. Discussion

A health facility-based survey dealing with 30 centers in Luanda (Angola), gathering 864 patients with fever (≥37.5 °C) or history of fever in the last 24 h, showed that 31 patients (3.6%) only had positive malaria blood smears (Thwing et al., 2009), and among patients with fever, 4.6% had positive blood smears, and 2.7% were positive even without fever. According to these authors, a very small minority of patients with fever at health facilities in Luanda actually had laboratory-confirmed *Plasmodium* infection, despite the large proportion of patients being diagnosed and treated for malaria (Thwing et al., 2009). They rightly underlined that "this low prevalence even among fever has two major implications: massive overuse of Artemisinin-based combination therapies (ACTs) or other antimalarials in patients who do not need it, and likely under-diagnosis of other causes of fever, some of which may be potentially life-threatening" (Thwing et al., 2009). A cross-sectional cluster survey was done in October-November 2007 in 33 health facilities of Huambo Province of Angola to assess the quality of malaria diagnosis and treatment (Rowe et al., 2009). Suspected malaria was defined as either fever (by history or measured axillary temperature ≥37.5 °C) or at least three of the following symptoms: headache, joint pain, chills, sweating, anemia, anorexia, fatigue, vomiting, or diarrhea. Rowe et al. (Rowe et al., 2009) imagined scenarios of hypothetical patients and noticed that in case of adults with fever and negative test (RDT or microscopy), most health workers (72.0–81.7%) seemed to ignore the result of the test and gave an incorrect diagnosis of malaria, and nearly all patients (96–100%), such as malaria diagnosed or suspected ones, were treated with an antimalarial drug. In this survey, it is worth underlining that even if fever seemed to be the main cause of consultation, temperature was measured in only 26% of consultations and assessment quality was poor for all other symptoms needed to identify suspected malaria. Combining the well-known lack of reliability of clinical symptoms (Baudon et al., 1988), the lack of pathognomonic symptoms and the poor quality of both clinical examinations (if any) and microscopy (if any), some concerns need to be addressed about the statistics, the actual burden of malaria, and its evolution which is of paramount importance for the evaluation of the efficacy of the different measures implemented to control the disease.

In a more recent survey done in the same Province of Huambo (Angola), laboratory supervision, including increase in number and level of training of laboratory technicians, allowed an improvement of malaria diagnostic capacity with a significant reduction in false-positive microscopy slide reading (Luckett et al., 2016).

The current monitoring implemented in the three health centers, one in the Lobito urban part and two in suburban and rural areas of the Benguela Province, showed that among outpatients, parasitological observations confirmed only 15% of malaria cases which were diagnosed according to clinical examination or "presumptive" malaria cases. Our data showed that with or without microscope, the rate of misdiagnosis was similar. In the case of Asseque center, plasmodial prevalence was significantly higher during the dry season than during the rainy season, which could be due to vegetables and other crops cultivated during the dry season that induce large scale use of water for irrigation which favored suitable breeding sites for vectors. This interesting seasonal variation is not indicated in the statistics of the health center where 98.3% of patients were supposed to have malaria (and received ACT treatment) when, in fact, nearly 22% only were

confirmed with positive blood smears (Table 1).

Therefore, according to official reports, malaria is considered as constituting 80% (and more) of consultation while in fact it represented about 12% for the three health centers. This large overdiagnosis leaded to a misusage of drugs and 80% of Coartem® was thus uselessly given. As a consequence, this cost was unnecessarily supported by the NMCP – Ministry of Health, and possible side effects in patients should not be disregarded.

Working in public health centers showed interesting observations on usual behavior of some nurses. For instance, sometimes the diagnosis is made by the patient him/herself at the health center and the nurse provides ACT. Then, the biology department will report the case as positive, otherwise the health agent will appear as incompetent. Besides, the use of microscope is a matter of concern and RDTs are recommended but even if it appears negative, the nurse may conclude "malaria in stage of incubation" due to the pressure of the patient, and provides ACT. Then, our study showed a lack of both (1) the supervision of the nurses and (2) training to improve their skills. As demonstrated in a recent study, laboratory supervision and training of the technicians have greatly improved the quality of malaria diagnostic in Huambo, Angola (Luckett et al., 2016). On a general basis, a good use of a microscope is obviously needed, as it was clearly demonstrated in the medical Department of the Sonamet Company (Besnard et al., 2006; Besnard et al., 2009), even if parasitaemia by itself could not be the ultimate criteria at individual level for clinical diagnosis. On the other hand, the lack of *Plasmodium* in thick blood smears has to be taken into consideration and should induce the search for other diseases and associated treatment.

From an epidemiological aspect, the median of parasitaemia appeared as an interesting parasitological criterion at community level. For a quick and relevant evaluation of malaria evolution according to the implementation of control operations of the NMCP, such criterion should receive some more considerations. It is crucial for the NMCP to have reliable data for an accurate evaluation, both epidemiological and cost/efficacy, of measures undertaken.

Such overdiagnosis and over evaluation of malaria cases were also noticed in other countries. In northern Niger, 95% of clinically diagnosed malaria during the dry season were in fact negative and such presumptive diagnosis of malaria resulted in a significant risk of mistreatment of children in urban Sahel (Olivar et al., 1991). In Nairobi (Kenya), a large scale survey was done during one year, including 22 facilities to estimate the actual burden of malaria among outpatients, and of the 37,544 blood samples, 5,540 (14.6%) malaria blood smears were recorded as positive (Mudhune et al., 2011); interestingly this is a percentage similar to the one noticed in our study. Evaluations of the malaria situation in African countries were recently implemented in Ouagadougou (Burkina Faso) (Wang et al., 2005), Abidjan (Côte d'Ivoire) (Wang et al., 2006c), Cotonou (Benin) (Wang et al., 2006b), Sekondi-Takoradi (Ghana) (Orish et al., 2016), Mocuba (Mozambique) (Hume et al., 2008), Dar es Salaam and Mto wa Mbu (Tanzania) (Mwanziva et al., 2008; Wang et al., 2006a), Garissa County (Kenya) (Njuguna et al., 2015), Khartoum State (Sudan) (A-Elgayoum et al., 2009), and the high rate of malaria overdiagnosis among febrile patients attending clinics was noticed for each study.

Overdiagnosis and antimalarial drugs overconsumption may produce serious effects on human health. Malaria overdiagnosis may increase patients risks of severe outcomes from undiagnosed conditions (Reyburn et al., 2004). For instance, the first diagnosis of the Marburg virus epidemic in 2005, in the Uige Province of Angola, was delayed, partly because of the general belief that the illness was hemorrhagic malaria, all cases being associated with a positive malaria diagnosis (Ministry of Health, 2005; Ministry of Health and WHO, 2005). In addition, antimalarial drugs overconsumption may increase unnecessary expense on limited public sector drug budgets or patients even if drugs are often given free of charge such as in the health centers monitored in Lobito. Furthermore, large systematic use of antimalarial drugs may increase the risk of mismanaged treatment course with too short duration of treatment. A direct consequence will be an increasing incidence of resistance to antimalarial treatments Overconsumption could then lead to decreasing efficiency of Artemisinin and all currently effective treatments.

Overestimation of malaria has been revealed with evidences for more than a decade (D'Acremont et al., 2009). This situation is now well recognized on a global scale. As it was recently underlined, it is "time to move from presumptive malaria treatment to laboratory confirmed diagnosis and treatment in African children with fever" (D'Acremont et al., 2009). Then, as clinical symptoms alone are not relevant for an accurate diagnosis of malaria, the simple observation of *Plasmodium* on thick smear provides an accurate result and sharply reduces the actual number of malaria crisis requiring ACT treatment. After many years of poor attention to parasitological evidence of malaria through microscopy, a global effort based on this "gold standard" must be achieved. The non-confirmed malaria cases must be ended, as well as antimalarial treatment of patients having negative thick blood smear, and other pathologies must be diagnosed and correctly cured. If positive thick blood smear is the proof for malaria case, a negative one must lead to the search of another pathology consequently stopping the too often systematically antimalarial drug treatment.

Competing interests

The authors declare that they have no competing interests.

Author's contributions

VF, PB and PC designed the study protocol; VF and PC carried out the field experiments and the study; SM, PB, and PC were involved in the analysis and interpretation of the data. SM, PB, and PC drafted the manuscript. FF supported the field study. All authors read and approved the final manuscript.

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