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Proactive and reactive case detection to optimise integrated community case management of malaria in a high transmission setting of Cameroon

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Proactive and reactive case detection to optimise integrated community case management of malaria in a high transmission setting of Cameroon

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Malaria, integrated community case management, active case detection, Cameroon

Abstract

Objective: Integrated community case management (iCCM) of childhood illness is a powerful intervention to reduce mortality. Yet, less than 20% of children with fever in sub-Saharan Africa have access to malaria testing. We sought to explore how incorporating proactive and reactive case detection of malaria into iCCM could help accelerate coverage.

Design: A community-led project to proactively screen febrile children under five years for malaria using rapid diagnostic testing and then using index cases to reactively detect more cases

Setting: Four primary schools, 4 health facilities and 13 neighbourhoods of the rural community of Bare-Bakem in Cameroon

Participants: Children and adults with fever

Intervention: Proactive and reactive case detection of malaria between 12 weeks between April and June 2018

Primary and secondary outcome measures: The proportion of index and secondary malaria cases detected during iCCM compared to the intervention

Results: We screened a total of 501 febrile cases of whom *Plasmodium* infection was confirmed in 425 (84.8%) cases including 176 (83.4%) among index cases and 249 (85.9%) among secondary cases. Of the 425 confirmed cases, 102 (24.0%) were index cases identified in the community during routine iCCM activity; 38 (8.9%) were index cases identified proactively in schools; 36 (8.5%) were index cases located in health facilities; and 249 (58.6%) were additional cases detected in the homes of index cases by RACD - showing the value of RACD over iCCM alone. Overall, by incorporating an active case detection approach, iCCM must have been improved by 67.5% to manage malaria cases in the community.

Conclusion: Most symptomatic cases of malaria remain undetected in the community despite the introduction of community case management of malaria but these undiagnosed cases can be mopped-up by adopting a proactive and reactive case detection approach. This approach should be targeted to schools, older children and large households.

Article Summary

Strengths and Limitations of this study

- The first study to show the clinical relevance of a reactive case detection strategy in a high malaria transmission area
- The study used existing community resources but in a more target manner to maximise access to malaria treatment in a poor and rural community

- A small-scale study with no control arm carried out during a relatively short period and during the high transmission season thus inclined towards over-estimating the value of the intervention

Introduction

In Cameroon, malaria-related morbidity has reduced from 40.6% in 2008 to 23.6% in 2016 while malaria mortality has reduced from 17.6% in 2000 to 12.4% in 2016[1-3]. Despite this remarkable effort, malaria remains a major public health problem in Cameroon where the entire population of more than 25 million inhabitants is at risk, with 71% living in high transmission areas[4]. In 2016, approximately 1.7 million malaria cases and 2637 deaths from malaria were recorded in health facilities in Cameroon. Children under five years of age were the most affected group in whom malaria was responsible for 41% of all case morbidity, 55% of hospital admissions and 69.7% of all malaria-attributed deaths in 2015[2]. To reduce childhood mortality, Cameroon and her development partners began implementing integrated community case management (iCCM) of pneumonia, diarrhoea, and malaria in 2009 to target communities with difficult access to health services. Community case management (CCM) of malaria can reduce overall and malaria-specific under-five mortality by 40% and 60%, respectively, and severe malaria morbidity by 53%[5, 6]. Yet in 2011, less than 20% of children with fever in sub-Saharan Africa received a finger/heel stick for malaria testing[7]. In some localities of Cameroon, iCCM strategy has been reported to have increased treatment rate for malaria, increased care seeking for fever and reduced burden on healthcare facilities[8, 9]. However, data from a community needs assessment conducted in 2016 in the rural community of Bare-Bakem in the Littoral Region of Cameroon indicated that malaria represented up to 80% of all-cause morbidity across health centres and that iCCM has been facing significant challenges including: passiveness in operation; low uptake, underutilisation and attrition of trained community health workers (CHW); prolonged and frequent stockouts of commodities for malaria diagnosis and treatment; inadequate supervision and motivation. School children though typically constituting the group with the highest prevalence of Plasmodium infection, have been virtually left out of this intervention despite receiving increasing attention recently[10-12]. In response to these challenges that threaten to reverse the initial iCCM gains, Peace Corps Cameroon has been supporting rural communities in Cameroon to effectively fight malaria. In 2018, the Peace Corps community of Bare-Bakem introduced a proactive and reactive case detection approach into the existing iCCM system with the objective to reduce malaria burden by expanding access to prompt malaria case

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3 management in the community. Integrating active (proactive and/or reactive) case detection
4 strategy with iCCM has not yet been documented in high transmission settings. We report
5 how in this community-led project, CHW proactively searched for cases of malaria in
6 children under five in schools, health facilities and households; and then using index cases,
7 they reactively detected and treated even more cases in the community by visiting the
8 households of the sick children with confirmed malaria.
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12 **Methods**

13 **Intervention site and priority setting**

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16 The intervention was carried out in the rural town of Baré, the headquarters of Baré -Bakem
17 municipality with a population of about 20000 inhabitants occupying a surface area of about
18 200km². Bare is situated at approximately 10 km from Nkongsamba (the divisional capital)
19 and 120 km from the coastal city of Douala (the regional capital). It has 13 neighbourhoods:
20 Bareko, Ebouth, Axe-Lourde, A, A bis, B, B bis, C, D, E, E bis, F and F bis. The locality's
21 low elevation and its equatorial warm and wet climate are conducive for the multiplication of
22 mosquitoes and eventually malaria endemicity. The town is host to a Peace Corps Volunteer
23 (PCV) for the period between 2016 and 2018 with the mission to support efforts to fight
24 infant and maternal mortality, malnutrition, malaria and HIV/AIDS. On average, across all
25 the four health facilities in Baré, malaria made up approximately 40% of all sicknesses
26 reported in 2016. Cases of malaria can even represent up to 80% of all sicknesses during the
27 wet season. A Community Needs Assessment (CNA) carried out in December 2016 and
28 January 2017 prior to the intervention indicated that malaria was the number one health
29 priority for the community. Of the 250 people that were interviewed, 84% claimed that
30 malaria was Baré's most important health problem. Malaria has a particularly devastating
31 effect on children under the age of five, over 50% of consultations for children under five
32 years old are confirmed cases of malaria. Despite the recognition that malaria is the
33 community's top health priority – only 34% of participants could correctly explain the mode
34 of transmission of malaria. Similarly, there is very limited access to health facilities and
35 inadequate health-seeking behaviour for malaria treatment. About 80% of the population
36 indicated that they initially seek care from traditional healers or road-side drug vendors. This
37 is why a focus on malaria prevention and education is important but prompt and expanded
38 access to malaria treatment so critical in Baré.
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Intervention description and evaluation

During 8 weeks of the high transmission period between April and June 2018, Baré's six CHW locally known in French as "*Agent de Santé Communautaire (ASC)*" conducted an active malaria case detection (ACD) involving both a proactive case detection (PACD) phase and a reactive case detection (RACD) phase.

Before launching, the project trained 25 primary and nursery school teachers on malaria detection and the promotion of prevention & care seeking behaviour. Each ASC was assigned to a school and a collaborative system among teachers and ASCs working together to detect sick children was developed. Consent forms were distributed to the teachers to pass along to parents of pupils for their approval to test their children. The four health centres were also invited to the training in order to build working relations with ASCs and all the health centres in Baré. The ASCs had been trained repeatedly over the past years by the National Malaria Control Programme (NMCP) on community management of malaria, iCCM but they were briefed alongside two supervisors on the specificities of this project. One supervisor was in charge of correct data collection, while the other inspected schools and visited households to ensure effectiveness of field work.

PACD was undertaken in 12 primary & nursery schools, 4 health centres, and 13 community neighbourhoods on a weekly basis. Each week on a Thursday, ASCs visited assigned schools and health centres for a febrile screening. Upon arriving at their schools, the trained teachers will indicate the pupils under five who recently had a fever (axillary temperature of 38°C or more). Health workers similarly helped to identify febrile children admitted in health facilities. Children with fever were identified as index cases, tested freely for Plasmodium infection using rapid diagnostic tests (RDT) approved and supplied by the NMCP. Those tested positive for malaria were further classified as either uncomplicated or severe malaria. Uncomplicated malaria cases were immediately treated with amodiaquine + artesunate, the first-line artemisinin-based combination therapy (ACT) recommended and supplied by the NMCP. Severe cases and RDT-negative cases were referred to health facilities for further investigation and management as per the NCMP guidelines. If an index case was absent from school the day the ASC arrived, the teacher would tell the ASC where the child lives. The ASC would visit the household and proceed as above. In the community however, ASCs continued to identify febrile children as per the conventional iCCM guidelines.

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3 As malaria cases tend to cluster geographically and temporally[13-16], ASCs then proceeded
4 with the RACD method to visit the home of an index case of confirmed malaria to find more
5 cases who presented symptoms of malaria in the past week. These secondary cases or
6 contacts would then be tested for free, classified and treated or referred to the nearest health
7 centre in a similar way like the index case.
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11 Data was collected using paper registers and later transcribed into a Microsoft Excel
12 electronic database available as a Supplementary File 1. Data collected from the index case
13 during PACD included: age, gender, place of residence, presence of fever, date of onset of
14 fever, date and location seen by an ASC, results of RDT for malaria, severity of malaria and
15 treatment received. During household visits, the same data were collected from febrile
16 contacts in addition to data pertaining to household size, long-lasting treated bed nets
17 ownership and current usage. Health facility malaria surveillance registers and ASC registers
18 were used as sources to abstract data on malaria cases notified between 2015 and 2018.
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22 Data analyses were performed using Stata version 14.2 (StataCorp. LP, College Station,
23 United States of America) and Microsoft Excel 2016 (Microsoft Corporation, Redmond,
24 USA) was used to plot curves. The data set was checked for logical inconsistencies, invalid
25 codes, omissions and improbable data by tabulating, summarizing, describing and plotting
26 variables, depending on their nature. Missing observations were systematically excluded.
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30 The value of PACD and RACD over iCCM alone was measured by the proportion of
31 additional cases detected.
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35 To describe similarities or differences between index cases and contacts, summary statistics
36 were presented as proportions for categorical variables, as means and standard deviations for
37 normally distributed continuous variables and as medians and interquartile ranges (IQRs) for
38 continuous variables with a skewed distribution. Associations between categorical variables
39 were assessed using Pearson's χ^2 test or Fisher's exact test for small samples, as appropriate.
40 For continuous variables, mean differences between index cases and contacts were assessed
41 using Student's t test. Associations between exposure variables and the likelihood of finding
42 a contact were evaluated by a univariate logistic regression model; crude odd ratios, 95%
43 confidence intervals (CIs) were reported. Subsequently, factors associated with the odds of a
44 finding a contact in the univariate analysis at a significance level below 5% were included in
45 a multiple logistic regression model with mixed effects to account for the variability in CHW
46 performance. Backward elimination based on a p-value lower than 0.05 was used to retain
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variables that were independently associated with contact tracing; the corresponding adjusted odds ratios (aORs) and 95% CIs for the final model were reported.

In late May we conducted one comparative sweep of three purposefully selected neighbourhoods (Ebouh, Bareko, and B Bis) to assess how many cases of malaria were detected using our strategy relative to a full door-to-door sweep.

Patient and public involvement statement

As a community-led project, the public and patients were involved in the project planning, implementation and data collection.

The study was approved by the Cameroon National Ethics Review Committee and Peace Corps Cameroon. Individual and parental consent was sought and all information was anonymised and de-identified prior to analysis.

Results

Detection and management of febrile cases

At the end of the three-month pilot study, we screened a total of 501 febrile cases of whom 211 were index cases with a mean age of 3.4 ± 0.1 years who triggered a further screening by RACD of 290 contacts of mean age 19.9 ± 1.1 years (Table 1). Out of these index cases, 65 (30.8%) children from schools led to additional 55 (19.0%) cases, 36 (17.1%) from health facilities led to a further 35 (12.0%) cases, and 110 (52.1%) cases from the community led to 200 (69.0%) secondary cases. On average, index cases were reached within 2.4 ± 0.2 days after onset of fever. Of those screened, 65 index cases were likely to be boys (60.2%) while secondary cases were mostly girls under five years but no gender specificity among older secondary cases. The prevalence of malaria as demonstrated by a positive RDT, was very high in both the index (83.4%) and the secondary cases (85.9%). Of these 425 confirmed malaria cases, 354 (83.3%) were classified as uncomplicated malaria cases who received ACT immediately from the ASCs including 142 (67.3%) from the index cases and 212 (73.1%) from the secondary cases. The 147 cases who did not receive immediate ACT, were classified as either RDT negative in 76 (15.2%) or as having severe malaria in 71 (16.7%) cases. A total of 113 cases who did not receive ACT were referred to the nearest health centre for further management including all the remaining 35 RDT negative index cases and 78 secondary cases.

Table 1. Characteristics of index and secondary cases of fever detected between April and June 2018

Characteristics		Index cases (n = 211)	Contacts (n = 290)	P-value of the difference between the groups
Reactive cases found per index case source				
	School	65 (30.8)	55 (19.0)	
	Health facility	36 (17.1)	35 (12.0)	
	Community	110 (52.1)	200 (69.0)	
	Total	211 (100)	290 (100)	<0.001
Gender, n (%)				
	Male	127 (60.2)	144 (49.7)	
	Female	84 (39.8)	146 (50.3)	
	Total	211 (100)	290 (100)	0.019
Age, mean(SD) years		3.4 (0.1)	19.9 (1.1)	<0.0001
Confirmed malaria, n (%)				
	RDT positive	176 (83.4)	249 (85.9)	
	RDT negative	35 (16.6)	41 (14.1)	
	Total	211 (100)	290 (100)	0.450
Immediate malaria treatment, n (%)				
	ACT	142 (67.3)	212 (73.1)	
	No ACT	69 (32.7)	78 (26.9)	
	Total	211 (100)	290 (100)	0.159
Referrals, n (%)				
	Yes	35 (16.6)	78 (26.9)	
	No	176 (83.4)	212 (73.1)	
	Total	211 (100)	290 (100)	0.006
Household size, mean (95%CI)		6.3 (6.0 – 6.5)		
Household LLIN ownership, mean (95%CI)		2.3 (2.2 – 2.4)		
LLIN coverage per household member (95%CI)		0.37 (0.35 – 0.38)		
LLIN in use per household member (95%CI)		0.33 (0.31 – 0.35)		

Proactive and Reactive case detection of confirmed malaria

During the RACD triggered by 176 index cases of confirmed malaria in children under five, 132 (75%) of these index cases investigated led to at least one additional case of confirmed malaria and a total of 249 secondary cases identified within 176 households visited. After a lag phase during the first half of the project, the number of cases detected increased sharply over the second half before returning to the initial stable level (Figure 1).

Figure 1. Trend in the number of cases of confirmed malaria between April and June 2018

There were approximately 6 persons on average per household with a bed net ownership of about 2 LLINs per household leading to a bed net coverage of about 1 LLIN for 3 persons. Of all the 425 confirmed cases, 38 (8.9%) were index cases identified proactively in schools and led to find 50 (11.8%) more cases; 36 (8.5%) were index cases located in health facilities and led to a further 24 (5.6%) cases; and 102 (24.0%) were index cases identified during routine iCCM activity and led to 175 (41.2%) additional cases showing the value of RACD over iCCM alone (Figure 2). Overall, this active case detection (ACD) strategy based on PACD and RACD identified 287 of the 425 cases thus indicating that the ongoing iCCM must have been improved by 67.5% to manage malaria cases in the community.

Across these three neighbourhoods in May 2018, there was a total of 86 confirmed cases of malaria of whom our project found 50 while the door-to-door sweep caught an additional 36 cases. Thus, suggesting that this project succeeded at detecting 63% of the cases that could be captured by an exhaustive door-to-door strategy.

Seasonally, across 12 weeks in April, May, and June in 2017 the ASCs detected 238 cases of malaria at a rate of ~20 cases per week. During our 8-week project across April, May and June in 2018, the ASCs detected 365 cases of malaria at a rate of ~45 cases per week computing to a 125% increase.

Figure 2. Relative contribution of active case detection strategies

The odds of finding a secondary case by RACD increased by 70% if the index case was one year younger (adjusted odd ratio (aOR) = 1.7, 95% CI: 1.5 – 1.9) and by 20% if a household increased by one person (aOR = 1.2, 95% CI: 1.1 – 1.3). Though RACD was likely to find female cases, the evidence to support gender discrimination was rejected in the multiple regression model in Table 2 (aOR = 1.2, 95% CI: 0.7 – 2.1).

Table 2. Multiple logistic regression model of factors associated with secondary case detection (N = 425)

Factor		Number of confirmed secondary cases, n (%)	Crude OR (95%CI)	p-value	Adjusted OR (95%)	p-value
Gender						
	Male	124 (53.7)	Reference		Reference	
	Female	125 (64.4)	1.6 (1.1 – 2.3)	0.024	1.2 (0.7 – 2.1)	0.477
Additional one year of age			1.7 (1.5 – 1.9)	<0.001	1.7 (1.5 – 1.9)	<0.001
Additional one household member			1.2 (1.1 – 1.3)	<0.001	1.2 (1.1 – 1.3)	0.015

Discussion

In this small-case quality improvement study, we sought to demonstrate in a high transmission area, the feasibility of embedding both the proactive and reactive case detection strategies into integrated community case management in order to maximise malaria case detection and prompt treatment. The study has indicated that by proactively searching for children under five years with malaria as index cases, and by reactively searching for more cases in the households of index cases, iCCM must have been improved by approximately 67.5%. The study has also confirmed that the burden of malaria lies in the community with only the tip of the iceberg seen in health facilities. While iCCM was introduced to respond to this challenge, it was currently underperforming in this rural setting. This project has suggested that iCCM can be adapted to achieve optimal results. While on one hand it may appear obvious that the malaria component of iCCM can be adapted to or opt for a PACD strategy, implementing RACD in a high transmission setting on the other hand may seem experimental or even controversial to some extent. This is because RACD is a surveillance approach recommended in low transmission or pre-elimination settings to disrupt transmission and is thought to be inefficient and unfeasible in high transmission settings. Conversely, RACD may also waste time and money when cases are few and sporadic[17-20].

Therefore, the choice of RACD as an approach depends on the objective to be attained, the proportion of cases it can detect and the resources needed. Our project was feasible and efficient because our aim was not to eliminate malaria but to detect and treat the maximum possible number of cases during a high transmission season when the proportion of cases is highest using resources already made available for iCCM in a rural setting where access to health services is limited. The extra resource needed is the time to visit schools, health facilities and households. CHWs told us that by conducting only a one-day visit per week to these facilities and only to households of index cases was more productive and made them more useful in their community. This strategy was not much different from what they were doing before, just a more targeted approach: - targeting schools, targeting households of index cases and targeting high transmission season when fever is likely to be caused by a *Plasmodium* infection as confirmed in this study where RDT was positive in 85% of persons screened for fever and with a probability of 75% that every index case led to at least one more case. Beyond CHW job satisfaction, teachers also expressed their satisfaction and were of great support in detecting fever or a history of fever amongst their pupils. Moreover, we found that teachers were far more likely to help CHW finding the households of sick children than healthcare workers. We thus strongly believe that RACD can be both feasible and efficient in a high transmission setting to maximise clinical case management. Consequently, we recommend that PACD and RACD become part of the ongoing iCCM strategy in Cameroon as an approach to optimise case detection. Yet incorporating PACD and RACD into iCCM will entail building a strong collaboration among CWH, HCW and teachers. Such a partnership already exists between the ministries of health and education in Cameroon in their concerted effort to fight neglected tropical diseases specifically soil-transmitted helminthiasis in school children[21]. The recurrent problem of stockouts of commodities will need to be resolved by the NMCP and field monitoring and supervision should become regular by iCCM programme coordination. Resolving these issues of multisector collaboration, delivery of commodities and field coordination were crucial as bottlenecks and explain in part why progress was slow in the first half of the project.

This study has further indicated that, while index cases were likely to be boys, RACD was likely to find girls and women in univariate analysis though such claims were not supported by evidence from multivariate analysis. Boys make up the majority of school children in Cameroon especially in the rural areas and this might be a reflection of this observation[22]. However, it is plausible that gender norms and values that determine the division of labour,

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3 leisure patterns, pregnancy, and sex-segregation of sleeping arrangements may lead to
4 different patterns of exposure to mosquitoes for men and women[22-24].
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7 Secondary cases were likely to be older than index cases and to be located in larger
8 households of the index case. Given that we purposely targeted children under five years, it
9 became obvious that we may likely find more of older children and adults as contacts.
10 Clustering of cases has previously been demonstrated in households of the contacts and
11 malaria eradication is thought to be feasible when household size drops below four persons
12 [25, 26]. The average household size in this study was six persons thus explaining while it
13 was very likely to find more cases in the community during RACD.
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19 This study had some limitations so that the results should be interpreted with caution. The
20 duration and period of the study was limited to only three months and to the first half of the
21 wet season. We could not therefore account for neither seasonality in malaria transmission
22 nor account for sustainability throughout the year. Older children and adults were not
23 included as index cases thus creating an outright difference between index and secondary
24 cases. This must have led to an overestimation of the value of RACD over iCCM in this field
25 study because in routine practice however, adults would be index cases as well. Targeting
26 school children for malaria treatment must have been a laudable effort but older school
27 children were also left out as index cases though they constitute a group with a higher
28 plasmodium infection prevalence than in the targeted younger age group[10]. However, these
29 children were among those screened in the community. We did not measure the effect of this
30 strategy on the pneumonia and diarrhoea components of iCCM but we believe that being an
31 integral part of the package of interventions, these two components were likely to have been
32 improved as well. We did not attempt to measure effect on malaria transmission as most
33 studies have done.
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44 **Conclusion**

45 This study has shown that most symptomatic cases of malaria remain undetected in the
46 community despite the introduction of integrated community management of malaria.
47 Schools are an important portal to locate children with undiagnosed malaria. Active case
48 detection based on a proactive and reactive case detection approaches is feasible in a high
49 transmission setting and has been shown to enhance in a synergistic manner the efficiency of
50 integrated community case management of malaria. We recommend that national malaria
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control programs adopt and implement this modified form of iCCM in similar settings to reduce the burden of malaria in our communities.

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Footnotes

Ethics approval and consent to participate

The study was approved by the National Ethics Review Board of Cameroon, Peace Corps Cameroon and local administrative and health authorities. Verbal consent was obtained from

household members after making public announcements and providing an information leaflets to explain the objectives of the project.

Consent for publication

Not Applicable

Availability of data and material

The datasets used and/or analysed during the current study are available as a supplementary file.

Competing interests

The authors declare that they have no competing interests

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Author Contributions

Conception, design and implementation: TDW, CEB

Data collection, analysis and interpretation: TDW, CEB

Drafting the manuscript: CEB

All authors read and approved the final manuscript

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TDW: Community Health Educator, Peace Corps Cameroon

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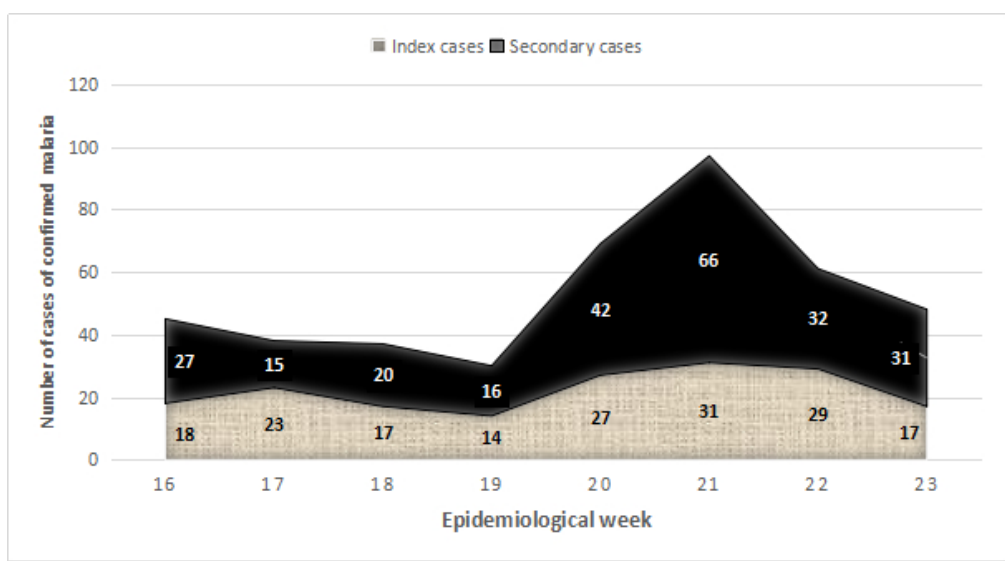


Figure 1

159x87mm (96 x 96 DPI)

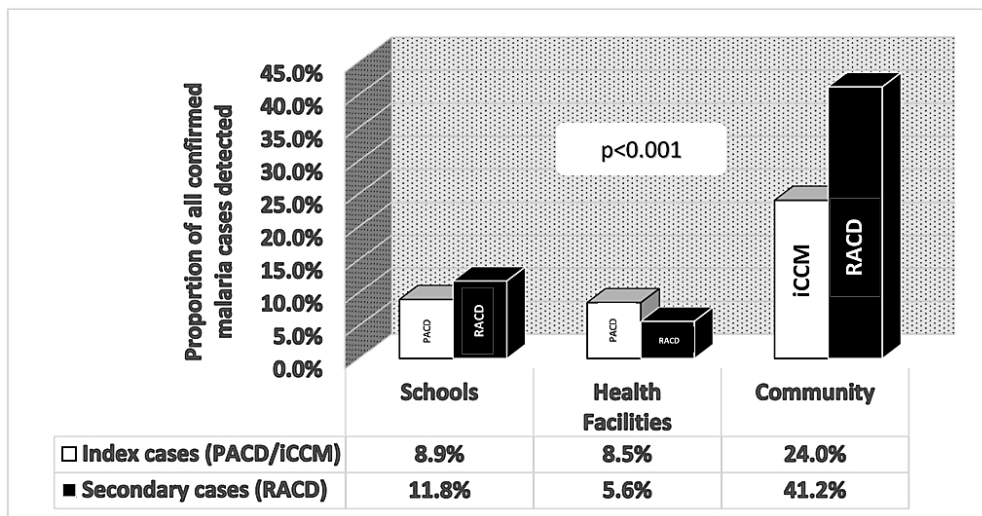


Figure 2

271x142mm (96 x 96 DPI)

Reporting checklist for quality improvement study.

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	Reporting Item	Page Number
	#1 Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patientcenteredness, timeliness, cost, efficiency, and equity of healthcare)	1
	#02a Provide adequate information to aid in searching and indexing	1
	#02b Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	2
Problem description	#3 Nature and significance of the local problem	3
Available knowledge	#4 Summary of what is currently known about the problem, including relevant previous studies	3
Rationale	#5 Informal or formal frameworks, models, concepts, and / or theories used to explain the problem, any reasons or	3

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		assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	
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4	Specific aims	#6 Purpose of the project and of this report	4
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6	Context	#7 Contextual elements considered important at the outset of introducing the intervention(s)	4
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10	Intervention(s)	#08a Description of the intervention(s) in sufficient detail that others could reproduce it	5,6
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14		#08b Specifics of the team involved in the work	5
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16	Study of the Intervention(s)	#09a Approach chosen for assessing the impact of the intervention(s)	6,7
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20		#09b Approach used to establish whether the observed outcomes were due to the intervention(s)	6,7
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23	Measures	#10a Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability	6
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29		#10b Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost	5,6
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34		#10c Methods employed for assessing completeness and accuracy of data	6
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38	Analysis	#11a Qualitative and quantitative methods used to draw inferences from the data	6,7
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42		#11b Methods for understanding variation within the data, including the effects of time as a variable	7
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46	Ethical considerations	#12 Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	7
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51		#13a Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project	n/a
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56		#13b Details of the process measures and outcome	n/a
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4			relevant contextual elements	
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8			problems, failures, or costs associated with the intervention(s).	
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13	Summary	#14a	Key findings, including relevance to the rationale and specific	10
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16		#14b	Particular strengths of the project	10
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19	Interpretation	#15a	Nature of the association between the intervention(s) and the	10
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23		#15b	Comparison of results with findings from other publications	10-12
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34	Limitations	#16a	Limits to the generalizability of the work	12
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52		#17e	Suggested next steps	12
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56			funding organization in the design, implementation,	
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interpretation, and reporting

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BMJ Open

Adding proactive and reactive case detection into the integrated community case management system (iCCM+) to optimise diagnosis and treatment of malaria in a high transmission setting of Cameroon

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Primary Subject Heading:	Public health
Secondary Subject Heading:	Infectious diseases
Keywords:	Malaria, integrated community case management, active case detection, Cameroon

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6 2 **integrated community case management system (iCCM+)**
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8 3 **to optimise diagnosis and treatment of malaria in a high**
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10 4 **transmission setting of Cameroon**

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43 16 **Key words**

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45 17 Malaria, integrated community case management, active case detection, Cameroon

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Abstract

Objective: Integrated community case management (iCCM) of childhood illness is a powerful intervention to reduce mortality. Yet, less than 20% of children with fever in sub-Saharan Africa have access to malaria testing. We conducted an action research to explore how iCCM+ based on incorporating proactive and reactive case detection of malaria into iCCM could help accelerate coverage.

Design: A community-led cross-sectional survey to measure the proportion of *Plasmodium* infection detected under iCCM+ compared with iCCM alone.

Setting: Four primary schools, 4 health facilities and 13 neighbourhoods of the rural community of Bare-Bakem in Cameroon

Participants: Children and adults with fever between April and June 2018

Intervention: A modified iCCM programme (iCCM+) comprised of a proactive screening of febrile children under five years old for malaria using rapid diagnostic testing to identify index cases and a reactive screening triggered by these index cases to detect secondary cases in the community

Primary and secondary outcome measures: The proportion of index and secondary malaria cases detected by iCCM+ compared with iCCM alone.

Results: We screened a total of 501 febrile patients of whom *Plasmodium* infection was confirmed in 425 (84.8%) cases including 176 (83.4%) index cases and 249 (85.9%) secondary cases. Of these cases, 102 (24.0%) were index cases identified in the community during routine iCCM activity and 36 (8.5%) cases detected passively in health facilities; 38 (8.9%) were index cases identified proactively in schools; and 249 (58.6%) were additional cases detected in the homes of index cases by RACD – computing to a total of 287 (67.5%) additional cases found by iCCM+ showing the added value of iCCM+ over iCCM alone.

Conclusion: Most symptomatic cases of malaria remain undetected in the community despite the introduction of community case management of malaria but most of these undiagnosed cases can be mopped-up by iCCM+.

55 **Article Summary**

56 **Strengths and Limitations of this study**

- 57 • The first study to show the clinical significance of a reactive case detection strategy in
58 a high malaria transmission area
- 59 • The study used existing community resources but in a more targeted manner to
60 maximise access to malaria treatment in a poor and rural community
- 61 • A small-scale study with no control arm carried out during a relatively short period and
62 during the high transmission season thus inclined towards over-estimating the value of
63 the intervention

64 **Introduction**

65 In Cameroon, malaria-related morbidity has reduced from 40.6% in 2008 to 23.6% in 2016
66 while malaria proportionate mortality has reduced from 17.6% in 2000 to 12.4% in 2016[1-3].
67 Despite this remarkable effort, malaria remains a major public health problem in Cameroon
68 where the entire population of more than 25 million inhabitants is at risk, with 71% living in
69 high transmission areas[4]. In 2016, approximately 1.7 million malaria cases and 2637 deaths
70 from malaria were recorded in health facilities in Cameroon. Children under five years of age
71 were the most affected group in whom malaria was responsible for 41% of all-cause morbidity,
72 55% of hospital admissions and 69.7% of all malaria-attributed deaths in 2015[2]. To reduce
73 childhood mortality, Cameroon and her development partners began implementing integrated
74 community case management (iCCM) of pneumonia, diarrhoea, and malaria in 2009 to target
75 communities with difficult access to health services. Community case management (CCM) of
76 malaria can reduce overall mortality and malaria-specific under-five mortality by 40% and
77 60%, respectively, and severe malaria morbidity by 53%[5, 6]. Yet in 2011, less than 20% of
78 children with fever in sub-Saharan Africa received a finger/heel stick for malaria testing[7]. In
79 some localities of Cameroon, iCCM strategy has been reported to have increased treatment rate
80 for malaria, increased care seeking for fever and reduced burden on healthcare facilities[8, 9].
81 However, data from a community needs assessment conducted in 2016 in the rural community
82 of Bare-Bakem in the Littoral Region of Cameroon indicated that malaria represented up to
83 80% of all-cause morbidity across health centres and that iCCM has been facing significant
84 challenges including: passive rather than active case detection; low uptake, underutilisation and
85 attrition of trained community health workers (CHWs); prolonged and frequent stockouts of
86 commodities for malaria diagnosis and treatment; inadequate supervision and motivation of
87 CHWs. School children though typically constituting the group with the highest prevalence of

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2
3 88 *Plasmodium* infection, have been virtually left out of this intervention despite receiving
4 89 increasing attention recently[10-12]. In response to these challenges that threaten to reverse the
5 90 initial iCCM gains, Peace Corps Cameroon has been supporting rural communities in
6 91 Cameroon to effectively fight malaria. In 2018, the Peace Corps community of Bare-Bakem
7 92 introduced a proactive and reactive case detection approach into the existing iCCM system
8 93 with the objective to reduce malaria burden by expanding access to prompt malaria case
9 94 management in the community. Integrating active (proactive and/or reactive) case detection
10 95 strategy with iCCM has not yet been documented in high transmission settings. We report how
11 96 in this community-led project, CHW proactively searched for cases of malaria in children under
12 97 five in schools, health facilities and households; and then using index cases, they reactively
13 98 detected and treated even more cases in the community by visiting the households of the sick
14 99 children with confirmed malaria.

100 **Methods**

101 **Design:** A community-led cross-sectional survey to measure the proportion of *Plasmodium*
102 infection detected under iCCM+ compared with iCCM alone.

103 **Intervention site and priority setting**

104 The intervention was carried out in the rural town of Baré, the headquarters of Baré -Bakem
105 municipality with a population of about 20000 inhabitants occupying a surface area of about
106 200km². Bare is situated at approximately 10 km from Nkongsamba (the divisional capital) and
107 120 km from the coastal city of Douala (the regional capital). It has 13 neighbourhoods:
108 Bareko, Ebouth, Axe Lourd, A, A bis, B, B bis, C, D, E, E bis, F and F bis. The locality's low
109 elevation and its warm and wet equatorial climate are conducive for high levels of malaria
110 transmission. The town was host to a Peace Corps Volunteer (PCV) for the period between
111 2016 and 2018 with the mission to support efforts to fight infant and maternal mortality,
112 malnutrition, malaria and HIV/AIDS. On average, across all the four health facilities in Baré,
113 malaria made up approximately 40% of all sicknesses reported in 2016. Cases of malaria can
114 even represent up to 80% of all sicknesses during the wet season. A Community Needs
115 Assessment (CNA) carried out in December 2016 and January 2017 prior to the intervention
116 indicated that malaria was the number one health priority for the community. Of the 250 people
117 that were interviewed, 84% claimed that malaria was Baré's most important health problem.
118 Malaria has a particularly devastating effect on children under the age of five, over 50% of
119 consultations for children under five years old were confirmed cases of malaria. Despite the

1
2
3 120 recognition that malaria is the community's top health priority – only 34% of participants could
4 121 correctly explain the mode of transmission of malaria. Similarly, there is very limited access
5 122 to health facilities and inadequate health-seeking behaviour for malaria treatment. About 80%
6
7 123 of the population indicated that they initially seek care from traditional healers or road-side
8
9 124 drug vendors. This is why a focus on malaria prevention and education is important but prompt
10 125 and expanded access to malaria treatment so critical in Baré. The iCCM programme was
11
12 126 introduced to respond to these needs but had its shortcomings that led to the implementation of
13
14 127 iCCM+.

18 128 **Intervention description and evaluation: Integrated Community Management** 19 20 129 **Plus (iCCM+)**

21 130 During 8 weeks of the high transmission period between April and June 2018, Baré's six CHWs
22
23 131 locally known in French as "*Agent de Santé Communautaire (ASC)*" conducted an active
24
25 132 malaria case detection (ACD) involving the addition of both the proactive case detection
26
27 133 (PACD) phase and the reactive case detection (RACD) approaches into their existing iCCM
28
29 134 activities. In operational terms, **iCCM+ = iCCM + PACD + RACD**

30
31 135 Before launching, the project trained 25 primary and nursery school teachers on malaria
32
33 136 detection and on the promotion of prevention & care seeking behaviour. Each CHW was
34
35 137 assigned to a school and a collaborative system between teachers and ASCs working together
36
37 138 to detect sick children was developed. Consent forms were distributed to the teachers to pass
38
39 139 along to parents of pupils for their approval to test their children. Health care workers from the
40
41 140 four health centres were also invited to the training in order to build working relations with
42
43 141 CHWs. The CHWs had been trained repeatedly over the past years by the National Malaria
44
45 142 Control Programme (NMCP) on community management of malaria, but they were briefed
46
47 143 alongside two supervisors on the specificities of this project. One supervisor was in charge of
48
49 144 correct data collection, while the other inspected schools and visited households to ensure
50
51 145 completeness of field work.

52
53 146 PACD was undertaken in 12 primary & nursery schools, 4 health centres, and 13 community
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55 147 neighbourhoods on a weekly basis. Each week on a Thursday, CHWs visited assigned schools
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57 148 and health centres for a febrile screening. Upon arriving at their schools, the trained teachers
58
59 149 will indicate the pupils under five who had a fever in a recent week (axillary temperature of
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150 38°C or more). Health workers similarly helped to identify febrile children admitted in health
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152 150 facilities. Children with fever were identified and tested at no cost for *Plasmodium* infection

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3 152 using rapid diagnostic tests (RDT) approved and supplied by the NMCP. Those tested positive
4 153 for malaria were named as “index cases” and were further classified as either uncomplicated
5 154 or severe malaria. Uncomplicated malaria cases were immediately treated with amodiaquine +
6 155 artesunate, the first-line artemisinin-based combination therapy (ACT) recommended and
7 156 supplied by the NMCP. Severe cases and RDT-negative cases were referred to health facilities
8 157 for further investigation and management as per the NMCP guidelines. If a febrile child was
9 158 absent from school the day the CHW arrived, the teacher would tell the CHW where the child
10 159 lives. The CHW then visited the household to identify and test the sick child. In the community
11 160 however, CHW continued to identify febrile children as per the conventional iCCM guidelines.
12
13 161 As malaria cases tend to cluster geographically and temporally[13-16], CHWs who also cluster
14 162 and work in the neighbourhoods in which they live, then proceeded with the RACD method to
15 163 visit the home of an index case. In the households, they made a list of all persons resident in
16 164 the household (contacts of the index case), identified and tested those who had a fever in the
17 165 past week. Those tested positive for malaria RDT were named as “secondary cases” and were
18 166 also classified and treated or referred to the nearest health centre in a similar way like the index
19 167 case as illustrated in Figure 1.

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32 168 **Figure 1. The flow chart of the augmented integrated community case management of malaria**
33 169 **(iCCM+)**

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35 170 Data was collected using paper registers and later transcribed into a Microsoft Excel electronic
36 171 database available as a Supplementary File 1. Data collected from the index case during PACD
37 172 included: age, sex, place of residence, presence of fever, date of onset of fever, date and
38 173 location seen by an ASC, results of RDT for malaria, severity of malaria and treatment
39 174 received. During household visits, the same data were collected from febrile contacts in
40 175 addition to data pertaining to household size, long-lasting treated bed nets ownership and
41 176 current usage. Health facility malaria surveillance registers and CHW registers were used as
42 177 sources to abstract data on malaria cases notified between 2015 and 2018.

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49 178 Data analyses were performed using Stata version 14.2 (StataCorp. LP, College Station, United
50 179 States of America) and Microsoft Excel 2016 (Microsoft Corporation, Redmond, USA) was
51 180 used to plot curves. The data set was checked for logical inconsistencies, invalid codes,
52 181 omissions and improbable data by tabulating, summarizing, describing and plotting variables,
53 182 depending on their nature. Missing observations were systematically excluded.

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3 183 The value of iCCM+ over iCCM alone was measured by the proportion of additional cases
4
5 184 detected.

6
7 185 To describe similarities or differences between index and secondary cases, summary statistics
8
9 186 were presented as proportions for categorical variables, as means and standard deviations for
10
11 187 normally distributed continuous variables and as medians and interquartile ranges (IQRs) for
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13 188 continuous variables with a skewed distribution. Associations between categorical variables
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15 189 were assessed using Pearson's χ^2 test or Fisher's exact test for small samples, as appropriate.
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17 190 For continuous variables, mean differences between index cases and contacts were assessed
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19 191 using Student's t test. Associations between exposure variables and the likelihood of finding a
20
21 192 contact were evaluated by a univariate logistic regression model; crude odd ratios, 95%
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23 193 confidence intervals (CIs) were reported. Subsequently, factors associated with the odds of a
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25 194 finding a contact in the univariate analysis at a significance level below 5% were included in a
26
27 195 multiple logistic regression model with mixed effects to account for the variability in CHW
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29 196 performance. Backward elimination based on a p-value lower than 0.05 was used to retain
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31 197 variables that were independently associated with contact tracing; the corresponding adjusted
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33 198 odds ratios (aOR) and 95% CIs for the final model were reported.

32 199 **Patient and public involvement statement**

33 200 As a community-led project, the public and patients were involved in the project planning,
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35 201 implementation and data collection.

36
37 202 The study was approved by the Cameroon National Ethics Review Committee and Peace Corps
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39 203 Cameroon. Individual and parental consent was sought and all information was anonymised
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41 204 and de-identified prior to analysis. An information letter was sent to parents and local
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43 205 administrations, and was announced in community meeting or worshipping places.

45 206 **Results**

47 207 **Detection and management of cases**

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49 208 At the end of the three-month pilot study, we screened a total of 501 febrile patients of whom
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51 209 *Plasmodium* infection was confirmed in 425 (overall prevalence of 84.8%) including 176 index
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53 210 cases with a mean age of 3.4 ± 0.1 years who triggered a further screening by RACD of 249
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55 211 contacts of mean age 19.2 ± 1.2 years (Table 1). On average, index cases were reached within
56
57 212 2.4 ± 0.2 days after onset of fever. Index cases were mostly boys (60.8% vs. 49.8%, $p = 0.025$)
58
59 213 while secondary cases were mostly girls under five years but no gender specificity among older
60
214 secondary cases. The prevalence of malaria was very high in both the index (83.4%) and the

215 secondary cases (85.9%). Of these 425 confirmed malaria cases, 354 (83.3%) were classified
 216 as uncomplicated malaria cases who received ACT immediately from the CHW. The 71 cases
 217 who did not receive immediate ACT, were classified as severe malaria cases who were referred
 218 to the nearest health centre for further management.

219

220 **Table 1. Characteristics of index and secondary cases of malaria detected between April and June 2018**

Characteristics		Index cases (n = 176)	Secondary cases (n = 249)	P-value of the difference between the groups of cases
Reactive cases found per index case source				
	School	38 (21.6)	50 (20.1)	
	Health facility	36 (20.4)	24 (9.6)	
	Community	102 (58.0)	175 (70.3)	
	Total	176 (100.0)	249 (100.0)	0.004
Sex, n (%)				
	Male	107 (60.8)	124 (49.8)	
	Female	69 (39.2)	125 (50.2)	
	Total	176 (100)	249 (100)	0.025
Age, mean (SD) years		3.4 (0.1)	19.2 (1.2)	<0.0001
Immediate malaria treatment, n (%)				
	ACT	142 (80.7)	212 (85.1)	
	No ACT	34 (19.3)	37 (14.9)	
	Total	176 (100)	249 (100)	0.225
Referrals, n (%)				
	Yes	34 (19.3)	37 (14.9)	
	No	142 (81.7)	212 (85.1)	
	Total	176 (100)	249 (100)	<0.001
Household size, mean (95%CI)		6.4 (6.2 – 6.6)		
Household LLIN ownership, mean (95%CI)		2.4 (2.3 – 2.6)		
LLIN coverage per household member (95%CI)		0.38 (0.36 – 0.40)		
LLIN in use per household member (95%CI)		0.34 (0.32 – 0.36)		

221

222

223 **Proactive and Reactive case detection of confirmed malaria**

224 During the RACD triggered by 176 index cases of confirmed malaria in children under five,
225 132 (75%) of these index cases investigated led to at least one additional case and a total of
226 249 secondary cases identified from 290 febrile contacts within 176 households visited. There
227 were approximately 6 persons on average per household with a bed net ownership of about 2
228 LLINs per household leading to a bed net coverage of about 1 LLIN for 3 persons. After a lag
229 phase during the first half of the project, the number of cases detected increased sharply over
230 the second half before returning to the initial stable level (Figure 2).

231 **Figure 2. Trend in the number of cases of confirmed malaria between April and June 2018**

232 Of all the 425 confirmed cases, 38 (8.9%) were index cases identified proactively in schools
233 and led to find 50 (11.8%) more cases; 36 (8.5%) were index cases located in health facilities
234 and led to a further 24 (5.6%) cases; and 102 (24.0%) were index cases identified during routine
235 iCCM activity and led to 175 (41.2%) additional cases showing the value of RACD over iCCM
236 alone (Figure 2). Overall, iCCM+ identified 287 of the 425 cases thus indicating that the
237 ongoing iCCM must have been improved by 67.5% to manage malaria cases in the community
238 (Figure 3).

239 **Figure 3. Flow diagram of cases detected and treated during iCCM and iCCM+**

240 During 12 weeks in April, May, and June in 2017 CHWs detected 238 cases of malaria at a
241 rate of ~20 cases per week. But during our 8-week project across April, May and June in 2018,
242 the CHWs detected 365 cases of malaria at a rate of ~45 cases per week computing to a 125%
243 increase from 2017 during the same transmission season.

244 The odds of finding a secondary case by RACD increased by 70% if the index case was one
245 year younger (adjusted odd ratio (aOR) = 1.7, 95% CI: 1.5 – 1.9) and by 20% if a household
246 increased by one person (aOR = 1.2, 95% CI: 1.1 – 1.3). Though RACD was likely to find
247 female cases, the evidence to support gender discrimination was rejected in the multiple
248 regression model in Table 2 (aOR = 1.2, 95% CI: 0.7 – 2.1).

249

250 **Table 2. Multiple logistic regression model of factors associated with secondary case detection (N = 425)**

Factor		Number of confirmed secondary cases, n (%)	Crude OR (95%CI)	p-value	Adjusted OR (95%)	p-value
Sex						
	Male	124 (53.7)	Reference		Reference	
	Female	125 (64.4)	1.6 (1.1 – 2.3)	0.024	1.2 (0.7 – 2.1)	0.477
Additional one year of age			1.7 (1.5 – 1.9)	<0.001	1.7 (1.5 – 1.9)	<0.001
Additional one household member			1.2 (1.1 – 1.3)	<0.001	1.2 (1.1 – 1.3)	0.015

251

252 Discussion

253 In this small-case quality improvement study, we sought to demonstrate in a high transmission
 254 area, the feasibility of embedding both the proactive and reactive case detection strategies into
 255 integrated community case management in order to maximise malaria case detection and
 256 prompt treatment. The study has indicated that by proactively searching for children under five
 257 years with malaria as index cases, and by reactively searching for more cases in the households
 258 of index cases, iCCM+ must have been increased the proportion of persons diagnosed and
 259 treated for *Plasmodium* infection by approximately 67.5%. The study has also confirmed that
 260 the burden of malaria lies in the community with only the tip of the iceberg seen in health
 261 facilities. While iCCM was introduced to respond to this challenge, it was currently
 262 underperforming in this rural setting. This project has suggested that iCCM can be adapted to
 263 achieve optimal results. While on one hand it may appear obvious that the malaria component
 264 of iCCM can be adapted to or opt for a PACD strategy, implementing RACD in a high
 265 transmission setting on the other hand may seem experimental or even controversial to some
 266 extent. This is because RACD is a surveillance approach recommended in low transmission or
 267 pre-elimination settings to disrupt transmission and is thought to be inefficient and unfeasible
 268 in high transmission settings. Conversely, RACD may also waste time and money when cases

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3 269 are few and sporadic[17-20]. Therefore, the choice of RACD as an approach depends on the
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5 270 objective to be attained, the proportion of cases it can detect and the resources needed. Our
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7 271 project was feasible and efficient because our aim was not to eliminate malaria but to detect
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9 272 and treat the maximum possible number of cases during a high transmission season when the
10
11 273 proportion of cases is highest using resources already made available for iCCM in a rural
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13 274 setting where access to health services is limited. The extra resource needed is the time to visit
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15 275 schools, health facilities and households. CHWs told us that by conducting only a one-day visit
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17 276 per week to these facilities and only to households of index cases was more productive and
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19 277 made them more useful in their community. This strategy was not much different from what
20
21 278 they were doing before, just a more targeted approach: - targeting schools, targeting households
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23 279 of index cases and targeting high transmission season when fever is likely to be caused by a
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25 280 *Plasmodium* infection as confirmed in this study where RDT was positive in 85% of persons
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27 281 screened for fever and with a high probability of 75% that every index case led to at least one
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29 282 secondary case. Beyond CHW job satisfaction, teachers also expressed their satisfaction and
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31 283 were of great support in detecting fever or a history of fever amongst their pupils. Moreover,
32
33 284 we found that teachers were far more likely to help CHW finding the households of sick
34
35 285 children than healthcare workers. We thus strongly believe that RACD can be both feasible
36
37 286 and efficient in a high transmission setting to maximise clinical case management.
38
39 287 Consequently, we recommend that PACD and RACD become part of the ongoing iCCM
40
41 288 strategy in Cameroon as an approach to optimise case detection. Yet incorporating PACD and
42
43 289 RACD into iCCM will entail building a strong collaboration among CWH, HCW and teachers.
44
45 290 Such a partnership already exists between the ministries of health and education in Cameroon
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47 291 in their concerted effort to fight neglected tropical diseases specifically soil-transmitted
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49 292 helminthiasis in school children[21]. The recurrent problem of stockouts of commodities will
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51 293 need to be resolved by the NMCP and field monitoring and supervision should become regular
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53 294 by iCCM programme coordination. Resolving these issues of multisector collaboration,
54
55 295 delivery of commodities and field coordination were crucial as bottlenecks and explain in part
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57 296 why progress was slow in the first half of the project.

52 297 This study has further indicated that, while index cases were likely to be boys, RACD was
53
54 298 likely to find girls and women in univariate analysis though such claims were not supported by
55
56 299 evidence from multivariate analysis. Boys make up the majority of school children in
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58 300 Cameroon especially in the rural areas and this might be a reflection of this observation[22].
59
60 301 However, it is plausible that gender norms and values that determine the division of labour,

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3 302 leisure patterns, pregnancy, and sex-segregation of sleeping arrangements may lead to different
4
5 303 patterns of exposure to mosquitoes for men and women[22-24].
6

7 304 Secondary cases were likely to be older than index cases and to be located in larger households
8
9 305 of the index case. Given that we purposely targeted children under five years, it became obvious
10
11 306 that we may likely find more of older children and adults as contacts. Clustering of cases has
12
13 307 previously been demonstrated in households of the contacts and malaria eradication is thought
14
15 308 to be feasible when household size drops below four persons [25, 26]. The average household
16
17 309 size in this study was six persons thus explaining while it was very likely to find more cases in
18
19 310 the community during RACD.

20 311 This study had some limitations so that the results should be interpreted with caution. There
21
22 312 was no control arm to clearly distinguish between iCCM+ from iCCM intervention areas. A
23
24 313 randomised community trial may be recommended as a solution. The duration and period of
25
26 314 the study was limited to only three months and to the first half of the wet season. We could not
27
28 315 therefore account for neither seasonality in malaria transmission nor account for sustainability
29
30 316 throughout the year. Older children and adults were not included as index cases thus creating
31
32 317 an outright difference between index and secondary cases. This must have led to an
33
34 318 overestimation of the value of RACD in this field study because in routine practice however,
35
36 319 adults would be index cases as well. Targeting school children for malaria treatment must have
37
38 320 been a laudable effort but older school children were also left out as index cases though they
39
40 321 constitute a group with a higher *Plasmodium* infection prevalence than in the targeted younger
41
42 322 age group[10]. However, these children were among those screened in the community. We did
43
44 323 not measure the effect of this strategy on the pneumonia and diarrhoea components of iCCM
45
46 324 but we believe that being an integral part of the package of interventions, these two components
47
48 325 were likely to have been improved as well. We did not attempt to measure effect on malaria
49
50 326 transmission as most studies have done.

51 327 **Conclusion**

52 328 This study has shown that most symptomatic cases of malaria remain undetected in the
53
54 329 community despite the introduction of integrated community management of malaria. Schools
55
56 330 are an important portal to locate children with undiagnosed malaria. Active case detection
57
58 331 based on a proactive and reactive case detection approaches is feasible in a high transmission
59
60 332 setting and has been shown to enhance in a synergistic manner the efficiency of integrated
333 community case management of malaria. We recommend that national malaria control

334 programs adopt and implement this modified form of iCCM in similar settings to reduce the
 335 burden of malaria in our communities.

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416

417 Footnotes

418

419 Ethics approval and consent to participate

420

421 The study was approved by the National Ethics Review Board of Cameroon, Peace Corps
422 Cameroon and local administrative and health authorities. Verbal consent was obtained from
423 household members after making public announcements and providing an information leaflets
424 to explain the objectives of the project.

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3 425 **Consent for publication**
4

5
6 426 Not Applicable
7

8 427 **Availability of data and material**
9

10 428

11 429 The datasets used and/or analysed during the current study are available as a supplementary
12 file.
13 430

14
15 431 **Competing interests**
16

17 432

18 433 The authors declare that they have no competing interests
19

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21

22 435

23 436 The study received no specific funding
24

25 437 **Author Contributions**
26

27 438

28 439 Conception, design and implementation: TDW, CEB
29

30 440 Data collection, analysis and interpretation: TDW, CEB
31

32 441 Drafting the manuscript: CEB
33

34 442 All authors read and approved the final manuscript
35

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37

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41 446
42 and collaboration.
43 447
44

45 448 **Authors' information**
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50 451 TDW: Community Health Educator, Peace Corps Cameroon
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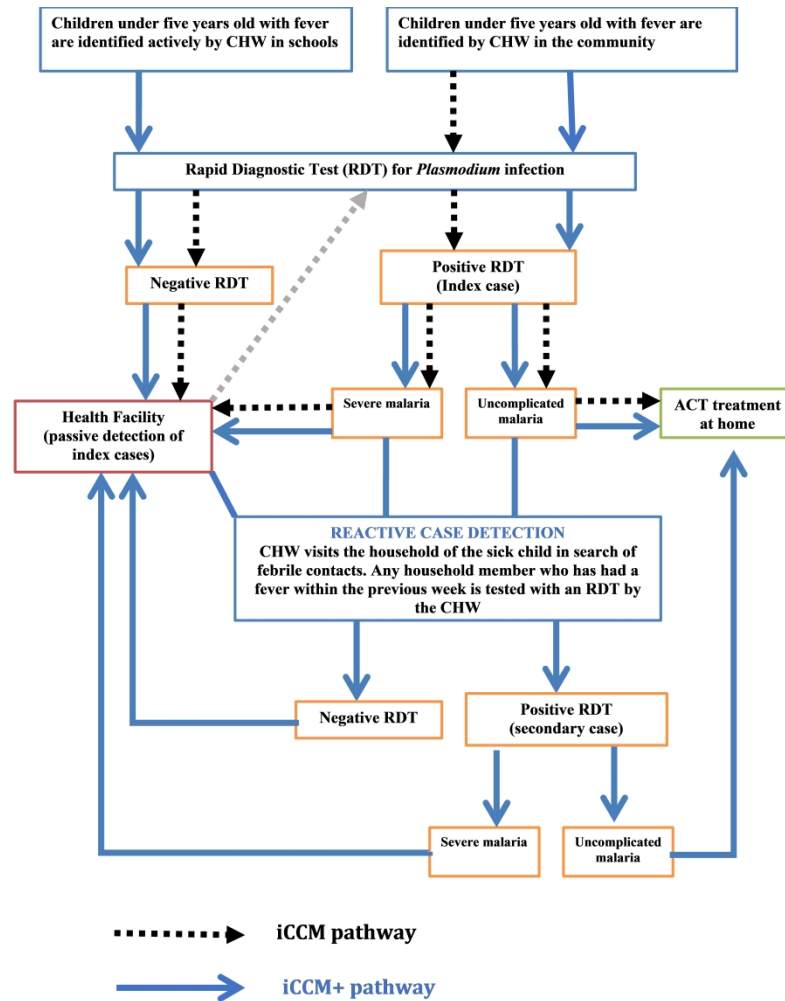


Figure 1. The flow-chart of the augmented integrated community case management of malaria (iCCM+)

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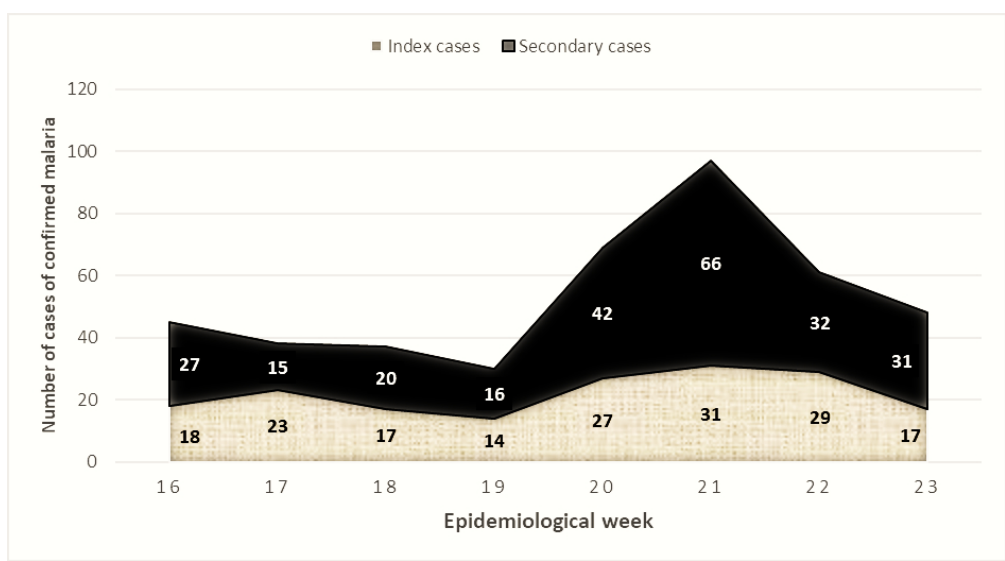
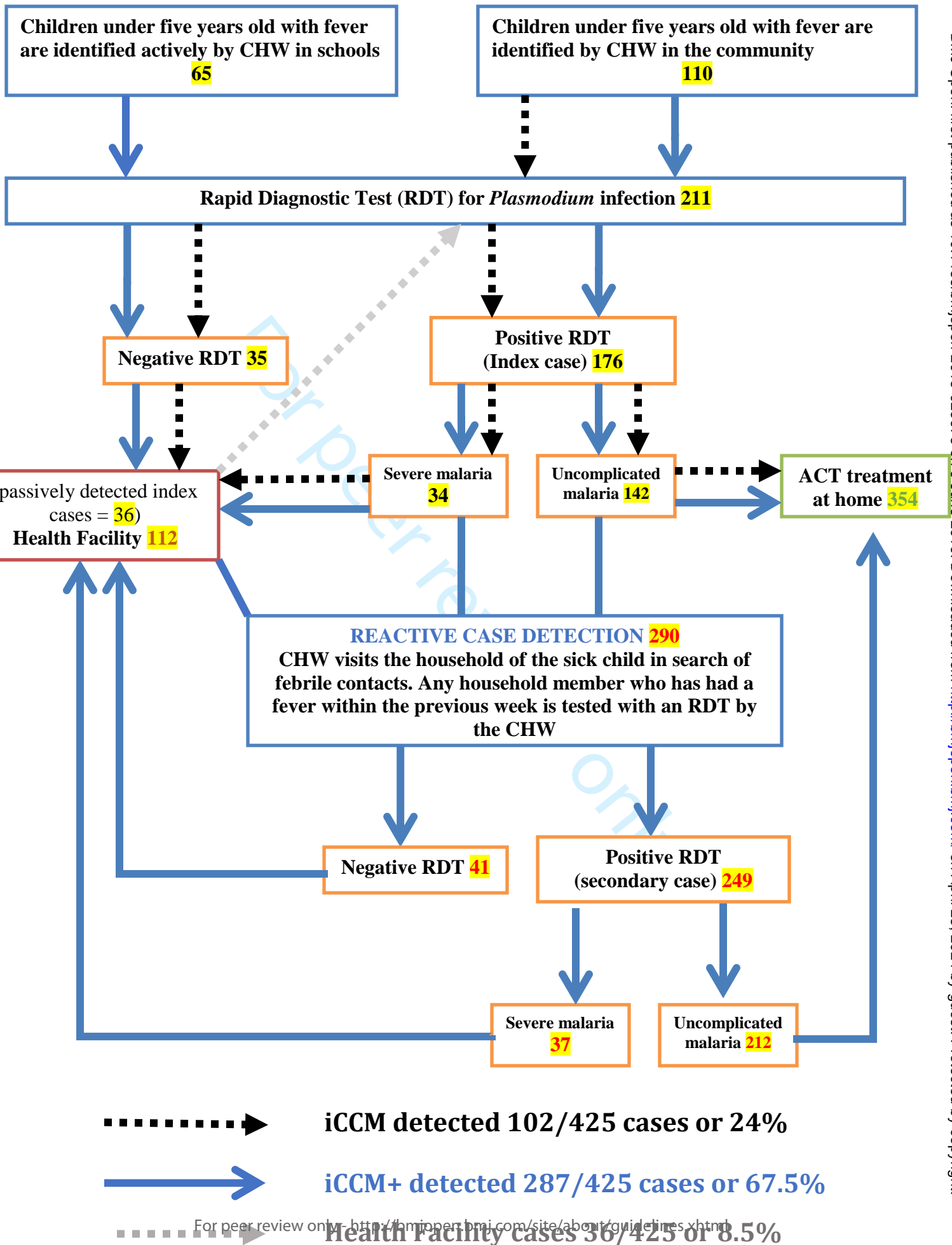


Figure 2. Trend in the number of cases of confirmed malaria

79x43mm (300 x 300 DPI)



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Number	Case Number	Case Type Primary: 1 Secondary: 2	Age	Sex Male: 1 Female: 2	Quarrier	Fever? 0 Yes: 1	RDT Result Negative: 0 Positive: 1	If simple malaria, ACT given? No: 0 Yes: 1	If complicated malaria or negative RDT, referred? No: 0 Yes: 1	Primary Case Location School: 1 Hospital: 2 Community: 3	Household population	Total LUN	Total LUN Attached	ASC	Week	Date of Fever	Date Found by ASC	How long it took? (Days)
1	1	1	4	1	8 Bis	0	0	0	0	2	4	3	1	JY	1	16/04/2018	19/04/2018	3
2	1.1	2	10	1	8 Bis	0	0	0	0	2				JY	1	19/04/2018	19/04/2018	
3	1.2	2	48	2	8 Bis	0	0	0	0	2				JY	1	19/04/2018	19/04/2018	
4	1.3	2	18	1	8 Bis	0	0	0	0	2				JY	2	19/04/2018	19/04/2018	
5	2	1	2	2	Bareko	1	1	1	0	2	3	2	2	JY	1	17/04/2018	19/04/2018	2
6	2.1	2	31	2	Bareko	0	0	0	0	2				JY	1	19/04/2018	19/04/2018	
7	2.2	2	41	1	Bareko	0	0	0	0	2				JY	1	19/04/2018	19/04/2018	
8	3	1	3	1	Ebouh	1	1	1	0	1	9	5	5	ZK	1	14/04/2018	19/04/2018	5
9	3.1	2	14	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
10	3.2	2	11	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
11	4	1	5	2	Ebouh	1	1	1	0	1	9	4	4	ZK	1	16/04/2018	19/04/2018	3
12	4.1	2	10	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
13	4.2	2	12	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
14	4.3	2	3	1	Ebouh	1	1	1	0	1				ZK	1	19/04/2018	19/04/2018	
15	4.4	2	5	2	Ebouh	1	1	1	0	1				ZK	1	19/04/2018	19/04/2018	
16	4.5	2	8	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
17	5	1	5	2	Ebouh	1	1	1	0	1	15	0	0	ZK	1	16/04/2018	19/04/2018	3
18	5.1	2	8	2	Ebouh	1	1	1	0	1				ZK	1	19/04/2018	19/04/2018	
19	5.2	2	10	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
20	5.3	2	10	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
21	6	1	4	1	Ebouh	1	1	1	0	1	4	2	2	ZK	1	15/04/2018	19/04/2018	4
22	6.1	2	35	1	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
23	7	1	5	2	Ebouh	1	1	1	0	1	6	6	6	ZK	1	10/04/2018	19/04/2018	9
24	7.1	2	48	2	Ebouh	1	1	0	1	1				ZK	1	19/04/2018	19/04/2018	
25	7.2	2	28	2	Ebouh	1	1	0	0	1				ZK	1	19/04/2018	19/04/2018	
26	8	1	4	1	Ebouh	1	1	1	0	1	6	3	3	ZK	1	15/04/2018	19/04/2018	4
27	8.1	2	2	1	Ebouh	1	1	1	0	1				ZK	1	19/04/2018	19/04/2018	
28	9	1	4	2	Ebouh	1	1	1	0	3	8	4	4	ZK	1	13/04/2018	21/04/2018	8
29	10	1	4	2	Ebouh	1	1	1	0	1	6	2	2	ZK	1	15/04/2018	19/04/2018	4
30	11	1	4	1	Ebouh	1	1	1	0	3	7	4	4	ZK	1	13/04/2018	19/04/2018	6
31	12	1	5	2	Ebouh	1	1	1	0	1	3	1	1	ZK	1	16/04/2018	19/04/2018	3
32	13	1	4	2	Ebouh	1	1	0	0	1	5	2	2	ZK	1	15/04/2018	19/04/2018	4
33	14	1	5	2	8 Bis	1	1	1	0	3	5	4	2	ZK	1	19/04/2018	21/04/2018	2
34	14.1	2	27	1	8 Bis	1	0	0	1	3				JL	1	21/04/2018	21/04/2018	
35	14.2	2	25	2	8 Bis	1	0	0	1	3				JL	1	21/04/2018	21/04/2018	
36	14.3	2	19	2	8 Bis	1	0	0	1	3				JL	1	21/04/2018	21/04/2018	
37	15	1	1	1	F	1	1	1	0	3	10	4	4	MN	1	17/04/2018	19/04/2018	2
38	15.1	2	5	2	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
39	15.2	2	38	2	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
40	15.3	2	18	1	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
41	15.4	2	10	2	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
42	15.5	2	12	2	F	1	0	0	1	3				MN	1	19/04/2018	19/04/2018	
43	15.6	2	21	2	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
44	15.7	2	8	1	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
45	15.8	2	47	1	F	0	0	0	0	3				MN	1	19/04/2018	19/04/2018	
46	16	1	4	2	E	0	0	0	1	3				MN	1	19/04/2018	19/04/2018	0
47	17	1	1	1	E	1	1	1	0	3	8	4	4	BN	1	21/04/2018	21/04/2018	0
48	17.1	2	5	1	E	1	1	1	0	3				BN	1	21/04/2018	21/04/2018	
49	17.2	2	11	2	E	1	1	0	1	3				BN	1	21/04/2018	21/04/2018	
50	17.3	2	50	1	E	0	0	0	0	3				BN	1	21/04/2018	21/04/2018	
51	17.4	2	39	2	E	0	0	0	0	3				BN	1	21/04/2018	21/04/2018	
52	18	1	5	1	E	1	1	1	0	3	12	6	4	BN	1	21/04/2018	21/04/2018	0
53	18.1	2	2	1	E	0	0	0	0	3				BN	1	21/04/2018	21/04/2018	
54	18.2	2	3	1	E	1	1	1	0	3				BN	1	21/04/2018	21/04/2018	
55	18.3	2	4	1	E	1	1	1	0	3				BN	1	21/04/2018	21/04/2018	
56	18.4	2	5	2	E	1	1	1	0	3				BN	1	21/04/2018	21/04/2018	
57	19	1	4	1	E	1	1	1	0	1	7	3	3	RT	1	18/04/2018	19/04/2018	1
58	19.1	2	68	1	E	1	1	0	1	1				RT	1	19/04/2018	19/04/2018	
59	19.2	2	50	2	E	1	1	0	1	1				RT	1	19/04/2018	19/04/2018	
60	19.3	2	13	2	E	1	1	0	1	1				RT	1	19/04/2018	19/04/2018	
61	19.4	2	11	2	E	1	1	0	1	1				RT	1	19/04/2018	19/04/2018	
62	19.5	2	9	1	E	1	1	0	1	1				RT	1	19/04/2018	19/04/2018	
63	19.6	2	7	2	E	1	1	0	1	1				RT	1	19/04/2018	19/04/2018	
64	20	1	3	1	F	1	1	1	0	1	6	2	1	RT	1	18/04/2018	19/04/2018	1
65	20.1	2	30	1	F	0	0	0	0	1				RT	1	19/04/2018	19/04/2018	
66	20.2	2	28	2	F	0	0	0	0	1				RT	1	19/04/2018	19/04/2018	
67	20.3	2	18	2	F	0	0	0	0	1				RT	1	19/04/2018	19/04/2018	
68	20.4	2	1	2	F	1	1	1	0	1				RT	1	19/04/2018	19/04/2018	
69	21	1	3	2	E Bis	1	1	1	0	1	4	2	1	JY	2	25/04/2018	25/04/2018	0
70	21.1	2	45	2	E Bis	0	0	0	0	1				JY	2	25/04/2018	25/04/2018	
71	22	1	3	2	F	1	0	0	1	1				JY	2	23/04/2018	26/04/2018	3
72	23	1	2	1	A Bis	1	1	0	0	2	6	3	2	JY	2	22/04/2018	28/04/2018	6
73	23.1	2	30	1	A Bis	0	0	0	0	2				JY	2	28/04/2018	28/04/2018	
74	23.2	2	1	1	A Bis	1	1	1	0	2				JY	2	28/04/2018	28/04/2018	
75	24	1	5	2	Bareko	1	1	0	0	2	No Visit			JY	2	23/04/2018	28/04/2018	5
76	25	1	1	1	Bareko	1	1	0	0	2	No Visit			JY	2	23/04/2018	28/04/2018	5
77	26	1	2	1	Ebouh	1	1	1	0	3	6	3	3	ZK	2	20/04/2018	24/04/2018	4
78	26.1	2	17	2	Ebouh	1	1	0	1	3				ZK	2	24/04/2018	24/04/2018	
79	26.2	2	7	1	Ebouh	1	1	0	1	3				ZK	2	24/04/2018	24/04/2018	
80	27	1	4	1	Ebouh	1	1	1	0	1				ZK	2	23/04/2018	26/04/2018	3
81	27.1	2	5	2	Ebouh	1	0	0	0	1				ZK	2	26/04/2018	26/04/2018	
82	28	1	5	1	Ebouh	1	1	0	1	1	5	3	3	ZK	2	21/04/2018	26/04/2018	5
83	28.1	2	4	1	Ebouh	1	1	1	0	1				ZK	2	26/04/2018	26/04/2018	
84	29	1	5	2	Ebouh	1	1	1	0	1	6	3	3	ZK	2	20/04/2018	26/04/2018	6
85	29.1	2	5	1	Ebouh	1	1	1	0	1				ZK	2	26/04/2018	26/04/2018	
86	30	1	5	2	Ebouh	1	0	0	1	1				ZK	2	23/04/2018	26/04/2018	3
87	31	1	3	2	Ebouh	1	1	1	0	1				ZK	2	21/04/2018		

128	45.1	2	5	2 B Bis	1	1	1	0	1			RT	2	26/04/2018		
129	45.2	2	14	2 B Bis	0	0	0	0	1			RT	2	26/04/2018		
130	46	1	4	2 E Bis	1	1	1	0	1	2	2	RT	2	26/04/2018	0	
131	46.1	2	36	2 E Bis	0	0	0	0	1			2	2	26/04/2018		
132	47	1	1	1 B	1	1	1	0	3	4	1	2	JL	3	02/05/2018	
133	47.1	2	45	2 B	1	1	0	0	1	3			JL	3	03/05/2018	
134	48	1	5	1 B	1	1	1	1	0	3	4	1	1	JL	3	03/05/2018
135	48.1	2	60	1 B	1	1	0	0	1	3			JL	3	03/05/2018	
136	49	1	2	1 Bareko	1	1	0	0	2	4	2		2	MN	3	03/05/2018
137	49.1	2	4	1 Bareko	1	1	1	1	0	2				MN	3	03/05/2018
138	50	1	5	1 B Bis	1	1	1	0	0	2	6	2	2	MN	3	27/04/2018
139	50.1	2	9	2 B Bis	1	1	1	0	1	2				MN	3	03/05/2018
140	50.2	2	3	2 B Bis	1	1	1	1	0	2				MN	3	03/05/2018
141	50.3	2	11	1 B Bis	1	1	0	1	2					MN	3	03/05/2018
142	51	1	3	1 B	1	1	1	0	0	2	7	4	0	MN	3	02/05/2018
143	51.1	2	9	1 B	1	1	1	0	1	2				MN	3	03/05/2018
144	52	1	2	1 F	1	1	1	0	0	2	10	3	3	MN	3	02/05/2018
145	52.1	2	4	2 F	1	1	1	1	0	2				MN	3	03/05/2018
146	52.2	2	7	2 F	1	1	1	0	1	2				MN	3	03/05/2018
147	52.3	2	10	2 F	1	1	1	0	1	2				MN	3	03/05/2018
148	53	1	5	2 D	1	1	1	0	0	2	4	0	0	MN	3	02/05/2018
149	53.1	2	2	2 D	1	1	1	1	0	2				MN	3	03/05/2018
150	53.2	2	0.17	1 D	1	1	1	0	2					MN	3	03/05/2018
151	54	1	0.58	2 Bareko	1	1	0	0	2	8	4	4	4	MN	3	02/05/2018
152	54.1	2	27	2 Bareko	1	1	1	0	1	2				MN	3	03/05/2018
153	55	1	4	1 B	1	1	1	0	0	4	2	2	2	MN	3	02/05/2018
154	55.1	2	2	1 E	1	1	1	1	0	2				MN	3	03/05/2018
155	56	1	5	1 Bareko	1	1	0	0	2	11	6	2	2	MN	3	03/05/2018
156	56.1	2	5	1 Bareko	1	1	1	1	0	2				BN	3	03/05/2018
157	56.2	2	2	1 Bareko	0	0	0	0	2					BN	3	03/05/2018
158	56.3	2	10	2 Bareko	1	1	0	1	2					BN	3	03/05/2018
159	56.4	2	18	2 Bareko	0	0	0	0	2					BN	3	03/05/2018
160	57	1	3	2 Ebouh	1	1	1	0	1	6	2	2	2	ZK	3	01/05/2018
161	57.1	2	14	1 Ebouh	1	1	0	1	1	3				ZK	3	03/05/2018
162	58	1	3	1 Ebouh	1	1	1	1	0	1	6	0	0	ZK	3	01/05/2018
163	58.1	2	8	2 Ebouh	1	1	0	0	1	1				ZK	3	03/05/2018
164	59	1	5	1 B Bis	1	1	1	1	0	1	4	2	2	ZK	3	01/05/2018
165	59.1	2	30	2 B Bis	1	1	0	1	1	1				ZK	3	03/05/2018
166	60	1	5	1 Ebouh	1	1	1	1	0	1	6	3	3	ZK	3	01/05/2018
167	60.1	2	35	2 Ebouh	1	0	0	0	1	1				ZK	3	03/05/2018
168	61	1	5	1 Ebouh	1	0	0	0	1	1				ZK	3	01/05/2018
169	62	1	3	1 Ebouh	1	0	0	1	1	4	2	1	2	ZK	3	02/05/2018
170	63	1	3	2 D	1	1	1	1	0	3	5	2	2	RT	3	02/05/2018
171	63.1	2	5	2 D	1	1	1	0	3					RT	3	02/05/2018
172	63.2	2	2	1 D	1	0	0	1	3					RT	3	02/05/2018
173	64	1	4	1 F Bis	1	1	1	1	0	1	5	2	2	RT	3	27/04/2018
174	64.1	2	3	1 F Bis	1	0	0	0	1	1				RT	3	03/05/2018
175	65	1	2	2 B	1	1	0	0	1	8	3	3	3	RT	3	01/05/2018
176	66	1	2	2 B	1	0	0	1	3	6	3	3	3	RT	3	03/05/2018
177	67	1	5	1 B Bis	1	0	0	1	1					RT	3	03/05/2018
178	68	1	5	1 D	1	0	0	0	1	1				RT	3	02/05/2018
179	69	1	4	1 A	1	0	0	0	1	1				RT	3	02/05/2018
180	70	1	3	1 E	1	1	1	0	0	2	10	0	0	JY	3	28/04/2018
181	70.1	2	9	2 E	1	1	1	0	1	2				JY	3	03/05/2018
182	70.2	2	3	1 E	1	1	1	1	0	2				JY	3	03/05/2018
183	71	1	5	2 B	1	1	1	1	0	3	5	3	3	MN	4	06/05/2018
184	71.1	2	8	1 B	1	1	1	0	1	3				MN	4	10/05/2018
185	72	1	4	1 F	1	1	1	1	0	3	5	2	2	MN	4	08/05/2018
186	72.1	2	3	1 F	1	1	1	0	3					MN	4	10/05/2018
187	72.2	2	5	2 F	1	1	1	1	0	3				MN	4	10/05/2018
188	72.3	2	2	1 F	1	1	1	0	1	3				MN	4	10/05/2018
189	73	1	1	1 F	1	0	0	0	1	3				MN	4	05/05/2018
190	74	1	3	2 F	1	0	0	1	3					MN	4	05/05/2018
191	75	1	4	2 Bareko	1	1	1	1	0	3	6	0	0	MN	4	07/05/2018
192	75.1	2	5	1 Bareko	1	1	1	1	0	3				MN	4	10/05/2018
193	75.2	2	3	2 Bareko	1	1	1	0	3					MN	4	10/05/2018
194	75.3	2	5	2 Bareko	1	1	1	1	0	3				MN	4	10/05/2018
195	76	1	5	2 Bareko	1	1	1	1	0	3	9	5	5	MN	4	07/05/2018
196	76.1	2	0.5	1 Bareko	1	1	1	1	0	3				MN	4	10/05/2018
197	76.2	2	3	1 Bareko	1	1	1	1	0	3				MN	4	10/05/2018
198	76.3	2	2	1 Bareko	1	1	1	1	0	3				MN	4	10/05/2018
199	76.4	2	4	1 Bareko	1	1	1	0	3					MN	4	10/05/2018
200	77	1	2	2 E	1	1	1	1	0	3				BN	4	10/05/2018
201	77.1	2	5	2 E	1	1	1	1	0	3				BN	4	10/05/2018
202	78	1	2	2 A	1	1	1	1	0	3				BN	4	08/05/2018
203	78.1	2	3	2 A	1	1	1	1	0	3				BN	4	11/05/2018
204	79	1	3	1 E Bis	1	1	1	1	0	1	2	1	1	RT	4	02/05/2018
205	79.1	2	22	2 E Bis	1	0	0	1	1					RT	4	03/05/2018
206	80	1	4	2 D	1	1	1	1	0	1	6	4	4	RT	4	01/05/2018
207	81	1	2	2 A	1	1	1	1	0	3	5	4	4	JY	4	09/05/2018
208	81.1	2	1	1 A	1	1	1	1	0	3				JY	4	10/05/2018
209	82	1	5	2 A	1	1	1	1	0	3	5	3	2	JY	4	10/05/2018
210	83	1	4	1 Ebouh	1	1	1	1	0	1	10	0	0	ZK	4	07/05/2018
211	83.1	2	6	1 Ebouh	1	1	0	1	1	1				ZK	4	10/05/2018
212	83.2	2	3	1 Ebouh	1	0	0	1	1	1				ZK	4	10/05/2018
213	84	1	1	1 B Bis	1	1	1	1	0	3	5	3	3	ZK	4	08/05/2018
214	84.1	2	27	2 B Bis	1	0	0	1	3					ZK	4	10/05/2018
215	85	1	5	1 Ebouh	1	0	0	1	1	1				ZK	4	09/05/2018
216	85	1	5	1 Ebouh	1	1	1	1	0	1	5	3	3	ZK	4	08/05/2018
217	86.1	2	35	2 Ebouh	1	1	0	1	1	4				ZK	4	10/05/2018
218	87	1	5	1 Ebouh	1	0	0	1	1	1				ZK	4	07/05/2018
219	88	1	4	1 Ebouh	1	0	0	1	1	1				ZK	4	08/05/2018
220	89	1	4	2 F	1	1	1	1	0	3	5	2	2	JL	4	06/05/2018
221	89.1	2	45	1 F	1	0	0	1	3					JL	4	07/05/2018
222	89.2	2	15	1 F	1	0	0	1	3					JL	4	07/05/2018
223	90	1	3	2 Ebouh	1	1	1	1	0	3	6	3	3	ZK	5	14/05/2018
224	90.1	2	6	2 Ebouh	1	1	1	1	0	3				ZK	5	15/05/2018
225	90.2	2	61	2 Ebouh	1	1	1	1	0	3				ZK	5	15/05/2018
226	90.3	2	6	1 Ebouh	1	1	1	1	0	3				ZK	5	15/05/2018
227	91	1	2	1 Ebouh	1	1	1	0	1	6	3	3	3	ZK	5	15/05/2018
228	91.1	2	7	1 Ebouh	1	1	1	1	0	1				ZK	5	17/05/2018
229	91.2	2	56	2 Ebouh	1	1	1	1	0	1				ZK	5	17/05/2018
230	92	1	3	1 Ebouh	1	1	1	1	0	1	8	3	3	ZK	5	15/05/2018
231	92.1	2	60	1 Ebouh	1	1	1	1	0	1				ZK	5	17/05/2018
232	92.2	2	10	1												

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398	154	1	5	1	B	1	1	1	0	3	9	0	0	JL	6	19/05/2018	21/05/2018	2
399	154.1	2	25	2	B	1	0	0	1	3				JL	6	21/05/2018		
400	155	1	3	1	F	1	1	1	0	3	4	1	1	JL	6	21/05/2018	23/05/2018	2
401	155.1	2	23	2	F	1	1	1	0	3				JL	6	21/05/2018	23/05/2018	
402	156	1	06	2	F Bis	1	1	1	0	3				JL	6	23/05/2018	24/05/2018	1
403	156.1	2	10	2	F Bis	1	1	1	0	3				JL	6	23/05/2018	24/05/2018	
404	156.2	2	11	1	F Bis	1	1	1	0	3				JL	6	24/05/2020		
405	156.3	2	7	2	F Bis	1	1	1	0	3				JL	6	24/05/2021		
406	157	1	2	1	F Bis	1	1	1	0	3	5	2	2	JL	6	23/05/2018	24/05/2018	1
407	157.1	2	39	2	F Bis	1	0	0	1	3				JL	6	24/05/2018		
408	158	1	5	1	C	1	1	1	0	3	9	3	3	RT	7	02/06/2018	02/06/2018	0
409	158.1	2	17	2	C	1	1	1	0	3				RT	7	02/06/2018		
410	158.2	2	18	2	C	1	1	1	0	3				RT	7	02/06/2018		
411	158.3	2	15	1	C	1	1	1	0	3				RT	7	02/06/2018		
412	158.4	2	9	1	C	1	1	1	0	3				RT	7	02/06/2018		
413	158.5	2	12	2	C	1	1	1	0	3				RT	7	02/06/2018		
414	159	1	5	2	B	1	0	0	1	3				RT	7	29/05/2018	31/05/2018	2
415	160	1	2	2	E Bis	1	1	1	0	3	6	3	3	RT	7	03/06/2018	03/06/2018	0
416	160.1	2	9	1	E Bis	1	1	1	0	3				RT	7	03/06/2018		
417	161	1	5	2	D	1	1	1	0	3	8	3	3	RT	7	29/05/2018	31/05/2018	2
418	161.1	2	4	1	D	1	1	1	0	3				RT	7	31/05/2018		
419	161.2	2	11	2	D	1	1	1	0	3				RT	7	31/05/2018		
420	162	1	6	1	Ebouh	1	1	1	0	3	10	5	5	ZK	7	24/05/2018	28/05/2018	4
421	163	1	3	1	Ebouh	1	1	1	0	3	6	3	3	ZK	7	27/05/2018	29/05/2018	2
422	163.1	2	30	1	Ebouh	1	1	1	0	3				ZK	7	29/05/2018		
423	163.2	2	18	1	Ebouh	1	1	1	0	3				ZK	7	29/05/2018		
424	164	1	3	1	Ebouh	1	1	1	0	3	8	4	4	ZK	7	24/05/2018	28/05/2018	4
425	165	1	3	1	Ebouh	1	0	0	1	1				ZK	7	24/05/2018	29/05/2018	5
426	166	1	3	1	Ebouh	1	0	0	1	1				ZK	7	25/05/2018	29/05/2018	4
427	167	1	3	1	Ebouh	1	0	0	1	1				ZK	7	26/05/2018	29/05/2018	3
428	168	1	3	1	Ebouh	1	0	0	1	1				ZK	7	26/05/2018	29/05/2018	3
429	169	1	2	1	B	1	0	0	1	1				ZK	7	25/05/2018	29/05/2018	4
430	170	1	3	1	B	1	0	0	1	1				ZK	7	24/05/2018	29/05/2018	5
431	171	1	5	1	Bareko	1	1	1	0	3	8	1	1	JL	7	29/05/2018	30/05/2018	1
432	171.1	2	33	1	Bareko	1	0	0	1	3				JL	7	30/05/2018		
433	171.2	2	11	2	Bareko	1	1	1	0	3				JL	7	30/05/2018		
434	171.3	2	11	1	Bareko	1	1	1	0	3				JL	7	30/05/2018		
435	172	1	5	2	F Bis	1	1	1	0	3	8	2	1	JL	7	28/05/2018	31/05/2018	3
436	172.1	2	9	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
437	172.2	2	9	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
438	172.3	2	62	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
439	172.4	2	38	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
440	173	1	3	1	F Bis	1	1	1	0	3	3	1	1	JL	7	27/05/2018	30/05/2018	3
441	173.1	2	28	2	F Bis	1	0	0	1	3				JL	7	30/05/2018		
442	174	1	5	1	A Bis	1	1	1	0	3	9	2	2	MN	7	28/05/2018	31/05/2018	3
443	174.1	2	17	1	A Bis	1	1	1	0	3				MN	7	31/05/2018		
444	174.2	2	7	2	A Bis	1	0	0	1	3				MN	7	31/05/2018		
445	174.3	2	15	1	A Bis	1	0	0	1	3				MN	7	31/05/2018		
446	174.4	2	44	1	A Bis	1	1	1	0	3				MN	7	31/05/2018		
447	175	1	2	1	B	1	1	1	0	3				MN	7	16/05/2018	31/05/2018	
448	176	1	2	2	F	1	1	1	0	3	15	0	0	MN	7	26/05/2018	31/05/2018	5
449	176.1	2	49	1	F	1	1	1	0	3				MN	7	31/05/2018		
450	176.2	2	14	1	F	1	1	1	0	3				MN	7	31/05/2018		
451	177	1	2	2	F	1	1	1	0	3	7	4	3	MN	7	30/05/2018	31/05/2018	1
452	177.1	2	8	1	F	1	1	1	0	3				MN	7	31/05/2018		
453	177.2	2	6	1	F	1	1	1	0	3				MN	7	31/05/2018		
454	177.3	2	6	2	F	1	1	1	0	3				MN	7	31/05/2018		
455	177.4	2	13	2	F	1	1	1	0	3				MN	7	31/05/2018		
456	177.5	2	37	2	F	1	1	1	0	3				MN	7	31/05/2018		
457	177.6	2	91	1	D	1	0	0	1	3				MN	7	31/05/2018		
458	178	1	5	1	D	1	1	1	0	3	2	1	0	MN	7	30/05/2018	30/05/2018	0
459	178.1	2	59	1	D	1	1	1	0	3				MN	7	30/05/2018		
460	179	1	3	2	F	1	1	1	0	3	6	3	3	MN	7	04/06/2018	04/06/2018	0
461	179.1	2	52	2	F	1	1	1	0	3				MN	7	04/06/2018		
462	180	1	4	2	E	1	1	1	0	3				MN	7	14/06/2018	31/05/2018	
463	181	1	4	1	D	1	1	1	0	3				MN	7	26/05/2018	31/05/2018	
464	182	1	3	1	D	1	1	1	0	3				MN	7	30/05/2018	31/05/2018	
465	183	1	4	2	E	1	1	1	0	3	4	2	2	MN	7	29/05/2018	31/05/2018	2
466	183.1	2	55	2	E	1	1	1	0	3				MN	7	31/05/2018		
467	184	1	5	2	F	1	1	1	0	3	6	1	1	MN	7	29/05/2018	02/06/2018	4
468	184.1	2	74	2	F	1	1	1	0	3				MN	7	02/06/2018		
469	185	1	3	1	A Bis	1	1	1	0	3				MN	7	16/05/2018	31/05/2018	
470	186	1	3	2	Bareko	1	1	0	0	2				JY	7	19/05/2018	19/05/2018	
471	187	1	2	1	Bareko	1	1	0	0	2				JY	7	15/05/2018	15/05/2018	
472	188	1	3	2	B Bis	1	1	1	0	3	4	2	2	JY	7	17/05/2018	18/05/2018	1
473	188.1	2	61	1	B Bis	1	1	1	0	3				JY	7	17/05/2018	18/05/2018	
474	189	1	1	2	Ebouh	1	1	0	0	2				JY	7	16/05/2018	24/05/2018	
475	190	1	2	1	Ebouh	1	1	0	0	2				JY	7	17/05/2018	17/05/2018	
476	191	1	3	1	A Bis	1	1	1	0	3	8	3	3	JY	7	30/05/2018	31/05/2018	1
477	192	1	3	2	B Bis	1	1	1	0	3	6	2	2	JY	7	31/05/2018	31/05/2018	0
478	193	1	3	2	B	1	1	1	0	3	8	4	4	BN	7	28/05/2018	28/05/2018	0
479	193.1	2	2	1	B	1	1	1	0	3				BN	7	28/05/2018		
480	193.2	2	2	1	B	1	1	1	0	3				BN	7	28/05/2018		
481	194	1	3	2	B	1	1	1	0	3	6	3	1	RT	8	05/06/2018	07/06/2018	2
482	194.1	2	7	2	B	1	1	1	0	3				RT	8	07/06/2018		
483	195	1	2	2	C	1	1	1	0	3	7	2	2	RT	8	30/05/2018	08/06/2018	9
484	195.1	2	8	2	C	1	1	1	0	3				RT	8	08/06/2018		
485	195.2	2	41	2	C	1	1	1	0	3				RT	8	08/06/2018		
486	196	1	4	1	A	1	1	1	0	3	6	0	0	RT	8	09/06/2018	10/06/2018	1
487	196.1	2	5	2	A	1	1	1	0	3				RT	8	10/06/2018		
488	197	1	1	2	F	1	1	1	0	3	5	2	2	MN	8	06/06/2018	06/06/2018	0
489	197.1	2	1	2	F</													

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60STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract Page 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found Page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 3
Objectives	3	State specific objectives, including any prespecified hypotheses Page 4
Methods		
Study design	4	Present key elements of study design early in the paper Page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 4-7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants Page 5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 6-7
Bias	9	Describe any efforts to address potential sources of bias Page 6
Study size	10	Explain how the study size was arrived at Not calculated
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Page 7
Statistical methods Page 7	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Page 7-8 (b) Give reasons for non-participation at each stage Figure 1 (c) Consider use of a flow diagram Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Table 1 (b) Indicate number of participants with missing data for each variable of interest Table 1
Outcome data	15*	Report numbers of outcome events or summary measures Tables 1 and 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Page 9 and Table 2 (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a

		meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Page 9
Discussion		
Key results	18	Summarise key results with reference to study objectives Page 10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 11
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 11-12
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Adding proactive and reactive case detection into the integrated community case management system (iCCM+) to optimise diagnosis and treatment of malaria in a high transmission setting of Cameroon: an observational quality improvement study

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Primary Subject Heading:	Public health
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Keywords:	Malaria, integrated community case management, active case detection, Cameroon

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Manuscripts

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4 1 **Adding proactive and reactive case detection into the**
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6 2 **integrated community case management system (iCCM+)**
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8 3 **to optimise diagnosis and treatment of malaria in a high**
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10 4 **transmission setting of Cameroon: an observational**
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12 5 **quality improvement study**
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Abstract

Objective: Integrated community case management (iCCM) of childhood illness is a powerful intervention to reduce mortality. Yet, only 29% and 59% of children with fever in sub-Saharan Africa had access to malaria testing and treatment between 2015 and 2017. We report how iCCM+ based on incorporating active case detection of malaria into iCCM could help improve testing and treatment.

Design: A community-led observational quality improvement study

Setting: The rural community of Bare-Bakem in Cameroon

Participants: Children and adults with fever between April and June 2018

Intervention: A modified iCCM programme (iCCM+) comprised of a proactive screening of febrile children under five years old for malaria using rapid diagnostic testing to identify index cases and a reactive screening triggered by these index cases to detect secondary cases in the community

Primary and secondary outcome measures: The proportion of additional malaria cases detected by iCCM+ over iCCM.

Results: We screened 501 febrile patients of whom *Plasmodium* infection was confirmed in 425 (84.8%) cases. Of these cases, 102 (24.0%) were index cases identified in the community during routine iCCM activity and 36 (8.5%) cases detected passively in health facilities; 38 (8.9%) were index cases identified proactively in schools; and 249 (58.6%) were additional cases detected by reactive case detection (RACD) – computing to a total of 287 (67.5%) additional cases found by iCCM+ over iCCM. The likelihood of finding additional cases increased with increasing family size [adjusted odd ratio (aOR) = 1.2, 95% CI: 1.1 – 1.3] and with increasing age [(aOR) = 1.7, 95% CI: 1.5 – 1.9].

Conclusion: Most symptomatic cases of malaria remain undetected in the community despite the introduction of community case management of malaria. iCCM+ can be adopted to diagnose and treat more of these undiagnosed cases especially when targeted to schools, older children and larger households.

54 **Article Summary**

55 **Strengths and Limitations of this study**

- 56 • The first study to show the public health significance of a reactive case detection
57 strategy in a high malaria transmission area
- 58 • The study used existing community resources but in a more targeted manner to
59 maximise access to malaria treatment in a poor and rural community
- 60 • A small-scale study with no control arm carried out during a relatively short period and
61 during the high transmission season thus inclined towards over-estimating the value of
62 the intervention

63 **Introduction**

64 In Cameroon, malaria-related morbidity has reduced from 40.6% in 2008 to 24.3% in 2017
65 while malaria proportionate mortality has reduced from 17.6% in 2000 to 12.8% in 2017¹⁻⁴.
66 Despite this remarkable effort, malaria remains a major public health problem in Cameroon
67 where the entire population of more than 25 million inhabitants is at risk, with 71% living in
68 high transmission areas⁵. In 2016, approximately 1.7 million malaria cases and 2637 deaths
69 from malaria were recorded in health facilities in Cameroon. Children under five years of age
70 were the most affected group in whom malaria was responsible for 41% of all-cause morbidity,
71 55% of hospital admissions and 69.7% of all malaria-attributed deaths in 2015². To reduce
72 childhood mortality, Cameroon and her development partners began implementing integrated
73 community case management (iCCM) of pneumonia, diarrhoea, and malaria in 2009 to target
74 communities with difficult access to health services. Community case management (CCM) of
75 malaria can reduce overall mortality and malaria-specific under-five mortality by 40% and
76 60%, respectively, and severe malaria morbidity by 53%^{6 7}. Yet between 2015 and 2017, only
77 59% of children with fever in sub-Saharan Africa received a malaria diagnostic test and only
78 29% had received any antimalarial drug^{8 9}. In some localities of Cameroon, iCCM strategy has
79 been reported to have increased treatment rate for malaria, increased care seeking for fever and
80 reduced burden on healthcare facilities^{10 11}. However, data from a community needs assessment
81 conducted in 2016 in the rural community of Bare-Bakem in the Littoral Region of Cameroon
82 indicated that malaria represented up to 80% of all-cause morbidity across health centres and
83 that iCCM has been facing significant challenges including: low uptake inherent to its passive
84 nature, underutilisation and attrition of trained community health workers (CHWs); prolonged
85 and frequent stockouts of commodities for malaria diagnosis and treatment; inadequate
86 supervision and motivation of CHWs. School children though typically constituting the group

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3 87 with the highest prevalence of *Plasmodium* infection, have been virtually left out of this
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5 88 intervention despite receiving increasing attention recently¹²⁻¹⁴. In response to these challenges
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7 89 that threaten to reverse the initial iCCM gains, Peace Corps Cameroon has been supporting
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9 90 rural communities in Cameroon to effectively fight malaria. In 2018, the Peace Corps
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11 91 community of Bare-Bakem introduced a proactive and reactive case detection approach into
12
13 92 the existing iCCM system with the objective to reduce malaria burden by expanding access to
14
15 93 prompt malaria case management in the community. Integrating active (proactive and/or
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17 94 reactive) case detection strategy with iCCM has not yet been documented in high transmission
18
19 95 settings. We report how in this community-led project, CHW proactively searched for cases of
20
21 96 malaria in children under five in schools, health facilities and households; and then using index
22
23 97 cases, they reactively detected and treated even more cases in the community by visiting the
24
25 98 households of the sick children with confirmed malaria.

99 **Methods**

100 **Design:** A community-led quality improvement study to measure the proportion of additional
101 *Plasmodium* infection detected under iCCM+ compared with iCCM alone.

102 **Intervention site and priority setting**

103 The intervention was carried out in the rural town of Baré, the headquarters of Baré -Bakem
104 municipality with a population of about 20000 inhabitants occupying a surface area of about
105 200km². Bare is situated at approximately 10 km from Nkongsamba (the divisional capital) and
106 120 km from the coastal city of Douala (the regional capital). It has 13 neighbourhoods:
107 Bareko, Ebouth, Axe Lourd, A, A bis, B, B bis, C, D, E, E bis, F and F bis. The locality's low
108 elevation and its warm and wet equatorial climate are conducive for high levels of malaria
109 transmission. The town was host to a Peace Corps Volunteer (PCV) for the period between
110 2016 and 2018 with the mission to support efforts to fight infant and maternal mortality,
111 malnutrition, malaria and HIV/AIDS. On average, across all the four health facilities in Baré,
112 malaria made up approximately 40% of all sicknesses reported in 2016. Cases of malaria can
113 even represent up to 80% of all sicknesses during the wet season. From a Community Needs
114 Assessment (CNA) carried out in December 2016 and January 2017 prior to the intervention,
115 84% reported malaria as the most important health problem, but only 34% of respondents knew
116 how malaria was transmitted. 80% of individuals reported first seeking care from traditional
117 healers. The iCCM programme was introduced to respond to these needs but had its

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3 118 shortcomings that led to the conception and implementation of iCCM+ as a modified iCCM
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5 119 intervention.

7 120 **Intervention description and evaluation**

9 121 **Integrated Community Management (iCCM)**

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12 123 In 2016, as part of the ongoing nation-wide iCCM programme, CHW were trained, supplied
13
14 124 and supervised to diagnose and treat children for malaria, pneumonia and diarrhoea, using
15
16 125 artemisinin-based combination therapies, oral antibiotics, oral rehydration salts and zinc.
17
18 126 Through home visits, patients of all ages in the community are screened for the 3 diseases and
19
20 127 treatment is administered based on the results of the examination and diagnostic testing that
21
22 128 includes malaria RDTs, disease history and respiratory rate. CHW also deliver health education
23
24 129 and promotion talks during these home visits. There are no visits to schools and there is neither
25
26 130 the proactive nor the reactive case detection effort. In this study, only the malaria component
27
28 131 of iCCM was considered (Figure 1).

29 132 **Integrated Community Management Plus (iCCM+)**

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32 134 During 8 weeks of the high transmission period between April and June 2018, Baré's six CHWs
33
34 135 locally known in French as "*Agent de Santé Communautaire (ASC)*" conducted an active
35
36 136 malaria case detection (ACD) involving the addition of both the proactive case detection
37
38 137 (PACD) phase and the reactive case detection (RACD) approaches into their existing iCCM
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40 138 activities. In operational terms, **iCCM+ = iCCM + PACD + RACD**

41 139 Before launching, the project trained 25 primary and nursery school teachers on malaria
42
43 140 detection and on the promotion of prevention & care seeking behaviour. Each CHW was
44
45 141 assigned to a school and a collaborative system between teachers and CHWs working together
46
47 142 to detect sick children was developed. Consent forms were distributed to the teachers to pass
48
49 143 along to parents of pupils for their approval to test their children. Health care workers from the
50
51 144 four health centres were also invited to the training in order to build working relations with
52
53 145 CHWs. The CHWs had been trained repeatedly over the past years by the National Malaria
54
55 146 Control Programme (NMCP) on community management of malaria, but they were briefed
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57 147 alongside two supervisors on the specificities of this project. One supervisor was in charge of
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59 148 correct data collection, while the other inspected schools and visited households to ensure
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149 completeness of field work.

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3 150 PACD was undertaken in 12 primary & nursery schools, 4 health centres, and 13 community
4 151 neighbourhoods on a weekly basis. Each week on a Thursday, CHWs visited assigned schools
5 152 and health centres to locate febrile children. Upon arriving at their schools, the trained teachers
6 153 indicated the pupils under five who had a fever in a recent week. Health workers similarly
7 154 helped to identify febrile children admitted in health facilities. Children with fever were
8 155 identified and tested at no cost for *Plasmodium* infection using rapid diagnostic tests (RDT)
9 156 approved and supplied by the NMCP. Those tested positive for malaria were named as “index
10 157 cases” and were further classified as either uncomplicated or severe malaria. Uncomplicated
11 158 malaria cases were immediately treated with amodiaquine + artesunate, the first-line
12 159 artemisinin-based combination therapy (ACT) recommended and supplied by the NMCP.
13 160 Severe cases and RDT-negative cases were referred to health facilities for further investigation
14 161 and management as per the NMCP guidelines. If a febrile child was absent from school the
15 162 day the CHW arrived, the teacher would tell the CHW where the child lives. The CHW then
16 163 visited the household to identify and test the sick child. In the community however, CHW
17 164 continued to identify febrile children as per the conventional iCCM guidelines.

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30 165 As malaria cases tend to cluster geographically and temporally¹⁵⁻¹⁸, CHWs who also cluster
31 166 and work in the neighbourhoods in which they live, then proceeded with the RACD method to
32 167 visit the home of an index case. In the households, they made a list of all persons resident in
33 168 the household (contacts of the index case), identified and tested those who had a fever in the
34 169 past week. Those tested positive for malaria RDT were named as “secondary cases” and were
35 170 also classified and treated or referred to the nearest health centre in a similar way like the index
36 171 case as illustrated in Figure 1.

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42 172 **Figure 1. The flow chart of the augmented integrated community case management of malaria**
43 173 **(iCCM+)**

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45 174 Data was collected using paper registers and later transcribed into a Microsoft Excel electronic
46 175 database available as a Supplementary File 1. Data collected from the index case during PACD
47 176 included: age, sex, place of residence, presence of fever, date of onset of fever, date and
48 177 location seen by a CHW, results of RDT for malaria, severity of malaria and treatment received.
49 178 During household visits, the same data were collected from febrile contacts in addition to data
50 179 pertaining to household size, long-lasting treated bed nets ownership and current usage. Health
51 180 facility malaria surveillance registers and CHW registers were used as sources to abstract data
52 181 on malaria cases notified between 2015 and 2018.

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3 182 Data analyses were performed using Stata version 14.2 (StataCorp. LP, College Station, United
4 States of America) and Microsoft Excel 2016 (Microsoft Corporation, Redmond, USA) was
5 183 used to plot curves. The data set was checked for logical inconsistencies, invalid codes,
6 184 omissions and improbable data by tabulating, summarizing, describing and plotting variables,
7 185 depending on their nature. Missing observations were systematically excluded.
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12 187 The value of iCCM+ over iCCM alone was measured by the proportion of additional cases
13 188 detected.

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16 189 To describe similarities or differences between index and secondary cases, summary statistics
17 190 were presented as proportions for categorical variables, as means and standard deviations for
18 191 normally distributed continuous variables and as medians and interquartile ranges (IQRs) for
19 192 continuous variables with a skewed distribution. Associations between categorical variables
20 193 were assessed using Pearson's χ^2 test or Fisher's exact test for small samples, as appropriate.
21 194 For continuous variables, mean differences between index cases and contacts were assessed
22 195 using Student's t test. Associations between exposure variables and the likelihood of finding a
23 196 contact were evaluated by a univariate logistic regression model; crude odd ratios, 95%
24 197 confidence intervals (CIs) were reported. Subsequently, factors associated with the odds of a
25 198 finding a contact in the univariate analysis at a significance level below 5% were included in a
26 199 multiple logistic regression model with mixed effects to account for the variability in CHW
27 200 performance. Backward elimination based on a p-value lower than 0.05 was used to retain
28 201 variables that were independently associated with contact tracing; the corresponding adjusted
29 202 odds ratios (aOR) and 95% CIs for the final model were reported.

203 **Patient and public involvement statement**

204 As a community-led project, the public and patients were involved in the project planning,
205 implementation and data collection.

206 The study was approved by the Cameroon National Ethics Review Committee and Peace Corps
207 Cameroon. Individual and parental consent was sought and all information was anonymised
208 and de-identified prior to analysis. An information letter was sent to parents and local
209 administrations, and was announced in community meeting or worshipping places.

210 Results

211 Detection and management of cases

212 At the end of the three-month pilot study, we screened a total of 501 febrile patients of whom
 213 *Plasmodium* infection was confirmed in 425 (overall test-positivity of 84.8%) including 176
 214 index cases with a mean age of 3.4 ± 0.1 years who triggered a further screening by RACD of
 215 249 contacts of mean age 19.2 ± 1.2 years (Table 1). On average, index cases were reached
 216 within 2.4 ± 0.2 days after onset of fever. Index cases were mostly boys (60.8% vs. 49.8%, p
 217 = 0.025) while secondary cases were mostly girls under five years but no gender specificity
 218 among older secondary cases. The RDT positivity for malaria was very high in both the index
 219 (83.4%) and the secondary cases (85.9%). Of these 425 confirmed malaria cases, 354 (83.3%)
 220 were classified as uncomplicated malaria cases who received ACT immediately from the
 221 CHW. The 71 cases who did not receive immediate ACT, were classified as severe malaria
 222 cases who were referred to the nearest health centre for further management.

224 Table 1. Characteristics of index and secondary cases of malaria detected between April and June 2018

Characteristics		Index cases (n = 176)	Secondary cases (n = 249)	P-value of the difference between the groups of cases
Reactive cases found per index case source				
	School	38 (21.6)	50 (20.1)	
	Health facility	36 (20.4)	24 (9.6)	
	Community	102 (58.0)	175 (70.3)	
	Total	176 (100.0)	249 (100.0)	0.004
Sex, n (%)				
	Male	107 (60.8)	124 (49.8)	
	Female	69 (39.2)	125 (50.2)	
	Total	176 (100)	249 (100)	0.025
Age, mean (SD) years		3.4 (0.1)	19.2 (1.2)	<0.0001
Immediate malaria treatment, n (%)				
	ACT	142 (80.7)	212 (85.1)	
	No ACT	34 (19.3)	37 (14.9)	
	Total	176 (100)	249 (100)	0.225
Referred to health facility, n (%)				
	Yes	34 (19.3)	37 (14.9)	
	No	142 (81.7)	212 (85.1)	

	Total	176 (100)	249 (100)	<0.001
Household size, mean (95%CI)		6.4 (6.2 – 6.6)		
Household LLIN ownership, mean (95%CI)		2.4 (2.3 – 2.6)		
LLIN coverage per household member (95%CI)		0.38 (0.36 – 0.40)		
LLIN in use per household member (95%CI)		0.34 (0.32 – 0.36)		

225

226

227 **Proactive and Reactive case detection of confirmed malaria**

228 During the RACD triggered by 176 index cases of confirmed malaria in children under five,
 229 132 (75%) of these index cases investigated led to at least one additional case and a total of
 230 249 secondary cases identified from 290 febrile contacts within 176 households visited. There
 231 were approximately 6 persons on average per household with a bed net ownership of about 2
 232 LLINs per household leading to a bed net coverage of about 1 LLIN for 3 persons. After a lag
 233 phase during the first half of the project, the number of cases detected increased sharply over
 234 the second half before returning to the initial stable level (Figure 2).

235 **Figure 2. Trend in the number of cases of confirmed malaria between April and June 2018**

236 Of all the 425 confirmed cases, 38 (8.9%) were index cases identified proactively in schools
 237 and led to find 50 (11.8%) more cases; 36 (8.5%) were index cases located in health facilities
 238 and led to a further 24 (5.6%) cases; and 102 (24.0%) were index cases identified during routine
 239 iCCM activity and led to 175 (41.2%) additional cases showing the value of RACD over iCCM
 240 alone (Figure 2). Overall, iCCM+ identified 287 of the 425 cases thus indicating that the
 241 ongoing iCCM must have been improved by 67.5% to detect malaria cases in the community
 242 (Figure 3).

243 **Figure 3. Flow diagram of cases detected and treated during iCCM and iCCM+**

244 During 12 weeks in April, May, and June in 2017 CHWs detected 238 cases of malaria at a
 245 rate of ~20 cases per week. But during our 8-week project across April, May and June in 2018,
 246 the CHWs detected 365 cases of malaria at a rate of ~45 cases per week computing to a 125%
 247 increase from 2017 during the same transmission season.

248 The odds of finding a secondary case by RACD increased by 70% if the index case was one
 249 year younger (adjusted odd ratio (aOR) = 1.7, 95% CI: 1.5 – 1.9) and by 20% if a household
 250 size increased by one person (aOR = 1.2, 95% CI: 1.1 – 1.3). Though RACD was likely to find
 251 female cases, the evidence to support gender discrimination was rejected in the multiple
 252 regression model in Table 2 (aOR = 1.2, 95% CI: 0.7 – 2.1).

254 **Table 2. Multiple logistic regression model of factors associated with secondary case detection (N = 425)**

Factor	Number of confirmed secondary cases, n (%)	Crude OR (95%CI)	p-value	Adjusted OR (95%)	p-value	
Sex						
	Male	124 (53.7)	Reference	Reference		
	Female	125 (64.4)	1.6 (1.1 – 2.3)	0.024	1.2 (0.7 – 2.1)	0.477
Additional one year of age			1.7 (1.5 – 1.9)	<0.001	1.7 (1.5 – 1.9)	<0.001
Additional one household member			1.2 (1.1 – 1.3)	<0.001	1.2 (1.1 – 1.3)	0.015

255

256 Discussion

257 In this small-scale quality improvement study, we sought to demonstrate in a high transmission
 258 area, the feasibility of embedding both the proactive and reactive case detection strategies into
 259 integrated community case management in order to maximise malaria case detection and
 260 prompt treatment. The study has indicated iCCM+ increased the proportion of persons
 261 diagnosed and treated for *Plasmodium* infection by approximately 67.5%. The study has also
 262 confirmed that the burden of malaria lies in the community with only the tip of the iceberg seen
 263 in health facilities. While iCCM was introduced to respond to this challenge, it was currently
 264 underperforming in this rural setting. This project has suggested that iCCM can be adapted to
 265 achieve optimal results. While on one hand it may appear obvious that the malaria component

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3 266 of iCCM can be adapted to or opt for a PACD strategy, implementing RACD in a high
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5 267 transmission setting on the other hand may seem experimental or even controversial to some
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7 268 extent. This is because RACD is a surveillance approach recommended in low transmission or
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9 269 pre-elimination settings to disrupt transmission and is thought to be inefficient and infeasible
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11 270 in high transmission settings. Conversely, RACD may also waste time and money when cases
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13 271 are few and sporadic¹⁹⁻²². Therefore, the choice of RACD as an approach depends on the
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15 272 objective to be attained, the proportion of cases it can detect and the resources needed. Our
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17 273 project was feasible and efficient because our aim was not to eliminate malaria but to detect
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19 274 and treat the maximum possible number of cases during a high transmission season when the
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21 275 proportion of cases is highest using resources already made available for iCCM in a rural
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23 276 setting where access to health services is limited. The extra resource needed is the time to visit
24
25 277 schools, health facilities and households. CHWs told us that by conducting only a one-day visit
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27 278 per week to these facilities and only to households of index cases was more productive and
28
29 279 made them more useful in their community. This strategy was not much different from what
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31 280 they were doing before, just a more targeted approach: - targeting schools, targeting households
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33 281 of index cases and targeting high transmission season when fever is likely to be caused by a
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35 282 *Plasmodium* infection as confirmed in this study where RDT was positive in 85% of persons
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37 283 screened for fever and with a high probability of 75% that every index case led to at least one
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39 284 secondary case. Beyond CHW job satisfaction, teachers also expressed their satisfaction and
40
41 285 were of great support in detecting fever or a history of fever amongst their pupils. Moreover,
42
43 286 we found that teachers were far more likely to help CHW finding the households of sick
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45 287 children than healthcare workers. We thus strongly believe that RACD can be both feasible
46
47 288 and efficient in a high transmission setting to maximise clinical case management.
48
49 289 Consequently, we recommend that PACD and RACD become part of the ongoing iCCM
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51 290 strategy in Cameroon as an approach to optimise case detection. Yet incorporating PACD and
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53 291 RACD into iCCM will entail building a strong collaboration among CWH, HCW and teachers.
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55 292 Such a partnership already exists between the ministries of health and education in Cameroon
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57 293 in their concerted effort to fight neglected tropical diseases specifically soil-transmitted
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59 294 helminthiasis in school children²³. The recurrent problem of stockouts of commodities will
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295 need to be resolved by the NMCP and field monitoring and supervision should become regular
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297 by iCCM programme coordination. Resolving these issues of multisector collaboration,
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299 delivery of commodities and field coordination were crucial as bottlenecks and explain in part
why progress was slow in the first half of the project. In response to the breakdown in the
delivery of commodities, the regional office for the NMCP is now distributing these

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3 300 commodities to health facilities and thus offsetting the transportation hurdles faced by the latter
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5 301 to purchase and pick them up from their regional head offices of NMCP. Moreover, under the
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7 302 ongoing performance-based financing (PBF) system, health facilities are becoming more and
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9 303 more autonomous and can get their commodities from local authorised outlets.

10
11 304 This study has further indicated that, while index cases were likely to be boys, RACD was
12
13 305 likely to find girls and women in univariate analysis though such claims were not supported by
14
15 306 evidence from multivariate analysis. Boys make up the majority of school children in
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17 307 Cameroon especially in the rural areas and this might be a reflection of this observation²⁴.
18
19 308 However, it is plausible that gender norms and values that determine the division of labour,
20
21 309 leisure patterns, pregnancy, and sex-segregation of sleeping arrangements may lead to different
22
23 310 patterns of exposure to mosquitoes for men and women²⁴⁻²⁶.

24
25 311 Secondary cases were likely to be older than index cases and to be located in larger households
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27 312 of the index case. Given that we purposely targeted children under five years, it became obvious
28
29 313 that we may likely find more of older children and adults as contacts. Clustering of cases has
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31 314 previously been demonstrated in households of the contacts and malaria eradication is thought
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33 315 to be feasible when household size drops below four persons^{27 28}. The average household size
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35 316 in this study was six persons thus explaining while it was very likely to find more cases in the
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37 317 community during RACD.

38
39 318 This study had some limitations so that the results should be interpreted with caution. There
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41 319 was no control arm to clearly distinguish between iCCM+ from iCCM intervention areas. A
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43 320 randomised community trial may be recommended as a solution. The duration and period of
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45 321 the study was limited to only three months and to the first half of the wet season. We could not
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47 322 therefore account for neither seasonality in malaria transmission nor account for sustainability
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49 323 throughout the year. Older children and adults were not included as index cases thus creating
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51 324 an outright difference between index and secondary cases. This must have led to an
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53 325 overestimation of the value of RACD in this field study because in routine practice however,
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55 326 adults would be index cases as well. Targeting school children for malaria treatment must have
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57 327 been a laudable effort but older school children were also left out as index cases though they
58
59 328 constitute a group with a higher *Plasmodium* infection prevalence than in the targeted younger
60
329 age group¹². However, these children were among those screened in the community. We did
330
331 not measure the effect of this strategy on the pneumonia and diarrhoea components of iCCM
but we believe that being an integral part of the package of interventions, these two components

332 were likely to have been improved as well. We did not attempt to measure effect on malaria
 333 transmission as most studies have done.

334 Conclusion

335 This study has shown that most symptomatic cases of malaria remain undetected in the
 336 community despite the introduction of integrated community management of malaria. Schools
 337 are an important portal to locate children with undiagnosed malaria. Active case detection
 338 based on a proactive and reactive case detection approaches is feasible in a high transmission
 339 setting and has been shown to enhance in a synergistic manner the efficiency of integrated
 340 community case management of malaria. We recommend that national malaria control
 341 programs adopt and implement this modified form of iCCM in similar settings to diagnose and
 342 treat more malaria cases in our communities.

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432 **Footnotes**

434 **Ethics approval and consent to participate**

435
436 The study was approved by the National Ethics Review Board of Cameroon, Peace Corps
437 Cameroon and local administrative and health authorities. Verbal consent was obtained from
438 household members after making public announcements and providing an information leaflets
439 to explain the objectives of the project.

440 **Consent for publication**

441 Not Applicable

442 **Availability of data and material**

443
444 The datasets used and/or analysed during the current study are available as a supplementary
445 file.

446 **Competing interests**

447
448 The authors declare that they have no competing interests

449 **Funding**

450
451 The study received no specific funding

452 **Author Contributions**

453
454 Conception, design and implementation: TDW, CEB
455 Data collection, analysis and interpretation: TDW, CEB
456 Drafting the manuscript: CEB

1
2
3 457 All authors read and approved the final manuscript
4

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7
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9
10 461 teachers, interns and the people of Bare – Bakem for their support and active participation
11
12 462 and collaboration.

13
14 463 **Authors' information**

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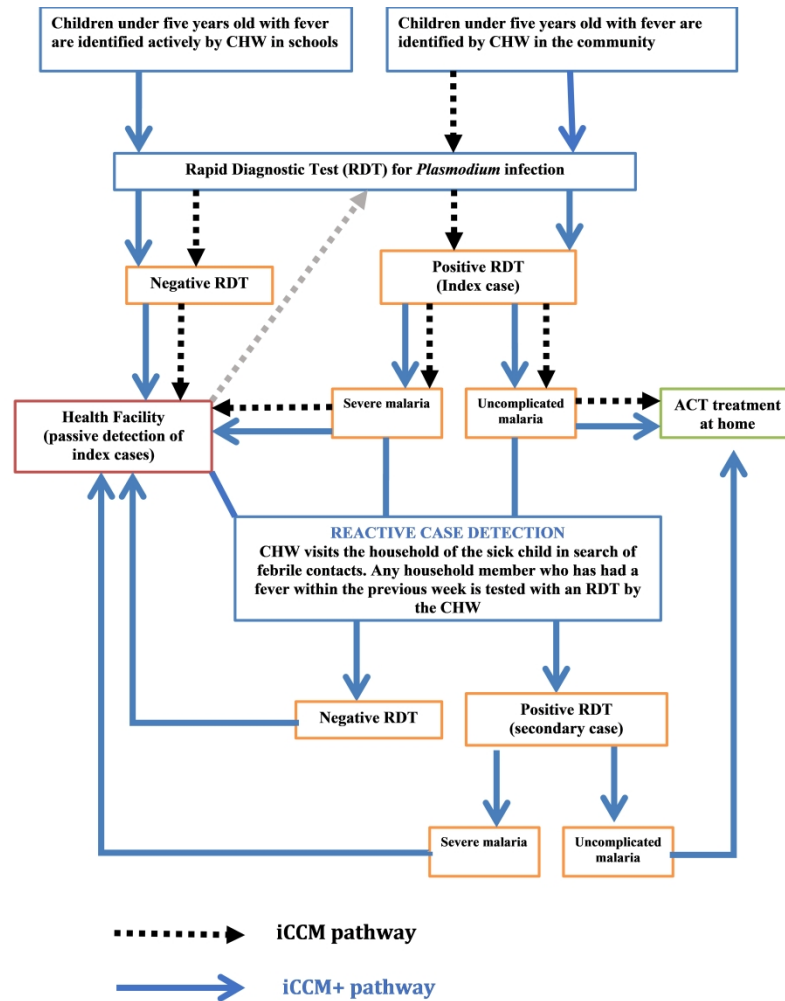


Figure 1. The flow-chart of the augmented integrated community case management of malaria (iCCM+)

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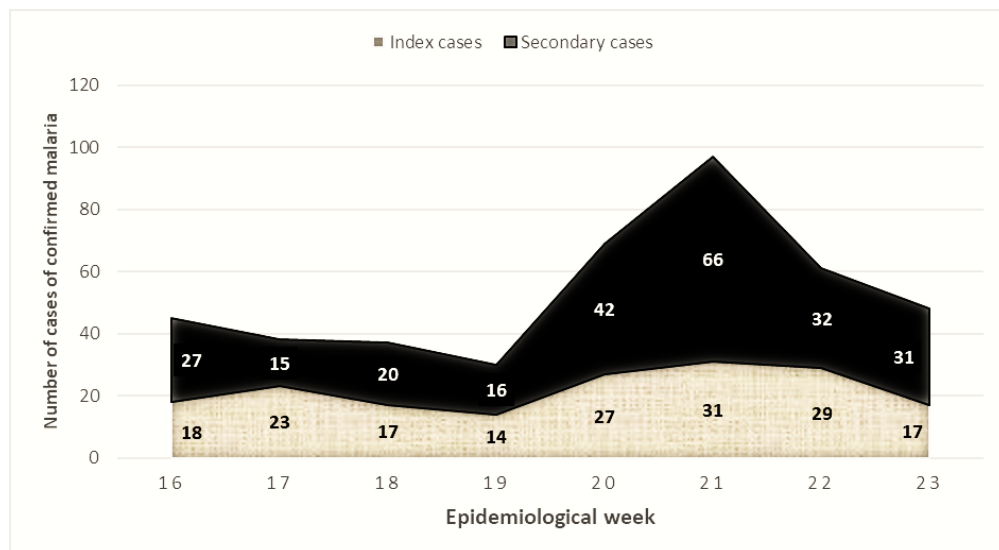
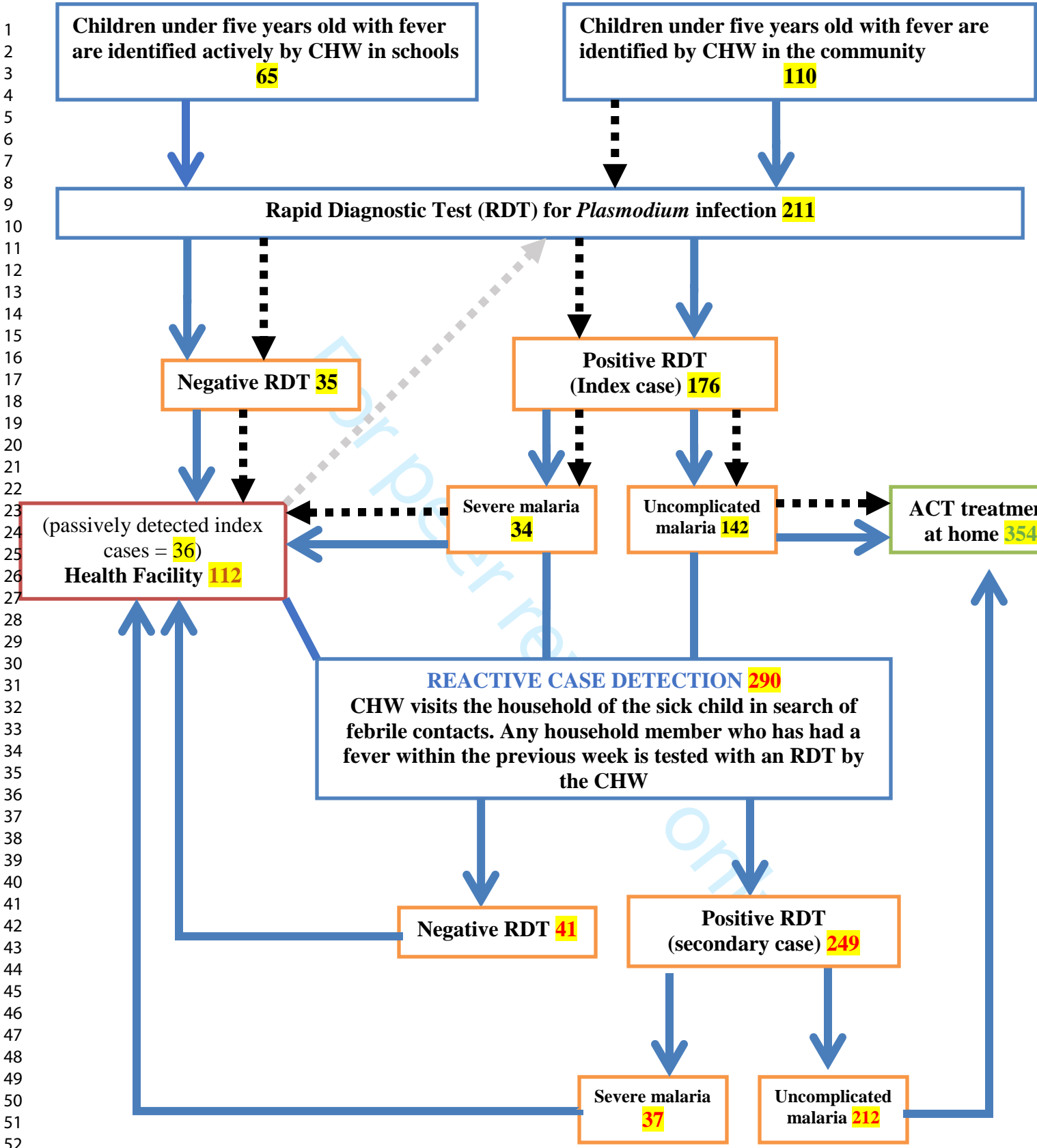


Figure 2. Trend in the number of cases of confirmed malaria

79x43mm (300 x 300 DPI)

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.....> iCCM detected 102/425 cases or 24%
 —————> iCCM+ detected 287/425 cases or 67.5%
 - - - - -> Health Facility cases 36/425 or 8.5%

Number	Case Number	Case Type Primary: 1 Secondary: 2	Age	Sex Male: 1 Female: 2	Quarrier	Fever?		RDT Result		If simple malaria, ACT given?		If complicated malaria or negative RDT, referred?		Primary Case Location School: 1 Hospital: 2 Community: 3	Household population	Total LUN	Total LUN Attached	ASC	Week	Date of Fever	Date Found by ASC	How long it took? (Days)
						0	Yes: 1	Positive: 1	Negative: 0	No: 0	Yes: 1	No: 0	Yes: 1									
1	1	1	4	1	8 Bis	0	1	0	0	0	0	0	0	2	4	3	1	JY	1	16/04/2018	19/04/2018	3
2	1.1	2	10	1	8 Bis	0	0	0	0	0	0	0	0	2				JY	1		19/04/2018	
3	1.2	2	48	2	8 Bis	0	0	0	0	0	0	0	0	2				JY	1		19/04/2018	
4	1.3	2	18	1	8 Bis	0	0	0	0	0	0	0	0	2				JY	1		19/04/2018	
5	2	1	2	2	Bareko	1	1	1	0	0	0	0	0	3	2	2	2	JY	1	17/04/2018	19/04/2018	2
6	2.1	2	31	2	Bareko	0	0	0	0	0	0	0	0	2				JY	1		19/04/2018	
7	2.2	2	41	1	Bareko	0	0	0	0	0	0	0	0	2				JY	1		19/04/2018	
8	3	1	3	1	Ebouh	1	1	1	0	0	0	0	0	9	5	5	ZK	1	14/04/2018	19/04/2018	5	
9	3.1	2	14	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
10	3.2	2	11	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
11	4	1	5	2	Ebouh	1	1	1	0	1	0	1	1	9	4	4	ZK	1	16/04/2018	19/04/2018	3	
12	4.1	2	10	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
13	4.2	2	12	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
14	4.3	2	3	1	Ebouh	1	1	1	0	1	0	1	1				ZK	1		19/04/2018		
15	4.4	2	5	2	Ebouh	1	1	1	0	1	0	1	1				ZK	1		19/04/2018		
16	4.5	2	8	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
17	5	1	5	2	Ebouh	1	1	1	0	1	0	1	1	15	0	0	ZK	1	16/04/2018	19/04/2018	3	
18	5.1	2	8	2	Ebouh	1	1	1	0	1	1	1	1				ZK	1		19/04/2018		
19	5.2	2	10	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
20	5.3	2	10	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
21	6	1	4	1	Ebouh	1	1	1	0	1	0	1	1	4	2	2	ZK	1	15/04/2018	19/04/2018	4	
22	6.1	2	35	1	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
23	7	1	5	2	Ebouh	1	1	1	0	1	0	1	1	6	6	6	ZK	1	10/04/2018	19/04/2018	9	
24	7.1	2	48	2	Ebouh	1	1	0	1	1	0	1	1				ZK	1		19/04/2018		
25	7.2	2	28	2	Ebouh	1	1	0	0	0	0	0	0				ZK	1		19/04/2018		
26	8	1	4	1	Ebouh	1	1	0	1	0	0	1	1	6	3	3	ZK	1	15/04/2018	19/04/2018	4	
27	8.1	2	2	1	Ebouh	1	1	1	0	1	0	1	1				ZK	1		19/04/2018		
28	9	1	4	2	Ebouh	1	1	1	0	1	0	1	3	8	4	4	ZK	1	13/04/2018	21/04/2018	8	
29	10	1	4	2	Ebouh	1	1	1	0	1	0	1	1	6	2	2	ZK	1	15/04/2018	19/04/2018	4	
30	11	1	4	1	Ebouh	1	1	1	0	1	0	1	3	7	4	4	ZK	1	13/04/2018	19/04/2018	6	
31	12	1	5	2	Ebouh	1	1	1	0	1	0	1	3	1	1	1	ZK	1	16/04/2018	19/04/2018	3	
32	13	1	4	2	Ebouh	1	1	0	0	0	0	0	1	5	2	2	ZK	1	15/04/2018	19/04/2018	4	
33	14	1	5	2	8 Bis	1	1	0	1	1	0	1	3	4	2	2	JL	1	19/04/2018	21/04/2018	2	
34	14.1	2	27	1	8 Bis	1	0	0	1	0	1	0	3				JL	1		21/04/2018		
35	14.2	2	25	2	8 Bis	1	0	0	1	0	0	1	3				JL	1		21/04/2018		
36	14.3	2	19	2	8 Bis	1	0	0	1	0	0	1	3				JL	1		21/04/2018		
37	15	1	1	1	F	1	1	1	0	0	0	0	3	10	4	4	MN	1	17/04/2018	19/04/2018	2	
38	15.1	2	5	2	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
39	15.2	2	38	2	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
40	15.3	2	18	1	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
41	15.4	2	10	2	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
42	15.5	2	12	2	F	1	0	0	0	1	0	1	3				MN	1		19/04/2018		
43	15.6	2	21	2	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
44	15.7	2	8	1	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
45	15.8	2	47	1	F	0	0	0	0	0	0	0	3				MN	1		19/04/2018		
46	16	1	4	2	E	0	0	0	0	1	0	1	3				MN	1	19/04/2018	19/04/2018	0	
47	17	1	1	1	E	1	1	1	0	0	0	0	3	8	4	4	BN	1	21/04/2018	21/04/2018	0	
48	17.1	2	5	1	E	1	1	1	0	1	0	1	3				BN	1		21/04/2018		
49	17.2	2	11	2	E	1	1	0	1	0	1	0	3				BN	1		21/04/2018		
50	17.3	2	50	1	E	0	0	0	0	0	0	0	3				BN	1		21/04/2018		
51	17.4	2	39	2	E	0	0	0	0	0	0	0	3				BN	1		21/04/2018		
52	18	1	5	1	E	1	1	1	0	1	0	1	3	12	6	4	BN	1	21/04/2018	21/04/2018	0	
53	18.1	2	2	1	E	0	0	0	0	0	0	0	3				BN	1		21/04/2018		
54	18.2	2	3	1	E	1	1	0	1	0	1	0	3				BN	1		21/04/2018		
55	18.3	2	4	1	E	1	1	1	0	0	0	0	3				BN	1		21/04/2018		
56	18.4	2	5	2	E	1	1	1	0	1	0	1	3				BN	1		21/04/2018		
57	19	1	4	1	E	1	1	1	0	1	0	1	7	3	3	RT	1	18/04/2018	19/04/2018	1		
58	19.1	2	68	1	E	1	1	0	1	1	0	1	1				RT	1		19/04/2018		
59	19.2	2	50	2	E	1	1	0	1	0	1	1	1				RT	1		19/04/2018		
60	19.3	2	13	2	E	1	1	0	0	1	0	1	1				RT	1		19/04/2018		
61	19.4	2	11	2	E	1	1	0	1	1	0	1	1				RT	1		19/04/2018		
62	19.5	2	9	1	E	1	1	0	1	0	0	1	1				RT	1		19/04/2018		
63	19.6	2	7	2	E	1	1	0	0	0	0	0	1				RT	1		19/04/2018		
64	20	1	3	1	F	1	1	1	0	1	0	1	6	2	2	1	RT	1	18/04/2018	19/04/2018	1	
65	20.1	2	30	1	F	0	0	0	0	0	0	0	1				RT	1		19/04/2018		
66	20.2	2	28	2	F	0	0	0	0	0	0	0	1				RT	1		19/04/2018		
67	20.3	2	18	2	F	0	0	0	0	0	0	0	1				RT	1		19/04/2018		
68	20.4	2	1	2	F	1	1	1	0	1	0	1	1				RT	1		19/04/2018		
69	21	1	3	2	E Bis	1	1	1	0	1	0	1	4	2	2	1	JY	1	25/04/2018	25/04/2018	0	
70	21.1	2	45	2	E Bis	0	0	0	0	0	0	0	1				JY	1		25/04/2018		
71	22	1	3	2	F	1	0	0	1	1	0	1	1				JY	1	23/04/2018	26/04/2018	3	
72	23	1	2	1	A Bis	1	1	0	0	0	0	0	2	6	3	2	JY	1	22/04/2018	28/04/2018	6	
73	23.1	2	30	1	A Bis	0	0	0	0	0	0	0	2				JY	1		28/04/2018		
74	23.2	2	1	1	A Bis	1	1	1	0	0	0	0	2				JY	1		28/04/2018		
75	24	1	5	2	Bareko	1	1	0	0	0	0	0	2	No Visit			JY	1	23/04/2018	28/04/2018	5	
76	25	1	1	1	Bareko	1	1	0	0	0	0	0	2	No Visit			JY	1	23/04/2018	28/04/2018	5	
77	26	1	2	1	Ebouh	1	1	1	0	1	0	1	3	6	3	3	ZK	1	20/04/2018	24/04/2018	4	
78	26.1	2	17	2	Ebouh	1	1	0	1	0	1	0	3				ZK	1	24/04/2018	24/04/2018	2	
79	26.2	2	7	1	Ebouh	1	1	0	1	0	1	0	3				ZK	1	24/04/2018	24/04/2018	2	
80	27	1	4	1	Ebouh	1	1	1	0	1	0	1	1				ZK	1	23/04/2018	26/04/2018	3	
81	27.1	2	5	2	Ebouh	1	0	0	0	0	0	0	1				ZK	1		26/04/2018		
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398	154	1	5	1	B	1	1	1	0	3	9	0	0	JL	6	19/05/2018	21/05/2018	2
399	154.1	2	25	2	B	1	0	0	1	3				JL	6	21/05/2018		
400	155	1	3	1	F	1	1	1	0	3	4	1	1	JL	6	21/05/2018	23/05/2018	2
401	155.1	2	23	2	F	1	1	1	0	3				JL	6	21/05/2018	23/05/2018	2
402	156	1	0.6	2	F Bis	1	1	1	0	3				JL	6	23/05/2018	24/05/2018	1
403	156.1	2	10	2	F Bis	1	1	1	0	3	12	0	0	JL	6	23/05/2018	24/05/2018	1
404	156.2	2	11	1	F Bis	1	1	1	0	3				JL	6	24/05/2018		
405	156.3	2	7	2	F Bis	1	1	1	0	3				JL	6	24/05/2018		
406	157	1	2	1	F Bis	1	1	1	0	3	5	2	2	JL	6	23/05/2018	24/05/2018	1
407	157.1	2	39	2	F Bis	1	0	0	1	3				JL	6	24/05/2018		
408	158	1	5	1	C	1	1	1	0	3	9	3	3	RT	7	02/06/2018	02/06/2018	0
409	158.1	2	17	1	C	1	1	1	0	3				RT	7	02/06/2018		
410	158.2	2	18	2	C	1	1	1	0	3				RT	7	02/06/2018		
411	158.3	2	15	1	C	1	1	1	0	3				RT	7	02/06/2018		
412	158.4	2	9	1	C	1	1	1	0	3				RT	7	02/06/2018		
413	158.5	2	12	2	C	1	1	1	0	3				RT	7	02/06/2018		
414	159	1	5	2	B	1	0	0	1	3				RT	7	29/05/2018	31/05/2018	2
415	160	1	2	2	E Bis	1	1	1	0	3	6	3	3	RT	7	03/06/2018	03/06/2018	0
416	160.1	2	9	1	E Bis	1	1	1	0	3				RT	7	03/06/2018		
417	161	1	5	2	D	1	1	1	0	3	8	3	3	RT	7	29/05/2018	31/05/2018	2
418	161.1	2	4	1	D	1	1	1	0	3				RT	7	31/05/2018		
419	161.2	2	11	2	D	1	1	1	0	3				RT	7	31/05/2018		
420	162	1	6	1	Ebouh	1	1	1	0	3	10	5	5	ZK	7	24/05/2018	28/05/2018	4
421	163	1	3	1	Ebouh	1	1	1	0	3	6	3	3	ZK	7	27/05/2018	29/05/2018	2
422	163.1	2	30	1	Ebouh	1	1	1	0	3				ZK	7	29/05/2018		
423	163.2	2	18	1	Ebouh	1	1	1	0	3				ZK	7	29/05/2018		
424	164	1	3	1	Ebouh	1	1	1	0	3	8	4	4	ZK	7	24/05/2018	28/05/2018	4
425	165	1	3	1	Ebouh	1	0	0	1	1				ZK	7	24/05/2018	29/05/2018	5
426	166	1	3	1	Ebouh	1	0	0	1	1				ZK	7	25/05/2018	29/05/2018	4
427	167	1	3	1	Ebouh	1	0	0	1	1				ZK	7	26/05/2018	29/05/2018	3
428	168	1	3	1	Ebouh	1	0	0	1	1				ZK	7	26/05/2018	29/05/2018	3
429	169	1	2	1	B	1	0	0	1	1				ZK	7	25/05/2018	29/05/2018	4
430	170	1	3	1	B	1	0	0	1	1				ZK	7	24/05/2018	29/05/2018	5
431	171	1	5	1	Bareko	1	1	1	0	3	8	1	1	JL	7	29/05/2018	30/05/2018	1
432	171.1	2	33	1	Bareko	1	0	0	1	3				JL	7	30/05/2018		
433	171.2	2	11	2	Bareko	1	1	1	0	3				JL	7	30/05/2018		
434	171.3	2	11	1	Bareko	1	1	1	0	3				JL	7	30/05/2018		
435	172	1	5	2	F Bis	1	1	1	0	3	8	2	1	JL	7	28/05/2018	31/05/2018	3
436	172.1	2	9	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
437	172.2	2	9	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
438	172.3	2	62	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
439	172.4	2	38	2	F Bis	1	1	1	0	3				JL	7	31/05/2018		
440	173	1	3	1	F Bis	1	1	1	0	3	3	1	1	JL	7	27/05/2018	30/05/2018	3
441	173.1	2	28	2	F Bis	1	0	0	1	3				JL	7	30/05/2018		
442	174	1	5	1	A Bis	1	1	1	0	3	9	2	2	MN	7	28/05/2018	31/05/2018	3
443	174.1	2	17	1	A Bis	1	1	1	0	3				MN	7	31/05/2018		
444	174.2	2	7	2	A Bis	1	0	0	1	3				MN	7	31/05/2018		
445	174.3	2	15	1	A Bis	1	0	0	1	3				MN	7	31/05/2018		
446	174.4	2	44	1	A Bis	1	1	1	0	3				MN	7	31/05/2018		
447	175	1	2	1	B	1	1	1	0	3				MN	7	16/05/2018	31/05/2018	
448	176	1	2	2	F	1	1	1	0	3	15	0	0	MN	7	26/05/2018	31/05/2018	5
449	176.1	2	49	1	F	1	1	1	0	3				MN	7	31/05/2018		
450	176.2	2	14	1	F	1	1	1	0	3				MN	7	31/05/2018		
451	177	1	2	2	F	1	1	1	0	3	7	4	3	MN	7	30/05/2018	31/05/2018	1
452	177.1	2	8	1	F	1	1	1	0	3				MN	7	31/05/2018		
453	177.2	2	6	1	F	1	1	1	0	3				MN	7	31/05/2018		
454	177.3	2	6	2	F	1	1	1	0	3				MN	7	31/05/2018		
455	177.4	2	13	2	F	1	1	1	0	3				MN	7	31/05/2018		
456	177.5	2	37	2	F	1	1	1	0	3				MN	7	31/05/2018		
457	177.6	2	91	1	F	1	0	0	1	3				MN	7	31/05/2018		
458	178	1	5	1	D	1	1	1	0	3	2	1	0	MN	7	30/05/2018	30/05/2018	0
459	178.1	2	59	1	D	1	1	1	0	3				MN	7	30/05/2018		
460	179	1	3	2	F	1	1	1	0	3	6	3	3	MN	7	04/06/2018	04/06/2018	0
461	179.1	2	52	2	F	1	1	1	0	3				MN	7	04/06/2018		
462	180	1	4	2	E	1	1	1	0	3				MN	7	14/06/2018	31/05/2018	
463	181	1	4	1	D	1	1	1	0	3				MN	7	26/05/2018	31/05/2018	
464	182	1	3	1	D	1	1	1	0	3				MN	7	30/05/2018	31/05/2018	
465	183	1	4	2	E	1	1	1	0	3	4	2	2	MN	7	29/05/2018	31/05/2018	2
466	183.1	2	55	2	E	1	1	1	0	3				MN	7	31/05/2018		
467	184	1	5	2	F	1	1	1	0	3	6	1	1	MN	7	29/05/2018	02/06/2018	4
468	184.1	2	74	2	F	1	1	1	0	3				MN	7	02/06/2018		
469	185	1	3	1	A Bis	1	1	1	0	3				MN	7	16/05/2018	31/05/2018	
470	186	1	3	2	Bareko	1	1	1	0	3				JY	7	19/05/2018	19/05/2018	
471	187	1	2	1	Bareko	1	1	1	0	3				JY	7	15/05/2018	15/05/2018	
472	188	1	3	2	B Bis	1	1	1	0	3	4	2	2	JY	7	17/05/2018	18/05/2018	1
473	188.1	2	61	1	B Bis	1	1	1	0	3				JY	7	17/05/2018	18/05/2018	1
474	189	1	1	2	Ebouh	1	1	1	0	3				JY	7	16/05/2018	24/05/2018	
475	190	1	2	1	Ebouh	1	1	1	0	3				JY	7	17/05/2018	17/05/2018	
476	191	1	3	1	A Bis	1	1	1	0	3	8	3	3	JY	7	30/05/2018	31/05/2018	1
477	192	1	3	2	B Bis	1	1	1	0	3	6	2	2	JY	7	31/05/2018	31/05/2018	0
478	193	1	3	2	B	1	1	1	0	3	8	4	4	BN	7	28/05/2018	28/05/2018	0
479	193.1	2	2	1	B	1	1	1	0	3				BN	7	28/05/2018		
480	193.2	2	2	1	B	1	1	1	0	3				BN	7	28/05/2018		
481	194	1	3	2	B	1	1	1	0	3	6	3	1	RT	8	05/06/2018	07/06/2018	2
482	194.1	2	7	2	B	1	1	1	0	3				RT	8	07/06/2018		
483	195	1	2	2	C	1	1	1	0	3	7	2	2	RT	8	30/05/2018	08/06/2018	9
484	195.1	2	8	2	C	1	1	1	0	3				RT	8	08/06/2018		
485	195.2	2	41	2	C	1	1	1	0	3				RT	8	08/06/2018		
486	196	1	4	1	A	1	1	1	0	3	6	0	0	RT	8	09/06/2018	10/06/2018	1
487	196.1	2	5	2	A	1	1	1	0	3				RT	8	10/06/2018		
488	197	1	1	2	F	1	1	1	0	3	5	2	2	MN	8	06/06/2018	06/06/2018	0
489	197.1	2																

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract Page 2 (b) Provide in the abstract an informative and balanced summary of what was done and what was found Page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 3
Objectives	3	State specific objectives, including any prespecified hypotheses Page 4
Methods		
Study design	4	Present key elements of study design early in the paper Page 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Page 4-7
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants Page 5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Page 6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Page 6-7
Bias	9	Describe any efforts to address potential sources of bias Page 6
Study size	10	Explain how the study size was arrived at Not calculated
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Page 7
Statistical methods Page 7	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Page 7-8 (b) Give reasons for non-participation at each stage Figure 1 (c) Consider use of a flow diagram Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Table 1 (b) Indicate number of participants with missing data for each variable of interest Table 1
Outcome data	15*	Report numbers of outcome events or summary measures Tables 1 and 2
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Page 9 and Table 2 (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a

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meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Page 9
Discussion		
Key results	18	Summarise key results with reference to study objectives Page 10
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 11
Generalisability	21	Discuss the generalisability (external validity) of the study results Page 11-12
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 15

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.