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# Successful introduction of artesunate combination therapy is not enough to fight malaria: results from an adherence study in Sierra Leone

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ABSTRACT

A study to measure adherence to artesunate and amodiaquine (AS+AQ) therapy in patients treated for uncomplicated malaria in community health centres (CHC) was conducted in Sierra Leone. Patients/caretakers were interviewed and remaining AS+AQ tablets at home after the last treatment dose were counted. Persons leaving CHCs with an AS+AQ prescription were also interviewed (exit interviews). In total, 118 patients were visited at home: 27 (22.9%) had one or more tablets left and were classed as certainly non-adherent; 34 (28.8%) were probably non-adherent [reported incorrect ($n = 27$) or incomplete ($n = 7$) intake]; and 57 (48.3%) were probably adherent. The main reasons for incomplete intake were sickness after one dose of AS+AQ, no food available for drug intake and forgetting to take them. For incorrect intake, reasons were vomiting after drug intake and incorrect instructions given by the CHC. Eighty-one percent of probably adherent patients reported following instructions given to them. In exit interviews, 82% of patients or caretakers of patients were able to repeat AS+AQ intake instructions correctly. Adherence to antimalarial treatment should not be taken for granted. Instructions on correct AS+AQ use should include discussion of disease symptoms as well as possible treatment side effects and how to manage them. Other factors are more difficult to influence, such as patients forgetting to take the treatment.



## 1. Introduction

Despite being treatable, malaria is still a life-threatening disease. Approximately one-half of the world's population is at risk for malaria, particularly those living in low-income countries where malaria is endemic.[1]

Apart from preventive measures, prompt and accurate diagnosis followed by treatment with an artemisinin-based combination therapy (ACT) is currently the main malaria control strategy. Widespread resistance to the common antimalarial monotherapies has led to an increased use of ACT as the first-line treatment for uncomplicated *Plasmodium falciparum* malaria.[2] In accordance with the national protocol of Sierra Leone and in collaboration with the Ministry of Health and Sanitation, ACT of artesunate and amodiaquine (AS+AQ) in a co-blister package has been used as the first-line drug in the Médecins Sans Frontières (MSF) project in the country. However, providing ACT alone cannot be considered the definitive solution to antimalarial resistance. A key element in the success of ACT is correct intake of the treatment.[3] Incorrect intake increases the

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risk of developing resistance in addition to treatment failure. New antimalarials are in the pipeline but research and development will take time, therefore it is important to protect the currently existing drugs.

Correct use of ACT is the sum of correct diagnosis, prescription and patient adherence. Numerous factors can influence patient adherence, such as frequency of dosing, number of pills prescribed, duration of treatment, side effects, clinical improvement, cost of treatment, concomitant treatment intake, patient education level, perception of disease, quality of explanation by health personnel and treatment packaging.[4,5] There are few published studies on patient adherence to ACT, and the methods and definitions of adherence vary widely.[6–10] Adherence reports range from 38% to 93%[11,12] and the main reasons for non-adherence include education level,[11,13] non-supervision of intake of the first dose[14] and problems with drug packaging.[15,16] Consequently, it is very difficult to make comparisons and to draw valid conclusions regarding the role of adherence in the success of ACT treatment.[17–19] This raises the concern that adherence studies are not considered a public health priority despite the recommendation that in order to ensure the long-term effectiveness of ACT, adherence assessments should be carried out on a regular basis at the national and programme levels and appropriate action taken to improve patient adherence, if indicated.[10,11] This study aimed to improve on previous studies by using three methods of measuring adherence. It was carried out as part of an ongoing programme evaluation. In addition, none of the studies have assessed adherence to the commonly used AS+AQ in Sierra Leone or West Africa.

The aim of this study was to measure adherence to AS+AQ in patients treated for uncomplicated malaria in MSF-supported community health centres (CHC) in southeast Sierra Leone and to identify the main reasons for non-adherence.

## 2. Materials and methods

### 2.1. Study area and population

The study area was located in the Bo and Pujehun districts in southeast Sierra Leone. All of Sierra Leone is hyperendemic for malaria with perennial transmission. The entire population of approximately 5.5 million people is at risk of contracting the disease, which accounts for >40% of outpatient morbidity in the general population (S. Baker, Head of National Malaria Control Program, Ministry of Health and Sanitation, Freetown, Sierra Leone, personal observation, 2009). MSF has provided free malaria diagnosis, treatment and prevention for a population of 158 000 living in and around 330 villages since 2005 (MSF, in-house mapping, 2007). Within this catchment area, MSF is working in five CHCs and 30 health posts forming Ministry of Health and Sanitation-related primary health units. The project also runs a referral hospital providing secondary-level health care. All together, approximately 280 local health personal are working in the health facilities. In 2008, there were 417 576 consultations in all MSF health facilities, with 181 711 confirmed cases of malaria (43.5%). Severe malaria was the principal cause of morbidity, accounting for 54.3% of all cases in the referral hospital (MSF, internal source, 2008/2009).

### 2.2. Study subjects

Patients were included in the study if they were: aged ≥1 year; had a confirmed diagnosis via a malaria rapid diagnostic test of uncomplicated *P. falciparum* malaria (with or without additional diagnoses); had received a course of AS+AQ in one of the five CHCs; were resident <45 min by car from the CHC; had no previous participation of a household member in the ongoing assessment; and had signed the informed consent on the day of the home visit.

### 2.3. Sample size and sampling procedure

In previous malaria adherence studies in similar areas, adherence was between 40% and 60%[13] (MSF, internal source, 2006). Estimating an adherence of 50%, a precision of 10%, an $\alpha$ error of 5% and a loss to follow-up or withdrawal of 20%, the total sample size required was calculated as 117 patients.

All five CHCs in the catchment area were equally included in the sampling. Patients were chosen systematically depending on the respective population size of each CHC area. As a second step, in the CHCs, patients or caretakers/parents to be visited at home were selected through systematic sampling. A sampling interval was calculated as the ratio of the number of eligible patients to the required sample size for the CHC. This sampling procedure was carried out in all five CHCs until the required number of patients was achieved.

### 2.4. Study procedure

Patients with confirmed uncomplicated malaria via a malaria rapid diagnostic test received the following ACT treatment: AS 4 mg/kg body weight together with AQ 10 mg/kg body weight taken once a day for 3 days.

The usual procedures were followed consisting of: patient registration; consultation; referral of suspected malaria cases for a malaria rapid diagnostic test; recording of the malaria rapid diagnostic test result on the patient card; referral of the patient back to the consultant for prescription of AS+AQ in the case of a positive malaria rapid diagnostic test together with further required drugs if necessary; referral to the pharmacy for dispensing; supervision of the first dose of AS+AQ at the pharmacy; observation of the patient over the first 30 min for immediate vomiting (with repetition of the first dose and further observation if vomiting occurred); and handing over the balance of treatment (second and third dose) with intake instructions to the patients or caretakers/parents of patients.

On completion, a short questionnaire was administered to all patients irrespective of their diagnosis. A full description of all drugs prescribed per patient was copied directly from the patient's card and a detailed address description was recorded.

**Table 1**
Final classification scheme of study patients according to treatment intake and the presence of the artesunate and amodiaquine co-blister package as well as adherence to artesunate and amodiaquine treatment for uncomplicated malaria in the study population in the Médecins Sans Frontières catchment area, Bo and Pujehun districts, Sierra Leone, July–August 2008

| Intake | Co-blister package | Final classification | Inclusions ($n$ = 118) | | |
|---|---|---|---|---|---|
| | | | $n$ | % | 95% CI |
| Incomplete | Present | Certain non-adherence | 27 | 22.9 | 15.2–30.6 |
| Incomplete | Not present | Probable non-adherence | 34 | 28.8 | 20.5–37.1 |
| Incorrect | Present or not present | Probable non-adherence | | | |
| Correct | Present or not present | Probable adherence | 57 | 48.3 | 39.2–57.5 |
| | | Non-adherence (certain and probable) | 61 | 51.7 | 42.5–60.8 |
| | | Adherence | 57 | 48.3 | 39.2–57.5 |
| | | Incomplete intake [$n$ = 27 blister seen (certain non-adherence), $n$ = 7 verbal account (probable non-adherence)] | 34 | 28.8 | 20.5–37.1 |
| | | Incorrect intake (probable non-adherence) | 27 | 22.9 | 15.2–30.6 |
| | | Correct intake (probable adherence) | 57 | 48.3 | 39.2–57.5 |

Health personnel of all five CHCs were informed about a study taking place, but the exact purpose of the study was not revealed in order not to change routine prescribing habits. In each CHC, the busiest days (mainly market days in the village) were selected for data collection. Data collection was carried out on 1–2 days in each CHC. On the day after the last treatment dose was supposed to be finished, patients who had received antimalarial treatment were visited at home. If these visits could not be completed, the interviewer would try again the following day. No interviews were carried out at a later date.

Patients or caretakers/parents of patients whom it was impossible to locate were classified as 'lost to follow-up' and were withdrawn from the analysis.

### 2.5. Data collection

A semistructured questionnaire (41 questions) to assess patient adherence was developed in English. The questionnaire started with general questions about the household (sex, age, education level of patient and/or caretaker/parent, household composition, occupation of head of household). Then, a systematic account was obtained regarding how the tablets were taken. Patients or caretakers/parents were also asked to show the original AS+AQ co-blister package. If the co-blister package was found, any remaining AS and/or AQ tablets were counted. Finally, two questions on general malaria knowledge were included. The questionnaire was anonymous.

Two interviewers conducted the questionnaires in the most appropriate language (Mende, Creole or English).

### 2.6. Definition of adherence

There is no standard definition for adherence and it varies broadly in the literature. In this study, definitions that had already proven their reliability in two similar settings were used.[13,20]

Patients were classified according to following three adherence categories: (i) certain non-adherence: patients who had any AS and/or AQ tablets remaining in the co-blister package at the time of the home visit; (ii) probable non-adherence: patients with a verbal account that not all the tablets were taken but no AS+AQ co-blister package could be shown or it was empty, and/or patients with a verbal account that AS+AQ was not taken according to the prescribed time schedule or in the prescribed dosage of the treatment protocol but no AS+AQ co-blister package could be shown or it was empty; and (iii) probable adherence: patients with a verbal account of complete treatment exactly following the treatment protocol but no AS+AQ co-blister package could be shown or it was empty.

Table 1 shows the final classification scheme of study patients according to the treatment intake and the presence of the AS+AQ co-blister package.

### 2.7. Exit interviews at the end of the consultation

Exit interviews were carried out at the CHCs regarding patient/caretaker attitudes towards AS+AQ prior to treatment and to assess prescription quality (dosages, information and instructions provided to the patient or parent/caretaker).

To calculate the required sample size, the same rationale was used as for the questionnaires during the home visits (minimum $n$ = 117). All persons who received a course of AS+AQ in one of the five CHCs were included in the sample size. The interviews were conducted on completion of all usual CHC procedures, just prior to leaving the CHC.

A semistructured questionnaire (18 questions) was developed in English. Patients or caretakers/parents were asked how they were planning to take/give the AS+AQ, followed by a series of systematic questions about each treatment dose. To avoid study bias, exit interviews were carried out after all the home visits had been finalised.

### 2.8. Statistical analysis

Data were entered into EpiData 3.0 software (The EpiData Association, Odense, Denmark). Data analysis was conducted using Stata 8.0 (Stata Corp., College Station, TX, USA) and SPSS 11.0 for Windows (SPSS Inc., Chicago, IL, USA).

The proportion of probable/certain non-adherence and probable adherence as well as the proportion of complete/incomplete/correct treatment intake were expressed

**Table 2**
General characteristics of the study population (patients and caretakers) visited at home in the Médecins Sans Frontières catchment area, Bo and Pujehun districts, Sierra Leone, July–August 2008

| Characteristic | Patients ($n$ = 118) | | Caretakers ($n$ = 89) | |
|---|---|---|---|---|
| | $n$ | % | $n$ | % |
| Age | | | | |
| <5 years | 67 | 56.8 | – | – |
| ≥5 years | 51 | 43.2 | 89 | 100.0 |
| Mean, median (min.–max.) (years) | 9.3, 4 (1–73) | | 29.2, 27.5 (12–80) | |
| Gender | | | | |
| Male | 56 | 47.5 | 5 | 5.6 |
| Female | 62 | 52.5 | 84 | 94.4 |
| Highest education level | | | | |
| Illiterate | 14 [a] | 48.3 | 69 | 77.5 |
| Primary level (not completed) | 15 [a] | 51.7 | 20 | 22.5 |
| Household size | | | | |
| 2–4 members | 10 | 8.5 | | |
| 5–15 members | 94 | 79.7 | | |
| >15 members | 14 | 11.9 | | |
| Mean household size (members) | 10.2 | | | |
| Household owns ≥1 long-lasting insecticidal mosquito net | 96 | 81.4 | | |
| No. of children under 5 years in household | | | | |
| 0–1 children | 50 | 42.4 | | |
| 2–4 children | 56 | 47.5 | | |
| 5–8 children | 12 | 10.2 | | |
| Mean no. of children under 5 years per household | 2.2 | | | |
| Main two professions of head of household | | | | |
| Subsistence farmer | 54 | 45.8 | | |
| Diamond miner | 22 | 18.6 | | |

[a] 14/29 or 15/29 patients who came to the community health centre without a caretaker.

with their 95% CI. Risk factors for non-adherence such as age, education level and knowledge of malaria were analysed. *P*-values and relative risks (with 95% CI) were calculated where appropriate.

### 2.9. Ethical considerations

Informed written consent was sought from patients or responsible caretakers/parents before the home interviews. Verbal consent was sought from patients or responsible caretakers/parents participating in the exit interviews at the end of their CHC consultation. All patients and caretakers/parents had the study purpose explained to them in a language they understood. Participation was completely voluntary.

## 3. Results

### 3.1. General characteristics of the study population visited at home

Data collection took place between July and August 2008. In total, 899 patients were screened at the five CHCs. Amongst these, 359 patients (39.9%) had received an AS+AQ prescription, 155 (43.2%) of whom were eligible for inclusion in the adherence study. In total, 118 home visits were performed. Thirty-seven patients were defined as lost to follow-up, primarily due to incomplete and incorrect address details. Nobody refused to participate in the study.

Of the 118 patients visited at home, 29 (24.6%) had come without a caretaker to the CHC and 89 (75.4%) came with a caretaker. General characteristics of the study population visited at home are shown in Table 2.

### 3.2. Patient adherence

Among the 118 patients interviewed, 27 (22.9%) had one or more tablets left at the time of the visit and were defined as certainly non-adherent. Of them, 25 had left both AS and AQ in the same quantity in their co-blister packages and 2 had taken AS but had left AQ. Thirty-four (28.8%) were defined as probably non-adherent [verbal account of incorrect ($n$ = 27) or incomplete ($n$ = 7) intake] and 57 (48.3%) were defined as probably adherent (correct intake) (Table 1).

### 3.3. Reasons for incomplete, incorrect or correct intake

The main self-reported reasons for incomplete intake ($n$ = 7 verbal account and $n$ = 27 co-blister package seen) were: sickness after the first dose of AS+AQ (32.4%; 11/34) and no food available for drug intake (14.7%; 5/34) (Table 3). As a consequence, 58.8% (20/34) of all study patients with incomplete intake omitted their last treatment dose.

The main reason for incorrect intake was immediate vomiting after drug intake (44.4%; 12/27). Ten patients (37.0%) said they were given incorrect instructions at the CHC (Table 3). The most common mistake resulting in

**Table 3**
Reasons for incomplete, incorrect or correct intake given by the study population in the Médecins Sans Frontières catchment area, Bo and Pujehun districts, Sierra Leone, July–August 2008

| | *n* | % |
|---|---|---|
| Incomplete intake (*n* = 34) | | |
| Sickness after first course of AS+AQ | 11 | 32.4 |
| No food available in the household for AS+AQ intake | 5 | 14.7 |
| No reason given | 5 | 14.7 |
| Forgot to take/give AS+AQ | 4 | 11.8 |
| Reported that wrong intake instructions were given at the CHC/instructions from the CHC were not understood | 4 | 11.8 |
| Reported no AS+AQ was given at CHC | 3 | 8.8 |
| Other reasons [a] | 2 | 5.9 |
| Incorrect intake (*n* = 27) | | |
| Reported vomiting immediately after AS+AQ intake | 12 | 44.4 |
| Reported that wrong intake instructions were given at the CHC/instructions from the CHC were not understood | 10 | 37.0 |
| AS+AQ made patient feel sick | 3 | 11.1 |
| Thought patient would get better faster | 1 | 3.7 |
| No reason given | 1 | 3.7 |
| Correct intake (*n* = 57) | | |
| Reported that correct intake instructions were given at the CHC | 46 | 80.7 |
| Wanted to cure the patient quickly | 9 | 15.8 |
| Knew how to take AS+AQ from previous treatment | 1 | 1.8 |
| No reason given | 1 | 1.8 |

AS+AQ: artesunate and amodiaquine; CHC: community health centre.
[a] Other reasons were: (i) one dose was taken by the caretaker as she did not feel well; and (ii) caretaker had to give too many other drugs to the patient (paracetamol, folic acid) and could therefore not give AS+AQ.

incorrect intake was to take/give the second dose of AS+AQ at the end of the first intake day at home (70%; 7/10).

The main reason stated for correct AS+AQ treatment intake was that they followed the instructions given at the CHC (80.7%, 46/57) (Table 3).

### 3.4. Assessment of possible risk factors and knowledge on malaria

To measure possible associations between risk factors and patient non-adherence to AS+AQ, relative risks (RR) were calculated. Calculations were made considering non-adherence as the outcome (*n* = 61; see Table 1).

Knowledge that only mosquito bites cause malaria showed a statistically significant association with adherence (RR = 1.7; *P* = 0.002).

When study patients or their respective parents/caretakers were asked about the cause of malaria, 55/118 (46.6%, 95% CI 37.9–55.6%) mentioned mosquito bites and 63/118 (53.4%, 95% CI 44.4–62.1%) claimed not to know the cause of malaria or mentioned a wrong cause.

None of the other factors, such as differences in patient age, education level or the number of concomitant treatments prescribed, were associated with an increased risk of non-adherence.

### 3.5. Exit interviews at the end of the consultation

#### 3.5.1. General characteristics of the study population in the exit interview group

Exit interviews were carried out at the five CHCs for 173 patients who had received an AS+AQ prescription. General characteristics of this population are shown in Table 4. Exit interview patients or caretakers/parents had the same sociodemographic and clinical characteristics as those who were interviewed for the adherence assessment (mean patient age, proportion of patients under 5 years, gender of patients/caretakers; all $P > 0.05$) except for significantly more illiterate caretakers in the exit interview group [93.2% (95% CI 87.5–96.8%) vs. 77.6% (95% CI 68.0–85.3%); $P = 0.001$].

#### 3.5.2. Understanding of artesunate and amodiaquine intake in the exit interview group

In the exit interview group, 98.8% (171/173) of the patients or caretakers/parents of patients knew that they had malaria or could name the correct signs/symptoms of malaria; 94.2% (163/173) of patients or caretakers/parents were able to identify the AS+AQ tablets as antimalarials among all the tablets given (Table 4).

In the exit interview group, 82.1% (142/173) of the patients were able to repeat correctly the full AS+AQ intake instructions given to them at the CHC. Of the 17.9% (31/173) who were not able to repeat these instructions correctly, the two most common errors were to take the second dose in the evening of Day 1 (54.8%; 17/31) or to split the dose in half and take the first half in the morning and the second half in the evening (25.8%; 8/31). Only 15.6% patients (27/173) were given additional information by health personnel related to AS+AQ. In most cases (74.1%; 20/27) this was that weakness was a possible side effect (Table 4).

## 4. Discussion

The results of this study have clearly shown that patient adherence to correct intake of AS+AQ should not be taken for granted. One of five patients did not complete the treatment within the time frame of 3 days and was certainly non-adherent. One-third took the treatment incorrectly.

**Table 4**
General characteristics and understanding of antimalarial treatment intake in the exit interview group in the community health centres in the Médecins Sans Frontières catchment area, Bo and Pujehun districts, Sierra Leone, July–August 2008

| Characteristic | Patients ($n$ = 173) [$n$ (%)] | Caretakers ($n$ = 119) [$n$ (%)] |
|---|---|---|
| Age | | |
| <5 years | 99 (57.2) | – |
| ≥5 years | 74 (42.8) | 119 (100.0) |
| Mean, median (min.–max.) (years) | 11, 3 (0–65) | 28, 26 (16–55) |
| Gender | | |
| Male | 84 (48.6) | 11 (9.2) |
| Female | 89 (51.4) | 108 (90.8) |
| Highest education level [a] | | |
| Illiterate | 42 (77.8) [b] | 110 (93.2) |
| Primary level (not completed) | 12 (22.2) [b] | 8 (6.8) |

| | $n$ | % |
|---|---|---|
| Perception of disease ($n$ = 173) | | |
| Able to name disease as malaria | 36 | 20.8 |
| Able to name signs/symptoms of malaria | 135 | 78.0 |
| Disease and its signs/symptoms unknown or other symptoms mentioned | 2 | 1.2 |
| Perception of antimalarial treatment ($n$ = 173) | | |
| Able to show AS+AQ as only malaria treatment | 163 | 94.2 |
| Unable to distinguish any given treatment | 8 | 4.6 |
| Able to show AS+AQ with other drugs | 2 | 1.2 |

| | $n$ | % |
|---|---|---|
| Patient or caretaker of patient: | | |
| Was able to repeat correctly the instructions for AS+AQ intake | 142/173 | 82.1 |
| Made errors while repeating the instructions for AS+AQ intake | 31/173 | 17.9 |
| Second dose will be wrongly taken on first intake day in the evening | 17/31 | |
| Split dose in half and take first half in the morning and second half in the evening | 8/31 | |
| Other reasons [c] | 6/31 | |
| Was asked in the CHC if she/he had understood instructions | 159/173 | 91.9 |
| Was asked to repeat back instructions | 114/173 | 65.9 |
| Was given additional information related to AS+AQ | 27/173 | 15.6 |
| Weakness during course of treatment | 20/27 | |
| Patient has to refer back to CHC if not better in 3 days | 5/27 | |
| AS+AQ is a treatment for malaria | 2/27 | |

AS+AQ: artesunate and amodiaquine; CHC: community health centre.
[a] One missing data for caretaker in the exit interview group.
[b] 42/54 or 12/54 patients who came to the community health centre without a caretaker.
[c] Other reasons were: impossible to repeat instructions; skip intake at second intake day; and extended intake for longer than 2 days.

The main reason patients gave for incomplete intake was that the treatment made them feel sick. Based on observations made during the interviews, another reason for not taking the third dose was simply that people had forgotten.

The only factor statistically significantly associated with good adherence was the knowledge that mosquito bites cause malaria. Poor knowledge of malaria associated with low adherence confirms the observation of a casual perception of malaria in this population. An adherence study in Northern Thailand validates this by showing a significant link between adherence and knowledge of malaria.[19] On the other hand, a study in Ethiopia showed that malaria was not perceived by the population to be a problem despite its high prevalence.[21]

Approximately one-half of the patients who took the drug incorrectly at home did so because they vomited immediately after they took the drug. Another one-third of these patients or caretakers claimed that the wrong instructions had been given to them in the CHCs.

However, one of the main reasons for good adherence was that patients/caretakers simply followed the instructions given to them at the CHC. Moreover, exit interviews showed a much better quality of AS+AQ prescriptions than a similar study in The Gambia where only one-third of caretakers were able to name the disease for which their child was brought to a health facility.[22]

Two different methods were used to measure adherence in patients: pill count in the AS+AQ co-blister package (an objective measurement); and a systematic questionnaire (more complete but non-verifiable information). By classifying patients as either certainly or probably non-adherent, the limitations of both methods were taken into account. Exit interviews were added to the study design to gain information on treatment attitudes and to assess prescription quality.

One of the most important but difficult things to avoid when carrying out an adherence study is influencing health personnel such that they change their routine prescription habits. It is also important not to alert patients that there might be a later 'control' regarding the treatment. The following measures were taken to limit this study bias: questionnaires were carried out for malaria and non-malaria patients attending the CHC to avoid

raising any suspicion among the health personnel or patients/caretakers. Informed written consent was only sought from those patients interviewed at home and not those interviewed at the CHC. The true nature of the study was not revealed to the CHC health personnel at the time of the study. Exit interviews took place only after all the home visits had been finalised so as not to influence anybody involved in the survey. To our knowledge, this is one of the first studies that used three complementary methods as a study design.

There are only a few published studies on patient adherence to ACT and their methods and definitions of adherence used are difficult to compare.[7–10] Focusing on studies that used a related study design, our results (23% certainly non-adherent) were comparable with two studies in South Sudan (18% certainly non-adherent)[20] and Zambia (21%).[13] Both settings were similar to this study: a remote rural area; low patient educational level; treatment intake over 3 days; and this specific treatment already implemented for some time. These characteristics might have contributed to the relatively low adherence. Furthermore, the results were in line with studies carried out in rural Sri Lanka (26% non-adherent)[8] and rural Senegal (62%).[12]

In Uganda, a study showed adherence to be as high as 93%[11] and in Tanzania adherence was still 75%.[10] However, in contrast, both adherence assessments were carried out immediately after the successful introduction of a new malaria treatment. Immediately following a new innovation, health personnel fresh from training are likely to be highly motivated and are more likely to pay attention to patient explanations. This could explain the higher adherence in these two studies.

Only some of the factors linked to adherence can be directly influenced in an operational setting. This study suggests that giving clear instructions on correct drug use should include discussion of disease symptoms as well as possible treatment side effects and how to manage them. Given the relatively high number of patients who vomited at home but did not come back to the health facility, it is important to inform patients on the consequences of vomiting. Mechanisms to prevent patients from vomiting should be investigated (i.e. dissolving the medication, taking it with food, training patients/caretakers to take/give the treatment slowly). In the absence of any information about disease symptoms and side effects (only 16% of the interviewees claimed to have been informed), patients may be less likely to complete their second and third dose at home if they fear the medicine might cause vomiting. Nevertheless, detailed information on side effects may result in reluctance to take the full course of medication.

Other factors are more difficult to influence, such as forgetfulness of patients to take the treatment. Alternative strategies, such as complete supervision of all three doses, may increase adherence, but the feasibility of this strategy must be carefully assessed. Development of simpler treatment regimens, including fixed-dose combinations or even single-dose ACT, might be another powerful tool in increasing patient adherence in the future.

In order to gain constant feedback of the quality of malaria care in health facilities, exit interviews of patients or parents/caretakers such as done in this study should be frequently repeated without the prior knowledge of the health personnel in question. This type of interview should not only be considered in relation to malaria treatment but for any other disease and its treatments prescribed at any health facility.

Although there is no doubt on the effectiveness of the ACT therapy as an antimalarial, this is highly dependent on patient adherence to the prescribed treatment protocol. Assessment of adherence to ACT is essential and needs to be constantly addressed by operational programmes where malaria is a major threat to the population in order to maximise the therapeutic value of the medication. Providing ACT alone is not enough.

**Authors' contributions:** SG designed the study protocol; SG, SD and AM carried out the field part of the study, mainly the adherence and exit interviews; SB supported the principal investigator considerably in carrying out the field part of the study; SB and JM had substantial input in data interpretation; SG drafted the manuscript; SD, AM, SB and JM undertook a critical revision of the manuscript. All authors read and approved the final manuscript. SG and SD are guarantors of the paper.

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