

# Quality of Care for Adult Inpatients with Malaria in a Tertiary Hospital in Uganda

Ronald Kiguba (✉ [kiguba@gmail.com](mailto:kiguba@gmail.com))

Makerere University College of Health Sciences <https://orcid.org/0000-0002-2636-4115>

Charles Karamagi

Clinical Epidemiology Unit, Makerere University College of Health Sciences

Sheila M. Bird

MRC Biostatistics Unit

---

## Research

**Keywords:** Antimalarials, antimalarial use, delayed initiation of antimalarials, malaria parasitaemia, malaria microscopy, malaria diagnosis, malaria treatment, missed day 1 dosing, risk factors, incomplete dosing

**Posted Date:** December 29th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-30045/v2>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

---

**Version of Record:** A version of this preprint was published at Malaria Journal on April 9th, 2021. See the published version at <https://doi.org/10.1186/s12936-021-03712-3>.

## Abstract

**Background:** Prompt detection and appropriate treatment of malaria prevents severe disease and death. The quality of care for adult malaria inpatients is not well documented in sub-Saharan Africa, particularly in Uganda. We sought to describe the patterns of malaria diagnosis and treatment among adult inpatients admitted to the medical and gynaecological wards of Uganda's 1790-bed Mulago National Referral Hospital from December 2013 to April 2014.

**Methods:** A prospective cohort of 762 consented inpatients aged  $\geq 18$  years was assembled. Proportions of inpatients who received preadmission and in-hospital antimalarials, missed Day 1 dosing of hospital-initiated antimalarials and/or had malaria microscopy done were determined. Multivariable logistic regression was used to identify risk-factors for missed Day 1 dosing of antimalarials.

**Results:** One in five (19%, 146/762) inpatients had an admitting or discharge malaria diagnosis or both; with median age of 29 years (IQR, 22 to 42 years). Microscopy was requested in 77% (108/141) of inpatients with an admitting malaria diagnosis; results were available for 46% (50/108), of whom 42% (21/50) tested positive for malaria parasitaemia. Only 13% (11/83) of inpatients who received in-hospital injectable artesunate (AS) or quinine (Q) received follow-up oral artemether-lumefantrine (AL); only 2 of 18 severe malaria cases received follow-up oral AL. Injectable AS only (47%, 47/100) was the most frequent hospital-initiated antimalarial followed by injectable Q only (23%, 23/100). A quarter (25%, 25/100; 95% CI: 17% to 35%) of inpatients missed Day 1 dosing of hospital-initiated antimalarials. Each additional admitting diagnosis was more than two-fold likely to increase the odds of missed Day 1 dosing of in-hospital antimalarials (aOR = 2.6, 95% CI: 1.52-4.56;  $P$ -value = 0.001).

**Conclusions:** Half the malaria microscopy results were not available; yet, the rate of testing was high. The majority of inpatients initiated on injectable AS or Q did not receive the recommended follow-up treatment of oral AL. One in four inpatients delayed to initiate hospital antimalarials by at least one calendar day. The hospital should encourage prompt availability of malaria test-results to promote the timely initiation and completion of antimalarial treatment, thereby improving the quality of care for hospitalized malaria patients in Uganda.

## Background

Around 405,000 people died from malaria globally in 2018, 94% of whom were from the World Health Organization (WHO) African Region. Prompt detection and appropriate treatment of malaria prevents severe disease and death [1]. The risk of mortality from severe malaria is highest during the first 24 hours of hospitalization [2]. Yet, in most moderate- to high-malaria-transmission settings, long transit-time to a suitable health facility where appropriate intravenous antimalarials can be administered could delay the initiation of appropriate antimalarials and increase the risk of patient deterioration or death [2]. Other impediments to the timely initiation of appropriate antimalarials include the lack of timely laboratory diagnosis and drug stock-outs [2, 3].

World Health Organization recommends confirmation of malaria diagnosis by quality microscopy or malaria rapid diagnostic testing within 2 hours of patient presentation and before administration of antimalarials. Otherwise, the decision to treat should be taken on clinical grounds. If severe malaria is suspected, parasitological diagnosis should not delay initiation of antimalarials [2]. Adults with severe malaria, including pregnant women in all trimesters and breast-feeding mothers, should be treated with three doses of injectable artesunate (AS) for 24 hours minimum at 0, 12 and 24 hours regardless of whether the patient can tolerate oral treatment earlier. If unable to take oral medication, the patient should continue with injectable AS once daily, for a maximum of 7-days. If injectable AS is not available, once daily injectable artemether (AT) or 8-hourly injectable quinine (Q) should be administered. Following injectable antimalarials, a full 3-day course of oral artemisinin-based combination therapy (ACT) - mainly artemether-lumefantrine (AL) (six doses) for Uganda - should be administered if the patient is able to take oral medication [2, 4-6]. Other recommended ACTs include artesunate-amodiaquine (AQ) and dihydroartemisinin-piperaquine (DP) (three doses for each ACT). If full treatment for severe malaria is not possible at a given health facility but injectables are available, adults and children should be given one intramuscular dose of AS or Q and referred to a suitable facility for appropriate management [2].

It is necessary for patients with severe malaria to initiate timely appropriate antimalarials and complete full courses of prescribed antimalarials, which promotes therapeutic success, reduces malaria-related mortality and prevents drug resistance [7-9]. However, SSA patients with severe malaria frequently receive incomplete doses of prescribed antimalarials and/or treatment meant for uncomplicated malaria [8, 10]. We have previously shown that one-third of hospitalized patients in our setting missed Day 1 of prescribed antibiotics [3], but similar data are scarce on antimalarial use. We aim to describe the patterns of malaria diagnosis and treatment [i.e. antimalarial use by extent of use, missed opportunity for treatment, frequency of administered-treatment, medication-

use-cycle (prescription-dispensing-administration), missed Day 1 dosing and mortality] among adult inpatients at Uganda's 1790-bed Mulago National Referral Hospital. We also evaluate patient-level risk-factors for missed Day 1 dosing of prescribed antimalarials and the relationship between missed Day 1 dosing of prescribed antimalarials and length of hospital stay among these Ugandan adult inpatients.

## Methods

Detailed account of the study design, setting, data collection and data management is documented elsewhere [3]. Briefly, key details are the following:

### Study design and setting

A prospective cohort study was conducted among inpatients, 18 years and older, at Mulago National Referral Hospital with bed capacity of 1,790 and an annual inpatient turnover of 140,000 patients. Three medical wards and one Gynaecological ward were included, each with an official bed capacity of 54 and average of 5-25 patient admissions per day [3].

Details on the prescription, dispensing and administration of medicines are hand-recorded in the patients' charts. Hospital pharmacists dispense the prescribed free-of-charge injectable and/or oral antimalarials, as appropriate, to inpatients/caregivers in quantities that discourage misuse of medicines. However, the inpatients/caregivers are instructed to return to the pharmacy early enough for more medication to avoid missing treatment [3].

### Data collection

The data were collected in December 2013 to April 2014 by four teams of trained research assistants. Each research team had a medical officer, clinical pharmacist and degree nurse. An internist on the medical wards and a gynaecologist/obstetrician on the gynaecology ward solved any clinical problems faced by the research assistants, while the principal investigator advised on pharmacological issues. The research team did not interrupt routine clinical care. Study patients provided written informed consent and were enrolled using a systematic sampling procedure following a daily random start from the first two (Infectious Diseases and Gastrointestinal Illnesses ward), three (Haematology, Neurology and Endocrinology ward) and four (Cardiovascular, Pulmonology and Nephrology ward & Gynaecology ward) new admissions; and subsequently every second, third and fourth admission, respectively. Patients were assessed at baseline (demographics, clinical conditions, medications) and on a daily basis (clinical conditions, medications) until discharge, transfer, death, or loss to follow-up [3].

Research assistants captured clinical data from patients' clinical charts and interviewed the patients, their caregivers and/or ward staff. Each research team's medical officer clerked the inpatients to obtain additional clinical data not documented in the clinical charts. Each research team's pharmacist captured baseline medication data at the time of hospital admission by interviewing the inpatients and reviewing all available medical documents. During hospital stay, research pharmacists obtained medication data from the patients' clinical charts, ward pharmacy records, pill counts of patients' oral medications (tablets, capsules), views of unused parenteral medicines possessed by the patients/caretakers and daily interviews with the patients/caregivers and/or ward staff. The data were collected daily from 8.00am to 6.00pm from Monday to Friday and from 10.00am to 6.00pm on weekends and public holidays [3].

### Data management

Epidata 3.1 software was programmed with checks to limit data entry errors and the electronic database password-secured to limit access to authorized personnel only [3].

## Statistical analysis

### Patterns of malaria diagnosis and antimalarial use

The proportions of inpatients who received antimalarials preadmission and during hospitalization were determined using, as numerator, the number of inpatients who received at least one antimalarial and, as denominator, the total number of study inpatients. We calculated the proportions of inpatients with available (positive, negative) and unavailable (not returned, not requested) malaria microscopy results and those who experienced missed Day 1 dosing of hospital-initiated antimalarials. See **Appendix** for details of the

analysis plan for post-admission time-to-first-dose among inpatients with an admitting malaria diagnosis; and parenteral-to-oral-switch of antimalarials.

We used Chi-squared tests to screen univariate-level relationships between patient-level characteristics and antimalarial use during hospitalization (yes/no); and potential patient-level risk-factors for missed Day 1 antimalarial dosing during hospitalization. Multivariable logistic regression was used to identify risk-factors for missed Day 1 dosing of antimalarials. Results were expressed as odds ratios (ORs) with their 95% confidence intervals (CIs). Poisson CIs were used for counts below 16. Stata 14.0 was used for all the analyses [11].

#### Identification of missed Day 1 dosing of antimalarials

Among inpatients for whom an antimalarial was prescribed during the current hospitalization and at least one dose was administered, missed Day 1 dosing was measured in two ways; i) calendar-day as proposed by Kiguba *et al* 2016 [3], see **Appendix**, and ii) 24-hour timescale using date-and-time of hospital admission and date-and-time of first in-hospital antimalarial dose.

## Results

### Study population

*Demographic and clinical characteristics:* The median age of 762 inpatients was 30 years (interquartile range, IQR, 24 to 42 years), see **Table 1**. About one in five (19%, 141/762; 95% CI: 16% to 21%) inpatients had an admitting malaria diagnosis, see **Tables 1 & 2**. About one in eight (12%, 88/762; 95% CI: 9% to 14%) inpatients had a discharge malaria diagnosis: 44% (39/88; 95% CI: 34% to 55%) had malaria as their single discharge diagnosis; recorded as severe malaria in 10 of 39 inpatients. About one-fifth (19%, 146/762; 95% CI: 16% to 22%) of inpatients had an admitting or discharge malaria diagnosis or both, and median age of 29 years (IQR, 22 to 42 years); of whom 15% (21/146; 95% CI: 9% to 21%) had a single admitting/discharge malaria diagnosis, see **Tables 2 & S1** and **Figure 1**, and 21% (30/146; 95% CI: 14% to 28%) had malaria-in-pregnancy. Eleven of the 21 inpatients with a single admitting/discharge malaria diagnosis had malaria-in-pregnancy, see **Table S1**; 20 of the 21 were female. Severe malaria was recorded for 12% (18/146, 95% CI: 7% to 19%) of inpatients with an admitting/discharge malaria diagnosis, see **Figure 1**.

### Laboratory diagnosis of malaria

Microscopy was requested in 26% (201/762) of inpatients; laboratory results were available for 42% (84/201; 95% CI: 34% to 48%) of them, of whom 30% (25/84; 95% CI: 20% to 41%) tested positive, see **Figure 1**. Microscopy was requested in 77% (108/141; 95% CI: 69% to 83%) of inpatients with an admitting malaria diagnosis; laboratory results were available for 46% (50/108; 95% CI: 37% to 56%) of them, of whom 42% (21/50; 95% CI: 28% to 57%) tested positive, see **Table 2** and **Appendix**. At bivariate level, inpatients with an admitting malaria-in-pregnancy diagnosis were ten-fold more likely to test positive for malaria when compared with non-pregnancy-related malaria inpatients (odds ratio, OR = 10.1; 95% CI: 1.55 to 65.96; 1 degree of freedom, df;  $\chi^2 = 9$ ; *P*-value = 0.003) i.e. [82% (9/11; 95% CI: 48% to 98%) vs. 31% (12/39; 95% CI: 17% to 48%)], respectively.

### Extent of antimalarial use

Thirteen percent (97/762; 95% CI: 10% to 15%) of inpatients received antimalarials during the 4-weeks pre-admission, see **Table 1**: of whom 44% (43/97; 95% CI: 34% to 55%) had an admitting malaria diagnosis. Thirteen percent (100/762; 95% CI: 11% to 16%) of inpatients received antimalarials during the current hospitalization, see **Table 1**: of whom 83% (83/100; 95% CI: 74% to 90%) had an admitting malaria diagnosis, see **Table 1**.

### Missed opportunity for hospital-initiated antimalarials

Four of 25 (16%, 95% CI: 5% to 36%) inpatients with a positive malaria test did not receive in-hospital antimalarials, see **Figure 1**. No admitting/discharge malaria diagnosis was recorded for three of the four inpatients, see **Figure 1**, two of whom had a malignancy; the fourth inpatient had poorly treated malaria on admission and run away from hospital due to delayed investigations and treatment, see **Table S1**. None of the inpatients died while in hospital, see **Box 1**; none had malaria-in-pregnancy.

missed opportunity for hospital-initiated antimalarial treatment for four inpatients with malaria parasitaemia as confirmed by microscopy, Uganda.

ars	Clinical notes
1	A 60-year-old female with unknown HIV-status, 6-year history of hypertension and type 2 diabetes mellitus (DM) presented with poorly controlled DM having defaulted on DM treatment for 8-months. Microscopy for malaria parasites was requested on the day of admission (Day 1). Results were returned on Day 1 with confirmed malaria parasitaemia. AL and paracetamol were prescribed on Day 2 but not dispensed. The patient was discharged on Day 3 without antimalarial treatment.
2	A 24-year-old female with unknown HIV-status was referred from a clinic where she had been treated for suspected malaria and typhoid with no improvement. She presented with poorly treated malaria and microscopy for malaria parasites was requested on Day 1. Results were returned on Day 2 with confirmed malaria parasitaemia. AL and paracetamol were prescribed on Day 2 but not dispensed and the patient was discharged on Day 2 without antimalarial treatment.
3	A 44-year-old HIV-negative male was transferred from a referral hospital. He presented with an admitting diagnosis of chronic lymphocytic leukaemia and confirmed malaria parasitaemia by microscopy. No fresh request for malaria microscopy was made during the current admission. The patient did not receive any antimalarial treatment prescription and/or administration both prior to admission and throughout the current hospitalization. He was transferred to Uganda Cancer Institute on Day 3.
4	A 43-year-old HIV-positive female with history of DM who was receiving second-line antiretroviral therapy (tenofovir, lamivudine, lopinavir/ritonavir) and co-trimoxazole presented with an admitting diagnosis of colon cancer. Microscopy for malaria parasites was requested on Day 2 and results were returned the same day with confirmed malaria parasitaemia. No antimalarial treatment was prescribed, dispensed or administered during hospitalization. The patient continued to receive her antiretrovirals and co-trimoxazole; and was transferred to Uganda Cancer Institute on Day 17.

Frequency of administered antimalarials

*Four-week preadmission period:* At patient-level, oral artemether-lumefantrine (AL) only (52%, 50/97; 95% CI: 41% to 62%) was most frequently administered followed by injectable quinine (Q) only (23%, 22/97; 95% CI: 15% to 32%), see **Table 3** and **Appendix**.

*Current hospitalization:* At patient-level, injectable AS only (47%, 47/100; 95% CI: 37% to 57%) was the most frequently administered followed by injectable Q only (23%, 23/100; 95% CI: 15% to 32%), oral AL only (15%, 15/100; 95% CI: 9% to 24%) and AS + AL only (8%, 8/100; 95% CI: 4% to 15%), among others; see **Table 3** and **Appendix**.

Medication-use-cycle

Overview of prescription, dispensing and administration of antimalarials

*Overall:* Antimalarials were prescribed for 15% (114/762) of inpatients, dispensed to 79% (90/114), yet, administered in 100 inpatients (93 of 100 had an antimalarial prescription), see **Appendix** for details on AS, Q and AL.

Incomplete dosing of in-hospital antimalarials

*Artesunate*: 25% (14/57; 95% CI: 14% to 38%) of inpatients in whom *in-hospital AS was administered* received <3 doses of *both dispensed and administered AS* irrespective of pregnancy, see **Appendix**.

*Quinine*: 21% (6/28; 95% CI: 8% to 41%) of inpatients in whom *in-hospital Q was administered* received <3 doses of *both dispensed and administered Q* irrespective of pregnancy, see **Appendix**.

*Artemether-Lumefantrine*: 71% (20/28; 95% CI: 51% to 87%) of inpatients in whom *in-hospital AL was administered* received <6 doses of *administered AL*.

*Artesunate or Quinine + Artemether-Lumefantrine*: About 13% (11/83) of the inpatients who received in-hospital injectable AS or Q also received at least one dose of follow-up oral AL during the current hospitalization, see **Table 3**; AL having been co-prescribed for 48 (58%) of the 83 inpatients. AL was co-prescribed for 12 (67%) of the 18 severe malaria cases and administered in 2 cases only during the current hospitalization.

#### Missed Day 1 dosing of hospital-prescribed antimalarials

*Overall*: A quarter (25%, 25/100; 95% CI: 17% to 35%) of inpatients who received antimalarials during the current hospitalization missed Day 1 dosing of hospital-initiated antimalarials based on calendar-day. A similar estimate of missed Day 1 dosing was obtained based on *post-admission 24-hour-delay*, see **Appendix**.

*Artesunate*: Around a quarter (28%, 16/57; 95% CI: 17% to 42%) of inpatients who initiated antimalarials with AS missed Day 1 dosing based on calendar-day, see **Table 4**.

*Quinine*: About one in five (18%, 5/28; 95% CI: 6% to 37%) of inpatients who initiated antimalarials with Q missed Day 1 dosing based on calendar-day, see **Table 5**.

#### Mortality among inpatients who received in-hospital antimalarials

Four of 100 inpatients who received in-hospital antimalarials died during hospitalization. All four inpatients had clinically-diagnosed malaria: microscopy was requested in three inpatients, but results were not available, see **Box 2**. An unconscious 88-year-old female of unknown HIV-status presented with a single admitting diagnosis of severe malaria and pulse rate of 98 beats per minute. She received a pre-referral intramuscular Q dose 23 hours preadmission and two Q doses 11 hours apart after admission. She died on Day 2 of hospitalization. The other three cases had multiple diagnoses, see **Box 2**.

: Mortality of four inpatients who received in-hospital antimalarial treatment, Uganda.	
Antimalarials	Clinical notes
None	One inpatient who received Q during admission died in hospital.
at 1-Q	An 88-year-old female of unknown HIV-status presented with a single admitting diagnosis of severe malaria which manifested with fever, chills and unconsciousness. She was referred from a clinic for further management after receiving an initial intramuscular dose of quinine (23 hours prior to the current admission). Her vitals on admission were: pulse rate (98 beats per minute); blood pressure (116/63 mmHg); temperature (35.9 °C). Microscopy for malaria parasites was requested on admission (Day 1) but the results were not returned by Day 2. She received 2-doses of Q which were administered 11 hours apart, the first dose being 2 hours after admission on Day 1. The patient died on Day 2 of hospitalization.
unate	Two inpatients who received AS during admission died in hospital. None of the two inpatients presented with either an admitting or a discharge malaria diagnosis:
at 1-AS	A 20-year-old female of unknown HIV-status was admitted with suspected severe sepsis of chest focus, bacterial pneumonia, urinary tract infection (UTI), salmonellosis and acute gastroenteritis. Microscopy for malaria parasites was requested on Day 1 but the results were not returned. She missed Day 1 dosing of AS and subsequently received 4 doses of AS. Her discharge diagnoses were UTI, pneumonia and salmonellosis. She died on Day 4.
at 2-AS	A 24-year-old HIV-positive female presented with severe immunosuppression, sepsis, disseminated tuberculosis and/or tuberculous meningitis, atypical measles syndrome and toxoplasmosis. Microscopy for malaria parasites was not requested on admission. She received 2 doses of AS and never missed Day 1 dosing. Her discharge diagnosis was severe immunosuppression. She died on Day 10.
ether + fantrine	One inpatient who received AL in hospital died.
at 1-AL	A 23-year-old HIV-positive female presented with working diagnoses of immunosuppression, malaria, septicaemia, urinary tract infection and anaemia. Microscopy for malaria parasites was requested on admission (Day 1) but the results were not returned. Duocotexcin (DP) was prescribed on Day 1 but was neither dispensed nor administered. One dose of AL was administered on Day 3. Her discharge diagnoses were immunosuppression and malaria. She died on Day 6.

### Patient-level risk-factors for missed Day 1 dosing of antimalarials

Number of admitting diagnoses was a statistically significant risk-factor for missed Day 1 dosing of hospital-initiated antimalarials based on calendar-day (aOR = 2.6, 95% CI: 1.52-4.56; *P*-value = 0.001), see **Table 6**. Similar results of missed Day 1 risk-factor were obtained based on *post-admission 24-hour-delay*, see **Table S2**. Malaria-in-pregnancy and severity of malaria were not significantly related to missed Day 1 dosing of antimalarials.

### Missed Day 1 dosing of hospital-initiated antimalarials versus length of hospital stay

No statistically significant association was observed between missed Day 1 dosing of antimalarials and length of hospital stay (OR = 1.1, 95% CI: 0.91-1.27; *P*-value <0.396). The mean length of hospital stay for missed Day 1 cases was 4.7 (SD=1.7) days versus 4.2 (SD=2.5) days for non-cases.

## Discussion

Malaria microscopy was requested in 77% of inpatients with an admitting malaria diagnosis, similar to estimates for the public sector (80%) in moderate- to high-transmission countries in sub-Saharan Africa (SSA) [1]. Unfortunately, only half the microscopy results were available to guide appropriate antimalarial treatment. Thus, despite decent microscopy rates, healthcare professionals still rely on clinical judgement to treat half the suspected malaria cases. Clinical judgement increases the risk of unnecessary antimalarial treatment and, in turn, depletes antimalarial stocks for inpatients who truly need them; and increases the incidence of associated adverse drug reactions and drug resistance [2]. Seven in ten inpatients with suspected non-pregnancy-related malaria tested negative for malaria and would therefore not need antimalarials; compared with only two in ten inpatients with suspected malaria-in-pregnancy. The value of a confirmed malaria diagnosis depends on prompt availability of parasitology results and whether the clinician uses the results to decide how to manage the patient. Malaria negative test-results as confirmed by microscopy - the gold standard - should

prompt clinicians to examine patients for other causes of illness and treat them accordingly [2]. However, the interpretation of negative microscopy results should take into account the high rates of antimalarial pre-treatment, which was as high as one in three admitted patients with suspected malaria in this patient cohort. A rapid diagnostic test (RDT), in addition to microscopy, could be used to detect the *HRP2* malaria antigen in patients who recently received antimalarials and whose blood films are, thus, likely to show no malaria parasitaemia [2]. RDTs can give positive results for up to 1-month after parasite clearance [2].

One in six cases of confirmed malaria, none of whom had severe symptoms, did not receive antimalarials during the current hospitalization, which raises concern over the safety of inpatient care at this tertiary care hospital. In high transmission zones, many patients with other causes of admission could carry malaria parasites without symptoms; however, they should receive antimalarial treatment when the infection is confirmed. Poor coordination between the laboratory and clinicians is likely to lead to missed antimalarial treatment, which is exacerbated by high inpatient loads of up to 80 admissions in wards with official bed capacity of 54 [3]. Introducing an integrated electronic health record (EHR) system to track inpatient care could significantly improve the flow of information between different hospital departments and, in so doing, promote efficient clinical management of inpatients [12].

Seven in eight inpatients initiated on injectable AS or Q did not receive the recommended follow-up oral AL. Also, one in four inpatients who received at least one in-hospital dose of prescribed antimalarials missed the first day of their antimalarial treatment. The missed treatment could be worsened by the observed disparities in prescribed, dispensed and administered antimalarials – similar to observations made elsewhere [8, 10]. Possible reasons for these system lapses include; i) drug stock-outs, ii) poor communication between clinician and patient/caregiver and, iii) work overload [3]. The hospital should improve its stock forecasting for in-demand antimalarials, promote intern-pharmacist-led bedside dispensing to reduce the clinicians' workload during drug administration, and improve supervision of junior and mid-level clinicians to promote accountability to inpatients and the hospital [3].

Each additional admitting diagnosis increases by more than two-fold the odds of missed Day 1 dosing of prescribed antimalarials, which underlines the need for prompt availability of malaria test-results to promote the timely initiation of antimalarials. Prompt and complete antimalarial treatment rapidly eliminates malaria parasites from a patient's bloodstream [13]. Patients with severe malaria should access timely appropriate antimalarials and complete full courses of prescribed antimalarials to promote therapeutic success, reduce malaria-related morbidity and mortality, and prevent the emergence and spread of drug resistance [7-9].

Inpatients with an admitting malaria-in-pregnancy diagnosis seemed more likely to have a microscopically-confirmed malaria diagnosis than inpatients with other admitting malaria diagnoses. This comparative advantage at diagnosis did not translate into better antimalarial treatment because no pregnancy-related difference was observed in the prescription, dispensing and administration of antimalarials. Improvement in the antimalarial medication-use-cycle should target systemic weaknesses.

Unlike Q, the hospital frequently encounters drug stock-outs of in-demand free-of-charge AS and AL, which inpatients must purchase from private community pharmacies to prevent lapses in prescribed treatment. Drugs bought from private community pharmacies are not recorded as dispensed in the hospital pharmacy registers [3], which explains why the reported number of inpatients with administered AS and AL exceeds the number of inpatients to whom these two drugs were dispensed. AS and AL are more in-demand than Q because; i) AS is the drug of choice for its faster parasite clearance, has a less tedious administration regime, and safer profile and, ii) AL is administered after both injectable AS and Q as the continuation of antimalarial treatment in severe malaria [2].

Death could be attributed to severe malaria and/or to quinine-related treatment in the 88-year-old female with a single admitting diagnosis of severe malaria. The caveat to this malaria-related attribution is diagnosis based on clinical judgement only (in the absence of microscopy results), unknown HIV-serostatus, advanced age, unknown random blood sugar levels and other comorbidities – especially cardiovascular comorbidities. That notwithstanding, Q was poorly administered at intervals of 23 hours (between first and second doses) and 11 hours (between second and third doses). Yet, 8-hourly intervals of injectable Q administration for at least 24 hours are recommended until the patient is able to take oral medication [2]. The unconsciousness manifested in this inpatient is a known key sign of hypoglycaemia in severe falciparum malaria and carries a high risk of mortality [2]. Unfortunately, hypoglycaemia can result from both severe malaria and quinine-induced hyperinsulinaemia. Thus, blood sugar levels should be checked frequently in severe malaria inpatients who receive Q [2]. Also, this inpatient had tachycardia which could have resulted from Q use and/or hypoglycaemia. With hindsight, this elderly inpatient should have been treated with injectable AS instead, although the frequent unavailability of in-demand AS, and its associated higher cost, often dictates treatment with Q. This fatal case of suspected severe malaria underpins the need for the rapid turnaround of microscopy test-results. To further improve the clinical management of

inpatients with severe malaria, the hospital should also invest in routine tests for random blood sugar, haemoglobin level/haematocrit, blood gases, urea and electrolytes; and in fluid balance charts as well as intensive nursing care.

In conclusion, half the malaria microscopy results were not available to guide the clinical management of malaria despite that the rate of testing was high. Seven in eight inpatients initiated on injectable AS or Q did not receive the recommended follow-up treatment of oral AL. One in four inpatients delayed to initiate hospital antimalarials by at least one calendar day. The hospital should review its workflows to encourage prompt availability of malaria test-results to promote timely antimalarial treatment based on confirmed diagnosis as opposed to clinical judgement only. Improved stock forecasting for in-demand antimalarials, intern-pharmacist-led bedside dispensing and frequent audits of junior and mid-level clinicians could improve the quality of treatment for malaria inpatients in Uganda.

The study's limitations have been reported elsewhere [3]. Briefly, the study was conducted at Uganda's National Referral and Teaching Hospital and the results might not be generalizable to facilities with lower calibres of inpatient care. Also, antimalarials that were purchased from private community pharmacies were not documented as dispensed in the hospital register so we obtained this dispensing information by interviewing the inpatients and/or their caregivers [3].

## Declarations

**Ethics approval and consent to participate:** Ethical approval was granted by the School of Medicine Research and Ethics Committee, Makerere University College of Health Sciences (REC REF No. 2011-113), Mulago Hospital Research and Ethics Committee (MREC 253), and Uganda National Council for Science and Technology (HS 1151). All participants gave written informed consent.

**Consent for publication:** Consent to publish this work was sought during the informed consent process.

**Availability of data and materials:** The dataset for this publication is available on reasonable request from the corresponding author.

**Competing interests:** SMB. holds GSK shares. RK and CK have nothing to declare.

**Funding:** The study received grant support from Wellcome Trust through the Training Health Researchers into Vocational Excellence in East Africa programme (grant number 087540); and the African Population and Health Research Centre (2013-2015 ADF 006).

**Authors' contributions:** RK conceived the study, supervised data collection and conducted data analysis. RK, SMB and CK designed the study, participated in interpretation of results and manuscript writing. All authors read and approved the final draft of the manuscript.

**Acknowledgements:** The authors are grateful to the study participants who consented; and the administration of Mulago Hospital which permitted the study.

## References

1. World Health Organization. World Malaria Report 2019. In: Organization WH, editor. Geneva: World Health Organization; 2019.
2. World Health Organization. Guidelines for the Treatment of Malaria. Treatment of Severe Malaria 2015 [cited 2020 30 April]; 3rd Edition:[Available from: <https://www.ncbi.nlm.nih.gov/books/NBK294445/>]
3. Kiguba R, Karamagi C, Bird SM. Extensive antibiotic prescription rate among hospitalized patients in Uganda: but with frequent missed-dose days. *The Journal of Antimicrobial Chemotherapy*. 2016; **71**(6): 1697-706.
4. Dondorp A, Nosten F, Stepniewska K, Day N, White N. Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial. *Lancet*. 2005; **366**(9487): 717-25.
5. Dondorp AM, Fanello CI, Hendriksen IC, Gomes E, Seni A, Chhaganlal KD, et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *Lancet*. 2010; **376**(9753): 1647-57.
6. Sinclair D, Donegan S, Isba R, Lalloo DG. Artesunate versus quinine for treating severe malaria. *The Cochrane Database of Systematic Reviews*. 2012; (6): CD005967.
7. Amboko BI, Ayieko P, Ogero M, Julius T, Irimu G, English M. Malaria investigation and treatment of children admitted to county hospitals in western Kenya. *Malaria Journal*. 2016; **15**(1): 506.

8. Ampadu HH, Asante KP, Bosomprah S, Akakpo S, Hugo P, Gardarsdottir H, et al. Prescribing patterns and compliance with World Health Organization recommendations for the management of severe malaria: a modified cohort event monitoring study in public health facilities in Ghana and Uganda. *Malaria Journal*. 2019; **18**(1): 36.
9. Riley C, Dellicour S, Ouma P, Kioko U, ter Kuile FO, Omar A, et al. Knowledge and Adherence to the National Guidelines for Malaria Case Management in Pregnancy among Healthcare Providers and Drug Outlet Dispensers in Rural, Western Kenya. *PloS One*. 2016; **11**(1): e0145616.
10. Dlamini SV, Kosgei RJ, Mkhonta N, Zulu Z, Makadzange K, Zhou S, et al. Case management of malaria in Swaziland, 2011-2015: on track for elimination? *Public Health Action*. 2018; **8**(Suppl 1): S3-S7.
11. StataCorp. *Stata Statistical Software: Release 12*. College Station, TX: StataCorp LP; 2011.
12. Schiza EC, Panos G, David C, Petkov N, Schizas CN. Integrated Electronic Health Record Database Management System: A Proposal. *Studies in Health Technology and Informatics*. 2015; **213**: 187-90.
13. World Health Organization. *Compendium of WHO malaria guidance – prevention, diagnosis, treatment, surveillance and elimination*. In: Organization WH, editor. Geneva: World Health Organization; 2019.

## Tables

**Table 1: Demographic and clinical characteristics of 762 inpatients, Uganda**

Characteristic	Antimalarial Use during the Current Hospitalization			Overall		
	Yes	No				
Age, years <sup>a</sup>	27 (21 - 35)	30 (25 - 43)		30 (24 - 42)		
Length of hospital stay, days <sup>a</sup>	4 ( 3 - 5)	4 (3 - 6)		4 ( 3 - 6)		
Patient-days of observation	454	3,287		3,741		
Extent of antimalarial use	Antimalarial Use during the Current Hospitalization, n (%)					
	Yes	No	Total			
Pre-admission antimalarials	97 (13)	665 (87)	762			
In-hospital antimalarials	100 (13)	662 (87)	762			
Pre-admission antimalarials	38 (38)	62 (62)	100			
Pre-/in-hospital co-trimoxazole	15 (15)	87 (87)	100			
In-hospital antibiotics	61 (61)	39 (39)	100			
In-hospital antiretrovirals	14 (14)	86 (86)	100			
Pre-/in-hospital antimalarials	159 (21)	603 (79)	762			
Subgroup analyses on key variables	Antimalarial Use, n (%)			Single factor analysis		
	Yes	No	Total, [% col] <sup>b</sup>	OR <sup>c</sup>	95% CI <sup>d</sup> for OR	P-value
Gender						
Male	20 ( 9)	208 (91)	228 [30]	1.0		
Female	80 (15)	454 (85)	534 [70]	1.8	1.09 - 3.07	0.022
Ward						
Gynaecological (GYN)	25 (13)	166 (87)	191 [25]	1.0		
Infectious Diseases and Gastrointestinal Illnesses (IDGI)	57 (18)	263 (82)	320 [42]	1.4	0.87 - 2.39	0.161
Haematology, Neurology and Endocrinology (HNE)	12 (10)	105 (90)	117 [15]	0.8	0.37 - 1.58	0.459
Cardiovascular, Pulmonology and Nephrology (CPN)	6 ( 4)	128 (96)	134 [18]	0.3	0.12 - 0.78	0.013
Number of working diagnoses						
One	21 (15)	122 (85)	143 [18]	1.0		
Two	26 (13)	177 (87)	203 [27]	0.9	0.46 - 1.59	0.616
Three	28 (15)	158 (85)	186 [24]	1.0	0.56 - 1.90	0.926
Four or more	25 (11)	205 (89)	230 [30]	0.7	0.38 - 1.32	0.277
Length of hospital stay, days						
Less than 5-days	64 (15)	368 (85)	432 [57]	1.0		
Five days or more	36 (11)	294 (89)	330 [43]	0.7	0.46 - 1.09	0.115
HIV-serostatus						
Negative	49 (14)	291 (86)	340 [45]	1.0		
Positive	23 (10)	209 (90)	232 [30]	0.7	0.39 - 1.11	0.113
Unknown	28 (15)	162 (85)	190 [25]	1.0	0.62 - 1.70	0.919
Hospitalization in past 3-months						
No	75 (14)	455 (86)	532 [70]	1.0		
Yes	25 (11)	205 (89)	230 [30]	0.7	0.46 - 1.20	0.227
Charlson's co-morbidity index score						
Zero	64 (16)	329 (84)	393 [52]	1.0		
One or more	36 (10)	333 (90)	369 [48]	0.6	0.36 - 0.86	0.008
Antiretroviral therapy use						
No	86 (14)	549 (86)	635 [83]	1.0		
Yes	14 (11)	113 (89)	127 [17]	0.8	0.43-1.44	0.444
Microscopy - Malaria Parasitaemia Results Available						
No	62 (62)	616 (93)	678 [89]	1.0		
Yes	38 (38)	46 ( 7)	84 [11]	8.2	4.81-14.0	<0.001
Major admitting diagnosis						
Malaria						
No	17 ( 3)	604 (97)	621 [81]	1.0		
Yes	83 (59)	58 (41)	141 [19]	50	28.3-91.5	<0.001
Immunosuppressed syndrome (ISS) or HIV/AIDS <sup>e</sup>						
No	86 (14)	524 (86)	610 [80]	1.0		
Yes	14 ( 9)	14 (91)	152 [20]	0.6	0.34 - 1.12	0.113

Tuberculosis (TB)

No	92 (14)	548 (86)	640 [84]	1.0		
Yes	8 ( 7)	114 (93)	122 [16]	0.4	0.20 - 0.88	0.023
Sepsis-related working diagnosis						
No	81 (12)	597 (88)	678 [89]	1.0		
Yes	19 (23)	65 (77)	84 [11]	2.2	1.23 - 3.78	0.007
Respiratory Conditions except TB						
No	85 (13)	547 (87)	632 [83]	1.0		
Yes	15 (12)	115 (88)	130 [17]	0.8	0.47 - 1.51	0.557
Miscellaneous infections						
No	78 (12)	571 (88)	649 [85]	1.0		
Yes	22 (19)	91 (81)	113 [15]	1.8	1.05 - 2.98	0.032

<sup>a</sup>Median (Interquartile Range, IQR); <sup>b</sup>% Column; <sup>c</sup>OR = Odds Ratio; <sup>d</sup>confidence interval; <sup>e</sup>Not all HIV-positive patients had the immunosuppressed syndrome, ISS

**Table 2: Malaria detection by laboratory diagnosis among 762 hospitalized patients, Uganda \***

Malaria suspected at admission (n = 141) <sup>b</sup>																Malaria not suspected at admission (n = 621)																	
Malaria at discharge (n = 83)								No malaria at discharge (n = 58)								Malaria at discharge (n = 5)								No malaria at discharge (n = 616)									
Microscopy requested, n (%) <sup>c</sup>																																	
Yes				No				Yes				No				Yes				No				Yes				No					
Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested	Returned Positive	Returned Negative	Not Returned	Not Requested		
21 (25)	13 (16)	31 (37)	18 (22)	0 (0)	16 (28)	27 (47)	15 (26)	1 (20)	0 (0)	1 (20)	3 (60)	3 (0)	30 (5)	58 (9)	525 (85)																		
In-hospital administration of antimalarials, n (%)																																	
Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
20 (95)	1 (5)	11 (85)	2 (15)	26 (84)	5 (16)	15 (83)	3 (17)	0 (0)	0 (0)	5 (31)	11 (69)	3 (11)	24 (89)	3 (20)	12 (60)	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	2 (100)	3 (100)	1 (100)	29 (97)	4 (7)	54 (95)	9 (2)	516 (98)
Single admitting diagnosis of malaria, n (%)																																	
Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
5 (24)	16 (76)	0 (0)	13 (60)	5 (16)	26 (84)	4 (22)	14 (78)	0 (0)	0 (0)	1 (6)	15 (94)	1 (4)	26 (96)	0 (0)	15 (100)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	3 (100)	0 (0)	3 (100)	0 (0)	30 (100)	0 (0)	58 (100)	0 (0)	525 (100)	
Received antimalarials during the 4-weeks preadmission, n (%)																																	
Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
7 (33)	14 (67)	5 (38)	8 (62)	8 (26)	23 (74)	7 (39)	11 (61)	0 (0)	0 (0)	5 (31)	11 (69)	8 (30)	19 (70)	3 (20)	12 (80)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	2 (100)	3 (100)	10 (67)	20 (91)	5 (9)	53 (91)	37 (93)
Single discharge diagnosis of malaria, n (%)																																	
Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
9 (43)	12 (57)	3 (23)	10 (77)	16 (52)	15 (48)	11 (61)	7 (39)	0 (0)	0 (0)	0 (0)	16 (100)	0 (0)	27 (100)	0 (0)	15 (100)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	1 (100)	0 (0)	3 (100)	0 (0)	3 (100)	0 (0)	30 (100)	0 (0)	58 (100)	0 (0)	525 (100)	

\*19% (146/762; 95% confidence interval (CI): 16% to 22%) of inpatients had either an admitting or discharge malaria diagnosis or both; <sup>b</sup>19% (141/762; 95% CI: 16% to 21%) had an admitting malaria diagnosis; <sup>c</sup>Only three of the 201 inpatients with microscopy requests had concurrent malaria rapid diagnostic testing (mRDT) done. However, mRDT results were available for only one inpatient, who tested positive.

**Table 3: Frequency of antimalarials used by hospitalized patients, Uganda, 2014**

Antimalarial	Number: n, %	
<b>Patient-level</b>		
<i>Pre-admission, n = 97</i>		
Artemether-Lumefantrine only	50	52%
Quinine only	22	23%
Sulfadoxine-Pyrimethamine only	9	9%
Artesunate only	5	5%
Coartem + Quinine only	4	4%
Duocotexcin only	2	2%
Artemether only	1	1%
Artesunate + Duocotexcin only	1	1%
P-alaxin + Quinine only	1	1%
Artemether + Quinine + Doxycycline only	1	1%
Dihydroartemisinin-Piperaquine only	1	1%
<i>In-hospital, n = 100*</i>		
Artesunate only <sup>±</sup>	47	47%
Quinine only <sup>~</sup>	23	23%
Artemether-Lumefantrine only	15	15%
Artesunate + Artemether-Lumefantrine only	8	8%
Quinine + Artemether/Lumefantrine only	3	3%
Sulfadoxine-Pyrimethamine only	2	2%
Artesunate + Quinine only	2	2%
<b>Drug-level</b>		
<i>Pre-admission, n = 105</i>		
Artemether-Lumefantrine	54	51%
Quinine	28	27%
Sulfadoxine-Pyrimethamine	9	9%
Artesunate	6	6%
Duocotexcin	3	3%
Artemether	2	2%
Dihydroartemisinin-Piperaquine	2	2%
Doxycycline	1	1%
<i>In-hospital, n = 113</i>		
Artesunate	57	50%
Quinine	28	25%
Artemether-Lumefantrine	26	23%
Sulfadoxine-Pyrimethamine	2	2%

\*Only 13% (11/83) of inpatients who received injectable artesunate or quinine received follow-up oral artemether-lumefantrine; <sup>±</sup>68% (32/47) of the inpatients presented with both admitting and discharge malaria diagnoses [median length of hospital stay: 4 (IQR, 3 to 5) days]; <sup>~</sup>91% (21/23) of the inpatients had both admitting and discharge malaria diagnoses [median length of hospital stay: 3 (IQR, 2 to 4) days]

Missed Day 1 dosing of artesunate injection among 57 hospitalized patients who received in-hospital intravenous artesunate, Uganda, 2014<sup>±</sup>

Length of stay, days	Preadmission antimalarial use	Admitting Malaria Diagnosis	Discharge Malaria Diagnosis	AL co-prescribed	Switched to AL	AS Doses Prescribed	AS Doses Received	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
3	No	Yes	No	No	No	3	1		1 dose						
3	No	Yes	Yes	Yes	No	2	3	1 dose	2 doses						
4	No	Yes	Yes	No	No	6	2	1 dose	1 dose						
5	No	Yes	Yes	Yes	No	3	3	1 dose	1 dose	1 dose					
2	No	Yes	Yes	Yes	No	2	1	1 dose							
4	Yes	Yes	Yes	Yes	No	10	3	1 dose		1 dose	1 dose				
5	No	No	No	No	No	3	2		2 doses						
2	No	Yes	Yes	Yes	Yes	3	2	2 doses							
4	No	Yes	No	Yes	Yes	3	2	1 dose	1 dose						
5	Yes	Yes	Yes	Yes	Yes	3	1	1 dose							
4	No	Yes	Yes	Yes	No	3	2	1 dose	1 dose						
5	No	Yes	Yes	No	No	3	4		1 dose	2 doses	1 dose				
5	No	Yes	Yes	No	No	3	3	1 dose	1 dose	1 dose					
5	No	Yes	No	No	No	3	3		1 dose	1 dose	1 dose				
10	Yes	Yes	No	No	No	3	2	1 dose	1 dose						
3	Yes	No	No	No	No	2	3	1 dose	2 doses						
5	Yes	Yes	Yes	Yes	No	2	2	1 dose	1 dose						
2	No	Yes	Yes	Yes	No	3	2	1 dose	1 dose						
3	No	Yes	Yes	Yes	No	2	3	2 doses	1 dose						
10	No	No	No	No	No	3	4		1 dose	1 dose	2 doses				
3	No	Yes	Yes	Yes	No	3	2		2 doses						
5	No	No	Yes	Yes	No	2	3		1 dose	1 dose	1 dose				
2	No	Yes	Yes	Yes	No	4	1	1 dose							
3	Yes	Yes	Yes	Yes	No	4	3	1 dose	1 dose	1 dose					
3	No	Yes	Yes	Yes	No	3	3	1 dose	2 doses						
3	Yes	Yes	Yes	No	No	3	3	1 dose	1 dose	1 dose					
3	Yes	Yes	Yes	Yes	No	3	2	1 dose	1 dose						
Length of stay, days	Preadmission antimalarial use	Admitting Malaria Diagnosis	Discharge Malaria Diagnosis	AL co-prescribed	Switched to AL	AS Doses Prescribed	AS Doses Received	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
5	Yes	Yes	Yes	Yes	No	3	4	1 dose	1 dose	1 dose	1 dose				
4	Yes	Yes	Yes	Yes	No	3	3	1 dose	1 dose	1 dose					
3	Yes	Yes	Yes	Yes	No	3	3	1 dose	1 dose	1 dose					
5	Yes	Yes	Yes	Yes	No	3	3	1 dose		1 dose	1 dose				
7	Yes	Yes	Yes	Yes	Yes	3	3	1 dose				1 dose	1 dose		
5	No	No	No	Yes	No	3	3		1	1	1				

									dose	dose	dose						
3	Yes	Yes	Yes	Yes	No	3	2	1 dose	1 dose								
4	No	Yes	Yes	No	No	3	2	1 dose	1 dose								
2	No	Yes	Yes	Yes	No	3	1	1 dose									
9	No	Yes	Yes	No	No	3	2	1 dose	1 dose								
6	No	Yes	Yes	No	No	3	3				1 dose	2 doses					
3	Yes	No	No	Yes	No	3	1	1 dose									
4	No	Yes	Yes	Yes	No	3	3		1 dose	2 doses							
3	Yes	Yes	No	Yes	No	3	3	1 dose	2 doses								
4	No	Yes	Yes	No	No	3	3	1 dose	1 dose	1 dose							
3	Yes	No	Yes	Yes	No	3	3	1 dose	2 doses								
4	Yes	Yes	Yes	Yes	No	3	3		1 dose	2 doses							
9	No	Yes	Yes	Yes	Yes	4	3			1 dose	1 dose	1 dose					
4	Yes	Yes	No	Yes	Yes	2	3		2 doses	1 dose							
4	No	Yes	Yes	Yes	No	6	2			1 dose	1 dose						
3	No	Yes	Yes	Yes	Yes	1	1	1 dose									
16	Yes	Yes	No	No	No	3	3	1 dose	2 doses								
4	No	Yes	Yes	No	No	3	1	1 dose									
6	No	Yes	No	No	No	3	4	1 dose	1 dose	2 doses							
5	No	Yes	Yes	Yes	No	3	3		2 doses	1 dose							
3	No	Yes	No	No	No	1	1	1 dose									
3	No	Yes	Yes	Yes	No	3	1		1 dose								
4	Yes	No	No	No	No	2	2	1 dose	1 dose								
15	Yes	No	Yes	No	No	3	8	1 dose	2 doses		1 dose	2 doses					2 doses
1	No	Yes	Yes	Yes	No	2	2	1 dose	1 dose								

dose day, n								16	10	8	1	1					
7 data unavailable, n1								0	5	27	44	52					
7 data available, N*								57	52	30	13	5					
n of inpatients with missed Day 1 data, n/N~								28%									

ation from 1 to 2 AS doses per calendar day depends on the time of day that an inpatient initiates treatment. Injectable AS is given at 0, 12, 24 hours then inpatient is to oral AL if he/she can tolerate it. Thus, an inpatient might receive 1 to 2 AS doses per calendar-day and very rarely 3 AS doses. \*N = [(The 57 artesunate users) - of inpatients who did not have artesunate dose-day data] or (57-n1); ~95% confidence intervals for the estimate is 28% (17% to 42%).

**Missed Day 1 dosing of quinine injection among 28 hospitalized patients who received in-hospital intravenous quinine, Uganda, 2014**

Length of stay, days	Preadmission antimalarial use	Admitting Malaria Diagnosis	Discharge Malaria Diagnosis	AL co-prescribed	Switched to AL	Doses Prescribed	Doses Received	Day 1	Day 2	Day 3	Day 4
2	No	Yes	Yes	Yes	No	3	2	1 dose	1 dose		
6	Yes	Yes	Yes	Yes	No	3	3	1 dose		1 dose	1 dose
8	Yes	No	No	No	No	3	1	1 dose			
4	Yes	Yes	Yes	No	No	3	3	1 dose	1 dose	1 dose	
3	No	Yes	Yes	No	No	3	3	1 dose	2 doses		
4	No	Yes	Yes	No	No	3	1	1 dose			
3	No	Yes	Yes	No	No	3	2	1 dose	1 dose		
2	Yes	Yes	Yes	No	No	3	2	1 dose	1 dose		
2	Yes	Yes	Yes	Yes	No	3	1	1 dose			
3	No	Yes	Yes	Yes	No	3	2	1 dose	1 dose		
5	Yes	Yes	Yes	No	No	3	3	2 doses	1 dose		
3	Yes	Yes	Yes	No	No	9	3	1 dose	1 dose	1 dose	
4	No	Yes	Yes	No	No	3	3	1 dose	1 dose	1 dose	
3	No	Yes	Yes	Yes	Yes	3	3	1 dose	2 doses		
4	No	Yes	Yes	No	No	6	2	1 dose	1 dose		
8	No	Yes	Yes	No	No	3	3	1 dose	2 doses		
5	Yes	Yes	Yes	Yes	Yes	3	3	1 dose		1 dose	1 dose
4	Yes	Yes	Yes	Yes	No	3	3	3 doses			
3	Yes	Yes	Yes	No	No	9	3	2 doses	1 dose		
2	No	Yes	Yes	No	No	3	2	1 dose	1 dose		
Length of stay, days	Preadmission antimalarial use	Admitting Malaria Diagnosis	Discharge Malaria Diagnosis	AL co-prescribed	Switched to AL	Doses Prescribed	Doses Received	Day 1	Day 2	Day 3	Day 4
9	No	Yes	No	No	No	6	3		2 doses	1 dose	
3	No	Yes	Yes	Yes	No	21	3	2 doses	1 dose		
2	No	Yes	Yes	Yes	No	0	1	1 dose			
10	No	Yes	Yes	Yes	Yes	6	3	2 doses	1 dose		
15	Yes	No	Yes	No	No	21	3			2 doses	1 dose
2	No	Yes	Yes	No	No	3	2	1 dose	1 dose		
2	No	Yes	Yes	No	No	3	2	1 dose	1 dose		
6	No	Yes	Yes	Yes	Yes	3	2	1 dose	1 dose		
Doses received, n								5	2	1	
Doses prescribed, n1								0	8	21	
Doses received, N *								28	20	7	
Number of inpatients with missed Day 1, n/N ~								18			

(Number of inpatients with missed Day 1, n/N ~ (Number of inpatients without quinine dose-day data) or (28-n1); ~95% confidence intervals for the estimate is 18% (6% to 37%).

Table 6: Missed Day 1 dosing of antimalarials by calendar-day, n (%); (N = 83)

Factor	Missed Calendar-Day 1 dosing			Crude Analysis			Adjusted Analysis		
	Yes	No	Total, [% col] <sup>a</sup>	OR <sup>b</sup>	95% for CI <sup>c</sup>	P-value	aOR <sup>b</sup>	95% for CI <sup>c</sup>	P-value
Antiretroviral therapy use									
	15 (20)	59 (80)	74 [89]	1.0			1.0		
	5 (56)	4 (44)	9 [11]	4.9	1.17-20.6	0.029	4.9	0.90-26.1	0.066
Malaria microscopy test results available									
	8 (17)	39 (83)	47 [57]	1.0			1.0		
	12 (33)	24 (67)	36 [43]	2.4	0.87-6.82	0.090	2.4	0.70-8.40	0.165
Duration on number of working days									
	20	63	83	2.6	1.56-4.35	<0.001	2.6	1.52-4.56	0.001

a: %OR = Odds Ratio; <sup>c</sup>confidence interval

## Figures

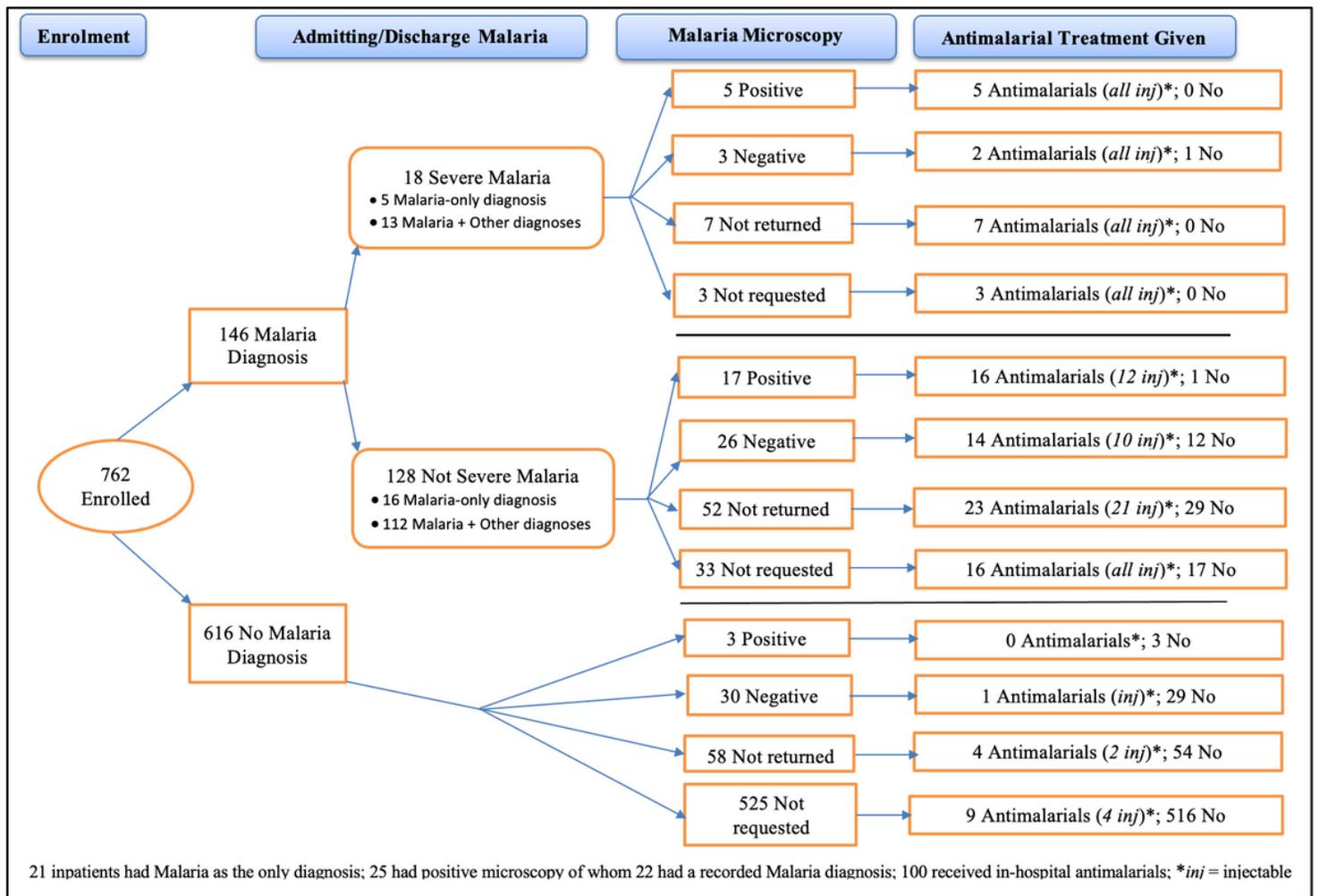


Figure 1

Schema of enrolment, malaria diagnosis and antimalarial treatment among 762 inpatients at a tertiary care hospital, Uganda

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Appendix11Dec2020.docx](#)