

# Evaluation of the Management of Severe Malaria in Pregnant Women, Children and Adults in Mali



# Preamble

## **National Malaria Control Programme**

We are pleased to present this report of an operational study evaluating the use of pre-referral rectal artesunate and injectable artesunate for the management of severe malaria in pregnant women, children under 6, and adults in several localities in Mali.

The study was performed by the Malaria Research and Training Centre (MRTC) in collaboration with the National Malaria Control Programme (NMCP) and with the financial and technical support of Medicines for Malaria Venture (MMV), to further malaria control efforts. It fell under the Ministry of Health's multiple activities and was conducted by the NMCP and its malaria control partners, with a view to eliminate the disease in the very near future.

This operational study addresses NMCP concerns regarding the management of severe malaria. It was designed to assess the implementation of the severe malaria treatment algorithm to improve clinical practice guidance at every tier of the health pyramid involved in the management of severe malaria. The study highlighted the potential barriers to the treatment of severe malaria in children, pregnant women and adults. We hope that the recommendations provided will help guide our practices in the interest of the vulnerable populations.

Together, we will win the fight against malaria.

Thank you.

NMCP Director

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# Principal Investigators

## **Principal Investigators**

Prof Kassoum Kayentao – MRTC  
Mrs Fady Toure – NMCP  
Dr Vincent Sanogo – NMCP  
Dr Mohamed Keïta – MRTC

## **Percentage of time spent**

Prof Kassoum Kayentao – 10%  
Mrs Fady Toure – 5%  
Dr Vincent Sanogo – 5%  
Dr Mohamed Keïta – 30%

## **Role**

Prof Kassoum Kayentao – Principal Investigator  
Mrs Fady Toure – Supervisor  
Dr Vincent Sanogo – Supervisor  
Dr Mohamed Keïta – Investigator

## Acronyms and abbreviations

ACT	Artemisinin-based combination therapy
CSREF	Reference Health Centre (Centre de Santé de Référence)
DHIS2	District Health Information Software 2
HCP	HealthCare Provider
IM	Intramuscular
IQR	Interquartile range
IV	Intravenous
MRTC	Malaria Research and Training Center
NLHIS	National Local Health Information System
NMCP	National Malaria Control Programme
ODK	Open Data Kit
WHO	World Health Organization

# 1. Introduction

Despite the progress made in the fight against malaria over the past decade, including a significant reduction in malaria-related morbidity and mortality in most sub-Saharan Africa countries, ~ 228 million cases and ~ 405'000 deaths were still recorded worldwide in 2018 (World Malaria Report 2019). Children under 5 and pregnant women are the most vulnerable and therefore the most affected by malaria.

In 2018, 32% of consultations in Mali were attributable to malaria, with 3'572'794 suspected cases and 3'457'267 cases tested, of which 66% were confirmed (DHIS2), and 1'178 malaria deaths, representing 22% of all deaths in the country (NLHIS). In pregnant women, 217'715 cases were suspected, of which 112'062 were confirmed (51.5%) (DHIS2).

To control malaria, the WHO recommends the use of artemisinin-based combination therapies (ACTs) for the treatment of target groups, including pregnant women as of the second trimester. For severe malaria, adults and children (including infants, pregnant women in all trimesters and lactating women) must be treated with IV or IM artesunate for at least 24h and until they can tolerate oral medication. Once a patient has received at least 24h of parenteral therapy and can tolerate oral medication, the treatment must be completed with a further 3 days of an oral ACT. In Mali, the National Malaria Control Programme (NMCP) makes the same recommendations. Injectable artesunate is the first-line treatment for severe malaria, followed by IM artemether, then quinine by IV infusion as last choice. However, in the weekly reports provided by malaria management sites, the use of artemisinin derivatives for severe malaria does not always comply with clinical practice guidelines. This survey will help determine the level of correct and incorrect use, and explore the reasons for healthcare providers' non-compliance with the severe malaria management guidelines.

## 2. Objectives

The study was designed to assess the use of pre-referral rectal artesunate and of injectable artesunate for the management of severe malaria in Mali. Its specific objectives included:

1. Determine the proportion of severe malaria patients correctly diagnosed and correctly treated in the selected health centres
2. Determine the level of use of the drugs selected by the national guidelines for the management of severe malaria in pregnant women, children and adults
3. Determine healthcare providers' level of knowledge regarding the diagnostic criteria for severe malaria, and the national guidelines for severe malaria management
4. Identify obstacles to healthcare providers' compliance with national guidelines regarding severe malaria management
5. Determine the availability of inputs for the treatment of severe malaria in the pharmacies of the selected health centres
6. Determine the most commonly used route of administration for injectable artesunate (IV or IM) based on health facility level
7. Determine the perception of healthcare providers' regarding the use of injectable artesunate
8. Determine the feasibility and acceptability of IM and rectal artesunate (pre-referral) in severe malaria management



## 3. Methodology

### 3.1. Study procedures

#### 3.1.1. Ethics committee approval

The study protocol was submitted to and approved by the ethics committee of the Faculty of Medicine, Pharmacy and Dentistry of Bamako (FMPOS). The approval letter was received on 4 May 2020 (NO 2020/70/CE/FMOS/FAPH).

#### 3.1.2. Site initiation visit

On 19-23 May 2020, we visited the study sites in Bamako, Sélingué, Sikasso, Mopti, and San to meet local health authorities, introduce the study and provide the data collecting tools for the collectors. These tools included tablets, copies of consent forms, notebooks, pens and bags.

**Table 1: Site initiation visit dates**

Date	Site	Health centres
19 May 2020	Sélingué	Reference Health Centre (CSREF)
20 May 2020	Sikasso	Hospital and CSREF
21 May 2020	Sévaré	Hôpital de Sévaré
21 May 2020	San	CSREF
22 May 2020	Bamako	CSREF de la Commune VI
23 May 2020	Bamako	Hôpital du Mali

#### 3.1.3. Training of investigators

A virtual training session on the BlueJeans platform took place on 27 May 2020, with the help of the CRO Pharmalys in charge of monitoring. The session covered three main topics:

1. Protocol presentation: The coordinator of the study procedures, Dr Mohamed Keïta, presented the study protocol and explained its purpose and methodology.
2. Good Clinical Practice (GCP): These sessions were given by Marieme Ba, Pharmalys' study monitor. She provided valuable information on Good Clinical Practice, even though this is not a clinical trial, and discussed personal data protection.
3. Data management: The study data manager explained how to enter data in the Open Data Kit (ODK) platform. He also explained how to correct data and how to export data to the server.

**Table 2: Training agenda**

Chair: Prof Kassoum Kayentao		
09:00 - 09:15	Self-Introduction	All
09:15 - 09:45	Protocol presentation	Dr Mohamed Keïta
09:45 - 11:45	Good Clinical Practice	Marieme Ba
11:45 - 12:45	Coffee break	
12:45 - 13:45	Data Management	Siriman Traoré
13:45 - 14:15	Coffee break	

**Table 3: Attendance list**

Names	Role	Site
Prof Kassoum Kayentao	Principal Investigator	Bamako
Mrs Marieme Ba	Study Monitor	Dakar
Dr Mohamed Keïta	Study Coordinator	All Mali sites
Mr Siriman Traoré	Data Manager	Bamako
Dr Moussa Djimdé	Supervisor	All Mali sites
Dr Hammadoun Diakité	Data Collector	Sikasso
Dr Issiaka Haidara	Data Collector	Sikasso
Dr Siaka Goïta	Data Collector	Bamako
Dr Fatoumata Djim	Data Collector	Bamako
Mr Amadou Ballo	Data Collector	Sévaré
Mr Ibrahim Cissé	Data Collector	Sévaré
Dr Daouda Diarra	Data Collector	Sélingué
Dr Bourema Koné	Data Collector	San

### 3.2. Study sites

The study was conducted in Bamako (Hôpital du Mali and CSREF of Commune VI), Sikasso (Hôpital Régional, CSREF of Sikasso and CSREF of Sélingué), Mopti (Hôpital Régional de Sévaré and CSREF of Mopti), and Ségou (CSREF of San).

### 3.3. Study period

The study's field activities were carried out from 19 May to 31 July 2020 in selected health centres. The data was collected from records dating from 1 January 2017 to 30 June 2019. Data analysis and report writing was done between 5 August and 1 September 2020.

### 3.4. Type of study

This study included two components:

- A retrospective evaluation based on the records of pregnant women at all trimesters of pregnancy, of children under 6 years of age, and of adults treated in those health centres for severe malaria (objectives a, b, f).
- An observational survey-based qualitative evaluation of the perception, satisfaction and acceptability of healthcare providers responsible for the management of severe and acute malaria in selected centres (objectives c, d, g, h).

### 3.5. Study population

The study population included:

- Pregnant women admitted for severe malaria in the selected centres.
- Children under 6 admitted for severe malaria in the selected centres
- Adults admitted for severe malaria in the selected centres.
- Healthcare providers responsible for the management of malaria at the selected centres.

#### 3.5.1. Data collection and analysis

Data collection was done on ODK electronic report forms using tablets and exported in Excel format. Frequencies and proportions of patients' general characteristics, diagnostics tools, treatments used and outcomes were computed using the R descr library. The median drug shortage duration was calculated. Pie charts were plotted using the plotrix library, and barplots were plotted using the R ggplot2 library. Statistical analysis was done using R version 3.5.1.

#### 3.5.2. Supervision

A supervision visit was performed by Kassoum Kayentao (MRTC), Mohamed Keita (MRTC), Moussa Djimde (MRTC), Moussa Yalcouyé (MRTC) and Fady Touré (NMCP) from 27 to 30 June 2020. The purpose was to monitor sites activities. All consent forms (228) were verified and corrective measures were recommended.

The sites visited were in Sévaré, Mopti, San, Sélingué, and Sikasso, as well as two sites in Bamako.



## 4. Results

### 4.1. Population characteristics

The general characteristics of the study population are described in Table 4. Data was collected from 7'272 patients in eight (8) different health centres, including 4'409 children under 6 treated for severe malaria in all sites (60.63%). The data of those aged 7 to 17 is not taken into account in this table. The total population included only 480 pregnant women treated for severe malaria, and 2'383 non-pregnant adults (32.77%). The sex ratio was 1.07 in favour of males. The largest number of patients whose data was collected was from the Sikasso CSREF (1'692; 23.27%), followed by San CSREF (1'582; 21.75%). Most cases of severe malaria were managed by medical doctors (3'513 cases; 48.31%), followed by nurses (2'295 cases; 31.56%).

**Table 4: Population characteristics (n = 7'272)**

Characteristics	n (%)
<b>Number of patient records examined</b>	
Children < 6 years	4409 (60.63)
Adults	2383 (32.77)
Pregnant women	480 (6.60)
<b>Gender</b>	
Female	3754 (51.62)
Male	3518 (48.3)
<b>Number of patients in each study site</b>	
Hôpital du Mali	403 (5.54)
CSREF de la Commune VI	651 (8.95)
CSREF San	1582 (21.75)
CSREF de Sélingué	955 (13.13)
CSREF de Sikasso	1692 (23.27)
Hôpital de Sikasso	544 (7.48)
CSREF de Mopti	636 (8.75)
Hôpital de Sévaré	809 (11.12)
<b>Numbers of healthcare providers</b>	
Medical doctor	3513 (48.31)
Medical student	1129 (15.53)
Midwife	37 (0.51)
Nurse	2295 (31.56)
Unknown	298 (4.10)

## 4.2. Proportion of patients correctly diagnosed and treated for severe malaria in the study health centres

Table 5 shows that among the centres surveyed, the highest rate of correct malaria diagnosis prior to treatment was achieved at Hôpital de Sévaré, with 809 cases (100%). According to the results of our survey, the Mopti CSREF provided the most presumptive treatment for severe malaria, with 374 cases (58.81%), followed by the Sikasso CSREF, with 559 cases (33.04%).

**Table 5: Malaria diagnostic confirmation by RDT or thick blood smear based on study sites**

Health centre	Diagnosis based on RDT or thick blood smear		
	Positive n (%)	Negative n (%)	Unknown n (%)*
Hôpital du Mali	399 (99.00)	2 (0.50)	2 (0.50)
CSREF de la Commune VI	625 (96.01)	0 (0.00)	26 (3.99)
CSREF de San	1546 (97.72)	0 (0.00)	36 (2.28)
CSREF de Sélingué	666 (69.74)	5 (0.52)	284 (29.74)
CSREF de Sikasso	1132 (66.90)	1 (0.06)	559 (33.04)
Hôpital de Sikasso	406 (74.63)	0 (0.00)	138 (25.37)
CSREF de Mopti	262 (41.19)	0 (0.00)	374 (58.81)
Hôpital de Sévaré	809 (100)	0 (0.00)	0 (0.00)

\* The high level of "Unknown diagnosis" in several sites can be explained by 1) there was a lack of completeness of documents for several hospitalized patients and 2) the survey was conducted at the referral center where diagnostic tools were not always available to confirm the clinical diagnosis before the patient received treatment - see Table 13

Regarding the accuracy of malaria diagnosis based on patient type (Table 6), malaria was confirmed prior to the treatment in 98.96% of pregnant women (475 cases), 82.06% of children under 6 (3618 cases), and 73.52% of adults (1752 cases).

**Table 6: Malaria diagnosis confirmed by RDT or thick blood smear based on patient type**

	Diagnosis based on RDT or thick blood smear		
	Positive n (%)	Negative n (%)	Unknown n (%)
Children < 6	3618 (82.06)	7 (0.16)	784 (17.78)
Adults	1752 (73.52)	1 (0.04)	630 (26.44)
Pregnant women	475 (98.96)	0 (0.00)	5 (1.04)

### 4.3. Use of drugs included in the national guidelines for the management of severe malaria in pregnant women, children, and adults

Table 7 show that injectable artesunate was used preferentially in children under 6 (77.2% of 3404 cases). In adults, injectable artemether was the most widely used (52.0% of 1238 cases), and in pregnant women, injectable artesunate was used in 270 cases (56.25%).

**Table 7: Use of antimalarial drugs recommended by national guidelines for severe malaria management**

Patients type	Injectable artesunate n (%)	Rectal artesunate n (%)	Injectable artemether n (%)	Injectable quinine n (%)
Children under 6; n= 4409	3404 (77.2)	5 (0.1)	933 (21.2)	114 (2.6)
Adults; n= 2383	522 (21.9)	1 (0.00)	1238 (52.0)	611 (25.6)
Pregnant women; n= 480	270 (56.25)	2 (0.4)	61 (12.7)	147 (30.6)
Total; n= 7272	4196 (57.7)	8 (0.1)	2232 (30.7)	872 (12.0)

Table 8 describes the choice of diagnostic tools based on the healthcare provider's qualification. The first choice of most surveyed people was thick blood smears over RDTs. Only matrons preferred RDTs to thick blood smears.

**Table 8: Choice of diagnostic tool based on the qualifications of the interviewed healthcare provider**

Healthcare provider	Thick blood smear n (%)	RDT n (%)
Medical doctor; n= 80	69 (86.2)	10 (12.5)
Medical student; n=44	39 (88.6)	5 (11.4)
Midwife; n= 26	20 (76.9)	6 (23.1)
Nurse level 2; n= 30	24 (80.0)	6 (20.0)
Nurse level 1; n= 33	25 (75.8)	8 (24.2)
Obstetric nurse; n= 12	8 (66.7)	4 (33.3)
Matron; n= 1	0 (0.00)	1 (100)
Pharmacist; n= 2	2 (100)	0 (0.00)
Total; n= 228	187 (82.0)	40 (17.5)

The first-line treatment was injectable artesunate for 163 healthcare providers (71.5%), followed by injectable quinine for 35 healthcare providers (15.4%). Almost no one chose rectal artesunate (Table 9).

**Table 9: Choice of first-line treatment by healthcare providers**

Healthcare providers qualification	Injectable artesunate n (%)	Rectal artesunate n (%)	Injectable artemether n (%)	Injectable quinine n (%)
Medical doctor; n= 80	64 (80.0)	0 (0.0)	4 (5.0)	12 (15.0)
Medical student; n=44	31 (70.5)	0 (0.0)	4 (9.1)	8 (18.2)
Midwife; n= 26	22 (84.6)	0 (0.0)	0 (0.0)	4 (15.4)
Nurse level 2; n= 30	17 (56.7)	0 (0.0)	8 (26.7)	5 (16.7)
Nurse level 1; n= 33	20 (60.6)	0 (0.0)	9 (27.3)	4 (12.1)
Obstetric nurse; n= 12	8 (66.7)	1 (8.3)	2 (16.7)	1 (8.3)
Matron; n= 1	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
Pharmacist; n= 2	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)
Total; n= 228	163 (71.5)	1 (0.4)	27 (11.8)	35 (15.4)

#### 4.4. Severe malaria training and awareness of national guidelines on severe malaria management in the healthcare centres

Severe malaria training had been provided mostly to doctors (58.8%). The study also showed that none of the matrons or pharmacists had received any training on severe malaria management (Table 10).

**Table 10: Training on severe malaria management**

Healthcare provider qualification	Number of people trained on severe malaria management n (%)
Medical doctor; n= 80	47 (58.8)
Medical student; n=44	17 (38.6)
Midwife; n= 26	15 (57.7)
Nurse level 2; n= 30	14 (46.7)
Nurse level 1; n= 33	9 (27.3)
Obstetric nurse; n= 12	5 (41.7)
Matron; n= 1	0 (0.0)
Pharmacist; n= 2	0 (0.0)
Total; n= 228	107 (46.9)

As shown in Table 11, 40 of the healthcare providers interviewed in Hôpital du Mali (76.9%) said that the national guidelines for severe malaria management were not available, and 29 of the 30 healthcare providers interviewed in Sévaré (96.7%) said they had been given the national guidelines. Overall, the availability of NMCP guidelines for severe malaria management was confirmed by 64.9% of healthcare providers (Table 11).

**Table 11: Availability of national guidelines for severe malaria management**

	National guidelines for severe malaria management			
	Presence	Absence	Unknown	Total
Hôpital du Mali	11 (21)	40 (77)	1 (2)	52 (23)
CSREF de la Commune VI	20 (87)	3 (13)	0 (0)	23 (10)
CSREF de San	17 (74)	4 (17)	2 (9)	23 (10)
CSREF de Sélingué	13 (59)	7 (32)	2 (9)	22 (10)
CSREF de Sikasso	31 (84)	6 (16)	0 (0)	37 (16)
Hôpital de Sikasso	10 (59)	7 (41)	0 (0)	17 (8)
CSREF de Mopti	17 (71)	6 (25)	1 (4)	24 (11)
Hôpital de Sévaré	29 (97)	1 (3)	0 (0)	30 (13)
Total	148 (65)	74 (33)	6 (3)	228

#### 4.5. Obstacles to healthcare provider compliance to national guidelines for severe malaria management

Table 12 describes the obstacles to national guidelines implementation for severe malaria management. Overall, 50.44% of healthcare providers declared that the major obstacle to using injectable artesunate was its high cost. Regarding rectal artesunate, 84.21% of healthcare providers reported not being aware of any obstacle limiting its use. Regarding injectable artemether, 64.47% of healthcare providers said that there were no constraints limiting its use. Regarding quinine, 107 (46.93%) of healthcare providers reported that side effects limited its use. The other barriers included the administration route (e.g. intramuscular injection) and healthcare providers' qualifications.

**Table 12: Obstacles to national guidelines implementation for severe malaria management**

Obstacles	Injectable artesunate n (%)	Rectal artesunate n (%)	Injectable artemether n (%)	Injectable quinine n (%)
High cost	115 (50.44)	6 (2.63)	20 (8.77)	2 (0.88)
Availability	14 (6.14)	11 (4.82)	2 (0.88)	1 (0.44)
Difficulty of preparation	30 (13.16)	2 (0.88)	2 (0.88)	2 (0.88)
Side effects	0 (0.00)	0 (0.00)	3 (1.32)	107 (46.93)
Other	28 (12.28)	5 (3.95)	38 (16.67)	14 (6.14)
None	35 (15.35)	6 (3.51)	147 (64.47)	84 (36.84)
Don't know	6 (2.63)	192 (84.21)	16 (7.02)	18 (7.89)

#### 4.6. Availability of inputs (drugs and diagnostic tools) for the treatment of severe malaria in selected health centre pharmacies

Table 13 shows that shortages of severe malaria management products are very common. Current issues regarding antimalarial availability were mentioned by 216 healthcare providers (94.74%). Diagnostic tool and antimalarial drug shortages were mentioned by 216 (94.74%) and 137 healthcare providers (60.09%), respectively. The median drug shortage duration was 15 days (IQR: 7 – 30).

**Table 13: Availability of severe malaria management tools**

Malaria management tool \ input or product issues	Availability n (%)
Current shortage of drugs for severe malaria	216 (94.74)
Diagnostic tool shortages	226 (99.12)
Drug shortages	137 (60.09)
Drug shortage duration, median (IQR)	15 days (7 – 30)

This survey showed (Table 14) that the most widely available antimalarial drug was injectable artesunate, administered to 206 children under 6 (90.4%) and 120 pregnant women (52.6%).

**Table 14: Availability of free antimalarial drugs (n = 228)**

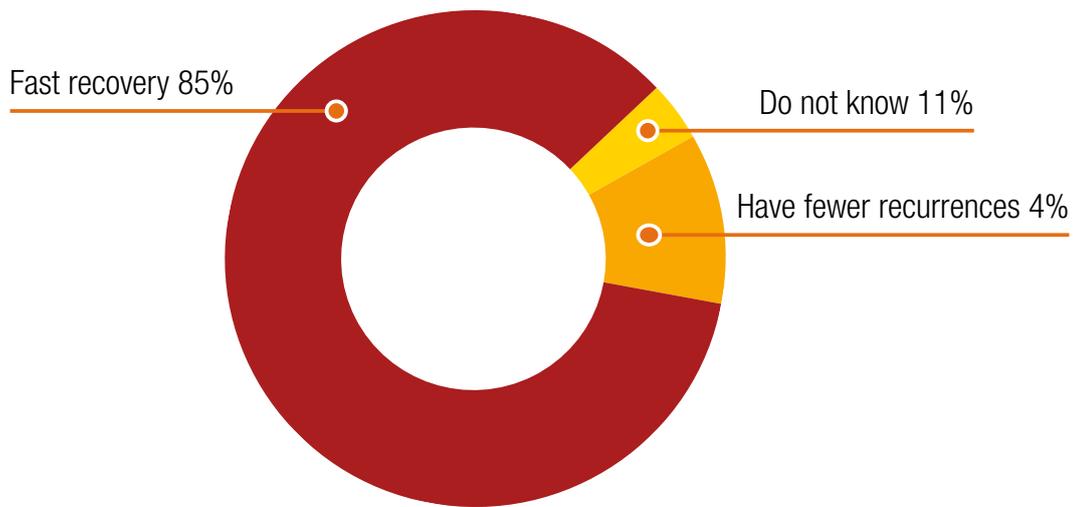
	Injectable artesunate n (%)	Rectal artesunate n (%)	Injectable artemether n (%)	Injectable quinine n (%)
Children under 6	206 (90.4)	22 (09.6)	49 (21.5)	66 (28.9)
Adults	3 (1.3)	2 (00.9)	2 (00.9)	2 (00.9)
Pregnant women	120 (52.6)	3 (01.3)	21 (09.2)	61 (26.8)



### 4.7. Healthcare providers' perception regarding the use of injectable artesunate

Figure 1 shows that 85% of healthcare providers thought that injectable artesunate in severe malaria patients provides a rapid recovery.

**Fig. 1: Perception of health providers regarding the use of injectable artesunate**



The survey (Fig. 2) shows that most healthcare providers reported not being aware of a patient refusing injectable artesunate for the treatment of severe malaria.

**Fig. 2: Patient refusal of injectable artesunate treatment**

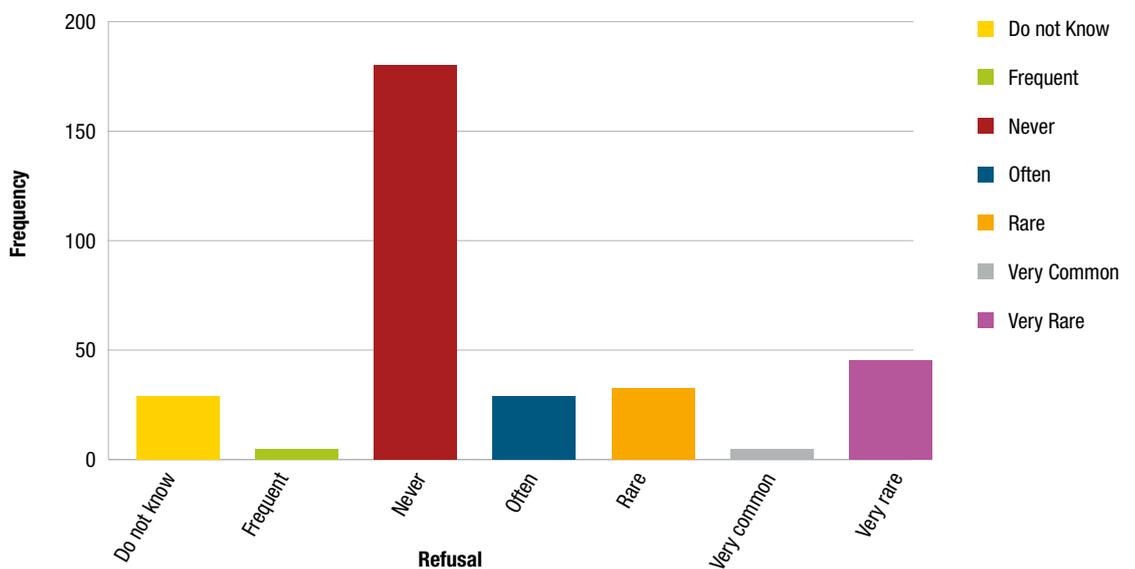
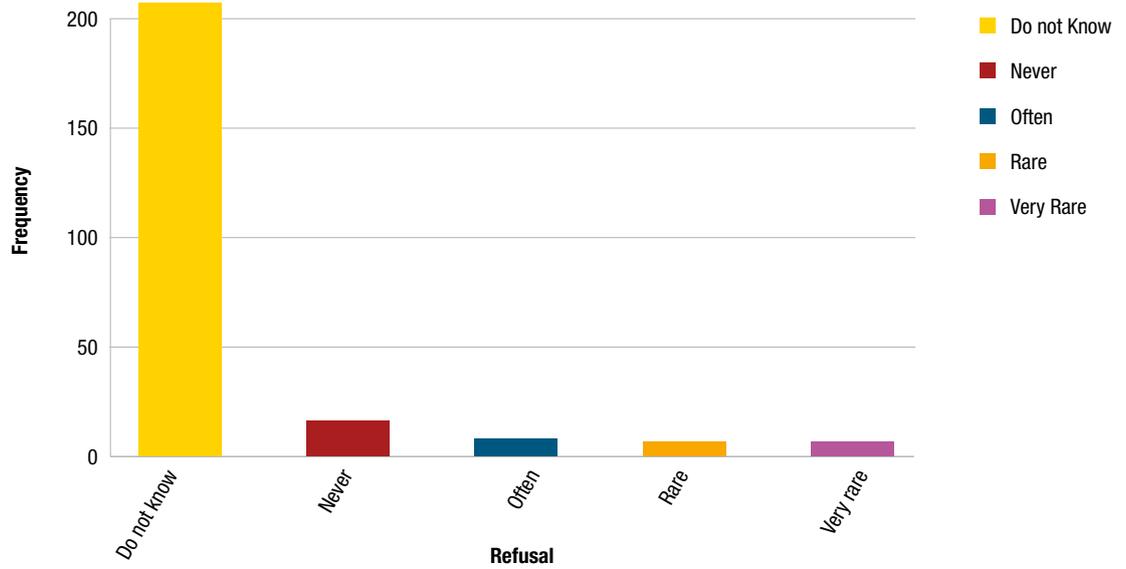


Fig. 3 below shows that most healthcare providers said they did not know if patients refused the administration of rectal artesunate for severe malaria. Rectal artesunate is mostly used as a pre-referral intervention in community health facilities. This explains why it is hardly ever used in reference health centres and hospitals surveyed for the study.

**Fig. 3: Patient refusal of rectal artesunate**



#### 4.8. Treatment outcome

Figure 4 below shows that only 267 out of 3'517 patients (8%) died. Overall, the recovery of 3'250 patients (92%) was recorded in medical registers or patients' files.

**Fig. 4: Treatment outcome.**

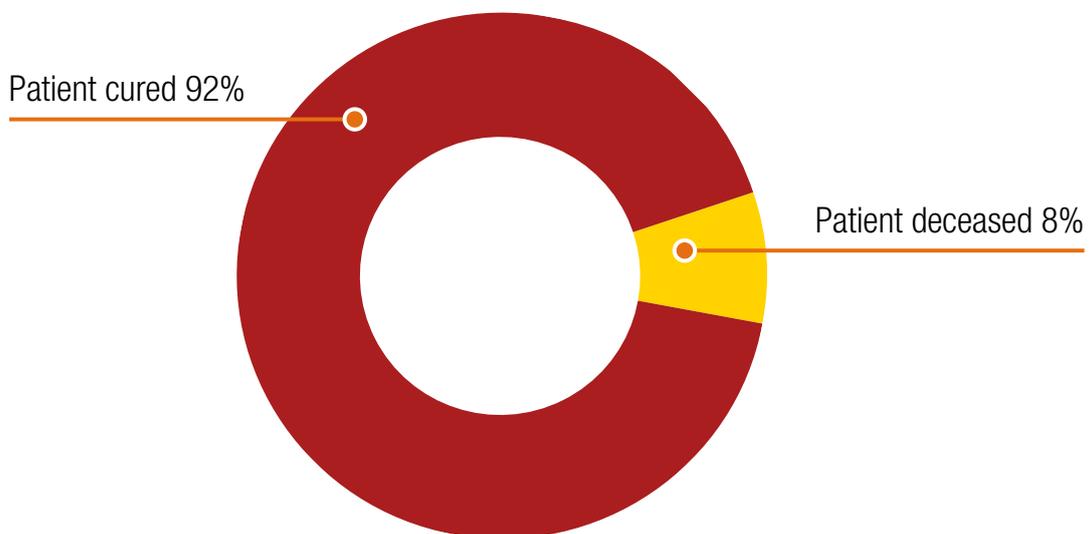


Table 15 shows that, when the management of severe malaria is provided by a nurse, the treatment outcome is not entered in the medical file or the register in 90.2% of cases. However, 51.4% of healthcare providers did not know the outcome of their patients' treatment for severe malaria. This can be explained by the fact that, for most patients, only baseline data was collected from registers.

**Table 15: Treatment outcome based on the health service provider's qualification**

	Patient cured n (%)	Patient deceased n (%)	Ongoing disease n (%)	Do not know n (%)
Medical doctor (n = 3513)	2176 (61.9)	170 (4.8)	12 (0.3)	1155 (32.9)
Medical student (n = 1129)	711 (63.0)	59 (5.2)	2 (0.2)	357 (31.6)
Midwife (n = 37)	33 (89.2)	0 (0.0)	0 (0.0)	4 (10.8)
Nurse (n = 2295)	193 (8.4)	31 (1.4)	2 (0.1)	2069 (90.2)
Unknown (n = 298)	137 (46.0)	7 (2.3)	0 (0.00)	154 (51.7)
Total (n = 7272)	3250 (44.7)	267 (3.7)	16 (0.2)	3739 (51.4)

Table 16 shows the treatment outcome based on the antimalarial drug used. The proportion of patients cured after treatment with injectable artesunate is similar in adults (56.9%) and in children (57.2%). Injectable artesunate seems most effective in pregnant women (91.5% of patients cured). The efficacy rates of the other drugs (injectable artemether and injectable quinine) were similar and greater in pregnant women. This could be explained by the fact that in adults and in children, treatment outcome was generally not entered in the source documents.

**Table 16: Treatment outcome based on antimalarial drug used**

	Patient cured n (%)	Patient deceased n (%)	Ongoing disease n (%)	Do not know n (%)
<b>Injectable artesunate</b>				
Adults	297 (56.9)	24 (4.6)	2 (0.4)	199 (38.1)
Children	1947 (57.2)	151 (4.4)	4 (0.1)	1302 (38.2)
Pregnant women	247 (91.5)	3 (1.1)	3 (1.1)	17 (6.3)
<b>Rectal artesunate</b>				
Adults	1 (100)	0 (0.0)	0 (0.0)	0 (0.0)
Children	0 (0.0)	0 (0.0)	0 (0.0)	5 (100)
Pregnant women	1 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)
<b>Injectable artemether</b>				
Adults	148 (12.0)	14 (1.1)	4 (0.3)	1072 (86.6)
Children	373 (40.0)	53 (5.7)	2 (0.2)	505 (54.1)
Pregnant women	50 (82.0)	1 (1.6)	0 (0.0)	10 (16.4)
<b>Injectable quinine</b>				
Adults	125 (20.5)	24 (3.9)	1 (0.2)	461 (75.5)
Children	42 (36.8)	4 (3.5)	0 (0.0)	68 (59.6)
Pregnant women	135 (91.8)	0 (0.0)	0 (0.0)	12 (8.2)

## 4.9. Administration route

Figure 5 shows that the intravenous route was the most used, with 57% of patients receiving IV artesunate and 12% receiving IV quinine. Intramuscular artemether was used in 31% of patients.

**Fig. 5: Administration routes**



As shown in Table 17, intravenous artesunate was used mostly at the Commune VI CSREF in Bamako (550 cases, 84.5%), followed by Hôpital du Mali (334 cases, 82.9%). Rectal artesunate was used only in the San CSREF (3 cases, 0.2%), the Sélingué CSREF (2 cases, 0.2%), and Hôpital de Sévaré (3 cases, 0.4%). Intramuscular artemether was used mostly in the Sélingué CSREF (532 cases, 55.7%) followed by Hôpital de Sikasso (292 cases, 53.7%). Intravenous quinine was used mostly in the Mopti CSREF (131 cases, 20.6%) followed by Hôpital de Sévaré (147 cases, 18.2%).

**Table 17: Administration route based on health centres**

Health centres	Administration route			
	IV artesunate n (%)	Rectal artesunate n (%)	IM artemether n (%)	IV quinine n (%)
Hôpital du Mali	334 (82.9)	0 (0.0)	43 (10.7)	35 (8.7)
CSREF de la Commune VI	550 (84.5)	0 (0.0)	74 (11.4)	45 (6.9)
CSREF de San	870 (55.0)	3 (0.2)	549 (34.7)	137 (8.7)
CSREF de Sélingué	276 (28.9)	2 (0.2)	532 (55.7)	72 (7.5)
CSREF de Sikasso	848 (50.1)	0 (0.0)	567 (33.5)	289 (17.1)
Hôpital de Sikasso	305 (56.1)	0 (0.0)	292 (53.7)	16 (2.9)
CSREF de Mopti	479 (75.3)	0 (0.0)	47 (7.4)	131 (20.6)
Hôpital de Sévaré	534 (66.0)	3 (0.4)	128 (15.8)	147 (18.2)
Total	4196 (41.96)	8 (0.1)	2232 (30.7)	872 (12.0)

IV= intravenous; IM= intramuscular

Table 18 shows that children received mostly IV artesunate (3404 cases; 81.1%), whereas adults received mostly IV quinine (611 cases; 70.1%) or IM artemether (1238 cases; 55.5%).

**Table 18: Administration route per patient type**

Patient type	Administration route			
	IV artesunate n (%)	Rectal artesunate n (%)	IM artemether n (%)	IV quinine n (%)
Adults	522 (12.4)	1 (12.5)	1238 (55.5)	611 (70.1)
Children	3404 (81.1)	5 (62.5)	933 (41.8)	114 (13.1)
Pregnant women	270 (6.4)	2 (25.0)	61 (2.7)	147 (16.9)

IV= intravenous; IM= intramuscular

Doses administered depended on patient type. As expected, the mean dose was higher in adults and pregnant women than in children. Treatment duration also varied based on patient type.

**Table 19: Doses of injectable, artemether and quinine per patient type**

Patient type	Type of patients		
	Children Mean (SD)	Adult Mean (SD)	Pregnant women Mean (SD)
Doses administrated (mg)	3404 (81.1)	161.93 (43.40)	159.43 (27.25)
Number of administration for attack dose	2.88 (0.45)	2.95 (0.27)	2.99 (0.14)
Number of day of treatment	2.84 (1.51)	4.03 (1.23)	3.89 (1.01)



## 5. Conclusions

This survey shows that four of the eight health centers surveyed registered a rate between 25-49% of unknown confirmation results, mainly due to lacking diagnostic tools, while patients were treated as severe malaria patients.

Injectable artesunate is the first-line treatment for children under 6 and pregnant women, followed by injectable artemether and quinine.

Pre-referral rectal artesunate is rarely used by healthcare providers across all sites.

As described by healthcare providers, the major obstacle to using injectable artesunate is its high cost. Diagnostic tools and drugs are available most of the time, and shortages do not last long.

The majority of healthcare providers is satisfied with injectable artesunate for the management of severe malaria because it provides a rapid recovery.

Although IV artesunate was the most frequently used drug, there were still 30% of patients who were treated with IM artemether.

Medical doctors are the most highly trained healthcare professionals involved in severe malaria management.

## 6. Recommendations

Based on the results of this study, we make the following recommendations:

1. For the NMCP
  - Monitor national guideline compliance when treating severe malaria in pregnant women, children and adults
  - Provide training on severe malaria management for all healthcare providers
  - Guarantee the availability of rectal artesunate and of diagnostic tools in all health centres
2. For healthcare providers
  - Apply the national guidelines correctly
  - Follow-up all severe malaria patients
  - Fill in data supports correctly (registers and patient files)
  - Monitor the safety of all drugs used, in compliance with national guidelines
3. For researchers
  - Continue to evaluate the efficacy of rectal and injectable artesunate for the treatment of severe malaria in pregnant women, children and adults in Mali
  - Monitor the tolerance of all drugs used, in compliance with national guidelines

