PASS information

Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa
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EU PAS Register Number	EUPAS43920
Active substance	ATC code: J07XA01 RTS,S (portion of *Plasmodium falciparum* circumsporozoite protein fused with hepatitis B surface antigen [RTS], and combined with hepatitis B surface antigen [S]). AS01 (liposome-based Adjuvant System containing the immunoenhancers MPL (3-O-desacyl-4'-monophosphoryl lipid A) and QS-21).
Medicinal product	Mosquirix™
Product reference	EMEA/H/W/002300/001
Procedure number	EMEA/H/W/002300/MEA/005
Marketing Authorisation Holder(s)	GlaxoSmithKline Biologicals Rue de l'Institut 89 1330 Rixensart, Belgium
Joint PASS	No

Research question and objectives	Co-Primary Objectives In participants aged 6 months to <10 years: • To obtain longitudinal estimates of *P. falciparum* parasite prevalence in order to characterize malaria transmission intensity in a standardised way at centers conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa. • To obtain longitudinal estimates of the use of malaria control interventions in centers conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.
Countries of study	Burkina Faso, Ghana, Kenya, Malawi, Tanzania, Senegal
Author	Coordinating author: PPD, Freelance Scientific Writer (on behalf of GSK)

Marketing authorization holder

Marketing authorization holder	GlaxoSmithKline Biologicals Rue de l'Institut 89, 1330 Rixensart, Belgium
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GlaxoSmithKline Biologicals (GSK) PASS Study Report INS-BIO-PASS-1010 version 02

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TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

1. ABSTRACT

Title

An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post-RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub Saharan Africa.

Keywords

RTS,S/AS01$_E$, malaria, sub-Saharan Africa, MTI, prevalence.

Study Report revision history

Final Interim Report (Surveys 1 & 2): 21 August 2017 [EPI-MAL-005 Study Group]

Final Interim Report (Surveys 3, 4 & 5): 17 March 2021

Erratum to Interim Report (Surveys 3, 4 & 5): 26 January 2022.

Rationale and background

GlaxoSmithKline Biologicals SA (GSK) has developed a pre-erythrocytic *Plasmodium falciparum* (*P. falciparum*) malaria vaccine, RTS,S/AS01$_E$, for routine immunization of infants and children living in sub-Saharan African malaria-endemic countries. The vaccine consists of sequences of the circumsporozoite protein and hepatitis B surface antigen (HBsAg) adjuvanted with AS01 i.e., liposome formulation with 3-O-desacyl-4'-monophosphoryl lipid A (MPL) and Quillaja saponaria Molina, fraction 21 (QS-21) immunostimulants.

To assess vaccine safety, effectiveness and impact, GSK designed a baseline (EPI-MAL-002) and a Phase 4 (EPI-MAL-003) observational study, allowing temporal and concurrent comparisons of the occurrence of malaria cases and adverse events in RTS,S vaccinated vs. unvaccinated children. In parallel with those studies, the present observational cross-sectional annual study (EPI-MAL-005) aimed to estimate *P. falciparum* parasite prevalence and the use of malaria control interventions (MCIs) during 10 consecutive years, using standardized methodologies and multiple diagnostic testing.

In 2015, the European Medicines Agency (EMA) gave a positive opinion for the use of the vaccine in children aged 6 weeks to 17 months at first dose. In January 2016, the World Health Organisation (WHO) recommended a pilot implementation of RTS,S/AS01$_E$ in children of 5–17 months of age in 3-5 epidemiological sub-Saharan African settings with moderate to high malaria transmission. In April 2017, WHO announced the pilot introduction of the vaccine based on a cluster-randomized design in selected areas of Ghana, Kenya and Malawi through the national Expanded Program on Immunisation (EPI), in the framework of the Malaria Vaccine Implementation Programme (MVIP).

Considering the WHO recommendation to operate the MVIP in moderate to high transmission areas, this study will allow (1) characterizing the malaria transmission intensity (MTI) before RTS,S/AS01$_E$ vaccine introduction in different countries/areas, including those participating in the MVIP; (2) over time, monitoring changes in MTI and changes in the use of MCIs before and after vaccine introduction in those areas in order to adjust the temporal and concurrent comparison analyses for potential year-to-year and/or geographical variations.

Research question and objectives

Co-Primary objectives
In participants aged 6 months to <10 years: • To obtain longitudinal estimates of *P. falciparum* parasite prevalence in order to characterize malaria transmission intensity in a standardized way at centers conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa. • To obtain longitudinal estimates of the use of malaria control interventions in centers conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.
Secondary objectives
In participants aged 6 months to <10 years: • To estimate trends in longitudinal estimates of the parasite prevalence of *P. falciparum* by vaccine eligible or ineligible subgroups and overall. • To obtain longitudinal estimates of the prevalence of *Plasmodium* species other than *P. falciparum*; overall and by age group. • To estimate longitudinal trends in receipt and timing of the third dose of DTP/HepB/Hib and the first dose of measles EPI vaccines, at around 14 weeks and 9 months of age respectively, as appropriate by country. • To describe changes in care seeking behaviors for reported fever or malaria in the previous 14 days. • To assess within-site geographical heterogeneity in malaria transmission intensity. To describe individual malaria prevention measures and risk factors for clinical malaria according to the parasite density observed.
Tertiary objectives
In participants aged 6 months to <10 years: • To compare asexual and sexual (gametocyte) parasitaemia (qualitative and quantitative-density) in the RTS,S/AS01$_E$ vaccinated and unvaccinated subjects. • To compare asexual and sexual (gametocyte) parasitaemia (qualitative and semi-quantitative-density) when measured by microscopy or NAAT.

DTP/HepB/Hib = Diphtheria-tetanus-whole-cell pertussis-hepatitis B- Haemophilus influenza type b pentavalent vaccine; EPI = Expanded Program on Immunisation; NAAT = Nucleic Acid Amplification Test

Study design

- A multi-center, epidemiology longitudinal cross-sectional study at centers in sub-Saharan Africa that participated in GSK's EPI-MAL-002 and EPI-MAL-003 studies.
- No study vaccine was administered in this epidemiology study.
- All medications that may influence malaria parasitemia within 14 days prior to each survey were recorded.
- Axillary body temperature of all participants at the time of the survey were recorded.

- A capillary blood sample was obtained for evaluation of malaria infection by blood slide and nucleic acid amplification test (NAAT). In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours or other symptoms/signs of clinical malaria, a rapid diagnostic test (RDT) was conducted, and if positive, treatment was given according to National guidelines. If a participant for whom no RDT was required was identified as being parasite positive following microscopy, National guidelines were to be followed for clinical management of the participant.
- Microscopy and NAAT were used to evaluate the level of asexual and sexual parasitemia.
- Serious adverse events (SAEs) associated with the study procedure (capillary blood sampling) were collected.
- Geographic Information System (GIS) was used to determine geographical variability in MTI locally. Study areas were mapped by villages using grid referencing. Participants were attributed to their village, however, to avoid personally identifiable information (PII), small villages were grouped when the number of participants was less than 10, so that it was not possible to identify 1 participant from 1 village. Therefore, the study area was divided into segments with a minimum of 10 participants by segment regrouping villages by proximity if needed. Villages were grouped at the time of random sampling of the study population. A map was drawn showing the location of numbered segments, each numbered with a unique ID code and containing 1 or more villages. This map was not submitted to GSK, but segments were reported by their ID code and surface (km^2) and participants were attributed to a segment code in the study database.
- Each study site was requested annually to provide center specific information about interventions from the malaria control program in the study area and to provide meteorological data for the study site such as rainfall and temperature.
- This study involved 10 annual cross-sectional surveys during malaria peak transmission.

Setting

The ancillary EPI-MAL-005 study was planned to be conducted in sites defined in the EPI-MAL-002 and EPI-MAL-003 protocols. In alignment with the MVIP, the study sites participating in EPI-MAL-005 from Survey 5 onwards were selected from the 3 countries where the RTS,S/AS01$_E$ vaccine was to be implemented: Ghana, Kenya and Malawi.

The study population was defined as study participants 6 months to <10 years of age living in Health and Demographic Surveillance System (HDSS), or equivalent system, catchment areas of the sites participating in the EPI-MAL-002 and EPI-MAL-003 studies. Participants already enrolled in EPI-MAL-002 and EPI-MAL-003 were eligible for participation in EPI-MAL-005.

The age group for enrolment was selected in this study as this permits analysis of parasite prevalence according to the WHO definition (2-9 years) and by the Joint Technical Expert Group (JTEG) requested age (<5 years).

At least 10 annual cross-sectional surveys at peak transmission would provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by the EPI-MAL-002 and EPI-MAL-003 studies. Malaria transmission is highly seasonal so surveys were carried out during the course of the rainy season preferably when rains decreased, which is the period of highest malaria transmission. Annual fluctuations may be seen in all endemic areas and a longitudinal assessment would allow for a better appreciation of the scale and trend of this annual variation. Endemicity is dependent on several environmental factors including climate (rain and temperature), access to malaria care, and use of other MCIs.

Participants and study size

The planned sample size per site and by survey was a maximum of 600 participants: 400 participants aged 6 months to <5 years (6M-4Y age group) and 200 participants aged 5 to <10 years (5Y-9Y age group).

Variables and data sources

Primary endpoints
• Occurrence of *P. falciparum* parasitemia (using microscopy). *Criteria/definitions: infection determined using a blood smear slide and determined using microscopy.* • Occurrence of malaria control interventions. *Criteria/definitions: malaria control measures are mosquito net usage (including ITN and LLIN), IRS, SMC, IPTi, and ACT therapy received within the last 14 days.*
Secondary endpoints
• Demography and history characteristics *Criteria/definitions: gender, age, medical history.* • Occurrence of *Plasmodium* species other than *P. falciparum* (using microscopy) *Criteria/definitions: infection with Plasmodium species other than P. falciparum determined using a blood smear slide and microscopy.* • Occurrence of uptake and timing of the third dose of DTP/HepB/Hib and the first measles EPI vaccines *Criteria/definitions: vaccination record of receipt of Dose 3 of the DTP/HepB/Hib and the first dose of the measles EPI vaccines.* • Occurrence of anti-malarial therapy *Criteria/definitions: any anti-malarial therapy received in the last 14 days.* • Occurrence of measured fever *Criteria/definitions: any measured fever at time of visit (axillary temperature ≥37.5°C).* • Occurrence of reported fever *Criteria/definitions: any reported fever occurring in the last 24 hours.* • Occurrence of care seeking behavior *Criteria/definitions: occurrence of visits to health providers following reported fever or malaria in the previous 14 days.* • Geo-referencing characteristics *Criteria/definitions: positioning of the subject's residence will be attributed to a segment with a unique ID from the grid referencing study area map in which the subject resides, where necessary, grouping small geographically proximate villages so that each segment has at least 10 study subjects to avoid PII, and proceeding as far as geographically appropriate.* • Occurrence of individual malaria prevention measures and risk factors *Criteria/definitions: malaria prevention measures are repellents and local herbs not specifically recommended by the national program and risk factors are rural/urban area, construction material for the house, floor and roof, type of eaves (open/closed), use of electricity and water source (distance from and type).*

Tertiary endpoints
• Occurrence of RTS,S/AS01$_E$ vaccine doses *Criteria/definitions: vaccination record of each dose received of the RTS,S/AS01$_E$ vaccine.* • Occurrence of *P. falciparum* parasitemia (using NAAT) *Criteria/definitions: detection of P. falciparum on dried blood spot and determined using NAAT.* • Occurrence of sexual *P. falciparum* parasitemia (using microscopy) *Criteria/definitions: detection of sexual P. falciparum using a blood smear slide and determined using microscopy.* • Occurrence of sexual *P. falciparum* (using NAAT/QT-NASBA) *Criteria/definitions: detection of sexual P. falciparum on dried blood spot and determined using NAAT.*

ACT = artemisinin based combination therapy; DTP/HepB/Hib = Diphtheria-tetanus-whole-cell pertussis-hepatitis B-Haemophilus influenza type b pentavalent vaccine; EPI = Expanded Program on Immunisation; IRS = indoor residual spraying; IPTi = intermittent preventative treatment in infants; ITN = insecticide treated nets; LLINs = long lasting insecticidal nets; NAAT = Nucleic Acid Amplification Test; PII = Personally Identifiable Information; QT-NASBA = Quantitative Nucleic Acid Sequence-Based Amplification; SMC = seasonal malaria chemoprevention

Data sources

All data were collected in the electronic case report form (eCRF), as summarized in the below table.

Malaria Control Program Questionnaire	• Survey date
	• Meteorological data (temperature/rain/humidity details)
	• Malaria control interventions:
	  ○ Bednet usage, including ITNs, LLINs
	  ○ IRS usage
	  ○ Other MCIs (ACT, IPT, SMC etc.)

Participant data	• Demography • Informed consent • Eligibility • Previous participation • Medical history
Household Questionnaire	• Malaria risk factors
Sample collection	• Malaria RDT • Slide readings details and slide readings results • Slide methodology used • Filter paper collection
Log status	• Concomitant vaccination details • Medication details
Expedited AEs	• SAE following capillary blood sample collection
Study conclusion	• Last information (date of last contact or last information etc.)

ACT = artemisinin based combination therapy; AE = adverse event; IRS = indoor residual spraying; IPT = intermittent preventative treatment; ITNs = insecticide treated nets; MCI = malaria control intervention; LLINs = long lasting insecticidal nets; RDT = rapid diagnostic test; SAE = serious adverse event; SMC = seasonal malaria chemoprevention

Results

Participants

EPI-MAL-005 was planned to be conducted in sites defined in the EPI-MAL-002 and EPI-MAL-003 protocols. From Survey 5 onwards, in alignment with the MVIP and implementation of RTS,S/AS01$_E$ vaccination, the study sites participating in EPI-MAL-005 were selected from the 3 countries where the RTS,S/AS01$_E$ vaccine was to be implemented (Ghana, Kenya and Malawi), and enrolment to sites in Burkina Faso, Senegal and Tanzania early terminated (Table 1).

Table 1 Study sites participating in each survey

	Surveys 1&2	Survey 3	Survey 4	Survey 5*	Survey 6*	Surveys 7-10*
BF_Nouna	X	X	X			
BF_Sapone	X	X	X			
SN_Keur Soce	X					
SN_Niakhar	X					
TZ_Korogwe	X					
GH_Kintampo_EXP	X	X	X	X	X	X
GH_Kintampo_UNEXP***					X	X
GH_Navrongo_EXP			X	X	X	X
GH_Navrongo_UNEXP***					X	X
KE_Kombewa_EXP	X	X	X	X	X	X
KE_Nyando_UNEXP***					X	X
KE_Bondo_UNEXP				X	X	X
KE_Gem_EXP				X	X	X
MA_Chikwawa_UNEXP**				X		X
MA_St Montfort_EXP**				X		X
MA_Mangochi_EXP				X	X	X
MA_Monkey Bay_UNEXP				X	X	X

Shaded fields represent sites not participating in a specific survey
BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania
EXP= exposed sites: Sites in which the RTS,S vaccine was planned to be / was implemented. Subject selection in the study was not based on their vaccination status, but vaccinated subjects might be randomly selected from the base population
UNEXP = unexposed sites: Sites in which the RTS,S vaccine was not planned to be / was not implemented during the course of the study. Subject selection in the study was not based on their vaccination status. Vaccinated subjects could still be randomly selected in this population if vaccination happened in an exposed cluster due to cross-cluster migration
*RTS,S vaccination started to be implemented concurrently to the conduct of Survey 5 in some of the exposed sites
**MA_Chikwawa and MA_St Montfort did not participate in Survey 6 due to the COVID-19 pandemic
***Unexposed sites in KE_Nyando, GH_Kintampo and GH_Navrongo did not participate in Survey 5 as the study sites could not be initiated on time

The number of participants included in the Total Cohort and the According to Protocol (ATP) Cohort according to *P. falciparum* infection status by survey are presented in Table 2.

Table 2 Number of participants included in the Total Cohort and ATP Cohort by survey

Survey	Total Cohort	ATP Cohort		
		PF_INF n (%)	NOT_INF n (%)	Total
1	4214	1187 (28.2)	3021 (71.8)	4208
2	4204	1232 (29.3)	2967 (70.7)	4199
3	2400	984 (41.0)	1415 (59.0)	2399
4	3003	958 (31.9)	2042 (68.1)	3000
5	5417	1022 (19.0)	4355 (81.0)	5377
6	5991	1246 (20.8)	4741 (79.2)	5987
7	7246	1138 (15.7)	6103 (84.3)	7241
8	7220	909 (12.6)	6308 (87.4)	7217
9	7203	888 (12.3)	6315 (87.7)	7203
10	7202	810 (11.2)	6392 (88.8)	7202

ATP = According to Protocol
Total Cohort = Total Effective Cohort, i.e., excludes participants with invalid inform consent (code 900)
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy

- As defined per protocol stratification design, the proportion of participants in the JTEG age group of 6M-4Y was similar across surveys, ranging from 66.5% (Surveys 2 and 6) to 66.8% (Surveys 3, 4, 8 and 10).
- The mean±standard deviation (SD) age ranged from 4.02±2.73 (Survey 8) to 4.05±2.75 years (Surveys 2 and 4).
- The male:female ratio was generally equal across surveys.

Summary description of main endpoints

Primary objectives

P. falciparum prevalence – Survey 1 to Survey 10

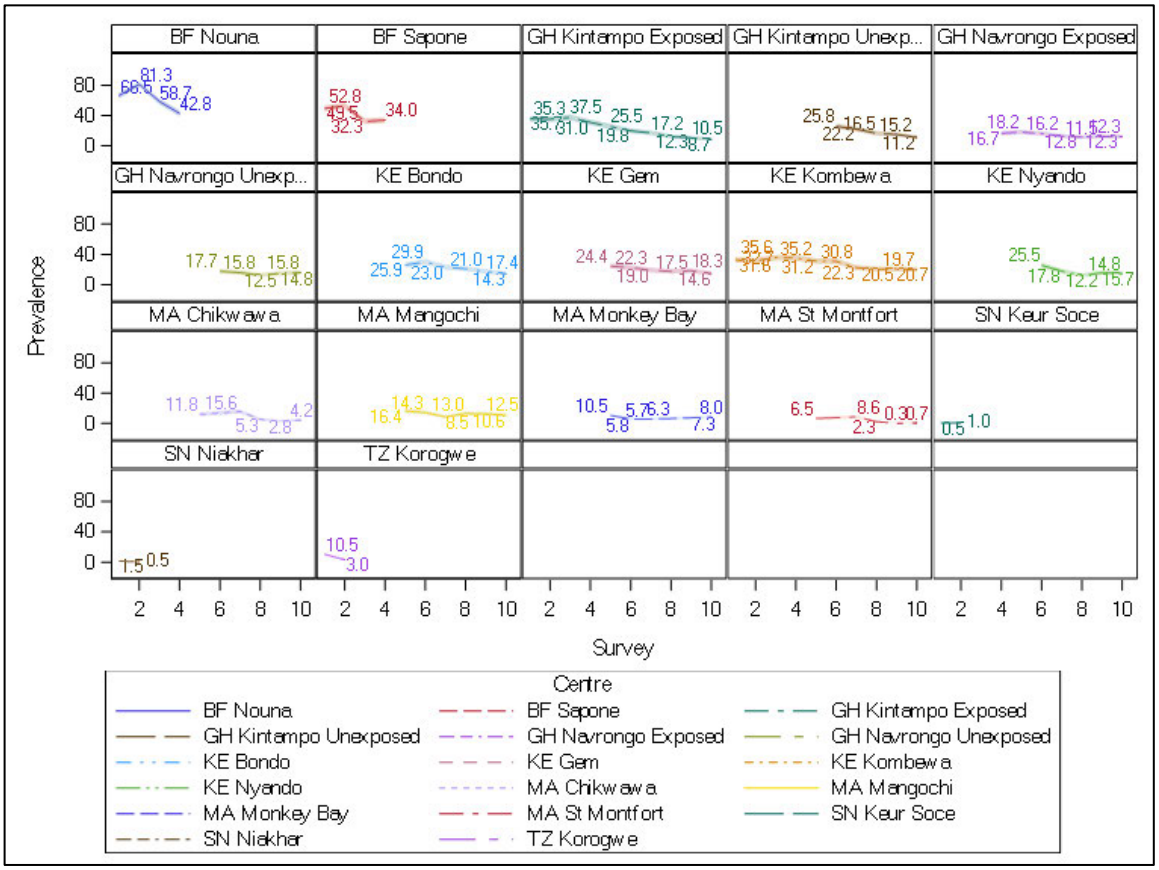
- Overall sites, *P. falciparum* parasitemia prevalence was highest in Survey 3 (41.02% of participants), after which prevalence decreased with subsequent surveys to Survey 8 (12.60% of participants) and remained at a similar level up to Survey 10 (11.25% of participants) (Table 3). The higher prevalence in Surveys 1-4 reflects the high malaria transmission intensity in the Burkina Faso sites participating in the earlier surveys. Post-RTS,S/AS01$_E$ vaccination (Survey 5 to Survey 10), *P. falciparum* prevalence generally decreased over surveys in most centers in Ghana, Kenya and Malawi (Figure 1).

Table 3 Overall *P. falciparum* parasitemia prevalence according to Survey year (ATP Cohort)

Survey year	n	N	Proportion (in %)	95% CI	
				LL	UL
Survey 1	1187	4208	28.21	26.85	29.59
Survey 2	1232	4199	29.34	27.97	30.74
Survey 3	984	2399	41.02	39.04	43.02
Survey 4	958	3000	31.93	30.27	33.64
Survey 5	1022	5377	19.01	17.97	20.08
Survey 6	1246	5987	20.81	19.79	21.86
Survey 7	1138	7241	15.72	14.88	16.58
Survey 8	909	7217	12.60	11.84	13.38
Survey 9	888	7203	12.33	11.58	13.11
Survey 10	810	7202	11.25	10.53	12.00

ATP = According to Protocol
N = number of subjects with known result for *P. falciparum* parasitemia test measured by microscopy
n = number of subjects *P. falciparum* parasitemia infected measured by microscopy
% = n/N x 100
LL, UL = 95% Lower and Upper exact confidence limits (CI)

Figure 1 *P. falciparum* parasitemia prevalence by center and survey (ATP Cohort)



ATP = according to protocol; BF = Burkino Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania
Prevalence % = number of subjects *P. falciparum* parasitemia infected measured by microscopy / number of subjects with known result for *P. falciparum* parasitemia test measured by microscopy x 100

- Overall, in all 10 surveys, the prevalence of *P. falciparum* was significantly lower in the JTEG age group of 6M-4Y vs. 5Y-9Y. This significant difference in prevalence of *P. falciparum* between JTEG age groups was also observed in most centers in each survey.
- *P. falciparum* prevalence varied across centers. Considering study sites from Ghana, Kenya and Malawi only, the prevalence of *P. falciparum* ranged from:
  - 0% in MA St Montfort EXP (Survey 9) to 32.75% in KE Kombewa EXP (Survey 4) in the 6M-4Y JTEG age group
  - 0.99% in MA St Montfort (Survey 10) to 57.50% in GH Kintampo EXP (Survey 1) in the 5Y-9Y JTEG age group.
- Overall, in all 10 surveys, the prevalence of *P. falciparum* was also lower in the WHO age group of 6M-1Y vs. 2Y-9Y.
- The *P. falciparum* prevalence generally increased with the annual age up to 6 years in all 10 surveys with no consistent trend in the 6-9 years of age group.
- The overall prevalence of *P. falciparum* was lower in vaccine eligible compared to ineligible subgroups, across all 10 surveys.
- Although participants were to receive the RTS,S/AS01$_E$ vaccine in exposed sites from Survey 5 onwards, only 4 participants were vaccinated in Survey 5. In Surveys 6 to 10, 4.3% (Survey 6), 15.0% (Survey 7), 22.4% (Survey 8), 27.3% (Survey 9) and 38.5% (Survey 10) of participants received at least 1 dose of RTS,S/AS01$_E$ vaccine. Overall in Surveys 6 to 10, the prevalence of *P. falciparum* was lower in RTS,S/AS01$_E$ vaccinated compared to unvaccinated participants.
- Overall sites, the prevalence of *P. falciparum* by microscopy was higher in participants with fever vs. no fever measured at the visit in all 10 surveys. The same finding was generally observed for each center.
- In all 10 surveys, the prevalence of *P. falciparum* was significantly heterogenous among centers ($p<0.0001$) for both JTEG and WHO age groups.
- There was no significant difference in the prevalence of *P. falciparum* between gender overall and in each center in all 10 surveys.

Malaria control interventions

- Overall sites, across all 10 surveys, bednet usage was high, ranging from 85.0% (Survey 9) to 91.1% (Survey 4), of which:
  - 44.6% (Survey 6) to 72.1% (Survey 3) were new bednets
  - 63.2% (Survey 3) to 89.9% (Survey 4) were impregnated bednets
  - 18.3% (Survey 4) to 41.7% (Survey 6) were pierced/torn bednets.
- Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), bednet usage the night before the visit remained high post-vaccination, ranging between 70.2% to 98.3% pre-vaccination and between 59.8% to 99.5% post-vaccination.

- Bednet usage showed some variations across centers. Considering study sites from Ghana, Kenya and Malawi only, the percentage of participants who used a bednet the night before the visit ranged from 59.8% in GH Kintampo EXP to 99.7% KE Nyando UNEXP, both in Survey 10, of which 0.6% in KE Kombewa EXP (Survey 3) to 100% in KE Kombewa EXP (Survey 10) were impregnated bednets.
- Overall sites, a higher proportion of participants slept under a bednet the night before the visit in the JTEG age group of 6M-4Y vs. 5Y-9Y in each survey. Considering study sites from Ghana, Kenya and Malawi only, this significant difference was observed in the majority of surveys in Malawi sites and KE Gem EXP.
- Overall sites, in all 10 surveys, a significantly higher percentage of participants slept under a bednet the night before the visit when comparing vaccine eligible vs. ineligible subgroups.
- There was no significant difference in bednet usage according to gender overall sites, with the exception of Survey 2 in which more females than males used bednets. There was no significant difference in bednet usage according to gender by center in any survey.
- Other MCIs (i.e., commercial/traditional repellents, mosquito coils, insecticide sprays) were rarely used. Across surveys, 74.0% (Survey 10) to 91.3% (Survey 3) of participants did not use any of these methods in the last 7 days before the visit.
- Considering study sites from Ghana, Kenya and Malawi only, the percentage of participants who did not use any commercial/traditional repellents, mosquito coils or insecticide sprays in the last 7 days before the visit ranged from 49.5% in GH Kintampo EXP (Survey 7) to 99.0% KE Kombewa EXP (Survey 8).
- The percentage of participants who did not use any commercial/traditional repellents, mosquito coils or insecticide sprays in the last 7 days before the visit was similar across surveys in the 6M-4Y and 5Y-9Y age groups, and in females and males.

Secondary objectives

Prevalence of Plasmodium species other than P. falciparum

- Across all 10 surveys, the overall proportion of participants infected with *P. malariae* was ≤3.0% and with *P. ovale* <1.0%. Participant infection with *P. vivax* was only recorded in 3 participants across surveys. The highest prevalence for *P. malariae* was measured in BF Nouna reaching 9.5% (Survey 2) and for *P. ovale* in KE Gem EXP reaching 3.0% (Survey 9). *P. vivax* was recorded in 1 participant each in TZ Korogwe (Survey 2), KE Kombewa EXP (Survey 3), and KE Bondo UNEXP (Survey 7).
- In all 10 surveys, the overall proportion of participants infected with *P. malariae* was higher in participants co-infected with *P. falciparum* compared to those not infected with *P. falciparum*. Although co-infected numbers were low, the proportion of participants infected with *P. falciparum* and *P. ovale* was higher than those infected with *P. ovale* alone. There were too few cases of *P. vivax* to assess any percentage difference by infection status.

Vaccination history

DTP/HepB/Hib (third dose) vaccination

- Overall, across the 10 surveys, 91.7% of participants had received the third dose of any combination of the DTP vaccine (i.e., pentavalent, tetravalent or DTP only): 69.4% (Survey 1), 87.8% (Survey 2), 84.6% (Survey 3), 90.9% (Survey 4), 96.1% (Survey 5), 92.9% (Survey 6), 93.2% (Survey 7), 94.8% (Survey 8), 95.2% (Survey 9) and 97.2% (Survey 10) of participants.
- A lower proportion of participants in the *P. falciparum* infected (PF INF) vs. not infected (NOT INF) group received the third dose of any combination of the DTP vaccine in all 10 surveys, ranging from 58.3% (Survey 1) to 93.6% (Survey 10) and 73.8% (Survey 1) to 97.6% (Survey 10), respectively.
- Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the proportion of participants who received the third dose of any combination of the DTP vaccine remained high post-RTS,S/AS01$_E$ vaccination, ranging from 62.6% to 100% (PF INF group) and 59.5% to 100% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 59.5% to 100% (PF INF group) and 75.3% to 100% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

Measles (first dose) vaccination

- Across all 10 surveys, 84.1% of participants had received the measles (first dose) vaccine: 53.7% (Survey 1), 80.4% (Survey 2), 79.1% (Survey 3), 84.5% (Survey 4), 89.0% (Survey 5), 87.2% (Survey 6), 86.8% (Survey 7), 87.5% (Survey 8), 88.0% (Survey 9) and 89.0% (Survey 10).
- In the majority of surveys, a lower proportion of participants in the PF INF vs. NOT INF group received the measles vaccine (first dose). Participants receiving the measles vaccine (first dose) varied across sites, ranging from 43.6% (Survey 1) to 89.2% (Survey 5) in the PF INF group, and 57.7% (Survey 1) to 89.1% (Survey 10) in the NOT INF group.
- Considering study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the proportion of participants who received the measles (first dose) vaccine ranged from 7.9% to 100% (PF INF group) and 11.9% to 94.8% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 58.1% to 97.0% (PF INF group) and 68.4% to 96.2% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

Care seeking behaviors

Anti-malarial or fever treatment sought in the last 14 days

- Overall sites, 15.7% (Survey 1), 12.8% (Survey 2), 15.1% (Survey 3), 19.0% (Survey 4), 20.6% (Survey 5), 16.9% (Survey 6), 10.0% (Survey 7), 9.8% (Survey 8), 12.5% (Survey 9) and 7.0% (Survey 10) of participants sought anti-malarial or fever treatment in the last 14 days, predominantly at the onset of symptoms across surveys.
- Overall sites, in participants seeking anti-malarial or fever treatment in the last 14 days, a significantly higher proportion was recorded in PF INF vs. NOT INF participants in Surveys 1, 2, 8 and 9, and a significantly lower proportion was recorded in PF INF vs. NOT INF participants in Survey 4; no significant difference was observed in Surveys 3, 5, 6, 7 and 10.
- Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the percentage of participants seeking anti-malarial or fever treatment in the last 14 days remained similar post-RTS,S/AS01$_E$ vaccination, ranging from 8.1% to 39.0% (PF INF group) and 11.1% to 34.7% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 1.0% to 44.3% (PF INF group) and 6.6% to 39.8% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

Malaria hospitalization in the last 3 months

- Overall sites, the proportion of participants hospitalized for malaria in the last 3 months before the visit was low: 2.6% (Survey 1), 2.8% (Survey 2), 3.0% (Survey 3), 3.1% (Survey 4), 2.1% (Survey 5), 2.5% (Survey 6), 1.8% (Survey 7), 2.4% (Survey 8), 2.4% (Survey 9) and 2.5% (Survey 10).
- The proportion of participants hospitalized for malaria in the last 3 months before the visit in the PF INF group ranged from 1.1% in Survey 5 to 3.4% in Survey 2, and in the NOT INF group from 1.8% in Survey 7 to 3.5% in Survey 4.
- Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the percentage of participants hospitalized for malaria in the last 3 months before the visit remained low post RTS,S/AS01$_E$ vaccination, ranging from 1.4% to 8.0% (PF INF group) and 0.5% to 9.8% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 0.0% to 12.7% (PF INF group) and 0.2% to 8.9% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

Medical history

Anti-malarial or any other medication taken in the last 14 days

- Overall sites, 16.6% (Survey 1), 16.0% (Survey 2), 19.0% (Survey 3), 22.0% (Survey 4), 24.1%, (Survey 5), 17.4% (Survey 6), 10.8% (Survey 7), 10.7% (Survey 8), 14.5% (Survey 9) and 7.2% (Survey 10) of participants had taken anti-malarial or any other medication in the last 14 days before the visit.

- Overall sites, in participants taking anti-malarial drugs in the last 14 days, a significantly lower proportion was recorded in PF INF vs. NOT INF participants in Surveys 3 and 4, and a significantly higher proportion was recorded in PF INF vs. NOT INF participants in Survey 5.

Fever at the visit

- The proportion of participants with fever measured at the visit was 5.1% (Survey 1), 4.8% (Survey 2), 3.9% (Survey 3), 4.2% (Survey 4), 4.6% (Survey 5), 3.7% (Survey 6), 2.2% (Survey 7), 2.8% (Survey 8), 3.5% (Survey 9) and 2.9% (Survey 10).
- Overall, in all 10 surveys, the proportion of participants with fever measured at the visit was significantly higher in PF INF vs. NOT INF participants, ranging from 6.2% (Survey 3) to 11.7% (Survey 5) and 1.3% (Survey 7) to 3.5% (Survey 1), respectively.

Geographical heterogeneity

- Significant geographical heterogeneity by segment varied across surveys for each center. Approximately 600 participants were included in each center, divided across 3 to 14 segments. Although random sampling of the study population was done, the number of participants in each segment at each site varied widely and could then influence the heterogeneity test performed.

Tertiary objectives/other analyses

RTS,S/AS01$_E$ vaccination

In alignment with the MVIP and implementation of RTS,S/AS01$_E$ vaccination, participants were to receive the RTS,S/AS01$_E$ vaccine in exposed sites from Survey 5 onwards. As only 4 participants received the RTS,S/AS01$_E$ vaccine in Survey 5, data are summarized in this section from Survey 6 onwards.

- Overall sites, 4.3% (Survey 6), 15.0% (Survey 7), 22.4% (Survey 8), 27.3% (Survey 9) and 38.5% (Survey 10) of participants received at least 1 dose of RTS,S/AS01$_E$ vaccine. In exposed sites, the percentage of participants across sites receiving at least 1 dose of RTS,S/AS01$_E$ vaccine increased with each subsequent survey: 0% to 15.0% in Survey 6, 22.3% to 35.7% in Survey 7, 39.8% to 48.9% in Survey 8, 40.7% to 53.0% in Survey 9 and 49.9% to 63.0% in Survey 10.
- A significantly lower proportion of participants in the PF INF vs NOT INF group had received RTS,S/AS01$_E$ vaccination in Surveys 6-10. This finding is partially attributable to the prevalence of *P. falciparum* being significantly lower in the 6M-4Y vs. 5Y-9Y age group, which is the age group eligible for RTS,S/AS01$_E$ vaccination.

Prevalence of P. falciparum measured by NAAT and microscopy

- Overall sites, across surveys, the prevalence of *P. falciparum* measured by NAAT ranged from 18.1% in Survey 10 to 45.9% in Survey 3, and measured by microscopy from 11.2% in Survey 10 to 41.0% in Survey 3.
- Overall sites, across surveys, the proportion of participants detected as positive by NAAT and negative by microscopy ranged from 20.9% in Survey 2 to 46.9% in Survey 9. The proportion of participants measured as negative by NAAT and detected as positive by microscopy ranged from 0.5% in Survey 10 to 12.2% in Survey 3.
- The concordance in *P. falciparum* prevalence between qualitative results from the 2 methods (NAAT vs. microscopy) reached a significant substantial overall agreement across all 10 surveys, with a κ coefficient ranging from 0.62 (Surveys 8 and 9) to 0.78 (Survey 2). The level of concordance between the 2 methods showed variation by center with a κ coefficient ranging from 0.13 (slight agreement) in MA St Montfort EXP (Survey 9) to 0.85 (almost perfect agreement) in MA Chikwawa UNEXP (Survey 8). Of note, the prevalence of *P. falciparum* measured by NAAT was not measured in SN Keur Soce in Survey 1.

Gametocyte results

- Overall sites, across surveys, gametocytes detected by microscopy ranged from 1.3% in Survey 10 to 6.9% in Survey 1, and measured by NAAT from 12.3% in Survey 10 to 27.4% in Survey 4.
- The concordance in gametocytemia between NAAT and microscopy reached a significant slight to fair overall agreement across all 10 surveys, with a κ coefficient ranging from 0.05 (Surveys 5 and 10) to 0.30 (Survey 1). The level of concordance between the 2 methods showed variation by center with a κ coefficient ranging from -0.09 (no agreement) in MA Chikwawa UNEXP (Survey 8) to 0.67 (substantial agreement) in SN Keur Soce (Survey 2). Of note, detection of gametocytes by NAAT was not measured in Keur Soce in Survey 1.

Analysis of parasite prevalence trends

The Cochran-Armitage trend test was computed only on centers with results for at least 3 surveys.

- The Cochran-Armitage trend test for parasite prevalence measured by microscopy was significant for all sites, with the exception of GH Navrongo UNEXP and MA Monkey Bay.

Slide reading results

- Overall, parasite density was mostly low (< 2500 parasites/µL of blood), with approximately half of participants with low parasite density among positive participants as measured by microscopy, approximately one-fifth of participants with medium density (2500–9999 parasites/µL) and one-quarter of participants with high (10 000–19 999 parasites/µL) to very high (≥ 20 000 parasites/µL) density.

- The proportion of participants with fever measured at the visit tended to increase with parasite density in all 10 surveys. In addition, a very high parasite density (≥ 20 000 parasites/µL of blood) was more frequently observed in participants with measured fever vs. no fever in each survey.

Rapid diagnostic test results

As per protocol, RDT was only performed in participants with measured fever at the visit or reported fever in the last 24 hours or in participants presenting signs/symptoms of clinical malaria at the visit; RDT results restricted to this subgroup are described below, with the exception of Survey 2 for which this subgroup analysis was not conducted.

- Overall sites, across surveys, among participants diagnosed as positive by microscopy (i.e., PF INF), most were also tested positive by RDT (96.8% Survey 1; 90.6% Survey 2; 92.7% Survey 3; 94.5% Survey 4; 94.4% Survey 5; 94.4% Survey 6; 93.4% Survey 7; 92.0% Survey 8; 92.7% Survey 9; 94.5% Survey 10).
- Overall sites, 27.1% (Survey 1), 24.9% (Survey 2), 42.7% (Survey 3), 33.0% (Survey 4), 31.7% (Survey 5), 30.5% (Survey 6), 28.0% (Survey 7), 23.8% (Survey 8), 16.2% (Survey 9) and 16.5% (Survey 10) of participants negative for *P. falciparum* by microscopy (i.e., NOT INF) had positive RDT results.

Discussion

- Overall sites, *P. falciparum* parasitemia prevalence was highest in Survey 3, after which prevalence decreased with subsequent surveys to Survey 8 and was remained at a similar level up to Survey 10. The higher prevalence in Surveys 1-4 reflects the high malaria transmission intensity in the Burkina Faso sites participating in the earlier surveys. Post-RTS,S/AS01$_E$ vaccination, *P. falciparum* prevalence generally decreased over surveys in most centers in Ghana, Kenya and Malawi.
- The observed prevalence of *P. falciparum* measured by microscopy varied by center and by age group. Overall for each survey and in most centers, the prevalence of *P. falciparum* was significantly lower in the 6M-4Y vs. 5Y-9Y JTEG age groups.
- The prevalence of *P. falciparum* varied across sites. Considering study sites from Ghana, Kenya and Malawi only, the prevalence of *P. falciparum* ranged from 0% in MA St Montfort EXP (Survey 9) to 32.75% in KE Kombewa EXP (Survey 4) in the 6M-4Y JTEG age group, and from 0.99% in MA St Montfort (Survey 10) to 57.50% in GH Kintampo EXP (Survey 1) in the 5Y-9Y JTEG age group.
- Overall in each survey (Survey 6 to Survey 10), the prevalence of *P. falciparum* was higher among the RTS,S/AS01$_E$ unvaccinated compared to vaccinated participants.
- Most participants slept under a bednet the night before the visit, ranging by center from 59.8% in GH Kintampo EXP to 99.7% KE Nyando UNEXP, both in Survey 10. The use of other MCIs was rare and showed variations among centers. Overall, a higher proportion of participants slept under a bednet the night before the visit in the 6M-4Y vs. 5Y-9Y age groups in each survey.

- Overall sites, in all 10 surveys, a significantly higher percentage of participants slept under a bednet the night before the visit when comparing vaccine eligible vs. ineligible subgroups.
- Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), bednet usage the night before the visit remained high post-vaccination, ranging between 70.2% to 98.3% pre-vaccination and between 59.8% to 99.5% post-vaccination.
- There was no significant difference in the prevalence of *P. falciparum* according to gender across surveys. There was no significant difference in bednet usage according to gender across surveys, with the exception of Survey 2 in which more females than males used bednets.
- Parasite density was low in approximately half, moderate in approximately 20% and high to very high in approximately 25% of *P. falciparum* positive participants measured by microscopy.
- Overall, the prevalence of *P. falciparum* by microscopy was higher in participants with fever vs. no fever measured at the visit in all 10 surveys. Fever measured at the visit tended to be reported more often in infected participants compared to non-infected participants, and observed among participants with a higher parasite density overall and by center.
- Data on care seeking behavior (child taken for treatment for reported fever or malaria in the last 14 days) did not show a clear trend in relation to infection status of the child across surveys. Considering exposed study sites participating pre- and post-vaccination introduction, the percentage of participants seeking anti-malarial or fever treatment in the last 14 days remained similar in pre- and post-RTS,S/AS01$_E$ vaccination periods.
- Overall, the proportion of participants hospitalized for malaria in the last 3 months before the visit was low (≤3.1% across surveys), and was comparable between infected and not infected cohorts. Considering exposed study sites participating pre- and post-vaccination, the percentage of participants hospitalized for malaria in the last 3 months remained similar in pre- and post-RTS,S/AS01$_E$ vaccination periods.
- The prevalence of *P. falciparum* measured by microscopy was lower compared to the results of prevalence obtained by NAAT. However, the concordance between qualitative results from the 2 methods (microscopy vs. NAAT) reached a substantial overall agreement in each survey.
- Overall, across surveys, among participants with fever or malaria symptoms diagnosed as positive by microscopy, most were also tested positive by RDT (>90.0%). The percentage of participants negative for *P. falciparum* by microscopy with positive RDT results ranged from 16.2% (Survey 9) to 42.7% (Survey 3).
- The proportion of participants positive for *Plasmodium* species other than *P. falciparum* was low across all surveys (≤3.0% *P. malariae*, ≤0.9% *P. ovale*, ≤0.3% *P. vivax*). The highest prevalence for *P. malariae* was measured in BF Nouna (9.5%) and for *P. ovale* in KE Gem EXP (3.0%); *P. vivax* was recorded for 3 participants across study sites/surveys.

- Overall, 69.4% (Survey 1) to 97.2% (Survey 10) of participants were vaccinated with any combination of the DTP vaccine (third dose), and 53.7% (Survey 1) to 89.0% (Survey 5 and Survey 10) of participants had received the measles (first dose) vaccine.

  A lower proportion of participants in *P. falciparum* infected compared to not infected cohorts received the third dose of any combination of the DTP vaccine in all 10 surveys. The same trend was not observed for participants receiving the first dose of measles vaccine.

  Considering exposed study sites participating pre- and post-vaccination, the proportion of participants who received the third dose of any combination of the DTP vaccine remained high post-RTS,S/AS01$_E$ vaccination. Results by site varied in participants who received the measles (first dose) vaccine.

- Overall, across surveys, gametocytes detected by microscopy were lower than measured by NAAT across surveys. The concordance in gametocytemia between NAAT and microscopy testing methods reached a significant slight to fair overall agreement across all 10 surveys.

- Overall, 4.3% (Survey 6), 15.0% (Survey 7), 22.4% (Survey 8), 27.3% (Survey 9) and 38.5% (Survey 10) of participants received at least 1 dose of RTS,S/AS01$_E$ vaccine. A significantly lower proportion of *P. falciparum* infected vs not infected participants had received RTS,S/AS01$_E$ vaccination in Surveys 6-10. This finding is partially attributable to the prevalence of *P. falciparum* being significantly lower in the 6M-4Y vs. 5Y-9Y age group, which is the age group eligible for RTS,S/AS01$_E$ vaccination.

- Significant geographical heterogeneity by segment was observed across surveys for each center. Approximately 600 participants were included in each center, divided across 3 to 14 segments. Although random sampling of the study population was done, the number of participants in each segment at each site varied widely and could then influence the heterogeneity test performed.

Conclusion

P. falciparum prevalence varied by age, center, and RTS,S/AS01$_E$ vaccination status, with younger children and vaccinated participants showing lower infection rates. Bednet use was common, especially among younger children, while the use of other preventive measures was limited. No gender differences were observed.

Bednet usage the night before the visit remained high post-RTS,S/AS01$_E$ vaccination periods. Other MCIs were rarely used. Care-seeking behaviors (anti-malarial or fever treatment, hospitalization for malaria) remained similar in pre- and post-RTS,S/AS01$_E$ vaccination periods. DTP/HepB/Hib and measles vaccine administration remained high in post-RTS,S/AS01$_E$ vaccination periods.

Microscopy detected less infection and gametocyte rates compared to NAAT, though both methods showed moderate agreement. Overall, high RTS,S/AS01$_E$ vaccine coverage and the protective impact of vaccination highlight the importance of integrated malaria control and accurate diagnostics.

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Names and affiliations of principal investigators

Refer to Modular Appendices for the list of investigators.

2. LIST OF ABBREVIATIONS

AE	Adverse event
ACT	Artemisinin based combination therapy
AMC	Academic Medical Center
AS01	GSK's proprietary Adjuvant System containing MPL, QS-21 and liposome
ATP	According to protocol
CI	Confidence interval
CNERS	Comité National d'Ethique et de Recherche en Santé
COVID-19	Coronavirus Disease 2019
CDQA	Clinical development quality assurance
CRA	Clinical Research Associate
DTP	Diphtheria, tetanus, pertussis trivalent vaccine
DTP/HepB/Hib	Diphtheria-tetanus-whole-cell pertussis-hepatitis B- Haemophilus influenza type b pentavalent vaccine
eCRF	Electronic case report form
EDC	Electronic data capture
EMA	European Medicines Agency
EPI	Expanded Program on Immunisation
EU PAS	European Union Post-Authorization Studies
EXP	Exposed
FSFV	First subject first visit
GCP	Good clinical practice
GH	Ghana
GHS-ERC	Ghana Health Service Ethics Review Committee
GPP	Good pharmacoepidemiology practices
GSK	GlaxoSmithKline
GVP	Good pharmacovigilance practices
HBsAg	Hepatitis B surface antigen
HDSS	Health and demographic surveillance system
IC	Informed consent
ICF	Informed consent form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IPTi	Intermittent preventative treatment in infants
IRB	Institutional Review Board
IRS	Indoor residual spraying
ITN	Insecticide treated nets
JTEG	Joint Technical Expert Group
KE	Kenya
KEMRI	Kenya Medical Research Institute
KHRC	Kintampo Health Research Centre
KHRC-IEC	Kintampo Health Research Centre Institutional Ethics Committee
LAR	Legally acceptable representative
LDL	Local delivery lead
LLIN	Long lasting insecticidal nets
LSLV	Last subject last visit
MA	Malawi
MAH	Marketing Authorization Holder
MCI	Malaria control intervention
MoH	Ministries of Health
MPL	3-O-desacyl-4'- monophosphoryl lipid A (produced by GSK)
MTI	Malaria transmission intensity
MVIP	Malaria Vaccine Implementation Program
NAAT	Nucleic acid amplification test
NOT INF	Not infected with *P. falciparum*
OR	Odds ratio

PASS	Post-Authorization Safety Study
PATH	Program for Appropriate Technology in Health
PCR	Polymerase chain reaction
PD	Protocol deviation
PDL	Project delivery lead
PF INF	*P. falciparum* infected
P. falciparum	*Plasmodium falciparum*
P. malariae	*Plasmodium malariae*
P. ovale	*Plasmodium ovale*
P. vivax	*Plasmodium vivax*
PII	Personally identifiable information
PRAC	Pharmacovigilance Risk Assessment Committee
QS-21	Quillaja saponaria Molina, fraction 21 (Licensed by GSK from Antigenics Inc, a wholly owned subsidiary of Agenus Inc., a Delaware, USA corporation)
QT-NASBA	Quantitative nucleic acid sequence-based amplification
RDT	Rapid diagnostic test
RMP	Risk management plan
RTS	Hybrid protein comprising HBs (hepatitis B surface antibody) and circumsporozoite (CS) protein portions
RTS,S	Particulate antigen, containing both RTS and HBs antigen (S) proteins
SAE	Serious adverse event
SAGE	Strategic Advisory Group of Experts
SAP	Statistical analysis plan
SAS	Statistical analysis system
SD	Standard deviation
SDL	Study delivery lead
SDV	Source data verification
SERU	Scientific and Ethics Research Unit
SMC	Seasonal malaria chemoprevention
SN	Senegal
SOP	Standard operating procedure
SPAP PC	Safety Post Approval Plan Partnership Committee
SQI	Significant quality issue
TCS	Tata Consultancy Services
UNEXP	Unexposed
WHO	World Health Organization
WRAIR	Walter Reed Army Institute of Research

3. ETHICS

3.1. Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The study protocol, any amendments, the informed consent, and other information that required pre-approval were reviewed and approved by a national, regional, or investigational center IEC or IRB.

3.2. Ethical conduct of the study

Overall, this study was conducted in accordance with the ICH Guideline for GCP, GPP [ISPE, 2015], other applicable guidelines, all applicable subject privacy requirements and the guiding principles of the Declaration of Helsinki.

The study was designed and conducted in accordance with the ICH Harmonised Tripartite Guideline for clinical investigation of medicinal products in the pediatric population (ICH E11) and all other applicable ethical guidelines.

During the course of the study, whenever potential issues with regard to the conduct of the study were identified, either via site monitoring activities or brought to GSK Biologicals' attention by other oversight mechanisms, these issues were investigated and appropriate corrective / preventive actions where possible were taken. Please refer to Section 10.10 for details.

3.3. Participant information and consent

Freely given and written or thumb printed informed consent was obtained from each participant's parent(s)/LAR(s) or the impartial witness and participant informed assent, as appropriate, prior to participation in the study. Electronic CRFs were provided for each participant's data to be recorded.

Refer to Protocol Section 5.1 for the IC process.

4. INVESTIGATORS

Refer to the Modular Appendices for the list of investigators.

5. OTHER RESPONSIBLE PARTIES

Safety Post Approval Plan Partnership Committee (SPAP PC):

Scope: The RTS,S/AS01$_E$ SPAP consisted of the GSK baseline (EPI-MAL-002), Phase 4 (EPI-MAL-003) and ancillary (EPI-MAL-005) studies, conducted to evaluate the benefit/risk profile of the RTS,S/AS01$_E$ vaccine when used in the framework of the MVIP in sub-Saharan Africa.

Principle: The SPAP PC was tasked with providing scientific and technical expertise and ensuring coordination between the study site investigators, GSK and PATH.

Composition: The SPAP PC was composed of 2 members from each study site, 2 members from PATH and 2 members from GSK. Each party selected its respective members.

Meetings: Face-to-face meetings and teleconferences were held annually. In addition, quarterly teleconferences between GSK, PATH and the chairs were held.

Third party contributors were as follows:

Supplier	Outsourced Activity
CCI [redacted]	Sample storage for microscopic slides
	Monitoring activities
	Data management activities
	Support for study management activities
	Data management activities
	Testing laboratory
	Translation of study documents
	Event organizer for investigator and monitor meetings
	Courier for shipment of samples
	Courier for shipment of samples
	Supplier of ancillaries/study supplies
	Supplier of equipment (weather stations)

6. MILESTONES

Milestone	Planned date	Actual date
Start of data collection	Q3 2014	Q4 2014
Last subject last visit (LSLV)	Q3 2024	Q3 2024
End of data collection	Q1 2025	Q2 2025
Interim report 1 (Surveys 1 & 2)	Q1 2017	Q3 2017
Interim report 2 (Surveys 3, 4 & 5)	Q2 2020	Q1 2021
Registration in the EU PAS register	-	Q4 2021
Final report of study results	Q2 2025	Q3 2025
Protocol Amendment 1 IEC/IRB approvals	-	Q3 2016
Protocol Amendment 2 IEC/IRB approvals	-	Q3 2018

7. RATIONALE AND BACKGROUND

7.1. Background

GSK has developed a pre-erythrocytic *P. falciparum* malaria vaccine, RTS,S/AS01$_E$, for routine immunization of infants and children living in sub-Saharan African malaria-endemic countries. The vaccine consists of sequences of the CS protein and HBsAg adjuvanted with AS01 i.e., liposome formulation with MPL and QS-21 immunostimulants.

In 2015, the EMA adopted a positive opinion for the use of the vaccine in children aged 6 weeks to 17 months at first dose [European Medicines Agency, 2015]. In January 2016, the WHO recommended a pilot implementation of RTS,S/AS01$_E$ in children of 5–17 months of age in 3-5 epidemiological sub-Saharan African settings with moderate to high malaria transmission [WHO, 2016]. In April 2017, WHO announced the vaccine introduction based on a cluster-randomised design in pilot areas of Ghana, Kenya and Malawi through the national EPI, in the framework of the MVIP [WHO, 2017].

7.2. Rationale

To assess vaccine safety, effectiveness and impact, GSK designed both a baseline (EPI-MAL-002) and a Phase 4 (EPI-MAL-003) observational studies, allowing temporal and concurrent comparisons of the occurrence of malaria cases and AEs in RTS,S/AS01$_E$ vaccinated vs. unvaccinated children. In parallel with those studies, the present observational cross-sectional annual study (EPI-MAL-005) aimed to estimate *P. falciparum* parasite prevalence and the use of MCIs over 10 consecutive years, using standardized methodologies and multiple diagnostic testing [Praet, 2022].

More specifically, considering the WHO recommendation to operate the MVIP in moderate to high transmission areas, this study will allow (1) characterizing the MTI before RTS,S/AS01$_E$ vaccine introduction in different countries/areas, including the ones participating in the MVIP; (2) over time, monitoring changes in MTI and changes in the use of MCIs before and after vaccine introduction in those areas in order to adjust the temporal and concurrent comparison for potential year-to-year and/or geographical variations.

8. RESEARCH QUESTION AND OBJECTIVES

See 'Objectives' in Section 1 'Abstract' of this Study Report.

Also, refer to Protocol Section 2 for the study objectives.

9. AMENDMENTS AND UPDATES

Two protocol amendments and 1 administrative change were required during the course of the study. A summary of the rationale for the amendments and administrative change is provided in the following table; for details, refer to Appendix C of the protocol.

Protocol Amendment/ Administrative Change	Date	Rationale/background for key changes
Amendment 1	21 September 2016	• Following RMP requirement for follow-up extension in EPI-MAL-003, the EPI-MAL-005 study was extended by 4 years to 9 years. • New sites selected for the EPI-MAL-002 and EPI-MAL-003 studies were included in this study. In addition, WHO proposed the use of RTS,S/AS01$_E$ in moderate to high malaria transmission settings, resulting in the 2 sites in Senegal and 1 site in Tanzania no longer participating in this study after Survey 2 due to low malaria transmission in these countries. • The sample size wording was updated to reflect the true reason for the limited sample size in children 5-9 years to reach a relative standard error equal to a maximum of 0.35 based on the PRAC's recommendation. • The criteria for when the RDT was to be done was updated from not only for fever >37.5 C, but also for participants with other symptoms/signs of clinical malaria.
Amendment 2	14 September 2018	• A delay in the implementation of the RTS,S/AS01$_E$ vaccine in the 3 countries participating in the WHO-led MVIP resulted in a delay to the start of EPI-MAL-003. As a consequence, EPI-MAL-005 needed to be extended to a total of 10 surveys in order to mirror the EPI-MAL-003 timeline. • Country and study site participation changed during the course of the study following WHO recommendations for pilot implementation of RTS,S/AS01$_E$ in settings with moderate to high transmission of malaria and WHO Regional Office for Africa selection for the initial introduction of RTS,S/AS01$_E$ in 3 countries (Ghana, Kenya and Malawi) through the MVIP. EPI-MAL-003 study site selection was performed following MoH pre-selection and according to WHO guidance in the framework of the MVIP, to include 4 sites in each of the 3 countries selected for the MVIP. Study sites in EPI-MAL-005 were aligned with study sites conducting EPI-MAL-002 and/or EPI-MAL-003.
Administrative Change 1	28 October 2021	• EPI-MAL-005 is referenced as a category 3 study in the RMP and was initially not classified as a PASS. In order to align with the GVP Module V Revision 2, where all category 3 studies assessing a risk are classified as PASS, this study was reclassified as a PASS.

10. RESEARCH METHODS

10.1. Study design

See ‘Study design’ in Section 1 ‘Abstract’ of this report for a summary of the study design.

Refer to Protocol Section 3 for an overview of the study design, Section 5 for details of the study design and conduct of the study, and Section 6 for safety assessments.

10.1.1. Sequence of analyses

Two interim Study Reports and an integrated Study Report at study end were planned. The interim Study Reports were written after Survey 2 (including Surveys 1 and 2) and Survey 5 (including Surveys 3, 4 and 5). This integrated report represents the final integrated Study Report for all surveys conducted (Surveys 1-10).

10.2. Setting

See 'Setting' in Section 1 'Abstract' of this report.

Refer to Protocol Section 4.1.1 for details of the study setting.

10.3. Participants

For details of the study population, refer to Protocol Section 4.1, and for sampling methods, refer to Protocol Section 4.1.2.

Study participants needed to have met all inclusion criteria and none of the exclusion criteria. Refer to Protocol Section 4.2 and Section 4.3 for eligibility criteria for enrolment.

10.4. Variables

See 'Variables' in Section 1 'Abstract' of this Study Report.

Also, refer to the SAP Section 4 for the study endpoints.

10.5. Data sources and measurement

See 'Data sources' in Section 1 'Abstract' of this report.

Also refer to Protocol Section 5.4 'Outline of study procedures' and Section 5.5 'Detailed description of study procedures to be conducted at each survey visit' for data sources for the study.

10.6. Bias

Bias is possible due to temporal differences and secular trends, e.g., climate change, socio-demographic factors, use of bednets and other prevention methods.

10.7. Study size

See 'Participants and study size' in Section 1 'Abstract' of this report.

Also refer to Protocol Section 7.2 for details of determination of study size.

10.8. Data transformation

For details of data management, refer to Protocol Section 8.1, and for derived and transformed data, refer to Protocol Section 7.4.

10.9. Statistical methods

The statistical analyses were performed using the SAS version 9.4.

Analyses for this Final Analysis are specified in detail in the SAP dated 08 April 2020; changes to analyses as specified in the SAP are detailed in Section 10.9.5.

10.9.1. Main summary measures

Continuous variables are described with number of non-missing observations, mean, SD, median, minimum and maximum and number of missing observations. Categorical variables are described with frequency tables; absolute numbers and percentages for each level are provided. For some categorical variables 95% CIs are also presented.

All the analyses concerning objectives were performed on the ATP Cohort.

The analysis was also to be done on the Total Cohort only if there were more than 5% of eliminated participants; except for the demography where all the tables are provided for both cohorts.

10.9.2. Main statistical methods

10.9.2.1. Demography, medical history and fever

The number of participants enrolled as well as the number excluded from the ATP analysis are presented.

The distribution of participants by center are tabulated according to *P. falciparum* infection status measured by microscopy, and by both JTEG and WHO age classification.

Refer to the SAP Section 6.1 for the presentation of distribution of participants by center, demographics (age at IC date, gender, previous enrolment), fever and concomitant medications.

10.9.2.2. Analysis of parasite prevalence

Refer to the SAP Section 6.2 for the presentation of the analysis of the co-primary objective regarding *P. falciparum* parasitemia prevalence. The pooled prevalence estimate was computed considering the center as random effect (see SAP Section 7.5). The heterogeneity among centers was tested using Cochran's Q test based upon inverse variance weights.

Refer to the SAP Section 7.7 for the determination of parasitemia prevalence trends across the surveys according to vaccine eligible status using the Cochran-Armitage trend test. As some sites were early terminated during the study and others started after the RTS,S/AS01$_E$ vaccine introduction, the Cochran-Armitage trend test was computed only on centers with results for at least 3 surveys.

10.9.2.3. Analysis of malaria control interventions

Refer to the SAP Section 6.3 for the presentation of bednet history information (sleeping under a mosquito net night before visit, new nets, pierced or impregnated bednets and how many holes).

The analysis of co-primary objective regarding the use of MCIs was done by computing the proportions of participants using MCIs among the participants for which this information was available (refer to the SAP Section 6.3 for details of presentation of data).

The CIs were computed using the exact method. ORs (unadjusted and adjusted) were computed (see SAP Section 7.6).

10.9.2.4. Analysis of parasite prevalence trends

The analysis of trends of parasitemia prevalence measured by microscopy was performed only for the final analysis (i.e., at the last cross-sectional survey). Refer to the SAP Section 6.4 for further details.

The pooled prevalence estimates were computed considering the center as random effect (refer to SAP Section 7.5).

10.9.2.5. Slide reading results

The analysis of slide readings included availability of slide readings, malaria RDT results, slide methodology used, filter paper collection, number of days between date of slide reading and collection date. Refer to the SAP Section 6.5 for details of presentation of data.

10.9.2.5.1. Microscopy

Descriptive analysis

The analyses of *P. falciparum*, distribution and density of *P. falciparum* parasitemia, gametocytes, and prevalence of *Plasmodium* species other than *P. falciparum* were performed using descriptive statistics. Refer to the SAP Section 6.5.1.1 for details of presentation of data.

Comparison analysis

The Fisher exact test was used to perform the comparison, by RTS,S/AS01$_E$ vaccination status, of *P. falciparum* results measured by microscopy (refer to SAP Section 6.5.1.2 for further details).

10.9.2.5.2. NAAT results

Descriptive analysis

The analyses of *P. falciparum* and gametocytes measured by NAAT were performed using descriptive statistics. Refer to the SAP Section 6.5.2.1 for details of presentation of data.

Comparison analysis

The Fisher exact test was used to perform the comparison, by RTS,S/AS01$_E$ vaccination status, of *P. falciparum* results measured by NAAT (see SAP Section 7.8 for further details).

10.9.2.5.3. Comparison between microscopy and NAAT

The comparison of *P. falciparum* results and density and gametocytes results, measured by microscopy and by NAAT, were performed using the Cohen's Kappa coefficient [Cohen, 1960].

Simple Kappa coefficient was used to compare the 2x2 contingency tables for the qualitative results (Positive/Negative; see SAP Section 7.4.4 for the details of categories).

For semi-quantitative results (see SAP Section 7.4.4 for the details of categories), simple and weighted Kappa coefficients were used to compare the 4x4 contingency tables.

The extent of the concordance was assessed using the Landis and Koch scale [Landis, 1977].

See SAP Section 6.5.3 for further details of analyses conducted.

10.9.2.6. Vaccination history

The vaccination history (vaccine, age at vaccination) regarding DTP, Pentavalent, Measles and RTS,S/AS01$_E$ were summarized using descriptive statistics. Refer to SAP Section 6.6 for details of data presentation.

10.9.2.7. Change in care seeking behaviors

Refer to SAP Section 6.7 for presentation of malaria or fever treatment taken in the past 14 days, and hospitalization for malaria.

10.9.2.8. Geographical heterogeneity

The heterogeneity among segment by center was tested using Cochran's Q test based upon inverse variance weights. Refer to SAP Section 6.8 for the presentation of the distribution of participants by segment, characteristics of segment and analyses of *P. falciparum* parasitemia prevalence by segment.

10.9.2.9. Malaria risk factors

Refer to SAP Section 6.9 for the presentation of malaria risk factors (number of participants in the same house, localization, house information). ORs were computed.

10.9.2.10. Malaria control program at center level

Center specific data regarding the malaria control program are summarized in data listings by center and by survey.

10.9.2.11. Analysis of SAEs related to study procedure

Refer to SAP Section 6.11 for the presentation of any SAEs reported, if applicable, during the entire study for the Total Cohort.

10.9.2.12. Output dataset

Annual fluctuations in malaria incidence occur as a result of changes in transmission intensity, which may be caused by changes in environmental factors such as rainfall or changes in usage of other MCIs (e.g., use of bednets). Therefore, by taking into account variations in MTI and MCI coverage, more accurate estimations of the vaccine impact on malaria disease diagnosed by RDT and/or microscopy during EPI-MAL-003 will be possible. Those estimations will be used as covariates in the models, as described in the protocol of the EPI-MAL-003 study.

EPI-MAL-005 ran in parallel with EPI-MAL-002 and EPI-MAL-003 and assessed the following parameters: prevalence of *P. falciparum* parasitemia, use of MCIs, changes in environmental factors such as rainfall, changes in health care seeking behaviors, within-site geographical heterogeneity in MTI and individual malaria prevention measures and risk factors for malaria. Compliance with DTP, measles and RTS,S/AS01$_E$ vaccines were also collected.

In order to adjust the comparison, and the estimation of the vaccine impact, an output dataset of the EPI-MAL-005 results will be considered for inclusion as covariates in the EPI-MAL-003 model. This dataset would consist of aggregated results by center, and by survey.

10.9.3. Missing values

No data handling was performed in case of missing data.

10.9.4. Sensitivity analyses

Not applicable.

10.9.5. Amendments to the statistical analysis plan

Not applicable.

10.10. Quality control

To comply with ICH GCP or other applicable guidelines administrative obligations relating to data collection, monitoring, archiving data, audits, confidentiality, ownership and publications were to be met.

A validated GSK defined electronic data collection tool (INFORM) was used as the method for data collection, details for which are provided in Section 8.1 of the protocol.

IQVIA monitored the study to verify that, among others; the data were authentic, accurate, and complete; safety and rights of participants were being protected; the study was conducted in accordance with the currently approved protocol, any other study agreements, GCP and all applicable regulatory requirements. GSK ensured necessary sponsor oversight. Further details are provided in Section 8.2 of the protocol.

Details for record retention are provided in Section 8.3 of the protocol.

The following meetings and trainings were conducted during the course of the study:

Investigator Meeting	Monitor Meeting
South Africa 02-03 October 2014	South Africa 01-02 October 2014
Navrongo (Ghana) 25-27 July 2017	Refresher training for Ghana only 30 August 2018 (online)
Kisumu (Kenya) 20-21 February 2019	Kisumu (Kenya) 19 February 2019

Audits of this study were conducted as part of the independent Sponsor quality assessment performed by GSK. The GH Kintampo center was subject to an audit during Survey 3 (May 2017) and the SN Niakhar center during Survey 1 (May 2015). Audit certificates are provided in the Audit Certificates appendix.

During the course of the study, the following SQIs with regard to the conduct of the study were identified, either via site monitoring activities or were brought to GSK's attention by other oversight mechanisms. These issues were investigated and where possible corrective and / or preventive actions were taken as described below.

Survey #	Description	Impact	Actions	Outcome
Survey 1	An ICF (Version 2 dated 15-Oct-2014) that was not approved by the site ethics committee was used to consent and enrol all 600 participants for Survey 1 in SN Keur Soce. The ICF used had not been submitted and approved by the National IRB CNERS Ethics Committee or by GSK and Quintiles.	The site had adapted the ICF of another GSK study (EPI-MAL-006) by changing the study identifying information on the ICF and used this for the EPI-MAL-005 study participants. The adapted ICF did not contain the correct study information.	• Reconsenting of the participants with the correct ICF. • Proper documentation and monitoring of the reconsenting. • IRB notification of the incident and the corrective action plan. • Additional GCP training of the site by IQVIA. • Assessment conducted for participation in following surveys of EPI-MAL-005 • Prior to start of Survey 2, Epidemiology team and LDL provided additional onsite GCP and operational training. • Site updated their site specific ICF SOP and trained all site staff involved in obtaining ICF on the updated ICF SOP.	Following CDQA assessment, based on the implementation of corrective actions and under the condition of implementation of the expected further preventive actions, there were no objections to the further use of the site for EPI-MAL-005.
Surveys 1&2	The approved local translated ICF Version 2 dated 20-Aug-2014 and Version 3 dated 27-Feb-2015 signed by 122 participants during Survey 1 and 114 participants in Survey 2 did not contain the header information as per the corresponding local approved English versions. Additional administrative errors were also noted.	The impact assessment on safety and study data was evaluated by the Epidemiologist, Project Delivery Lead and the Study Delivery Lead and considered unlikely that there was any impact on safety and rights of a participant. It was considered that there was no impact on reliability and robustness of the data generated.	• The KHRC-IEC was notified. The local translated ICF was updated and the below proposed actions by the site sent to the IRB. • Site created a notification letter to be approved by KHRC-IEC • GHS-ERC was notified of all the errors and KHRC-IEC approval. • On approval of the notification letter by KHRC-IEC and acknowledgment by GHS-ERC, the participants parents/LARs were contacted regarding the errors in the ICFs already signed. • Quintiles was employed to perform monitoring activities and responsibilities were conducted according to GSK's SOPs.	As per corrective actions taken and outcome of the impact assessment, no further investigation was needed.
Survey 5	For 1 participant in KE Siaya, PII was mistakenly encoded in the EDC application (eCRF in InForm).	Participants full name was entered in the eCRF and could be seen by unauthorized GSK personnel (potential data privacy breach).	• Actions were taken to remove the PII and ensure that it could not be further seen. • Principal Investigators and site staff were retrained on how to properly encode data in EDC.	As per corrective actions taken and measures put in place to prevent future re-occurrence, no further investigation was needed.
Survey 5	For 20 participants in KE Siaya and 6	Study procedures were carried out	• Issue was mainly caused by inexperience of	As per corrective actions taken

Survey #	Description	Impact	Actions	Outcome
	participants in MA Chikwawa, site staff initiated some study procedures (e.g., assessment of body temperature, taking capillary blood samples) before the ICF was signed. These procedures are study-specific and should not be performed before signed agreement by the participant and Principal Investigator.	prior to consent given by participants.	some field workers and the lack of coordination between them. • Preventive actions were taken in both KE Siaya and MA Chikwawa centers: site staff were retrained on the consent process and Principal Investigator further investigated on the root cause to put in place preventive actions.	and measures put in place to prevent future re-occurrence, no further investigation was needed.
Surveys 8&9	Source data files went missing for 29 participants in Survey 8 and 6 participants in Survey 9 in KE Kombewa. All data had already been entered into the database and SDV completed.	There was a potential impact to participants' privacy rights, as well as to data integrity, as although the data had already been entered into the eCRF, the audit trail could not be reconstructed.	• Site staff were retrained on site Archiving of study records SOP. • Notification of the issue was sent to the Ethics Committees KEMRI SERU and WRAIR. • Site created a documented process for management of active/ongoing study records, including access control and tracking of documents removal and return to the records room. • Training was conducted in the new process for all staff handling active / ongoing study records at the site.	As per corrective actions taken and measures put in place to prevent future re-occurrence, no further investigation was needed.
Survey 7	At the monitoring enrolment checkpoint/quality gate for MW Mangochi, the ICFs for the first 100 participants enrolled were correctly signed but not dated by the parent/LAR as the local ICF template did not have a dedicated space for entering the date. Dates were however captured in the participants' source documentation by the site staff	The issue/non-compliance could potentially impact the study's data quality as it may have led to those 100 participants' data elimination from the study.	• Ethics Committees were notified and recommendations from the Ethics Committees completed. • The issue was to be documented in the Study Report. • Study Team were retrained on PD escalation, SQI detection and process.	As measures were put in place to prevent future re-occurrence, no further investigation was needed.
Survey 4	123 participants in GH Navrongo who presented with fever in the last 24 hours prior to the visit did not have an RDT as per protocol and ICF.	The impact on safety of the participants was unlikely as several cross-checks were made with the Principal Investigator to ensure that	• Site staff, monitor and study team were retrained. • Manual cleaning for RDT data was performed to identify any similar issue in the other sites.	As per corrective actions taken and measures put in place to prevent future re-occurrence, no further investigation was needed.

Survey #	Description	Impact	Actions	Outcome
		every participant who did not receive RDT as per protocol, who was not already under treatment during home visit, and who later tested positive by microscopy received treatment with the shortest delay.	• RDT monitoring was included as part of enrolment checks. • The requirement for RDT was highlighted via newsletters. • An automated check in the integrated Data Review Plan was added to identify missing RDTs prior to the start of Survey 5.	
Survey 5	In total, data for 396 participants across 4 sites (MW Mangochi; KE Kombewa; KE Siaya; MW Chikwawa) could not be entered into Inform.	Timely data capture in the system (demography page onwards) was not possible, therefore potentially impacting data quality, with data backlog accumulation, and delay in answering data queries timely, possibly becoming unresolvable.	• Study timelines for Survey 5 were postponed in order to allow proper data entry, monitoring, cleaning and impact assessment. • IQVIA monitoring visits were performed to conduct 100% Source Data Review to replace remote monitoring.	The issue was resolved resulting in a backlog for data entry, monitoring and data cleaning. The risk in data integrity was added to the study risk register on 11th July 2019 as confirmed by Matthieu Lamy, Epidemiologist Lead.
Survey 8	In KE Nyando, the LAR section of the ICFs for 12 participants were incorrectly completed by consenting staff on behalf of the LARs, although the LARs signed the document.	This non-compliance and lack of oversight by the study staff potentially adversely affected the rights of the participants, quality and integrity of data.	• Independent study staff reconsented the LARs. • The root cause was determined, EC notified, measures put in place to prevent future re-occurrence by retraining, withdrawing fieldworkers, adding additional quality control measures and updating the applicable SOP.	As measures were put in place to prevent future re-occurrence, no further investigation was warranted.
Survey 8	In MA Mangochi, the IAF section for the witness was unsigned, although the participant was illiterate for 14 participants.	This non-compliance and lack of oversight by the study staff potentially adversely affected the rights of the participants, quality and integrity of data.	• EC was consulted: IAF should have witness section signed and "Impartial witness" in cases where LAR is the literate parent of the child can be the parent. • Review of all IAFs was conducted to identify any similar issue. • Site ICF SOP was updated, and staff trained. • LAR signed the witness section of IAF for all concerned participants. • The non-compliance with a list of concerned participants was reported to the EC.	As measures were put in place to prevent future re-occurrence, no further investigation was warranted.

CDQA = clinical development quality assurance; CNERS = Comité National d'Ethique et de Recherche en Santé; EC = Ethics Committee; eCRF = electronic case report form; EDC = electronic data capture; GCP = good clinical practice; GHS-ERC = Ghana Health Service Ethics Review Committee; IAF = informed assent form; ICF = informed consent form; IRB = Institutional Review Board; KE = Kenya; KEMRI = Kenya Medical Research Institute; KHRC-IEC = Kintampo Health Research Centre Institutional Ethics Committee; LAR = legally acceptable representative; LDL = local delivery lead; MA = Malawi; PD = protocol deviation; PDL = project delivery lead; PII = personally identifiable information; RDT = rapid diagnostic test; SDL = study delivery lead; SDV = source data verification; SERU = Scientific and Ethics Research Unit; SOP = standard operating procedure; SQI = Significant quality issue; WRAIR = Walter Reed Army Institute of Research

11. RESULTS

11.1. Participants

Enrolment dates (FSFV, LSLV) for each cross-sectional survey are provided in Table 4.

Table 4 Timelines of analysis and enrolment by survey

Survey	FSFV	LSLV
1	22 October 2014	07 August 2015
2	21 September 2015	12 July 2016
3	19 September 2016	13 June 2017
4	20 September 2017	04 June 2018
5	17 September 2018	14 October 2019
6	30 September 2019	13 August 2020
7	24 September 2020	09 August 2021
8	04 October 2021	03 August 2022
9	19 September 2022	25 July 2023
10	11 September 2023	06 July 2024

FSFV = first subject first visit; LSLV = last subject last visit

The list of study sites participating in each survey is presented in Table 5:

- EPI-MAL-005 was planned to be conducted in sites defined in the EPI-MAL-002 and EPI-MAL-003 protocols. From Survey 5 onwards, in alignment with the MVIP and implementation of RTS,S/AS01$_E$ vaccination, the study sites participating in EPI-MAL-005 were selected from the 3 countries where the RTS,S/AS01$_E$ vaccine was to be implemented (Ghana, Kenya and Malawi), and enrolment to sites in Burkina Faso, Senegal and Tanzania early terminated. See EPI-MAL-005 Protocol Section 4.1.1 for further details of site selection.

Table 5 Study sites participating in each survey

	Surveys 1&2	Survey 3	Survey 4	Survey 5*	Survey 6*	Surveys 7-10*
BF_Nouna	X	X	X			
BF_Sapone	X	X	X			
SN_Keur Soce	X					
SN_Niakhar	X					
TZ_Korogwe	X					
GH_Kintampo_EXP	X	X	X	X	X	X
GH_Kintampo_UNEXP					X	X
GH_Navrongo_EXP			X	X	X	X
GH_Navrongo_UNEXP					X	X
KE_Kombewa_EXP	X	X	X	X	X	X
KE_Nyando_UNEXP					X	X
KE_Bondo_UNEXP				X	X	X
KE_Gem_EXP				X	X	X
MA_Chikwawa_UNEXP**				X		X
MA_St Montfort_EXP**				X		X
MA_Mangochi_EXP				X	X	X
MA_Monkey Bay_UNEXP				X	X	X

Shaded fields represent sites not participating in a specific survey
BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania
EXP = exposed sites: Sites in which the RTS,S vaccine was planned to be / was implemented. Subject selection in the study was not based on their vaccination status, but vaccinated subjects might be randomly selected from the base population
UNEXP = unexposed sites: Sites in which the RTS,S vaccine was not planned to be / was not implemented during the course of the study. Subject selection in the study was not based on their vaccination status. Vaccinated subjects could still be randomly selected in this population if vaccination happened in an exposed cluster due to cross-cluster migration
*RTS,S vaccination started to be implemented concurrently to the conduct of Survey 5 in some of the exposed sites
**MA_Chikwawa and MA_St Montfort did not participate in Survey 6 due to the COVID-19 pandemic
Source: Table D2.1_S1 to Table D2.1_S10

11.2. Descriptive data

11.2.1. Disposition of participants

The number of participants included in the Total Cohort and the ATP Cohort according to *P. falciparum* infection status by survey are presented in Table 6.

Table 6 Number of participants included in the Total Cohort and ATP Cohort by survey

Survey	Total Cohort	ATP Cohort		
		PF_INF n (%)	NOT_INF n (%)	Total
1	4214	1187 (28.2)	3021 (71.8)	4208
2	4204	1232 (29.3)	2967 (70.7)	4199
3	2400	984 (41.0)	1415 (59.0)	2399
4	3003	958 (31.9)	2042 (68.1)	3000
5	5417	1022 (19.0)	4355 (81.0)	5377
6	5991	1246 (20.8)	4741 (79.2)	5987
7	7246	1138 (15.7)	6103 (84.3)	7241
8	7220	909 (12.6)	6308 (87.4)	7217
9	7203	888 (12.3)	6315 (87.7)	7203
10	7202	810 (11.2)	6392 (88.8)	7202

ATP = According To Protocol Cohort
Total Cohort = Total Effective Cohort, i.e., excluding participants with invalid inform consent (code 900)
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy
Source: Table D1_S1 to Table D1_S10

The number of participants by center according to *P. falciparum* infection status are presented in Table D2.1_S1 to Table D2.1_S10 for the JTEG age groups and Table D3.1_S1 to Table D3.1_S10 for the WHO age groups for the Total Cohort, and in Table D2.2_S1 to Table D2.2_S10 and Table D3.2_S1 to Table D3.2_S10 for the ATP Cohort, respectively.

A summary of participants previously enrolled in the study by center according to *P. falciparum* infection status are presented in Table D6.2_S1 to Table D6.2_S10 (ATP Cohort) and Table D6.1_S1 to Table D6.1_S10 (Total Cohort).

11.2.2. Protocol deviations

The number of participants excluded, and reasons for exclusion, from the ATP Cohort for each survey are presented in Table 7.

Table 7 Number of participants excluded from ATP Cohort and reasons for exclusion by survey

Survey #	Total excluded	Reasons for exclusion
Survey 1	7	• At 1 site the ICFs were re-signed but 1 participant was not available for re-signing and therefore the data could not be considered for analysis. • 4 participants due to age exclusion criteria. • 1 participant due to consent withdrawal • 1 participant had a sample taken for slide reading which could not be used due to clotting
Survey 2	5	• 4 participants due to age exclusion criteria. • 1 participant had a sample taken for slide reading which could not be used due to clotting
Survey 3	1	• 1 participant due to inclusion/exclusion criteria not met
Survey 4	4	• 1 participant due to issues related to the informed consent form (ICF), i.e., ICF process not respected and/or ICF not adequately completed • 1 participant due to inclusion/exclusion criteria not met • 2 participants due to missing or incomplete information on slide readings (primary endpoint)
Survey 5	44	• 4 participants due to issues related to the informed consent form (ICF), i.e., ICF process not respected and/or ICF not adequately completed • 3 participants due to inclusion/exclusion criteria not met • 37 participants due to missing or incomplete information on slide readings (primary endpoint)
Survey 6	12	• 2 participants due to inclusion/exclusion criteria not met • 2 participants due to missing or incomplete information on slide readings (primary endpoint) • 8 participants due to missing parent/LAR/child signature or thumbprint on Consent Form
Survey 7	5	• 5 participants due to missing or incomplete information on slide readings (primary endpoint)
Survey 8	4	• 1 participant due to consent given by a minor representing the child • 3 participants due to missing or incomplete information on slide readings (primary endpoint)
Survey 9	0	-
Survey 10	0	-

Source: Table D1_S1 to Table D1_S10

Other important deviations to the protocol are as follows:

- As per protocol, each segment defined to assess geographical heterogeneity had to include a minimum of 10 participants, regrouping villages by proximity if needed in order to avoid identification of PII. However, the following segments had less than 10 participants recruited:

  Survey 5, 4 segments: 1 segment in MA Mangochi EXP, 1 segment in MA St Montfort EXP, 2 segments in MA Monkey Bay UNEXP

Survey 6, 2 segments: 1 segment in MA Monkey Bay UNEXP, 1 segment in KE Nyando UNEXP

Survey 7, 4 segments: 3 segments in GH Navrongo UNEXP, 1 segment in MA St Montfort EXP

Survey 8, 5 segments: 3 segments in GH Navrongo UNEXP, 2 segments in MA Chikwawa UNEXP

Survey 9, 6 segments: 1 segment in KE Kombewa EXP, 2 segments in GH Navrongo UNEXP, 1 segment in MA Mangochi EXP, 1 segment in MA Chikwawa UNEXP, 1 segment in KE Nyando UNEXP

Survey 10, 13 segments: 3 segments in GH Navrongo UNEXP, 2 segments in MA Mangochi EXP, 1 segment in MA Monkey Bay UNEXP, 1 segment in MA Chikwawa UNEXP, 3 segments in MA St Montfort EXP, 3 segments in KE Nyando UNEXP.

Results for geographical heterogeneity are presented in Section 11.4.2.5.

- In Survey 6, following a data quality check, it was identified that segment information for 19 participants from GH Navrongo were incorrectly recorded, creating virtually more options than expected, and potentially diluting the homogeneity/heterogeneity statistical calculations. On further assessment, the impact was estimated to be negligible, as despite the data being linked to a secondary objective, it affected only 19 participants out of 1200 enrolled in the survey and consequently there would be no change to the current study outcomes, and no impact on the overall study conclusions. The GH Navrongo site verified the data and sent the corrected information.
- During Survey 6, at site KE Siaya, a participant personal identifier was entered into InForm when the study staff was responding to CRA query. The staff was retrained and the PI was asked to report this incident as a critical protocol deviation to the ethics committee. Moreover this was reported to the Computer Security Incident Response.

11.2.3. Demography

A summary of the number of participants included in the JTEG 6M-4Y age group and demographic characteristics for the ATP Cohort are described below and detailed in Table 8.

- As defined per protocol stratification design, the proportion of participants in the JTEG age group of 6M-4Y was similar across surveys, ranging from 66.5% in Surveys 2 and 6 to 66.8% in Surveys 3, 4, 8 and 10.
- The mean±SD age ranged from 4.02±2.73 (Survey 8) to 4.05±2.75 years (Surveys 2 and 4).
- The male:female ratio was generally equal across surveys.

No major differences were observed in the demographic characteristics of the Total Cohort compared to the ATP Cohort.

Table 8 Demographic and baseline characteristics by survey (ATP Cohort)

Survey	JTEG age group: 6M-4Y n (%)	Age (years) Mean±SD	Female:Male
Survey 1	2808 (66.7)	4.02±2.75	48.7:51.3
Survey 2	2794 (66.5)	4.05±2.75	49.7:50.3
Survey 3	1603 (66.8)	4.04±2.75	50.4:49.6
Survey 4	2004 (66.8)	4.05±2.75	48.2:51.8
Survey 5	3584 (66.7)	4.05±2.72	48.8:51.2
Survey 6	3980 (66.5)	4.03±2.72	49.5:50.5
Survey 7	4830 (66.7)	4.05±2.73	50.1:49.9
Survey 8	4818 (66.8)	4.02±2.73	50.7:49.3
Survey 9	4797 (66.6)	4.04±2.74	48.7:51.3
Survey 10	4814 (66.8)	4.03±2.74	49.9:50.1

ATP = according to protocol; JTEG = Joint Technical Expert Group; 6M-4Y = 6 months to 4 years; SD = standard deviation
n (%) = number (percentage) of participants overall in JTEG age group
Source: Table D4.2_S1 to Table D4.2_S10

Further details are presented of demographic characteristics according to *P. falciparum* infection status in Table D4.2_S1 to Table D4.2_S10 (ATP Cohort) and Table D4.1_S1 to Table D4.1_S10 (Total Cohort) and according to vaccine eligible or ineligible subgroups in Table D5.2_S1 to Table D5.2_S10 (ATP Cohort) and Table D5.1_S1 to Table D5.1_S10 (Total Cohort). The definitions of vaccine eligible/ineligible subgroups are provided in Annex 2 ‘Glossary of terms’.

11.3. Outcome data

The number of participants in the Total Cohort and ATP Cohort with reasons for exclusion are presented in Section 11.2.2.

11.4. Main results

11.4.1. Results of co-primary objectives

Of the participants included in the ATP Cohort, results of co-primary objectives are described below.

11.4.1.1. Prevalence of *P. falciparum*

P. falciparum prevalence – Survey 1 to Survey 10

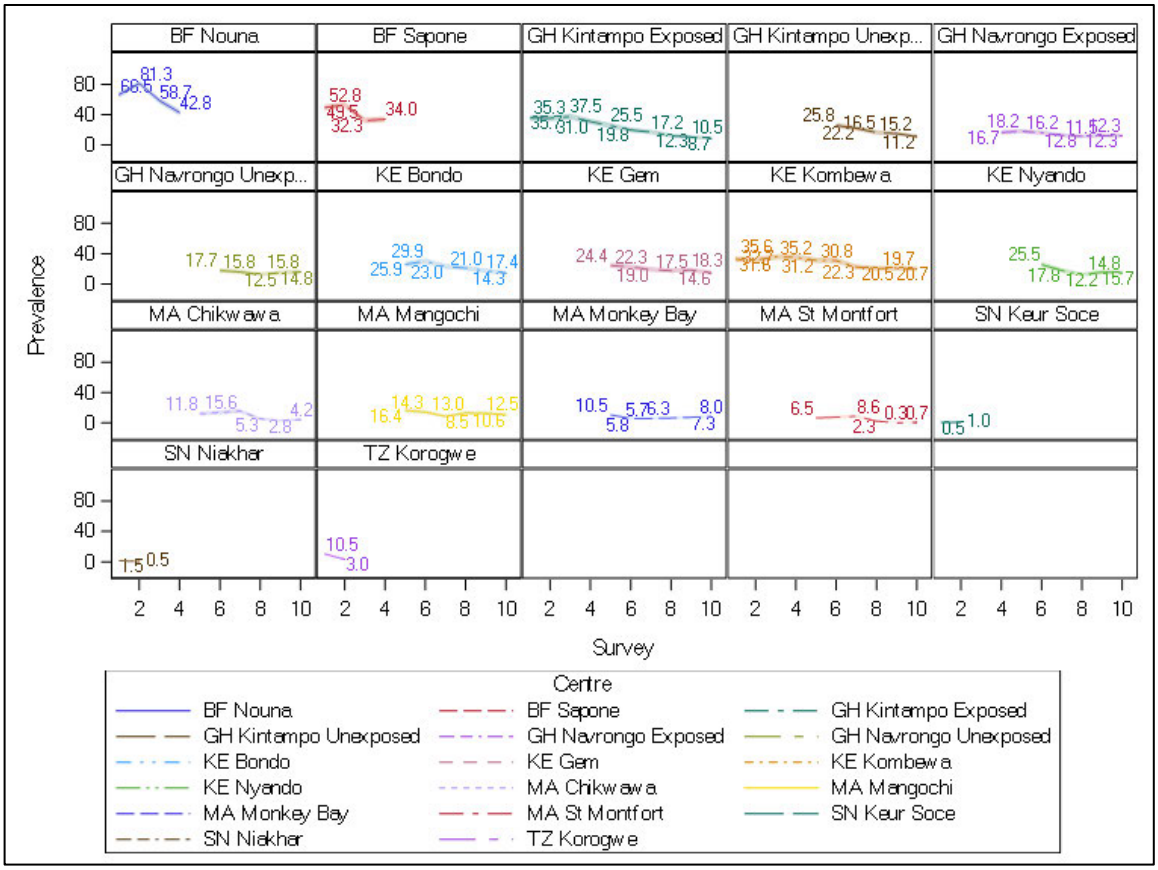
Overall sites, *P. falciparum* parasitemia prevalence was highest in Survey 3 (41.02% of participants), after which prevalence decreased with subsequent surveys to Survey 8 (12.60% of participants) and remained at a similar level up to Survey 10 (11.25% of participants) (Table 9). The higher prevalence in Surveys 1-4 reflects the high malaria transmission intensity in the Burkina Faso sites participating in the earlier surveys. Post-RTS,S/AS01$_E$ vaccination (Survey 5 to Survey 10), *P. falciparum* prevalence generally decreased over surveys in most centers in Ghana, Kenya and Malawi (Figure 2).

Table 9 Overall *P. falciparum* parasitemia prevalence according to Survey year (ATP Cohort)

					95% CI	
Survey year		**n**	**N**	**Proportion (in %)**	**LL**	**UL**
Survey 1	Total	1187	4208	28.21	26.85	29.59
	Pooled - GEE model	.	.	28.13	14.30	47.87
Survey 2	Total	1232	4199	29.34	27.97	30.74
	Pooled - GEE model	.	.	29.35	13.12	53.35
Survey 3	Total	984	2399	41.02	39.04	43.02
	Pooled - GEE model	.	.	41.01	31.37	51.40
Survey 4	Total	958	3000	31.93	30.27	33.64
	Pooled - GEE model	.	.	31.93	24.93	39.86
Survey 5	Total	1022	5377	19.01	17.97	20.08
	Pooled - GEE model	.	.	18.93	14.33	24.59
Survey 6	Total	1246	5987	20.81	19.79	21.86
	Pooled - GEE model	.	.	20.82	16.66	25.70
Survey 7	Total	1138	7241	15.72	14.88	16.58
	Pooled - GEE model	.	.	15.72	12.84	19.11
Survey 8	Total	909	7217	12.60	11.84	13.38
	Pooled - GEE model	.	.	12.59	9.76	16.08
Survey 9	Total	888	7203	12.33	11.58	13.11
	Pooled - GEE model	.	.	12.33	9.35	16.08
Survey 10	Total	810	7202	11.25	10.53	12.00
	Pooled - GEE model	.	.	11.25	8.69	14.44

ATP = According To Protocol Cohort; GEE = generalized estimating equations
N = number of subjects with known result for *P. falciparum* parasitemia test measured by microscopy
n = number of subjects *P. falciparum* parasitemia infected measured by microscopy
% = n/N x 100
Pooled - GEE model = Estimated proportion using PROC GENMOD with 'Center' as random effect
LL, UL = 95% Lower and Upper exact confidence limits (CI)
Source: Table T3 (Annex – Report Tables Survey 10)

Figure 2 ***P. falciparum*** **parasitemia prevalence by center and survey (ATP Cohort)**



ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania
Prevalence % = number of subjects *P. falciparum* parasitemia infected measured by microscopy / number of subjects with known result for *P. falciparum* parasitemia test measured by microscopy x 100
Source: Table T3 (Annex – Report Tables Survey 10)

In Annex – Report Tables Survey 10: Survey year effect on participants infected with *P. falciparum* parasitemia according to RTS,S/AS01 vaccine eligible or ineligible subgroup are presented in Table T2; *P. falciparum* parasitemia prevalence according to survey year are presented in Table T3; *P. falciparum* prevalence by vaccine eligibility by survey for each study site are presented in Figure T1A (BF Nouna), Figure T1B (BF Sapone), Figure T2A (SN Niakhar), Figure T2B (SN Keur Soce), Figure T3A (TZ Korogwe), Figure T4A (KE Kombewa EXP), Figure T4B (KE Bondo UNEXP), Figure T4C (KE Gem EXP), Figure T4D (KE Nyando UNEXP), Figure T5A (GH Kintampo EXP), Figure T5B (GH Kintampo UNEXP), Figure T5C (GH Navrongo EXP), Figure T5D (GH Navrongo UNEXP), Figure T6A (MA Mangochi EXP), Figure T6B (MA Monkey Bay UNEXP), Figure T6C (MA Chikwawa UNEXP), Figure T6D (MA St Montfort EXP) and Figure T7 (all study sites).

P. falciparum prevalence – by JTEG and WHO age groups

Overall, in all 10 surveys, the prevalence of *P. falciparum* was significantly lower in the JTEG age group of 6M-4Y vs. 5Y-9Y (Table 10 and Figure 3). This significant difference in prevalence of *P. falciparum* between JTEG age groups was also observed in most sites in each survey.

P. falciparum prevalence varied across sites. Considering study sites from Ghana, Kenya and Malawi only, the prevalence of *P. falciparum* ranged from:

- 0% in MA St Montfort EXP (Survey 9) to 32.75% in KE Kombewa EXP (Survey 4) in the 6M-4Y JTEG age group
- 0.99% in MA St Montfort (Survey 10) to 57.50% in GH Kintampo EXP (Survey 1) in the 5Y-9Y JTEG age group.

Overall, in all 10 surveys, the prevalence of *P. falciparum* was also lower in the WHO age group of 6M-1Y vs. 2Y-9Y (Table P2_S1 to Table P2_S10).

P. falciparum prevalence – by annual age

The *P. falciparum* prevalence generally increased with the annual age up to 6 years in all 10 surveys with no consistent trend in the 6-9 years of age group (Table P5_S1 to Table P5_S10).

P. falciparum prevalence – by vaccine eligibility

The overall prevalence of *P. falciparum* was lower in vaccine eligible compared to ineligible subgroups, in all 10 surveys (Table P6_S1 to Table P6_S10).

P. falciparum prevalence – by vaccination status

In alignment with the MVIP and implementation of RTS,S/AS01$_E$ vaccination, participants were to receive the RTS,S/AS01$_E$ vaccine in exposed sites from Survey 5 onwards. Only 4 participants received the RTS,S/AS01$_E$ vaccine (at least 1 dose) in Survey 5 (see Section 11.4.3.1); data are therefore summarized for prevalence of *P. falciparum* by vaccination status from Survey 6 onwards.

Overall in each survey (Survey 6 to Survey 10), the prevalence of *P. falciparum* was lower in RTS,S/AS01$_E$ vaccinated compared to unvaccinated participants (Table 11, Figure 4). In total, 4.3% (Survey 6), 15.0% (Survey 7), 22.4% (Survey 8), 27.3% (Survey 9) and 38.5% (Survey 10) of participants received at least 1 dose of RTS,S/AS01$_E$ vaccine (Table V2_S6 to Table V2_S10).

Table 10 ***P. falciparum*** **parasitemia prevalence by center and survey, according to JTEG age group (ATP Cohort)**

JTEG		Survey 1			Survey 2			Survey 3			Survey 4		
age group	Study site	%	95% CI		%	95% CI		%	95% CI		%	95% CI	
0.5-4Y	BF_Nouna	61.63	56.70	66.40	80.25	76.01	84.04	49.50	44.49	54.51	33.67	29.05	38.52
	BF_Sapone	40.20	35.37	45.17	45.61	40.65	50.64	18.70	15.01	22.87	23.56	19.48	28.04
	SN_Niakhar	1.51	0.56	3.25	0.25	0.01	1.40						
	TZ_Korogwe_EXP	7.23	4.90	10.22	1.50	0.55	3.24						
	KE_Kombewa_EXP	24.88	20.72	29.40	26.93	22.65	31.56	29.68	25.24	34.41	32.75	28.19	37.57
	GH_Kintampo_EXP	24.75	20.60	29.28	27.25	22.94	31.90	29.18	24.77	33.89	25.88	21.64	30.48
	GH_Navrongo_EXP										7.69	5.29	10.74
	SN_Keur Soce	0.50	0.06	1.79	1.01	0.28	2.56						
	Overall Total	**23.04**	**21.49**	**24.64**	**26.16**	**24.54**	**27.84**	**31.75**	**29.48**	**34.09**	**24.70**	**22.83**	**26.65**
	Pooled - GEE model	**22.96**	**11.11**	**41.53**	**26.12**	**11.02**	**50.21**	**31.76**	**21.96**	**43.51**	**24.71**	**17.44**	**33.77**
5-9Y	BF_Nouna	76.24	69.76	81.93	83.50	77.62	88.36	77.00	70.54	82.64	61.31	54.16	68.11
	BF_Sapone	68.16	61.24	74.54	67.00	60.02	73.47	59.80	52.63	66.67	54.73	47.57	61.74
	SN_Niakhar	1.50	0.31	4.32	0.98	0.12	3.50						
	TZ_Korogwe_EXP	17.00	12.07	22.94	6.00	3.14	10.25						
	KE_Kombewa_EXP	48.73	41.56	55.94	40.91	33.99	48.10	47.47	40.35	54.68	40.10	33.20	47.31
	GH_Kintampo_EXP	57.50	50.33	64.44	51.50	44.35	58.61	54.27	47.08	61.33	41.09	34.23	48.21
	GH_Navrongo_EXP										35.03	28.38	42.13
	SN_Keur Soce	0.50	0.01	2.75	0.99	0.12	3.51						
	Overall Total	**38.57**	**36.01**	**41.18**	**35.66**	**33.15**	**38.23**	**59.67**	**56.17**	**63.10**	**46.49**	**43.35**	**49.64**
	Pooled - GEE model	**38.52**	**19.99**	**61.10**	**35.84**	**16.95**	**60.45**	**59.64**	**48.63**	**69.76**	**46.45**	**37.98**	**55.14**

JTEG		Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
age group	Study site	%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
0.5-4Y	KE_Kombewa_EXP	27.11	22.83	31.74	27.82	23.48	32.50	19.00	15.27	23.19	16.92	13.38	20.94	15.96	12.51	19.92	12.85	9.72	16.54
	GH_Kintampo_EXP	20.00	16.19	24.26	13.18	10.03	16.89	11.25	8.33	14.76	6.28	4.11	9.13	6.00	3.88	8.80	5.75	3.68	8.50
	GH_Kintampo_UNEXP				20.20	16.38	24.47	16.54	13.03	20.56	14.39	11.11	18.20	10.53	7.69	13.96	8.27	5.76	11.42
	GH_Navrongo_EXP	9.98	7.22	13.34	8.00	5.54	11.11	4.77	2.90	7.35	3.51	1.93	5.82	6.25	4.09	9.09	5.50	3.48	8.21
	GH_Navrongo_UNEXP				6.50	4.29	9.38	6.98	4.69	9.93	6.77	4.51	9.69	7.02	4.71	9.98	8.85	6.27	12.04
	MA_Mangochi_EXP	12.78	9.67	16.46	9.80	7.06	13.15	6.72	4.47	9.62	8.74	6.13	12.00	6.02	3.89	8.82	7.00	4.70	9.96
	MA_Monkey Bay_UNEXP	6.84	4.55	9.79	2.00	0.87	3.90	4.51	2.70	7.04	3.69	2.08	6.02	4.79	2.91	7.37	5.46	3.45	8.15
	MA_Chikwawa_UNEXP	8.44	5.88	11.65				10.36	7.60	13.70	2.51	1.21	4.57	1.75	0.71	3.58	3.02	1.57	5.22
	MA_St Montfort_EXP	4.37	2.57	6.91				6.52	4.34	9.35	1.24	0.41	2.88	0.00	0.00	0.92	0.50	0.06	1.79
	KE_Bondo_UNEXP	23.21	19.18	27.63	25.38	21.14	30.01	18.27	14.63	22.39	15.56	12.17	19.46	13.65	10.45	17.39	11.00	8.11	14.48
	KE_Gem_EXP	19.90	16.11	24.14	16.28	12.77	20.31	11.94	8.94	15.52	13.58	10.40	17.31	12.06	9.03	15.67	10.70	7.85	14.14
	KE_Nyando_UNEXP				20.91	17.01	25.24	12.15	9.10	15.79	9.95	7.24	13.26	10.67	7.83	14.10	9.56	6.89	12.84
	Overall Total	**14.82**	**13.67**	**16.02**	**14.97**	**13.88**	**16.12**	**10.75**	**9.89**	**11.65**	**8.61**	**7.84**	**9.44**	**7.90**	**7.15**	**8.70**	**7.37**	**6.65**	**8.15**
	Pooled - GEE model	**14.74**	**10.45**	**20.40**	**15.01**	**10.64**	**20.74**	**10.75**	**8.29**	**13.83**	**8.60**	**6.06**	**12.05**	**7.89**	**5.66**	**10.89**	**7.37**	**5.67**	**9.53**
5-9Y	KE_Kombewa_EXP	39.39	32.54	46.57	36.82	30.14	43.89	29.00	22.82	35.82	27.78	21.66	34.57	30.15	23.86	37.04	33.00	26.58	39.93
	GH_Kintampo_EXP	36.50	29.82	43.58	33.33	26.81	40.36	29.00	22.82	35.82	24.26	18.52	30.77	19.50	14.25	25.68	14.50	9.93	20.16
	GH_Kintampo_UNEXP				37.19	30.46	44.30	33.33	26.86	40.31	20.81	15.37	27.16	24.38	18.61	30.92	16.92	12.01	22.83
	GH_Navrongo_EXP	34.31	27.83	41.27	32.66	26.20	39.65	28.71	22.58	35.48	27.50	21.44	34.24	24.50	18.71	31.06	26.00	20.07	32.66
	GH_Navrongo_UNEXP				40.00	33.15	47.15	33.67	27.14	40.69	23.88	18.16	30.39	30.35	24.08	37.21	30.57	24.16	37.59
	MA_Mangochi_EXP	23.74	17.99	30.29	23.04	17.45	29.43	12.18	7.96	17.58	20.85	15.58	26.96	25.25	19.41	31.82	17.91	12.87	23.92
	MA_Monkey Bay_UNEXP	17.73	12.74	23.70	13.50	9.09	19.03	7.96	4.62	12.61	11.86	7.67	17.26	12.38	8.17	17.73	13.27	8.85	18.83
	MA_Chikwawa_UNEXP	18.75	13.49	25.00				26.21	20.35	32.78	10.89	6.95	16.02	4.98	2.41	8.96	6.50	3.51	10.86
	MA_St Montfort_EXP	10.77	6.79	15.99				13.07	8.72	18.56	4.55	2.10	8.45	1.00	0.12	3.55	0.99	0.12	3.53
	KE_Bondo_UNEXP	31.07	24.82	37.87	38.46	31.82	45.44	32.66	26.20	39.65	31.84	25.46	38.76	25.00	19.16	31.60	21.00	15.57	27.31
	KE_Gem_EXP	33.50	26.95	40.56	34.36	27.72	41.48	33.17	26.72	40.12	25.37	19.51	31.97	30.69	24.41	37.55	22.50	16.91	28.92
	KE_Nyando_UNEXP				34.48	27.97	41.46	28.78	22.69	35.50	17.01	12.01	23.05	25.89	19.92	32.59	26.04	19.99	32.85
	Overall Total	**27.38**	**25.33**	**29.51**	**32.39**	**30.34**	**34.48**	**25.67**	**23.94**	**27.47**	**20.59**	**18.99**	**22.27**	**21.16**	**19.54**	**22.84**	**19.05**	**17.50**	**20.69**
	Pooled - GEE model	**27.32**	**21.66**	**33.81**	**32.38**	**27.81**	**37.32**	**25.65**	**21.01**	**30.91**	**20.56**	**16.53**	**25.26**	**21.17**	**16.30**	**27.03**	**19.10**	**14.49**	**24.75**

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; JTEG = Joint Technical Expert Group; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania

EXP = exposed sites; UNEXP = unexposed sites; GEE = generalized estimating equations

0.5-4Y = 6 months - 4 years at IC (Informed Consent) date; 5-9Y = 5 - 9 years at IC date; 95% CI = 95% Lower and Upper exact confidence limits

Pooled - GEE model = Estimated proportion using PROC GENMOD with 'Center' as random effect

Source: Table P1_S1 to Table P1_S10

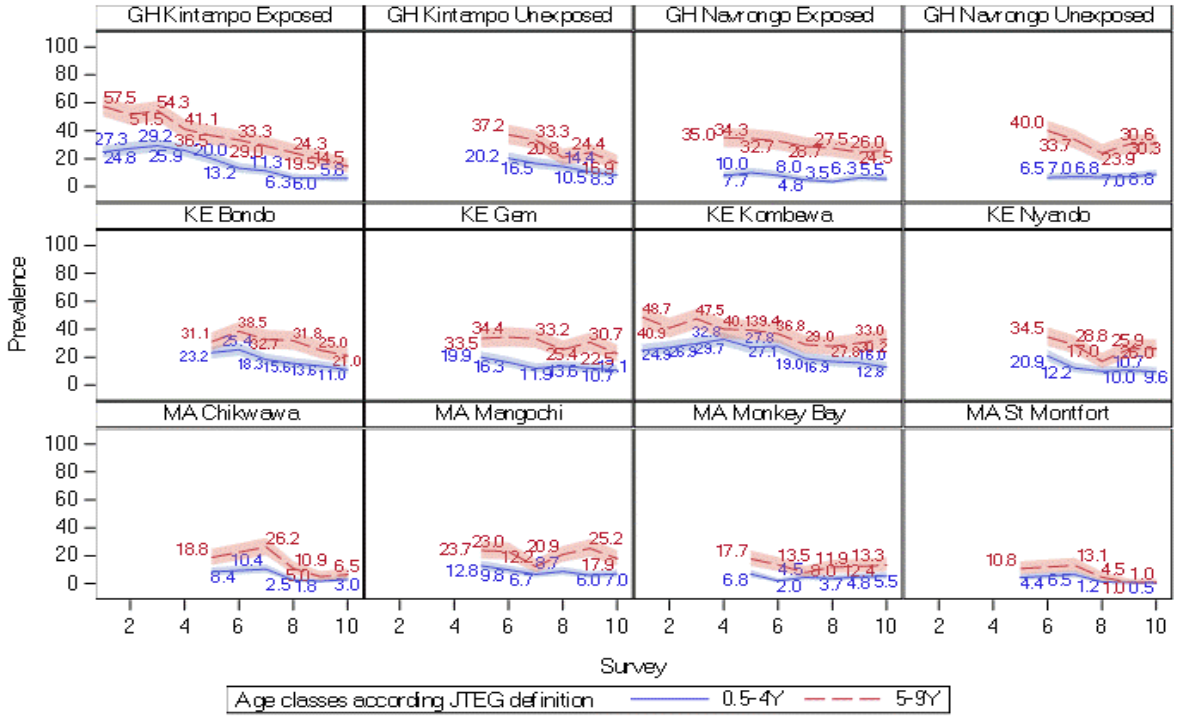
Table 11 ***P. falciparum*** **parasitemia prevalence by center and survey, according to RTS,S/AS01 vaccination status (Surveys 6-10; ATP Cohort)**

Vaccination status	Study center	Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
Vaccinated	KE_Kombewa_EXP	24.44	16.00	34.64	14.18	8.76	21.25	12.55	8.63	17.43	13.77	10.11	18.15	11.11	8.13	14.72
	GH_Kintampo_EXP	2.17	0.06	11.53	6.33	3.08	11.33	4.69	2.45	8.04	3.64	1.83	6.42	4.20	2.37	6.84
	GH_Kintampo_UNEXP	-	-	-	-	-	-	0.00	0.00	97.50	-	-	-	0.00	0.00	70.76
	GH_Navrongo_EXP	-	-	-	1.74	0.36	5.01	2.73	1.19	5.31	2.55	1.11	4.96	4.42	2.55	7.08
	GH_Navrongo_UNEXP	-	-	-	-	-	-	-	-	-	-	-	-	1.14	0.03	6.17
	MA_Mangochi_EXP	2.70	0.07	14.16	2.31	0.63	5.81	5.26	2.83	8.83	5.65	3.27	9.02	6.33	3.86	9.71
	MA_Monkey Bay_UNEXP	-	-	-	0.00	0.00	97.50	0.00	0.00	97.50	5.88	0.15	28.69	7.69	3.15	15.21
	MA_Chikwawa_UNEXP	-	-	-	0.00	0.00	84.19	0.00	0.00	33.63	0.00	0.00	8.22	0.91	0.02	4.96
	MA_St Montfort_EXP	-	-	-	4.11	1.90	7.66	0.76	0.09	2.71	0.00	0.00	1.50	0.27	0.01	1.50
	KE_Bondo_UNEXP	-	-	-	20.00	0.51	71.64	10.53	1.30	33.14	4.35	0.53	14.84	8.47	4.82	13.59
	KE_Gem_EXP	8.33	3.42	16.42	8.49	5.11	13.09	9.78	6.55	13.91	12.26	8.87	16.38	7.45	4.83	10.89
	KE_Nyando_UNEXP	-	-	-	12.50	0.32	52.65	0.00	0.00	36.94	6.45	2.40	13.52	6.57	3.64	10.78
	Overall Total	**12.06**	**8.34**	**16.68**	**6.00**	**4.66**	**7.58**	**5.83**	**4.73**	**7.08**	**6.36**	**5.32**	**7.53**	**5.60**	**4.77**	**6.52**
	Pooled - GEE model	**9.83**	**3.78**	**23.23**	**6.47**	**3.93**	**10.45**	**5.79**	**3.48**	**9.49**	**5.66**	**3.33**	**9.44**	**5.39**	**3.75**	**7.70**
Unvaccinated	KE_Kombewa_EXP	31.96	27.93	36.20	24.68	20.83	28.85	25.76	21.33	30.60	27.80	22.76	33.28	34.23	28.02	40.88
	GH_Kintampo_EXP	21.30	17.96	24.95	21.04	17.33	25.14	18.02	14.11	22.50	17.45	13.32	22.24	15.23	10.95	20.37
	GH_Kintampo_UNEXP	25.83	22.37	29.53	22.17	18.90	25.71	16.53	13.64	19.75	15.17	12.39	18.29	11.22	8.80	14.03
	GH_Navrongo_EXP	16.19	13.33	19.39	17.29	13.83	21.21	19.93	15.61	24.86	23.08	18.32	28.40	24.37	19.06	30.33
	GH_Navrongo_UNEXP	17.67	14.70	20.96	15.83	13.00	19.00	12.50	9.96	15.42	14.83	12.08	17.93	18.36	15.10	21.99
	MA_Mangochi EXP	15.04	12.20	18.26	11.03	8.22	14.40	18.41	14.51	22.86	18.55	14.43	23.27	14.95	11.12	19.49
	MA_Monkey Bay UNEXP	5.83	4.10	8.02	5.68	3.96	7.84	6.34	4.53	8.60	7.39	5.40	9.82	8.07	5.85	10.79
	MA_Chikwawa_UNEXP	-	-	-	15.67	12.90	18.78	5.41	3.73	7.56	3.05	1.79	4.84	4.93	3.18	7.24
	MA_St Montfort EXP	-	-	-	11.17	8.23	14.70	3.57	1.86	6.16	0.56	0.07	2.01	1.28	0.27	3.70
	KE_Bondo UNEXP	29.93	26.29	33.78	23.04	19.72	26.62	21.29	18.05	24.83	18.49	15.35	21.97	16.78	13.35	20.69
	KE_Gem EXP	24.60	20.90	28.61	24.74	20.55	29.33	23.94	19.44	28.92	25.18	20.22	30.67	22.86	18.07	28.23
	KE_Nyando UNEXP	25.50	22.06	29.19	17.91	14.90	21.24	12.37	9.84	15.28	17.36	14.16	20.94	19.38	15.56	23.68
	Overall Total	**21.20**	**20.15**	**22.29**	**17.43**	**16.49**	**18.40**	**14.54**	**13.63**	**15.49**	**14.57**	**13.62**	**15.55**	**14.78**	**13.75**	**15.86**
	Pooled - GEE model	**21.38**	**17.12**	**26.36**	**17.51**	**14.49**	**21.01**	**15.29**	**11.74**	**19.68**	**15.67**	**11.66**	**20.73**	**15.89**	**11.65**	**21.30**

Shaded fields represent sites not participating in a specific survey
Fields with no data (-) represent no participants with known result for *P. falciparum* parasitemia test measured by microscopy

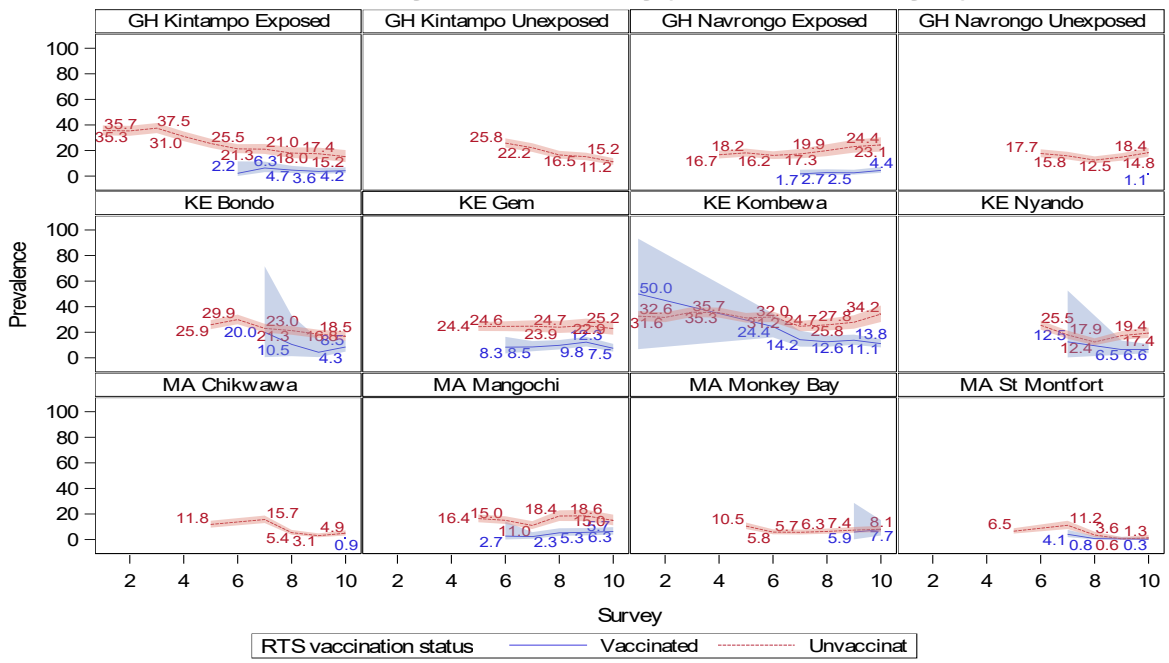
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites; GEE = generalized estimating equations
Vaccinated = children vaccinated with at least 1 dose of RTS,S/AS01 malaria vaccine; Unvaccinated = children unvaccinated with RTS,S/AS01 malaria vaccine
95% CI = 95% Lower and Upper exact confidence limits; Pooled - GEE model = Estimated proportion using PROC GENMOD with 'Center' as random effect
Source: Table P7_S6 to Table P7_S10

Figure 3 ***P. falciparum*** **parasitemia prevalence by center (Ghana, Kenya and Malawi sites only) and survey, according to JTEG age group (ATP Cohort)**



ATP = according to protocol; JTEG = Joint Technical Expert Group; GH = Ghana; KE = Kenya; MA = Malawi
0.5-4Y = 6 months - 4 years at IC (Informed Consent) date; 5-9Y = 5 - 9 years at IC date
Shaded area = 95% Lower and Upper exact confidence limits
Source: Table P1_S1 to Table P1_S10

Figure 4 ***P. falciparum*** **parasitemia prevalence by center (Ghana, Kenya and Malawi sites only) and survey, according to RTS,S/AS01 vaccination status (ATP Cohort)**



ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi
Vaccinated = children vaccinated with at least 1 dose of RTS,S/AS01 malaria vaccine; Unvaccinat= children unvaccinated with RTS,S/AS01 malaria vaccine
Shaded area = 95% Lower and Upper exact confidence limits
Source: Table P7_S6 to Table P7_S10

P. falciparum prevalence – according to presence of fever

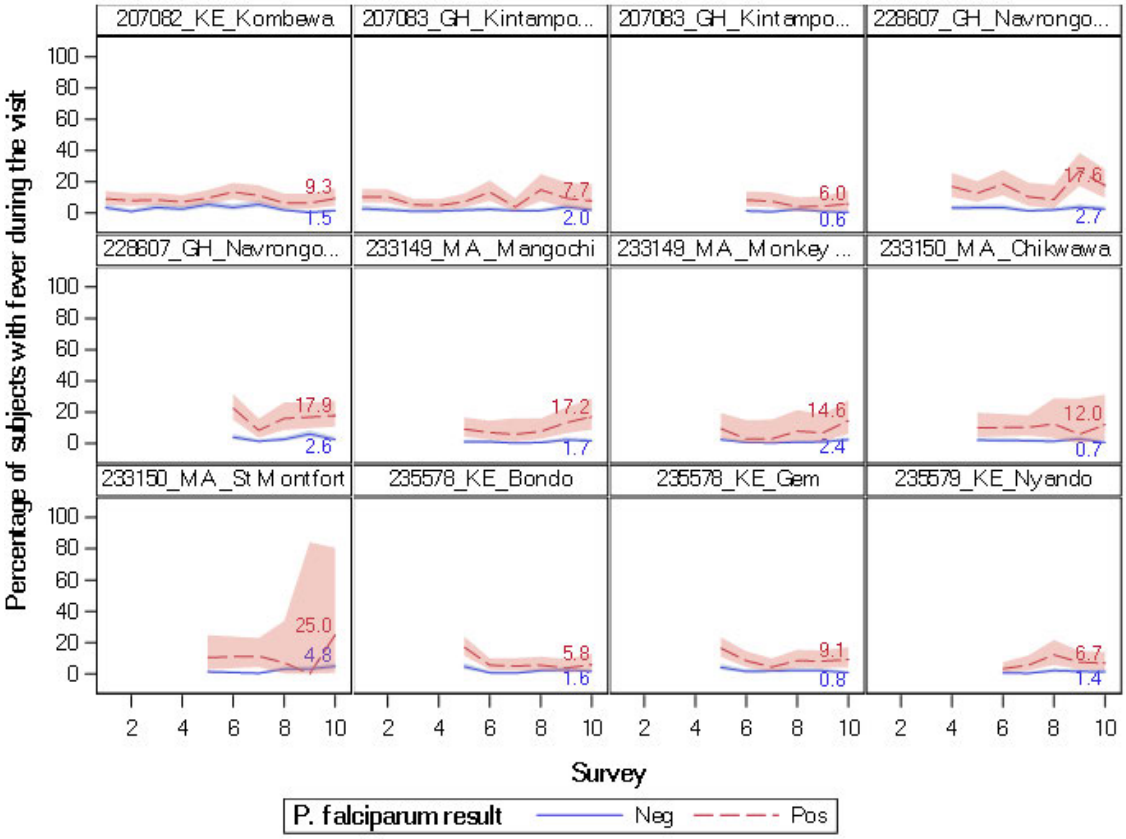
Overall sites, the prevalence of *P. falciparum* by microscopy was higher in participants with fever vs. no fever measured at the visit in all 10 surveys (Table 12). The same finding was generally observed for each center (Figure 5).

Table 12 ***P. falciparum*** **measured by microscopy by survey, according to the presence of fever at the visit (ATP Cohort)**

	Fever % (95% CI)	No fever % (95% CI)
Survey 1	50.2 (43.4-57.1)	27.0 (25.6-28.4)
Survey 2	49.0 (41.9-56.1)	28.4 (27.0-29.8)
Survey 3	64.9 (54.4-74.5)	40.0 (38.0-42.1)
Survey 4	62.2 (53.2-70.7)	30.6 (28.9-32.3)
Survey 5	49.0 (42.6-55.4)	17.6 (16.5-18.6)
Survey 6	57.8 (51.1-64.4)	19.4 (18.4-20.4)
Survey 7	51.6 (43.6-59.5)	14.9 (14.1-15.8)
Survey 8	40.0 (33.2-47.1)	11.8 (11.1-12.6)
Survey 9	34.8 (28.9-41.1)	11.5 (10.8-12.3)
Survey 10	42.5 (35.7-49.4)	10.3 (9.6-11.0)

ATP = according to protocol; 95% CI = Exact 95% Lower and Upper confidence limits
Fever = Positive presence of fever at the visit; no fever = Negative presence of fever at the visit
Source: Table S16_S1 to Table S16_S10

Figure 5 ***P. falciparum*** **measured by microscopy by center (Ghana, Kenya and Malawi sites only) and survey, according to the presence of fever at the visit (ATP Cohort)**



ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi; Neg = negative; Pos = positive
Shaded area = 95% Lower and Upper exact confidence limitsSource: Table S16_S1 to Table S16_S10

P. falciparum prevalence – heterogeneity by center

In all 10 surveys, the prevalence of *P. falciparum* was significantly heterogenous among centers (p<0.0001) for both JTEG (Table P3_S1 to Table P3_S10) and WHO (Table P4_S1 to Table P4_S10) age groups. There was no significant difference in the prevalence of *P. falciparum* between gender overall and in each center in all 10 surveys (Table P8_S1 to Table P8_S10).

11.4.1.2. Malaria control interventions

Overall, across all 10 surveys, bednet usage was high, ranging from 85.0% (Survey 9) to 91.1% (Survey 4) (Table 13), of which:

- 44.6% (Survey 6) to 72.1% (Survey 3) were new bednets
- 63.2% (Survey 3) to 89.9% (Survey 4) were impregnated bednets
- 18.3% (Survey 4) to 41.7% (Survey 6) were pierced/torn bednets.

Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), bednet usage the night before the visit remained high post-vaccination, ranging between 70.2% to 98.3% pre-vaccination to between 59.8% to 99.5% post-vaccination.

Table 13 Bednet history information overall by survey (ATP Cohort)

Survey	Bednet usage			New bednets			Impregnated bednets			Pierced/torn bednets		
	%	95% CI		%	95% CI		%	95% CI		%	95% CI	
Survey 1	89.5	88.6	90.5	67.0	65.5	68.5	68.7	67.2	70.2	24.0	22.7	25.4
Survey 2	86.4	85.3	87.4	57.4	55.7	59.0	77.9	76.5	79.2	24.0	22.7	25.5
Survey 3	89.7	88.4	90.9	72.1	70.2	74.0	63.2	61.1	65.2	20.0	18.4	21.8
Survey 4	91.1	90.0	92.1	67.4	65.6	69.2	89.9	88.7	91.0	18.3	16.9	19.8
Survey 5	89.4	88.5	90.2	60.3	58.9	61.7	87.4	86.5	88.4	37.6	36.2	39.0
Survey 6	85.9	84.9	86.7	44.6	43.2	46.0	86.7	85.8	87.6	41.7	40.3	43.0
Survey 7	86.8	86.0	87.5	61.0	59.7	62.2	89.5	88.7	90.3	29.8	28.7	31.0
Survey 8	87.5	86.7	88.2	64.7	63.5	65.9	84.6	83.7	85.5	32.0	30.8	33.1
Survey 9	85.0	84.2	85.9	48.8	47.5	50.0	88.1	87.3	88.9	40.6	39.4	41.8
Survey 10	85.5	84.7	86.4	63.1	61.9	64.3	88.4	87.6	89.2	28.6	27.5	29.7

ATP = according to protocol
95% CI = Exact 95% Lower and Upper confidence limits
Source: Table MCI1_S1 to Table MCI1_S10

Bednet usage showed some variations across centers (Table 14). Considering study sites from Ghana, Kenya and Malawi only, the percentage of participants who used a bednet the night before the visit ranged from:

- 59.8% in GH Kintampo EXP to 99.7% KE Nyando UNEXP, both in Survey 10, of which:
  - 0.6% in KE Kombewa EXP (Survey 3) to 100% in KE Kombewa EXP (Survey 10) were impregnated bednets.

Table 14 Bednet usage by center and survey (ATP Cohort)

		Survey 1			Survey 2			Survey 3			Survey 4		
	Study site	**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**	
Bednet usage	BF_Nouna	90.3	87.6	92.5	88.3	85.5	90.8	97.3	95.7	98.5	93.5	91.2	95.3
	BF_Sapone	92.2	89.8	94.2	89.1	86.4	91.5	95.8	93.9	97.3	92.5	90.1	94.5
	SN_Niakhar	91.5	88.9	93.6	69.6	65.7	73.2						
	TZ_Korogwe	90.5	87.9	92.7	99.2	98.1	99.7						
	KE_Kombewa_EXP	97.5	95.9	98.6	89.1	86.4	91.5	85.6	82.6	88.4	98.3	97.0	99.2
	GH Kintampo_EXP	70.2	66.3	73.8	82.8	79.6	85.8	80.0	76.6	83.1	76.3	72.7	79.7
	GH_Navrongo_EXP										94.8	92.7	96.5
	SN Keur Soce	94.7	92.6	96.3	86.7	83.7	89.3						
	Overall Total	**89.5**	**88.6**	**90.5**	**86.4**	**85.3**	**87.4**	**89.7**	**88.4**	**90.9**	**91.1**	**90.0**	**92.1**
Impregnated bednets*	BF_Nouna	96.0	94.0	97.5	94.5	92.2	96.3	100	99.4	100	99.3	98.2	99.8
	BF_Sapone	98.4	97.0	99.3	97.6	95.9	98.7	99.8	99.0	100	95.7	93.6	97.2
	SN_Niakhar	87.9	84.9	90.5	100	99.1	100						
	TZ_Korogwe	51.8	47.5	56.1	95.3	93.3	96.9						
	KE_Kombewa_EXP	46.7	42.6	50.9	9.7	7.4	12.6	0.6	0.1	1.7	96.9	95.2	98.2
	GH Kintampo_EXP	39.7	35.0	44.5	99.6	98.6	100	41.3	36.8	45.8	60.0	55.4	64.6
	GH_Navrongo_EXP										91.7	89.2	93.9
	SN Keur Soce	55.3	51.1	59.4	52.1	47.7	56.5						
	Overall Total	**68.7**	**67.2**	**70.2**	**77.9**	**76.5**	**79.2**	**63.2**	**61.1**	**65.2**	**89.9**	**88.7**	**91.0**

		Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
	Study site	**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**	
Bednet usage	KE_Kombewa_EXP	96.7	94.9	98.0	95.7	93.7	97.2	99.5	98.5	99.9	98.2	96.7	99.1	96.2	94.3	97.6	99.3	98.3	99.8
	GH_Kintampo_EXP	78.0	74.5	81.3	76.8	73.2	80.2	72.2	68.4	75.7	73.0	69.3	76.5	65.3	61.4	69.1	59.8	55.8	63.8
	GH_Kintampo_UNEXP				65.8	61.9	69.6	60.0	56.0	63.9	76.0	72.4	79.4	68.2	64.3	71.9	71.0	67.2	74.6
	GH_Navrongo_EXP	92.2	89.8	94.2	90.2	87.5	92.4	93.7	91.4	95.5	89.8	87.1	92.1	90.5	87.9	92.7	91.3	88.8	93.5
	GH_Navrongo_UNEXP				97.2	95.5	98.3	96.8	95.1	98.1	91.8	89.3	93.9	93.7	91.4	95.5	94.5	92.4	96.2
	MA_Mangochi_EXP	91.5	88.9	93.6	77.9	74.4	81.2	74.5	70.8	77.9	74.5	70.8	77.9	69.4	65.5	73.0	67.1	63.1	70.8
	MA_Monkey Bay_UNEXP	92.3	89.9	94.3	80.5	77.1	83.6	77.5	73.9	80.8	70.2	66.3	73.8	69.9	66.1	73.6	71.0	67.1	74.6
	MA_Chikwawa_UNEXP	88.5	85.6	91.0				90.5	87.9	92.7	92.8	90.5	94.8	87.5	84.6	90.0	87.8	84.9	90.3
	MA_St Montfort_EXP	86.3	83.2	89.0				81.6	78.3	84.6	94.7	92.6	96.3	91.8	89.3	93.9	90.4	87.7	92.6
	KE_Bondo_UNEXP	90.7	88.1	92.9	93.5	91.2	95.3	98.7	97.4	99.4	95.5	93.6	97.0	95.4	93.4	96.9	98.7	97.4	99.4
	KE_Gem_EXP	88.0	85.1	90.5	83.2	79.9	86.1	96.7	94.9	98.0	93.4	91.1	95.2	94.0	91.8	95.8	96.0	94.1	97.4
	KE_Nyando_UNEXP				97.8	96.3	98.8	99.3	98.3	99.8	99.3	98.3	99.8	98.5	97.2	99.3	99.7	98.8	100
	Overall Total	**89.4**	**88.5**	**90.2**	**85.9**	**84.9**	**86.7**	**86.8**	**86.0**	**87.5**	**87.5**	**86.7**	**88.2**	**85.0**	**84.2**	**85.9**	**85.5**	**84.7**	**86.4**
Impregnated bednets*	KE_Kombewa_EXP	98.8	97.5	99.5	99.7	98.7	100	99.7	98.8	100	99.2	98.0	99.7	99.8	99.0	100	100	99.4	100
	GH_Kintampo_EXP	94.7	92.2	96.5	87.6	84.3	90.5	96.1	93.8	97.7	99.5	98.4	99.9	74.0	69.3	78.3	97.8	95.7	99.0
	GH_Kintampo_UNEXP				99.7	98.6	100	99.7	98.5	100	0.7	0.1	1.9	92.2	89.1	94.6	95.5	93.1	97.3
	GH_Navrongo_EXP	98.0	96.5	99.0	93.1	90.7	95.1	77.0	73.3	80.5	99.6	98.7	100	91.7	89.1	93.9	98.0	96.4	99.0
	GH_Navrongo_UNEXP				98.3	96.9	99.2	99.5	98.5	99.9	99.3	98.2	99.8	97.5	95.9	98.6	98.8	97.5	99.5
	MA_Mangochi_EXP	73.1	69.1	76.8	90.4	87.4	92.9	99.1	97.7	99.8	93.5	90.8	95.6	89.7	86.4	92.4	95.3	92.7	97.1
	MA_Monkey Bay_UNEXP	75.2	71.4	78.7	87.4	84.1	90.2	98.9	97.5	99.6	98.1	96.3	99.2	75.2	70.8	79.2	83.5	79.7	86.9
	MA_Chikwawa_UNEXP	94.6	92.3	96.4				85.9	82.8	88.7	88.2	85.2	90.7	81.1	77.5	84.4	56.9	52.5	61.2
	MA_St Montfort_EXP	57.5	53.1	61.9				25.0	21.3	29.0	37.5	33.5	41.6	53.5	49.3	57.8	38.2	34.1	42.4
	KE_Bondo_UNEXP	97.8	96.2	98.9	85.7	82.5	88.5	98.5	97.2	99.3	98.4	97.1	99.3	99.0	97.7	99.6	98.6	97.4	99.4
	KE_Gem_EXP	95.6	93.5	97.2	96.5	94.5	98.0	97.1	95.4	98.3	97.2	95.4	98.4	97.3	95.7	98.5	99.1	98.0	99.7
	KE_Nyando_UNEXP				36.6	32.7	40.7	97.1	95.5	98.3	96.7	94.9	98.0	98.1	96.7	99.1	99.7	98.8	100
	Overall Total	**87.4**	**86.5**	**88.4**	**86.7**	**85.8**	**87.6**	**89.5**	**88.7**	**90.3**	**84.6**	**83.7**	**85.5**	**88.1**	**87.3**	**88.9**	**88.4**	**87.6**	**89.2**

*Impregnated bednets' are a subset of 'Bednet usage'
Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
Source: Table MCI1_S1 to Table MCI1_S10

Overall sites, a higher proportion of participants slept under a bednet the night before the visit in the JTEG age group of 6M-4Y vs. 5Y-9Y in each survey (Table 15). Considering study sites from Ghana, Kenya and Malawi only, this significant difference was observed in the majority of surveys in Malawi sites and KE Gem EXP.

Overall sites, in all 10 surveys, a significantly higher percentage of participants slept under a bednet the night before the visit when comparing vaccine eligible vs. ineligible subgroups (Table MCI17_S1 to Table MCI17_S10).

There was no significant difference in bednet usage according to gender overall sites, with the exception of Survey 2 in which more females than males used bednets. There was no significant difference in bednet usage according to gender by center in any survey (Table MCI15_S1 to Table MCI15_S10).

Table 15 Bednet usage by center and survey, according to JTEG age group (ATP Cohort)

JTEG age group	Study site	Survey 1			Survey 2			Survey 3			Survey 4		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
0.5-4Y	BF_Nouna	92.8	89.9	95.1	89.5	86.1	92.3	98.3	96.4	99.3	95.5	93.0	97.3
	BF_Sapone	93.3	90.4	95.5	91.0	87.7	93.6	96.8	94.5	98.3	94.0	91.2	96.1
	SN_Niakhar	93.0	90.0	95.3	69.8	65.0	74.3						
	TZ_Korogwe_EXP	93.3	90.4	95.5	99.8	98.6	100						
	KE_Kombewa_EXP	99.0	97.5	99.7	94.0	91.2	96.1	92.3	89.2	94.7	98.5	96.8	99.5
	GH_Kintampo_EXP	72.3	67.6	76.6	84.8	80.8	88.1	83.0	79.0	86.6	79.1	74.8	83.0
	GH_Navrongo_EXP										95.5	93.0	97.3
	SN_Keur Soce	96.0	93.6	97.7	89.9	86.5	92.7						
	Overall Total	**91.4**	**90.3**	**92.4**	**88.4**	**87.2**	**89.6**	**92.6**	**91.2**	**93.8**	**92.6**	**91.3**	**93.7**
5-9Y	BF_Nouna	85.1	79.5	89.8	86.0	80.4	90.5	95.5	91.6	97.9	89.4	84.3	93.3
	BF_Sapone	90.0	85.1	93.8	85.5	79.8	90.1	94.0	89.7	96.8	89.6	84.5	93.4
	SN_Niakhar	88.5	83.2	92.6	69.1	62.3	75.4						
	TZ_Korogwe_EXP	85.0	79.3	89.6	98.0	95.0	99.5						
	KE_Kombewa_EXP	94.4	90.2	97.2	79.3	73.0	84.7	72.2	65.4	78.3	98.0	94.9	99.4
	GH_Kintampo_EXP	66.0	59.0	72.5	79.0	72.7	84.4	73.9	67.2	79.8	70.8	64.0	77.0
	GH_Navrongo_EXP										93.4	89.0	96.4
	SN_Keur Soce	92.0	87.3	95.4	80.3	74.1	85.5						
	Overall Total	**85.9**	**83.9**	**87.6**	**82.4**	**80.3**	**84.4**	**83.9**	**81.2**	**86.4**	**88.2**	**86.0**	**90.1**

JTEG age group	Study site	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
0.5-4Y	KE_Kombewa_EXP	98.3	96.4	99.3	96.5	94.2	98.1	99.8	98.6	100	99.3	97.8	99.8	98.5	96.8	99.4	99.0	97.4	99.7
	GH_Kintampo_EXP	78.5	74.1	82.4	79.4	75.1	83.2	74.3	69.7	78.5	73.9	69.3	78.1	66.3	61.4	70.9	63.8	58.8	68.5
	GH_Kintampo_UNEXP				70.8	66.1	75.2	64.7	59.8	69.4	79.2	74.9	83.0	68.4	63.6	73.0	74.4	69.9	78.6
	GH_Navrongo_EXP	93.0	90.1	95.3	91.5	88.3	94.0	94.2	91.5	96.3	92.7	89.7	95.1	93.0	90.0	95.3	92.5	89.5	94.9
	GH_Navrongo_UNEXP				97.5	95.5	98.8	96.5	94.2	98.1	93.5	90.6	95.7	94.5	91.8	96.5	94.8	92.2	96.8
	MA_Mangochi_EXP	94.0	91.2	96.1	81.4	77.2	85.1	78.6	74.3	82.5	81.0	76.7	84.8	74.4	69.9	78.6	74.5	69.9	78.7
	MA_Monkey Bay_UNEXP	94.2	91.4	96.3	84.0	80.0	87.5	82.7	78.6	86.3	77.8	73.5	81.8	76.1	71.6	80.2	78.4	74.1	82.3
	MA_Chikwawa_UNEXP	90.0	86.6	92.8				93.2	90.4	95.5	95.7	93.2	97.5	90.2	86.9	93.0	91.7	88.5	94.2
	MA_St Montfort_EXP	88.4	84.8	91.4				86.0	82.3	89.2	96.5	94.2	98.1	95.0	92.4	96.9	93.3	90.4	95.5
	KE_Bondo_UNEXP	93.6	90.7	95.8	94.9	92.2	96.8	99.5	98.2	99.9	98.3	96.5	99.3	97.3	95.2	98.6	98.8	97.1	99.6
	KE_Gem_EXP	92.8	89.8	95.1	87.5	83.9	90.6	98.8	97.1	99.6	96.0	93.7	97.7	96.5	94.2	98.1	96.8	94.5	98.3
	KE_Nyando_UNEXP				98.5	96.7	99.4	99.2	97.8	99.8	99.3	97.9	99.8	99.3	97.8	99.8	99.8	98.6	100
	Overall Total	**91.4**	**90.5**	**92.3**	**88.2**	**87.1**	**89.2**	**89.0**	**88.0**	**89.8**	**90.3**	**89.4**	**91.1**	**87.5**	**86.5**	**88.4**	**88.2**	**87.2**	**89.1**
5-9Y	KE_Kombewa_EXP	93.4	89.0	96.5	94.0	89.8	96.9	99.0	96.4	99.9	96.0	92.2	98.2	91.5	86.7	94.9	100	98.2	100
	GH_Kintampo_EXP	77.0	70.5	82.6	71.7	64.9	77.9	68.0	61.1	74.4	71.3	64.5	77.4	63.5	56.4	70.2	52.0	44.8	59.1
	GH_Kintampo_UNEXP				55.8	48.6	62.8	50.7	43.6	57.9	69.5	62.6	75.9	67.7	60.7	74.1	64.2	57.1	70.8
	GH_Navrongo_EXP	90.7	85.8	94.3	87.4	82.0	91.7	92.6	88.0	95.8	84.0	78.2	88.8	85.5	79.8	90.1	89.0	83.8	93.0
	GH_Navrongo_UNEXP				96.5	92.9	98.6	97.5	94.2	99.2	88.6	83.3	92.6	92.0	87.4	95.4	93.8	89.4	96.7
	MA_Mangochi_EXP	86.4	80.8	90.8	71.1	64.3	77.2	66.0	58.9	72.6	62.6	55.7	69.1	59.4	52.3	66.2	52.2	45.1	59.3
	MA_Monkey Bay_UNEXP	88.7	83.5	92.7	73.5	66.8	79.5	67.2	60.2	73.6	54.1	46.8	61.3	57.9	50.8	64.8	55.6	48.4	62.7
	MA_Chikwawa_UNEXP	85.4	79.6	90.1				85.0	79.3	89.5	87.1	81.7	91.4	82.1	76.1	87.1	80.0	73.8	85.3
	MA_St Montfort_EXP	82.1	75.9	87.2				72.4	65.6	78.5	90.9	86.0	94.5	85.6	79.9	90.1	84.7	78.9	89.3
	KE_Bondo_UNEXP	85.0	79.3	89.5	90.9	86.1	94.4	97.0	93.6	98.9	90.0	85.1	93.8	91.5	86.7	95.0	98.5	95.7	99.7
	KE_Gem_EXP	78.2	71.7	83.7	74.4	67.6	80.3	92.6	88.0	95.8	88.1	82.8	92.2	89.1	84.0	93.0	94.5	90.4	97.2
	KE_Nyando_UNEXP				96.6	93.0	98.6	99.5	97.3	100	99.5	97.2	100	97.0	93.5	98.9	99.5	97.1	100
	Overall Total	**85.2**	**83.5**	**86.8**	**81.3**	**79.5**	**83.0**	**82.3**	**80.7**	**83.8**	**81.7**	**80.1**	**83.3**	**80.2**	**78.5**	**81.8**	**80.3**	**78.6**	**81.9**

Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; JTEG = Joint Technical Expert Group; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
0.5-4Y = 6 months - 4 years at Informed Consent (IC) date, 5-9Y = 5 - 9 years at IC date
95% CI = 95% Lower and Upper exact confidence limits
Source: Table MCI16_S1 to Table MCI16_S10

Other MCIs (i.e., commercial/traditional repellents, mosquito coils, insecticide sprays) were rarely used. Across surveys, 74.0% (Survey 10) to 91.3% (Survey 3) of participants did not use any of these methods in the last 7 days before the visit (Table 16).

Considering study sites from Ghana, Kenya and Malawi only, the percentage of participants who did not use any commercial/traditional repellents, mosquito coils or insecticide sprays in the last 7 days before the visit ranged from 49.5% in GH Kintampo EXP (Survey 7) to 99.0% KE Kombewa EXP (Survey 8) (Table 16).

Data for SMC, IPTi and ACT therapy received within the last 14 days were collected at the center and not participant level, and are therefore not included in summary tabulations at the participant level. Data for ACT usage are available in Appendix Table V.8 and Appendix Table V.9, for IPT and SMC in Appendix Table V.10 and Appendix Table V.11 and for IPT alone in Appendix Table V.12.

Table 16 Malaria control interventions – no usage of commercial/traditional repellents, mosquito coils or insecticide sprays - by center and survey (ATP Cohort)

Study site	Survey 1			Survey 2			Survey 3			Survey 4		
	%	95% CI		%	95% CI		%	95% CI		%	95% CI	
BF_Nouna	78.1	74.5	81.3	60.7	56.6	64.6	90.5	87.9	92.7	92.8	90.5	94.8
BF_Sapone	99.0	97.9	99.6	96.3	94.5	97.7	97.8	96.3	98.8	78.2	74.6	81.4
SN_Niakhar	79.8	76.3	82.9	94.0	91.8	95.8						
TZ_Korogwe	98.5	97.2	99.3	92.0	89.5	94.0						
KE_Kombewa_EXP	94.8	92.7	96.5	98.5	97.2	99.3	96.5	94.7	97.8	98.8	97.6	99.5
GH Kintampo_EXP	81.7	78.3	84.7	93.3	91.0	95.2	80.5	77.1	83.6	77.0	73.4	80.3
GH_Navrongo_EXP										75.7	72.0	79.0
SN_Keur Soce	96.8	95.1	98.1	85.7	82.6	88.4						
Overall Total	**89.8**	**88.9**	**90.7**	**88.6**	**87.6**	**89.6**	**91.3**	**90.1**	**92.4**	**84.5**	**83.2**	**85.8**

Study site	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
	%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
KE_Kombewa_EXP	97.7	96.1	98.7	97.0	95.3	98.2	98.3	97.0	99.2	99.0	97.8	99.6	88.8	86.0	91.2	85.7	82.6	88.4
GH_Kintampo_EXP	73.3	69.6	76.8	75.0	71.3	78.4	49.5	45.4	53.6	56.8	52.8	60.8	61.7	57.6	65.6	61.5	57.5	65.4
GH_Kintampo_UNEXP				57.7	53.6	61.7	63.0	59.0	66.9	49.7	45.6	53.7	51.0	46.9	55.1	58.5	54.4	62.5
GH_Navrongo_EXP	78.0	74.5	81.3	77.1	73.6	80.4	60.2	56.1	64.1	62.9	58.9	66.8	68.7	64.8	72.4	70.7	66.8	74.3
GH_Navrongo_UNEXP				89.2	86.4	91.5	76.3	72.7	79.7	76.5	72.9	79.8	77.0	73.4	80.3	67.8	63.9	71.6
MA_Mangochi_EXP	84.6	81.4	87.4	82.7	79.5	85.7	82.0	78.7	85.0	79.7	76.2	82.8	81.5	78.2	84.6	66.7	62.8	70.5
MA_Monkey Bay_UNEXP	94.0	91.8	95.7	82.8	79.6	85.8	88.3	85.5	90.8	81.3	78.0	84.4	66.1	62.2	69.9	67.8	63.9	71.5
MA_Chikwawa_UNEXP	87.5	84.5	90.1				82.6	79.4	85.5	87.7	84.8	90.2	85.0	81.9	87.8	90.1	87.4	92.4
MA_St Montfort_EXP	81.7	78.3	84.7				85.0	81.9	87.7	91.2	88.6	93.3	81.3	78.0	84.4	87.1	84.1	89.6
KE_Bondo_UNEXP	94.3	92.1	96.0	86.3	83.3	88.9	90.6	87.9	92.8	88.6	85.8	91.0	77.1	73.6	80.4	77.5	73.9	80.8
KE_Gem_EXP	95.8	93.9	97.3	96.3	94.4	97.6	96.0	94.1	97.4	95.4	93.4	96.9	94.3	92.2	96.0	97.0	95.3	98.2
KE_Nyando_UNEXP				74.3	70.6	77.8	74.5	70.8	77.9	71.1	67.3	74.7	66.2	62.2	69.9	58.2	54.1	62.1
Overall Total	**87.4**	**86.5**	**88.3**	**81.8**	**80.8**	**82.8**	**78.9**	**77.9**	**79.8**	**78.3**	**77.4**	**79.3**	**74.9**	**73.9**	**75.9**	**74.0**	**73.0**	**75.1**

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites

95% CI = Exact 95% Lower and Upper confidence limits

Source: Table MCI3_S1 to Table MCI3_S10

The percentage of participants who did not use any commercial/traditional repellents, mosquito coils or insecticide sprays in the last 7 days before the visit was similar across surveys in the 6M-4Y and 5Y-9Y age groups (Table 17).

Table 17 Malaria control interventions – no usage of commercial/traditional repellents, mosquito coils or insecticide sprays - by JTEG age group and survey (ATP Cohort)

Survey	6M-4Y age group			5-9Y age group		
	%	95% CI		%	95% CI	
Survey 1	89.7	88.6	90.8	89.9	88.2	91.5
Survey 2	88.0	86.7	89.2	89.9	88.2	91.4
Survey 3	91.1	89.6	92.5	91.7	89.6	93.5
Survey 4	84.7	83.0	86.2	84.1	81.7	86.4
Survey 5	87.9	86.8	89.0	86.4	84.8	88.0
Survey 6	82.1	80.9	83.3	81.2	79.4	82.9
Survey 7	78.9	77.7	80.0	78.9	77.2	80.5
Survey 8	78.7	77.5	79.8	77.7	76.0	79.4
Survey 9	74.9	73.7	76.2	74.8	73.0	76.5
Survey 10	74.5	73.2	75.7	73.2	71.3	74.9

ATP = according to protocol; JTEG = Joint Technical Expert Group; 6M-4Y = 6 months to 4 years; 5-9Y = 5 to 9 years
95% CI = Exact 95% Lower and Upper confidence limits
Source: Table MCI20_S1 to Table MCI20_S10

The percentage of participants who did not use any commercial/traditional repellents, mosquito coils or insecticide sprays in the last 7 days before the visit was similar across surveys in females and males (Table 18).

Table 18 Malaria control interventions – no usage of commercial/traditional repellents, mosquito coils or insecticide sprays - by gender and survey (ATP Cohort)

Survey	Female			Male		
	%	95% CI		%	95% CI	
Survey 1	89.3	87.9	90.6	90.3	88.9	91.5
Survey 2	89.7	88.3	91.0	87.6	86.1	89.0
Survey 3	92.3	90.6	93.7	90.4	88.6	92.0
Survey 4	83.8	81.8	85.7	85.1	83.3	86.9
Survey 5	87.6	86.3	88.8	87.3	86.0	88.5
Survey 6	81.7	80.2	83.0	82.0	80.5	83.3
Survey 7	79.1	77.8	80.4	78.7	77.3	80.0
Survey 8	78.0	76.7	79.4	78.7	77.3	80.0
Survey 9	75.3	73.9	76.8	74.5	73.0	75.9
Survey 10	73.2	71.7	74.6	74.9	73.5	76.3

ATP = according to protocol
95% CI = Exact 95% Lower and Upper confidence limits
Source: Table MCI19_S1 to Table MCI19_S10

Results for the use of bednets and other MCIs according to parasite density are presented in Table MCI2_S1 to Table MCI2_S10 and Table MCI4_S1 to Table MCI4_S10, respectively, and according to vaccine eligibility subgroups in Table MCI5_S1 to Table MCI5_S10. The unadjusted OR of the association between the use of MCIs (vs. no use) and *P. falciparum* infection are presented in Table MCI6_S1 to Table MCI6_S10. Results of the association between MCIs or risk factors and *P. falciparum* infection are described in Section 11.4.2.6.

11.4.2. Results of secondary objectives

Of the participants included in the ATP Cohort, results of secondary objectives are described below.

11.4.2.1. Prevalence of *Plasmodium* species other than *P. falciparum*

Across all 10 surveys, the overall proportion of participants infected with *P. malariae* was ≤3.0% and with *P. ovale* <1.0% (Table 19). Participant infection with *P. vivax* was only recorded in 3 participants across surveys.

Table 19 Proportion of participants infected with *P. malariae*, *P. vivax* and *P. ovale* by survey (ATP Cohort)

	P. malariae n (%)	*P. vivax* n (%)	*P. ovale* n (%)
Survey 1	62 (1.5)	0 (0)	23 (0.5)
Survey 2	128 (3.0)	1 (0.0)	10 (0.2)
Survey 3	51 (2.1)	1 (0.0)	11 (0.5)
Survey 4	57 (1.9)	0 (0)	21 (0.7)
Survey 5	39 (0.7)	0 (0)	21 (0.4)
Survey 6	87 (1.5)	0 (0)	52 (0.9)
Survey 7	83 (1.1)	1 (0.0)	20 (0.3)
Survey 8	34 (0.5)	0 (0)	9 (0.1)
Survey 9	50 (0.7)	0 (0)	32 (0.4)
Survey 10	61 (0.8)	0 (0)	14 (0.2)

ATP = according to protocol
Source: Table S12_S1 to Table S12_S10

In all 10 surveys, the overall proportion of participants infected with *P. malariae* was higher in participants co-infected with *P. falciparum* compared to those not infected with *P. falciparum* (Table 20). Although co-infected numbers were low, the proportion of participants infected with *P. falciparum* and *P. ovale* was higher than those infected with *P. ovale* alone. There were too few cases of *P. vivax* to assess any percentage difference by infection status.

Table 20 Proportion of participants infected with *P. malariae*, *P. vivax* and *P. ovale* by infection status and survey (ATP Cohort)

	P. malariae **n (%)**		***P. vivax*** **n (%)**		***P. ovale*** **n (%)**	
	PF INF	**NOT INF**	**PF INF**	**NOT INF**	**PF INF**	**NOT INF**
Survey 1	55 (4.6)	7 (0.2)	0 (0)	0 (0)	13 (1.1)	10 (0.3)
Survey 2	91 (7.4)	37 (1.2)	1 (0.1)	0 (0)	6 (0.5)	4 (0.1)
Survey 3	40 (4.1)	11 (0.8)	0 (0)	1 (0.1)	8 (0.8)	3 (0.2)
Survey 4	31 (3.2)	26 (1.3)	0 (0)	0 (0)	12 (1.3)	9 (0.4)
Survey 5	26 (2.5)	13 (0.3)	0 (0)	0 (0)	11 (1.1)	10 (0.2)
Survey 6	65 (5.2)	22 (0.5)	0 (0)	0 (0)	26 (2.1)	26 (0.5)
Survey 7	56 (4.9)	27 (0.4)	1 (0.1)	0 (0)	8 (0.7)	12 (0.2)
Survey 8	16 (1.8)	18 (0.3)	0 (0)	0 (0)	4 (0.4)	5 (0.1)
Survey 9	26 (2.9)	24 (0.4)	0 (0)	0 (0)	15 (1.7)	17 (0.3)
Survey 10	27 (3.3)	34 (0.5)	0 (0)	0 (0)	6 (0.7)	8 (0.1)

ATP = according to protocol
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy
Source: Table S12_S1 to Table S12_S10

The prevalence of *Plasmodium* species other than *P. falciparum* remained low in each center. The highest prevalence for *P. malariae* was measured in BF Nouna reaching 9.5% (Survey 2) and for *P. ovale* in KE Gem EXP reaching 3.0% (Survey 9). *P. vivax* was recorded in 1 participant each in TZ Korogwe (Survey 2), KE Kombewa EXP (Survey 3) and KE Bondo UNEXP (Survey 7) (Table 21).

Table 21 Other Plasmodium parasitemia results by survey - participant level measured by microscopy (ATP Cohort)

Study center	Plasmodium species	Survey 1		Survey 2		Survey 3		Survey 4	
		n	%	n	%	n	%	n	%
BF_Nouna	*P. malaria*	4	0.7	57	9.5	16	2.7	9	1.5
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	3	0.5	0	0.0	1	0.2	1	0.2
BF_Sapone	*P. malaria*	31	5.1	35	5.8	13	2.2	7	1.2
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	1	0.2	0	0.0	0	0.0	2	0.3
SN_Niakhar	*P. malaria*	0	0.0	0	0.0				
	P. vivax	0	0.0	0	0.0				
	P. ovale	0	0.0	0	0.0				
TZ_Korogwe	*P. malaria*	0	0.0	1	0.2				
	P. vivax	0	0.0	1	0.2				
	P. ovale	3	0.5	1	0.2				
KE_Kombewa_EXP	*P. malaria*	16	2.7	17	2.8	14	2.3	17	2.8
	P. vivax	0	0.0	0	0.0	1	0.2	0	0.0
	P. ovale	8	1.3	7	1.2	2	0.3	10	1.7
GH_Kintampo_EXP	*P. malaria*	11	1.8	18	3.0	8	1.3	22	3.7
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	8	1.3	2	0.3	8	1.3	8	1.3
GH_Navrongo_EXP	*P. malaria*							2	0.3
	P. vivax							0	0.0
	P. ovale							0	0.0
SN_Keur Soce	*P. malaria*	0	0.0	0	0.0				
	P. vivax	0	0.0	0	0.0				
	P. ovale	0	0.0	0	0.0				
Overall Total	***P. malaria***	**62**	**1.5**	**128**	**3.0**	**51**	**2.1**	**57**	**1.9**
	P. vivax	**0**	**0.0**	**1**	**0.0**	**1**	**0.0**	**0**	**0.0**
	P. ovale	**23**	**0.5**	**10**	**0.2**	**11**	**0.5**	**21**	**0.7**

Study center	Plasmodium species	Survey 5		Survey 6		Survey 7		Survey 8		Survey 9		Survey 10	
		n	%	n	%	n	%	n	%	n	%	n	%
KE_Kombewa_EXP	*P. malaria*	15	2.5	17	2.8	29	4.8	19	3.2	16	2.7	22	3.7
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	3	0.5	11	1.8	7	1.2	4	0.7	4	0.7	6	1.0
GH_Kintampo_EXP	*P. malaria*	10	1.7	4	0.7	9	1.5	3	0.5	3	0.5	1	0.2
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	2	0.3	3	0.5	1	0.2	3	0.5	0	0.0	1	0.2
GH_Kintampo_UNEXP	*P. malaria*			8	1.3	4	0.7	1	0.2	1	0.2	4	0.7
	P. vivax			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale			3	0.5	0	0.0	0	0.0	0	0.0	1	0.2
GH_Navrongo_EXP	*P. malaria*	0	0.0	0	0.0	1	0.2	0	0.0	1	0.2	0	0.0
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
GH_Navrongo_UNEXP	*P. malaria*			0	0.0	0	0.0	0	0.0	3	0.5	3	0.5
	P. vivax			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
MA_Mangochi_EXP	*P. malaria*	4	0.7	2	0.3	0	0.0	2	0.3	0	0.0	2	0.3
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
MA_Monkey Bay_UNEXP	*P. malaria*	0	0.0	0	0.0	2	0.3	2	0.3	0	0.0	0	0.0
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
MA_Chikwawa_UNEXP	*P. malaria*	0	0.0			0	0.0	0	0.0	1	0.2	0	0.0
	P. vivax	0	0.0			0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	4	0.7			4	0.6	0	0.0	0	0.0	1	0.2
MA_St Montfort_EXP	*P. malaria*	0	0.0			1	0.2	1	0.2	0	0.0	0	0.0
	P. vivax	0	0.0			0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	2	0.3			0	0.0	0	0.0	0	0.0	0	0.0
KE_Bondo_UNEXP	*P. malaria*	6	1.0	23	3.8	14	2.3	1	0.2	10	1.7	11	1.8
	P. vivax	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
	P. ovale	5	0.8	13	2.2	3	0.5	0	0.0	8	1.3	2	0.3
KE_Gem_EXP	*P. malaria*	4	0.7	15	2.6	14	2.3	4	0.7	9	1.5	15	2.5
	P. vivax	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale	5	0.8	9	1.5	3	0.5	2	0.3	18	3.0	1	0.2

Study center	Plasmodium species	Survey 5		Survey 6		Survey 7		Survey 8		Survey 9		Survey 10	
		n	%	n	%	n	%	n	%	n	%	n	%
KE_Nyando_UNEXP	*P. malaria*			18	3.0	9	1.5	1	0.2	6	1.0	3	0.5
	P. vivax			0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
	P. ovale			12	2.0	1	0.2	0	0.0	1	0.2	2	0.3
Overall Total	***P. malaria***	**39**	**0.7**	**87**	**1.5**	**83**	**1.1**	**34**	**0.5**	**50**	**0.7**	**61**	**0.8**
	P. vivax	**0**	**0.0**	**0**	**0.0**	**1**	**0.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**
	P. ovale	**21**	**0.4**	**52**	**0.9**	**20**	**0.3**	**9**	**0.1**	**32**	**0.4**	**14**	**0.2**

Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
Source: Table S12_S1 to Table S12_S10

Details on the proportion of participants infected with *Plasmodium* species other than *P. falciparum* according to vaccine eligibility subgroups are presented in Table S13_S1 to Table S13_S10 and according to RDT results in Table S18_S1 to Table S18_S10, Table S18b_S1 and Table S18b_S3 to Table S18b_S10.

11.4.2.2. Vaccination history

11.4.2.2.1. DTP/HepB/Hib (third dose) vaccination

Overall, across the 10 surveys, 91.7% of participants had received the third dose of any combination of the DTP vaccine (i.e., pentavalent, tetravalent or DTP only) (Table V4 [Annex – Report Tables Survey 10]): 69.4% (Survey 1), 87.8% (Survey 2), 84.6% (Survey 3), 90.9% (Survey 4), 96.1% (Survey 5), 92.9% (Survey 6), 93.2% (Survey 7), 94.8% (Survey 8), 95.2% (Survey 9) and 97.2% (Survey 10) of participants (Table V1_S1 to Table V1_S10).

A lower proportion of participants in the PF INF vs. NOT INF group received the third dose of any combination of the DTP vaccine in all 10 surveys, ranging from 58.3% (Survey 1) to 93.6% (Survey 10) and 73.8% (Survey 1) to 97.6% (Survey 10), respectively (Table 22).

By center, the proportion of participants vaccinated with any combination of the DTP vaccine (third dose) in the PF INF group was lowest in BF Sapone (25.4%) in Survey 1, reaching 100% in single sites in Surveys 1, 4 and 6, 3 sites in Survey 9, 2 sites in Survey 2, 4 sites in surveys 5 and 8, 5 sites in Survey 7 and 7 sites in Survey 10 (Table 22, Figure 6). In the NOT INF group, the proportion of participants vaccinated with any combination of the DTP vaccine (third dose) was lowest in SN Keur Soce (29.8%) in Survey 1, reaching 100% in GH Navrongo EXP in Survey 4, and in KE Kombewa EXP in Surveys 7 and 8.

Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the proportion of participants who received the third dose of any combination of the DTP vaccine remained high post-RTS,S/AS01$_E$ vaccination, ranging from 62.6% to 100% (PF INF group) and 75.1% to 100% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 59.5% to 100% (PF INF group) and 75.3% to 100% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

Table 22 DTP/HepB/Hib vaccination history by center and survey, according to *P. falciparum* infection status (ATP Cohort)

***Pf* infection status**	**Study center**	**Survey 1**			**Survey 2**			**Survey 3**			**Survey 4**		
		%	**95% CI**		**%**	**95% CI**		**%**	**95% CI**		**%**	**95% CI**	
PF INF	BF_Nouna	57.3	52.3	62.2	64.8	60.3	69.0	68.2	63.0	73.0	69.6	63.6	75.2
	BF_Sapone	25.4	20.6	30.7	98.7	96.8	99.7	83.0	76.9	88.0	98.5	95.8	99.7
	SN_Niakhar	100	66.4	100	100	29.2	100						
	TZ_Korogwe	92.1	82.4	97.4	94.4	72.7	99.9						
	KE_Kombewa_EXP	93.4	88.9	96.4	99.5	97.1	100	99.1	96.6	99.9	98.6	95.9	99.7
	GH Kintampo_EXP	62.6	55.8	69.1	72.6	66.1	78.5	67.1	60.6	73.2	73.1	66.1	79.3
	GH_Navrongo_EXP										100	96.4	100
	SN_Keur Soce	33.3	0.8	90.6	100	54.1	100						
	Overall Total	**58.3**	**55.4**	**61.1**	**80.8**	**78.5**	**83.0**	**77.5**	**74.8**	**80.1**	**86.0**	**83.7**	**88.1**
NOT INF	BF_Nouna	72.9	66.2	78.9	54.5	44.8	63.9	81.9	76.5	86.4	81.3	76.8	85.3
	BF_Sapone	44.9	39.2	50.7	99.3	97.5	99.9	91.4	88.2	93.9	99.2	97.8	99.8
	SN_Niakhar	98.8	97.6	99.5	90.3	87.6	92.6						
	TZ_Korogwe	92.6	90.0	94.6	97.3	95.6	98.4						
	KE_Kombewa_EXP	98.5	96.8	99.5	98.8	97.2	99.6	99.7	98.6	100	99.5	98.2	99.9
	GH Kintampo_EXP	75.1	70.5	79.4	82.5	78.3	86.1	81.9	77.6	85.6	83.3	79.4	86.8
	GH_Navrongo_EXP										100	99.3	100
	SN_Keur Soce	29.8	26.2	33.7	87.4	84.4	89.9						
	Overall Total	**73.8**	**72.2**	**75.4**	**90.7**	**89.6**	**91.8**	**89.5**	**87.8**	**91.0**	**93.2**	**92.1**	**94.3**

Pf infection status	Study center	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	100	98.0	100	99.5	97.0	100	100	97.3	100	100	97.0	100	99.2	95.6	100	100	96.9	100
	GH_Kintampo_EXP	65.4	57.3	72.9	89.1	82.0	94.1	62.1	52.0	71.5	59.5	47.4	70.7	93.7	84.5	98.2	92.3	81.5	97.9
	GH_Kintampo_UNEXP				57.4	49.2	65.3	52.6	43.8	61.3	76.8	67.2	84.7	69.2	58.7	78.5	100	94.6	100
	GH_Navrongo_EXP	96.4	91.0	99.0	87.6	79.4	93.4	87.0	77.4	93.6	91.3	82.0	96.7	68.9	57.1	79.2	67.6	55.7	78.0
	GH_Navrongo_UNEXP				62.3	52.3	71.5	80.0	70.5	87.5	69.3	57.6	79.5	83.1	73.7	90.2	77.9	68.2	85.8
	MA_Mangochi_EXP	99.0	94.4	100	100	95.8	100	100	93.0	100	98.7	93.1	100	98.7	92.8	100	98.4	91.6	100
	MA_Monkey Bay_UNEXP	100	94.3	100	94.3	80.8	99.3	100	89.7	100	100	90.7	100	100	92.0	100	100	92.6	100
	MA_Chikwawa_UNEXP	100	94.8	100				100	96.3	100	100	89.1	100	100	80.5	100	100	86.3	100
	MA_St Montfort_EXP	100	90.7	100				100	93.3	100	100	76.8	100	100	15.8	100	100	39.8	100
	KE_Bondo_UNEXP	94.3	89.5	97.4	99.4	96.9	100	98.6	94.9	99.8	98.4	94.4	99.8	98.1	93.3	99.8	100	95.8	100
	KE_Gem_EXP	99.3	96.2	100	97.7	93.5	99.5	95.7	90.1	98.6	99.1	94.9	100	99.1	95.0	100	97.7	92.0	99.7
	KE_Nyando_UNEXP				97.4	93.4	99.3	98.1	93.4	99.8	98.6	92.7	100	96.8	91.0	99.3	100	95.9	100
	Overall Total	**93.3**	**91.6**	**94.8**	**88.6**	**86.7**	**90.3**	**87.7**	**85.6**	**89.6**	**90.4**	**88.3**	**92.3**	**91.2**	**89.2**	**93.0**	**93.6**	**91.7**	**95.2**
NOT INF	KE_Kombewa_EXP	99.3	97.9	99.8	99.8	98.7	100	100	99.2	100	100	99.2	100	99.8	98.8	100	99.8	98.8	100
	GH_Kintampo_EXP	80.3	76.3	83.9	91.1	88.1	93.5	79.5	75.7	82.9	75.3	71.4	78.9	97.0	95.2	98.3	98.0	96.4	99.0
	GH_Kintampo_UNEXP				70.3	65.9	74.5	66.8	62.3	71.1	91.4	88.6	93.7	78.0	74.1	81.5	99.8	99.0	100
	GH_Navrongo_EXP	97.8	96.1	98.9	93.6	91.1	95.6	93.5	91.0	95.5	95.1	92.9	96.8	89.7	86.8	92.2	88.8	85.8	91.4
	GH_Navrongo_UNEXP				91.3	88.5	93.6	90.3	87.4	92.7	87.4	84.3	90.1	88.3	85.1	90.9	89.9	86.9	92.4
	MA_Mangochi_EXP	98.6	97.1	99.4	99.0	97.8	99.7	99.8	99.0	100	98.3	96.8	99.2	98.9	97.5	99.6	98.0	96.4	99.0
	MA_Monkey Bay_UNEXP	99.3	98.1	99.8	99.6	98.7	100	99.6	98.7	100	99.6	98.7	100	99.8	99.0	100	99.5	98.4	99.9
	MA_Chikwawa_UNEXP	99.6	98.6	100				99.8	98.9	100	99.8	99.0	100	99.5	98.5	99.9	99.8	99.0	100
	MA_St Montfort_EXP	98.4	96.9	99.2				99.6	98.7	100	99.7	98.8	100	98.8	97.6	99.5	98.8	97.6	99.5
	KE_Bondo_UNEXP	96.2	94.1	97.8	98.3	96.6	99.3	98.7	97.2	99.5	99.4	98.2	99.9	99.4	98.2	99.9	99.8	98.9	100
	KE_Gem_EXP	99.3	98.1	99.9	97.4	95.5	98.6	99.4	98.2	99.9	99.8	98.9	100	99.8	98.9	100	99.4	98.3	99.9
	KE_Nyando_UNEXP				98.7	97.1	99.5	99.8	98.9	100	99.2	98.1	99.8	99.0	97.7	99.7	99.2	98.0	99.8
	Overall Total	**96.7**	**96.1**	**97.2**	**94.0**	**93.3**	**94.7**	**94.2**	**93.5**	**94.7**	**95.5**	**94.9**	**96.0**	**95.7**	**95.2**	**96.2**	**97.6**	**97.2**	**98.0**

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites;

DTP/HepB/Hib = diphtheria-tetanus-whole-cell pertussis-hepatitis B- Haemophilus influenza type b pentavalent vaccine

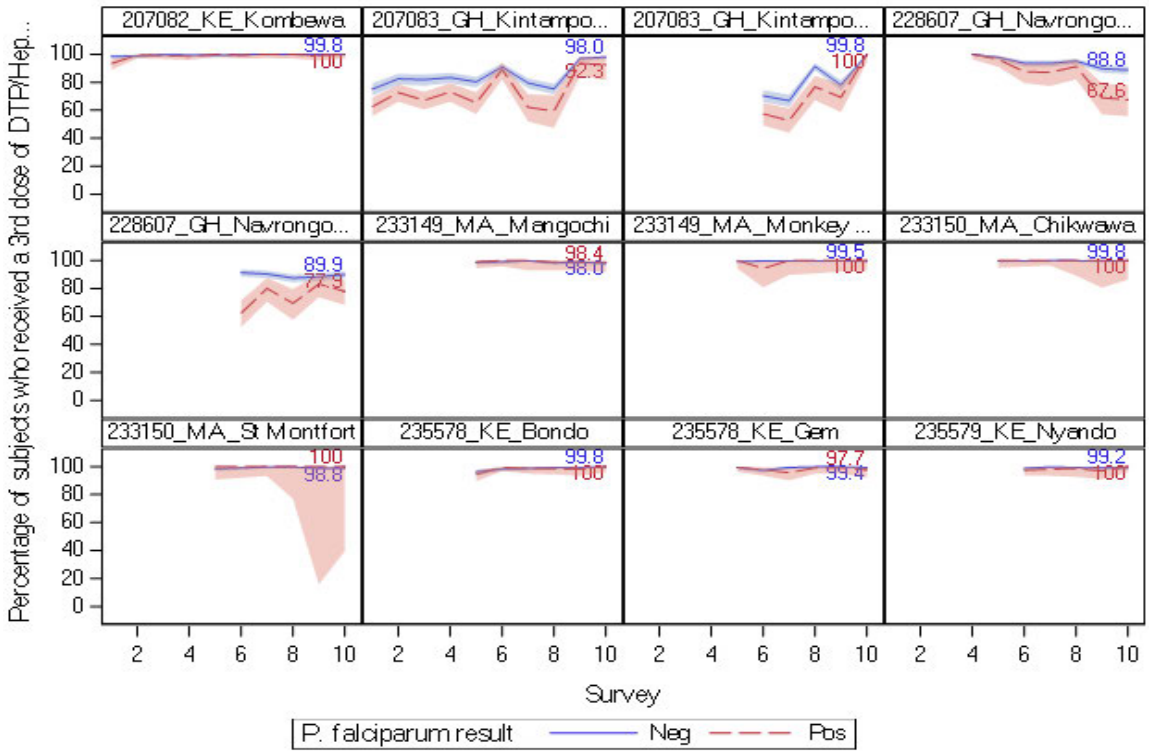
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy

NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy

95% CI = Exact 95% Lower and Upper confidence limits

Source: Table V1_S1 to Table V1_S10

Figure 6 DTP/HepB/Hib vaccination history by center (Ghana, Kenya and Malawi sites only) and survey, according to *P. falciparum* infection status (ATP Cohort)



Shaded area = Exact 95% Lower and Upper confidence limits
ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi; DTP/HepB/Hib = diphtheria-tetanus-whole-cell pertussis-hepatitis B- Haemophilus influenza type b pentavalent vaccine; Neg = negative; Pos = positive
Source: Table V1_S1 to Table V1_S1

Vaccination history according to RTS,S/AS01$_E$ vaccination status is presented in Table V3_S5 to Table V3_S10.

11.4.2.2.2. Measles (first dose) vaccination

Across all 10 surveys, 84.1% of participants had received the measles (first dose) vaccine (Table V4 [in Survey 10 final analysis]): 53.7% (Survey 1), 80.4% (Survey 2), 79.1% (Survey 3), 84.5% (Survey 4), 89.0% (Survey 5), 87.2% (Survey 6), 86.8% (Survey 7), 87.5% (Survey 8), 88.0% (Survey 9) and 89.0% (Survey 10) (Table V1_S1 to Table V1_S10).

In the majority of surveys, a lower proportion of participants in the PF INF vs. NOT INF group received the measles vaccine (first dose). Participants receiving the measles vaccine (first dose) varied across sites, ranging from 43.6% (Survey 1) to 89.2% (Survey 5) in the PF INF group, and 57.7% (Survey 1) to 89.1% (Survey 10) in the NOT INF group (Table 23).

By center, the proportion of participants vaccinated with the measles vaccine (first dose) in the PF INF group was lowest in GH Kintampo EXP (7.9%) in Survey 1, reaching 100% in single sites in Surveys 2, 4, 5 and 9 and in 2 sites in Survey 10 (Table 23, Figure 7). In the NOT INF group the proportion of participants vaccinated with the measles vaccine (first dose) was lowest in GH Kintampo EXP (11.9%) in Survey 1 and highest in KE Kombewa EXP (96.2%) in Survey 9.

Considering study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the proportion of participants who received the measles (first dose) vaccine ranged from 7.9% to 100% (PF INF group) and 11.9% to 94.8% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 58.1% to 97.0% (PF INF group) and 68.4% to 96.2% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

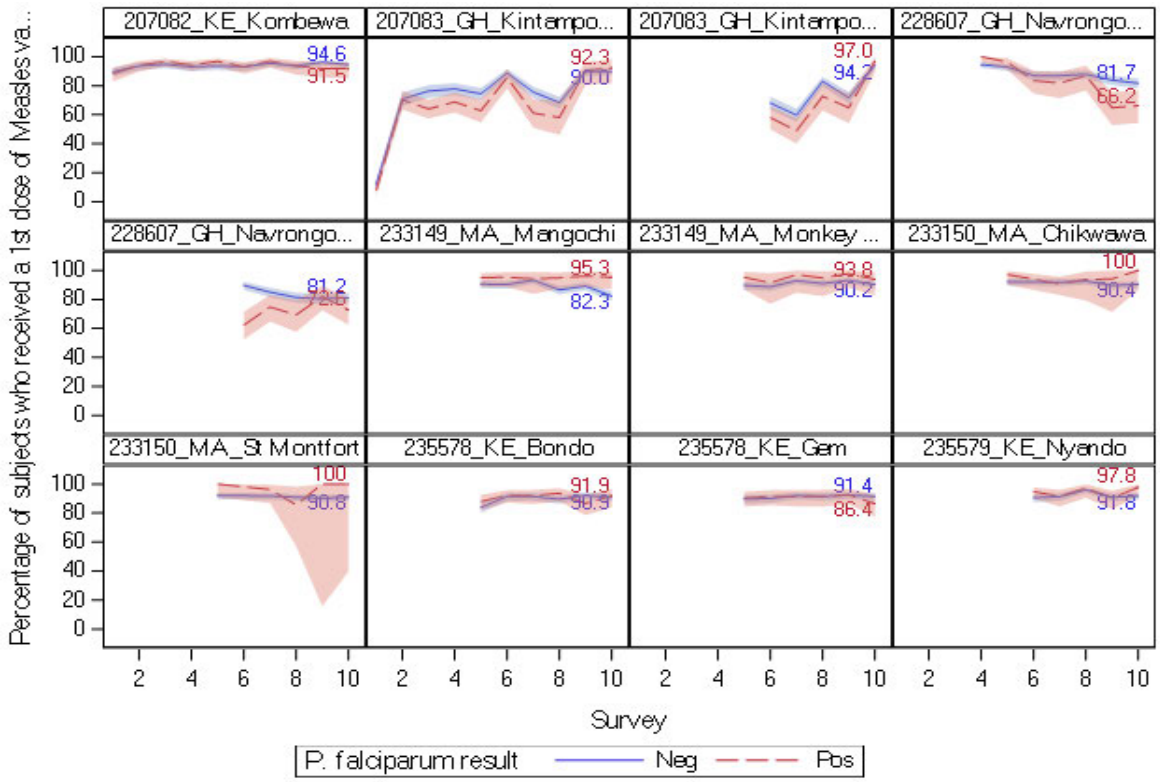
Table 23 Measles vaccination history by center and survey, according to *P. falciparum* infection status (ATP Cohort)

Pf infection status	Study center	Survey 1			Survey 2			Survey 3			Survey 4		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	BF_Nouna	49.1	44.1	54.1	59.8	55.3	64.2	59.9	54.6	65.1	63.4	57.2	69.3
	BF_Sapone	23.1	18.4	28.3	96.5	93.9	98.2	82.5	76.4	87.5	94.1	90.0	96.9
	SN_Niakhar	77.8	40.0	97.2	100	29.2	100						
	TZ_Korogwe	84.1	72.7	92.1	88.9	65.3	98.6						
	KE_Kombewa_EXP	88.3	82.9	92.4	94.2	89.8	97.1	96.7	93.3	98.7	94.3	90.3	97.0
	GH_Kintampo_EXP	7.9	4.7	12.4	70.3	63.6	76.3	64.0	57.4	70.3	68.8	61.6	75.4
	GH_Navrongo_EXP										100	96.4	100
	SN_Keur Soce	33.3	0.8	90.6	83.3	35.9	99.6						
	Overall Total	**43.6**	**40.8**	**46.5**	**76.9**	**74.5**	**79.3**	**73.3**	**70.4**	**76.0**	**81.6**	**79.0**	**84.0**
NOT INF	BF_Nouna	61.6	54.5	68.3	47.3	37.8	57.0	71.4	65.3	76.9	69.7	64.5	74.5
	BF_Sapone	36.1	30.7	41.7	90.8	86.8	93.9	85.5	81.7	88.7	90.2	86.8	92.9
	SN_Niakhar	89.5	86.7	91.8	84.6	81.5	87.4						
	TZ_Korogwe	85.7	82.4	88.5	90.0	87.3	92.3						
	KE_Kombewa_EXP	89.6	86.2	92.4	93.7	90.8	95.8	94.8	92.1	96.8	93.1	90.1	95.4
	GH Kintampo_EXP	11.9	8.9	15.6	70.9	66.1	75.4	76.3	71.6	80.5	77.8	73.5	81.7
	GH_Navrongo_EXP										94.6	92.2	96.4
	SN_Keur Soce	18.9	15.9	22.3	72.2	68.4	75.8						
	Overall Total	**57.7**	**55.9**	**59.5**	**81.8**	**80.4**	**83.2**	**83.1**	**81.1**	**85.0**	**85.8**	**84.3**	**87.3**

Pf infection status	Study center	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	96.8	93.1	98.8	93.0	88.3	96.2	97.0	92.5	99.2	93.5	87.6	97.2	91.9	85.7	96.1	91.5	85.0	95.9
	GH_Kintampo_EXP	62.7	54.6	70.4	85.7	78.1	91.5	61.2	51.1	70.6	58.1	46.1	69.5	90.5	80.4	96.4	92.3	81.5	97.9
	GH_Kintampo_UNEXP				58.1	49.9	65.9	48.9	40.1	57.7	72.7	62.9	81.2	64.8	54.1	74.6	97.0	89.6	99.6
	GH_Navrongo_EXP	96.4	91.0	99.0	83.5	74.6	90.3	81.8	71.4	89.7	87.0	76.7	93.9	64.9	52.9	75.6	66.2	54.3	76.8
	GH_Navrongo_UNEXP				62.3	52.3	71.5	74.7	64.8	83.1	69.3	57.6	79.5	82.0	72.5	89.4	72.6	62.5	81.3
	MA_Mangochi_EXP	94.9	88.5	98.3	95.3	88.5	98.7	94.1	83.8	98.8	94.9	87.4	98.6	96.0	88.8	99.2	95.3	86.9	99.0
	MA_Monkey Bay_UNEXP	95.2	86.7	99.0	91.4	76.9	98.2	97.1	84.7	99.9	94.7	82.3	99.4	97.7	88.0	99.9	93.8	82.8	98.7
	MA_Chikwawa_UNEXP	97.1	89.9	99.6				90.7	83.1	95.7	93.8	79.2	99.2	94.1	71.3	99.9	100	86.3	100
	MA_St Montfort_EXP	100	90.7	100				96.2	87.0	99.5	85.7	57.2	98.2	100	15.8	100	100	39.8	100
	KE_Bondo_UNEXP	88.0	81.9	92.6	92.2	87.2	95.7	92.1	86.3	96.0	93.7	88.0	97.2	86.7	78.6	92.5	91.9	83.9	96.7
	KE_Gem_EXP	90.4	84.4	94.7	91.6	85.5	95.7	91.3	84.6	95.8	91.5	84.5	96.0	92.7	86.2	96.8	86.4	77.4	92.8
	KE_Nyando_UNEXP				94.8	90.0	97.7	91.6	84.6	96.1	97.3	90.6	99.7	90.4	82.6	95.5	97.8	92.1	99.7
	Overall Total	**89.2**	**87.2**	**91.1**	**84.7**	**82.5**	**86.6**	**82.9**	**80.5**	**85.0**	**86.0**	**83.6**	**88.2**	**85.8**	**83.3**	**88.0**	**88.4**	**86.0**	**90.5**
NOT INF	KE_Kombewa_EXP	93.7	90.9	95.8	93.0	90.1	95.3	95.5	93.2	97.2	93.7	91.1	95.7	96.2	94.1	97.7	94.6	92.2	96.4
	GH_Kintampo_EXP	74.5	70.2	78.5	88.8	85.6	91.5	75.7	71.6	79.4	68.4	64.3	72.4	89.8	86.9	92.2	90.0	87.1	92.3
	GH_Kintampo_UNEXP				68.1	63.5	72.4	59.7	55.1	64.2	83.0	79.5	86.2	71.7	67.6	75.6	94.2	91.8	96.0
	GH_Navrongo_EXP	92.9	90.3	95.0	87.1	83.8	89.9	87.0	83.8	89.8	87.9	84.8	90.6	83.8	80.4	86.9	81.7	78.2	85.0
	GH_Navrongo_UNEXP				89.7	86.6	92.2	85.0	81.5	88.0	81.3	77.7	84.6	80.4	76.7	83.8	81.2	77.5	84.5
	MA_Mangochi_EXP	90.6	87.7	93.0	90.3	87.4	92.7	93.2	90.8	95.2	86.6	83.4	89.4	89.2	86.2	91.7	82.3	78.8	85.4
	MA_Monkey Bay_UNEXP	89.7	86.8	92.2	88.7	85.8	91.2	92.9	90.5	94.9	90.9	88.2	93.2	93.2	90.7	95.1	90.2	87.4	92.6
	MA_Chikwawa_UNEXP	92.2	89.6	94.4				91.8	89.1	94.0	92.6	90.1	94.6	89.7	87.0	92.1	90.4	87.7	92.7
	MA_St Montfort_EXP	92.1	89.5	94.2				91.8	89.2	93.9	91.0	88.3	93.2	90.3	87.6	92.6	90.8	88.2	93.0
	KE_Bondo_UNEXP	83.9	80.2	87.2	91.4	88.3	93.9	91.4	88.5	93.8	89.6	86.5	92.2	92.2	89.4	94.4	90.9	88.0	93.2
	KE_Gem_EXP	89.6	86.4	92.3	90.2	87.0	92.7	92.0	89.3	94.3	91.4	88.6	93.7	92.4	89.7	94.6	91.4	88.7	93.7
	KE_Nyando_UNEXP				90.6	87.5	93.1	91.3	88.4	93.6	96.1	94.0	97.5	90.9	88.1	93.3	91.8	89.1	94.0
	Overall Total	**89.0**	**88.0**	**89.9**	**87.8**	**86.8**	**88.7**	**87.5**	**86.7**	**88.3**	**87.7**	**86.9**	**88.5**	**88.3**	**87.5**	**89.1**	**89.1**	**88.3**	**89.9**

Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy
95% CI = Exact 95% Lower and Upper confidence limits
Source: Table V1_S1 to Table V1_S10

Figure 7 Measles vaccination history by center (Ghana, Kenya and Malawi sites only) and survey, according to *P. falciparum* infection status (ATP Cohort)



ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi; Neg = negative; Pos = positive
Shaded area = Exact 95% Lower and Upper confidence limits
Source: Table V1_S1 to Table V1_S10

Vaccination history according to RTS,S/AS01 vaccination status is presented in Table V3_S5 to Table V3_S10.

11.4.2.3. Care seeking behaviors

11.4.2.3.1. Anti-malarial or fever treatment sought in the last 14 days

Overall sites, 15.7% (Survey 1), 12.8% (Survey 2), 15.1% (Survey 3), 19.0% (Survey 4), 20.6% (Survey 5), 16.9% (Survey 6), 10.0% (Survey 7), 9.8% (Survey 8), 12.5% (Survey 9) and 7.0% (Survey 10) of participants sought anti-malarial or fever treatment in the last 14 days, predominantly at the onset of symptoms across surveys (Table B1_S1 to Table B1_S10).

Overall sites, in participants seeking anti-malarial or fever treatment in the last 14 days, a significantly higher proportion was recorded in PF INF vs. NOT INF participants in Surveys 1, 2, 8 and 9, and a significantly lower proportion was recorded in PF INF vs. NOT INF participants in Survey 4; no significant difference was observed in Surveys 3, 5, 6, 7 and 10 (Table 24). Results by center are presented in Table 24 and Figure 8.

Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the percentage of participants seeking anti-malarial or fever treatment in the last 14 days remained similar post-RTS,S/AS01$_E$ vaccination, ranging from 8.1% to 39.0% (PF INF group) and 11.1% to 34.7% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 1.0% to 44.3% (PF INF group) and 6.6% to 39.8% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

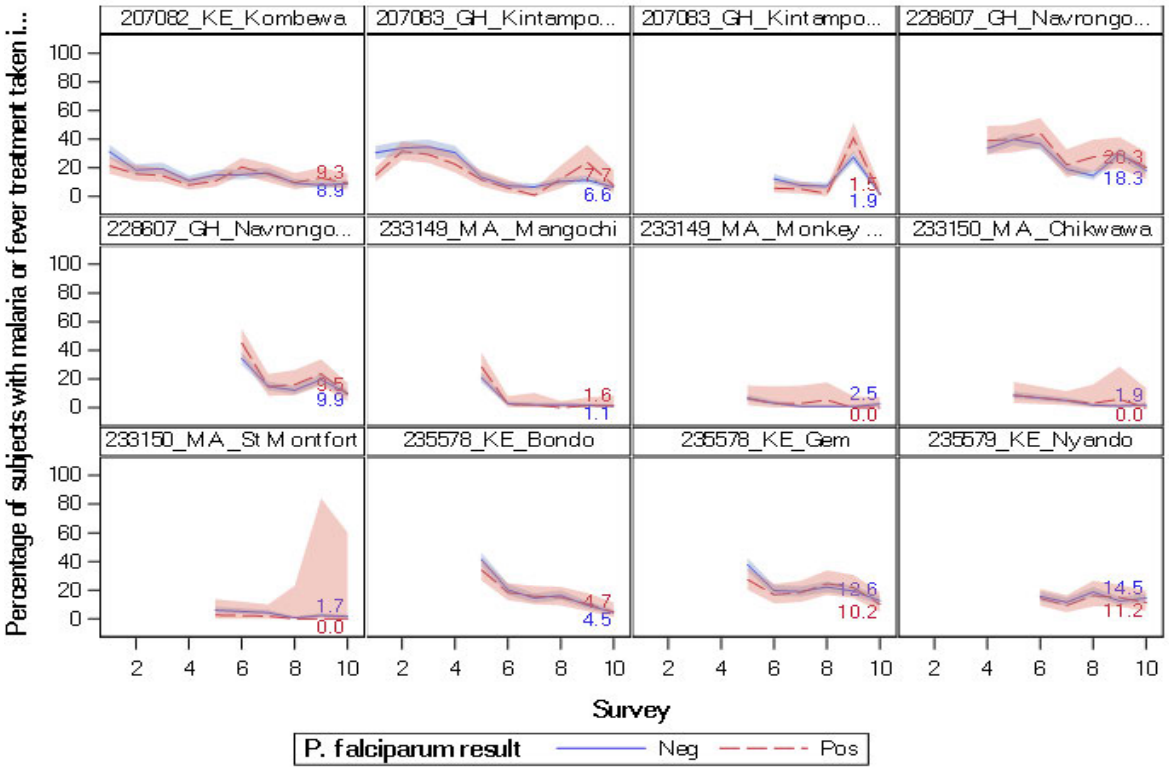
Table 24 Malaria or fever treatment taken in the past 14 days by center and survey, according to *P. falciparum* infection status (ATP Cohort)

Pf infection	Study center	Survey 1			Survey 2			Survey 3			Survey 4		
status		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	BF_Nouna	32.8	28.2	37.6	25.6	21.8	29.7	6.5	4.2	9.6	14.0	10.0	18.9
	BF_Sapone	4.0	2.1	6.9	6.6	4.2	10.0	3.1	1.1	6.6	9.8	6.1	14.7
	SN_Niakhar	0.0	0.0	33.6	0.0	0.0	70.8						
	TZ_Korogwe	31.7	20.6	44.7	22.2	6.4	47.6						
	KE_Kombewa_EXP	21.4	15.9	27.8	15.9	11.0	21.9	14.6	10.1	20.0	8.1	4.8	12.6
	GH_Kintampo_EXP	15.0	10.5	20.4	31.6	25.4	38.3	29.3	23.5	35.8	22.6	16.8	29.3
	GH_Navrongo_EXP										39.0	29.4	49.3
	SN_Keur Soce	0.0	0.0	70.8	0.0	0.0	45.9						
	Overall Total	**20.1**	**17.8**	**22.4**	**20.0**	**17.8**	**22.4**	**12.8**	**10.8**	**15.1**	**16.1**	**13.8**	**18.6**
NOT INF	BF_Nouna	34.5	28.0	41.5	29.5	21.2	38.8	6.0	3.4	9.8	11.1	8.0	14.9
	BF_Sapone	8.2	5.4	11.9	8.8	5.8	12.8	3.9	2.3	6.3	10.4	7.5	13.8
	SN_Niakhar	1.0	0.4	2.2	0.0	0.0	0.6						
	TZ_Korogwe	14.7	11.8	18.0	4.3	2.8	6.3						
	KE_Kombewa_EXP	31.3	26.8	36.0	18.5	14.9	22.6	19.4	15.6	23.7	11.1	8.1	14.6
	GH_Kintampo_EXP	30.6	26.0	35.4	33.8	29.1	38.7	34.7	29.9	39.7	30.7	26.3	35.4
	GH_Navrongo_EXP										33.6	29.5	37.9
	SN_Keur Soce	0.0	0.0	0.6	0.0	0.0	0.6						
	Overall Total	**14.0**	**12.8**	**15.3**	**9.8**	**8.7**	**10.9**	**16.7**	**14.8**	**18.7**	**20.4**	**18.7**	**22.2**

Pf infection status	Study center	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	10.7	6.7	16.0	20.5	15.0	27.1	15.7	10.0	23.0	9.8	5.1	16.4	12.9	7.6	20.1	9.3	4.7	16.1
	GH_Kintampo_EXP	11.8	7.1	18.0	5.9	2.4	11.7	1.0	0.0	5.3	12.2	5.7	21.8	23.8	14.0	36.2	7.7	2.1	18.5
	GH_Kintampo_UNEXP				5.8	2.7	10.7	5.3	2.1	10.5	2.0	0.2	7.1	40.7	30.5	51.5	1.5	0.0	8.0
	GH_Navrongo_EXP	40.0	30.8	49.8	44.3	34.2	54.8	22.1	13.4	33.0	27.5	17.5	39.6	29.7	19.7	41.5	20.3	11.8	31.2
	GH_Navrongo_UNEXP				45.3	35.6	55.2	14.7	8.3	23.5	16.0	8.6	26.3	23.6	15.2	33.8	9.5	4.4	17.2
	MA_Mangochi_EXP	28.6	19.9	38.6	2.3	0.3	8.1	2.0	0.0	10.4	0.0	0.0	4.6	1.3	0.0	7.2	1.6	0.0	8.4
	MA_Monkey Bay_UNEXP	6.3	1.8	15.5	2.9	0.1	14.9	2.9	0.1	15.3	5.3	0.6	17.7	0.0	0.0	8.0	0.0	0.0	7.4
	MA_Chikwawa_UNEXP	8.7	3.3	18.0				5.2	1.7	11.6	3.1	0.1	16.2	5.9	0.1	28.7	0.0	0.0	13.7
	MA_St Montfort_EXP	2.6	0.1	13.8				1.9	0.0	10.1	0.0	0.0	23.2	0.0	0.0	84.2	0.0	0.0	60.2
	KE_Bondo_UNEXP	34.2	26.8	42.1	18.4	13.0	24.9	15.8	10.2	23.0	15.0	9.3	22.4	10.5	5.3	18.0	4.7	1.3	11.5
	KE_Gem_EXP	27.4	20.3	35.4	16.8	10.8	24.3	18.3	11.7	26.5	24.5	16.7	33.8	21.8	14.5	30.7	10.2	4.8	18.5
	KE_Nyando_UNEXP				14.4	9.2	21.0	9.3	4.6	16.5	16.2	8.7	26.6	14.9	8.4	23.7	11.2	5.5	19.7
	Overall Total	**21.0**	**18.6**	**23.7**	**18.1**	**16.0**	**20.3**	**10.6**	**8.9**	**12.6**	**12.5**	**10.5**	**14.9**	**18.2**	**15.8**	**20.9**	**7.9**	**6.1**	**10.0**
NOT INF	KE_Kombewa_EXP	15.0	11.7	18.8	15.2	11.9	19.0	16.5	13.3	20.2	9.4	7.0	12.4	8.0	5.7	10.8	8.9	6.5	11.8
	GH_Kintampo_EXP	13.4	10.4	16.9	7.5	5.3	10.2	6.6	4.6	9.2	10.5	8.0	13.4	11.5	9.0	14.6	6.6	4.6	9.0
	GH_Kintampo_UNEXP				12.4	9.4	15.8	7.7	5.5	10.5	7.2	5.1	9.8	27.5	23.7	31.6	1.9	0.9	3.4
	GH_Navrongo_EXP	39.8	35.5	44.3	36.9	32.6	41.2	19.1	15.8	22.8	14.5	11.6	17.8	29.7	25.8	33.8	18.3	15.0	21.8
	GH_Navrongo_UNEXP				34.2	30.0	38.6	14.9	11.9	18.3	12.2	9.5	15.3	19.6	16.2	23.3	9.9	7.4	12.8
	MA_Mangochi_EXP	20.8	17.4	24.7	2.7	1.5	4.5	2.0	1.0	3.6	1.9	0.9	3.5	1.7	0.8	3.2	1.1	0.4	2.4
	MA_Monkey Bay_UNEXP	6.7	4.8	9.2	3.2	1.9	5.0	0.9	0.3	2.0	0.7	0.2	1.8	0.7	0.2	1.8	2.5	1.4	4.2
	MA_Chikwawa_UNEXP	8.6	6.3	11.3				5.0	3.3	7.2	1.8	0.8	3.2	1.2	0.5	2.5	1.9	1.0	3.4
	MA_St Montfort_EXP	6.0	4.2	8.4				4.3	2.8	6.3	0.7	0.2	1.7	2.3	1.3	3.9	1.7	0.8	3.0
	KE_Bondo_UNEXP	41.5	36.9	46.2	20.3	16.5	24.5	14.4	11.3	17.9	16.3	13.1	19.9	9.4	7.0	12.4	4.5	2.9	6.6
	KE_Gem_EXP	37.7	33.3	42.4	19.7	16.1	23.6	19.0	15.6	22.8	22.2	18.6	26.1	19.4	16.0	23.2	12.6	9.9	15.8
	KE_Nyando_UNEXP				15.7	12.4	19.4	11.6	8.9	14.7	18.8	15.6	22.4	12.5	9.7	15.6	14.5	11.5	17.8
	Overall Total	**20.6**	**19.4**	**21.8**	**16.6**	**15.5**	**17.6**	**9.9**	**9.2**	**10.7**	**9.4**	**8.7**	**10.2**	**11.6**	**10.9**	**12.5**	**6.9**	**6.2**	**7.5**

Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy
95% CI = Exact 95% Lower and Upper confidence limits
Source: Table B1_S1 to Table B1_S10

Figure 8 **Malaria or fever treatment taken in the past 14 days by center (Ghana, Kenya and Malawi sites only) and survey, according to *P. falciparum* infection status (ATP Cohort)**



ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi; Neg = negative; Pos = positive
Shaded area = Exact 95% Lower and Upper confidence limits
Source: Table B1_S1 to Table B1_S10

11.4.2.3.2. Malaria hospitalization in the last 3 months

Overall sites, the proportion of participants hospitalized for malaria in the last 3 months before the visit was low: 2.6% (Survey 1), 2.8% (Survey 2), 3.0% (Survey 3), 3.1% (Survey 4), 2.1% (Survey 5), 2.5% (Survey 6), 1.8% (Survey 7), 2.4% (Survey 8), 2.4% (Survey 9) and 2.5% (Survey 10) (Table B2_S1 to Table B2_S10).

Overall, the proportion of participants hospitalized for malaria in the last 3 months before the visit in the PF INF group ranged from 1.1% in Survey 5 to 3.4% in Survey 2, and in the NOT INF group from 1.8% in Survey 7 to 3.5% in Survey 4 (Table 25). Results by center are presented in Table 25 and Figure 9.

Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), the percentage of participants hospitalized for malaria in the last 3 months before the visit remained low post-RTS,S/AS01$_E$ vaccination, ranging from 1.4% to 8.0% (PF INF group) and 0.5% to 9.8% (NOT INF group) pre-RTS,S/AS01$_E$ vaccination, and 0.0% to 12.7% (PF INF group) and 0.2% to 8.9% (NOT INF group) post-RTS,S/AS01$_E$ vaccination.

Table 25 Malaria hospitalization in the last 3 months by center and survey, according to *P. falciparum* infection status (ATP Cohort)

Pf infection status	Study center	Survey 1			Survey 2			Survey 3			Survey 4		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	BF_Nouna	1.7	0.7	3.5	2.5	1.3	4.3	1.7	0.6	3.7	1.2	0.2	3.4
	BF_Sapone	0.7	0.1	2.4	1.3	0.3	3.2	1.5	0.3	4.5	2.5	0.8	5.6
	SN_Niakhar	0.0	0.0	33.6	0.0	0.0	70.8						
	TZ_Korogwe	6.3	1.8	15.5	0.0	0.0	18.5						
	KE_Kombewa_EXP	5.6	2.8	9.8	4.8	2.2	8.8	1.4	0.3	4.1	1.9	0.5	4.8
	GH_Kintampo_EXP	4.2	1.9	7.8	8.0	4.7	12.5	6.2	3.4	10.2	1.6	0.3	4.6
	GH_Navrongo_EXP										7.0	2.9	13.9
	SN_Keur Soce	0.0	0.0	70.8	0.0	0.0	45.9						
	Overall Total	**2.8**	**1.9**	**3.9**	**3.4**	**2.5**	**4.6**	**2.6**	**1.7**	**3.8**	**2.3**	**1.4**	**3.5**
NOT INF	BF_Nouna	2.5	0.8	5.7	2.7	0.6	7.6	2.0	0.7	4.6	1.7	0.6	3.8
	BF_Sapone	1.3	0.4	3.3	1.8	0.6	4.1	1.0	0.3	2.5	2.5	1.2	4.6
	SN_Niakhar	0.0	0.0	0.6	0.0	0.0	0.6						
	TZ_Korogwe	2.2	1.2	3.9	1.0	0.4	2.2						
	KE_Kombewa_EXP	5.2	3.3	7.9	5.9	3.8	8.6	1.3	0.4	3.0	0.5	0.1	1.8
	GH_Kintampo_EXP	8.5	6.0	11.8	9.8	7.0	13.2	8.3	5.7	11.5	5.6	3.6	8.2
	GH_Navrongo_EXP										6.2	4.3	8.7
	SN_Keur Soce	0.2	0.0	0.9	0.2	0.0	0.9						
	Overall Total	**2.5**	**2.0**	**3.1**	**2.6**	**2.1**	**3.2**	**3.2**	**2.3**	**4.2**	**3.5**	**2.8**	**4.4**

Pf infection status	Study center	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	0.0	0.0	2.0	0.5	0.0	3.0	0.7	0.0	4.1	0.0	0.0	3.0	0.8	0.0	4.4	0.8	0.0	4.6
	GH_Kintampo_EXP	2.6	0.7	6.6	1.7	0.2	5.9	7.8	3.4	14.7	5.4	1.5	13.3	12.7	5.6	23.5	3.8	0.5	13.2
	GH_Kintampo_UNEXP				1.3	0.2	4.6	3.0	0.8	7.5	1.0	0.0	5.5	2.2	0.3	7.7	1.5	0.0	8.0
	GH_Navrongo_EXP	1.8	0.2	6.4	5.2	1.7	11.6	2.6	0.3	9.1	2.9	0.4	10.1	2.7	0.3	9.4	10.8	4.8	20.2
	GH_Navrongo_UNEXP				5.7	2.1	11.9	3.2	0.7	9.0	8.0	3.0	16.6	6.7	2.5	14.1	14.7	8.3	23.5
	MA_Mangochi_EXP	1.0	0.0	5.6	1.2	0.0	6.3	0.0	0.0	7.0	0.0	0.0	4.6	0.0	0.0	4.8	1.6	0.0	8.4
	MA_Monkey Bay_UNEXP	3.2	0.4	11.0	0.0	0.0	10.0	2.9	0.1	15.3	0.0	0.0	9.3	0.0	0.0	8.0	0.0	0.0	7.4
	MA_Chikwawa_UNEXP	1.4	0.0	7.8				4.1	1.1	10.2	3.1	0.1	16.2	0.0	0.0	19.5	0.0	0.0	13.7
	MA_St Montfort_EXP	0.0	0.0	9.3				0.0	0.0	6.7	0.0	0.0	23.2	0.0	0.0	84.2	0.0	0.0	60.2
	KE_Bondo_UNEXP	0.6	0.0	3.5	0.6	0.0	3.1	0.0	0.0	2.6	0.0	0.0	2.9	0.0	0.0	3.5	0.0	0.0	4.2
	KE_Gem_EXP	0.0	0.0	2.5	0.8	0.0	4.2	0.0	0.0	3.2	0.9	0.0	5.1	0.9	0.0	5.0	0.0	0.0	4.1
	KE_Nyando_UNEXP				1.3	0.2	4.6	0.9	0.0	5.1	1.4	0.0	7.3	0.0	0.0	3.8	0.0	0.0	4.1
	Overall Total	**1.1**	**0.5**	**1.9**	**1.7**	**1.0**	**2.6**	**2.1**	**1.4**	**3.1**	**1.8**	**1.0**	**2.8**	**2.3**	**1.4**	**3.5**	**3.3**	**2.2**	**4.8**
NOT INF	KE_Kombewa_EXP	0.5	0.1	1.7	1.7	0.7	3.4	0.2	0.0	1.2	0.2	0.0	1.2	0.6	0.1	1.8	0.8	0.2	2.1
	GH_Kintampo_EXP	3.6	2.1	5.7	4.0	2.4	6.1	4.4	2.8	6.6	8.9	6.6	11.7	4.8	3.2	7.0	6.2	4.3	8.6
	GH_Kintampo_UNEXP				4.7	2.9	7.1	2.8	1.5	4.7	4.4	2.8	6.6	4.5	2.9	6.7	1.5	0.7	2.9
	GH_Navrongo_EXP	4.4	2.8	6.7	6.8	4.7	9.3	4.4	2.8	6.5	6.2	4.3	8.6	7.4	5.3	10.0	7.0	5.0	9.6
	GH_Navrongo_UNEXP				5.7	3.8	8.1	4.0	2.4	6.1	4.6	3.0	6.7	6.7	4.7	9.2	11.1	8.5	14.2
	MA_Mangochi_EXP	2.4	1.2	4.2	0.4	0.0	1.4	0.2	0.0	1.0	0.6	0.1	1.7	1.7	0.8	3.2	0.2	0.0	1.0
	MA_Monkey Bay_UNEXP	2.4	1.3	4.1	1.2	0.5	2.5	1.1	0.4	2.3	1.8	0.9	3.2	0.0	0.0	0.7	0.7	0.2	1.8
	MA_Chikwawa_UNEXP	1.6	0.7	3.0				2.3	1.2	4.0	0.5	0.1	1.5	0.5	0.1	1.5	0.2	0.0	1.0
	MA_St Montfort_EXP	1.5	0.6	2.9				1.1	0.4	2.3	0.5	0.1	1.5	1.3	0.6	2.6	0.3	0.0	1.2
	KE_Bondo_UNEXP	1.5	0.6	3.2	1.2	0.4	2.8	0.2	0.0	1.2	0.8	0.2	2.1	0.2	0.0	1.1	0.0	0.0	0.7
	KE_Gem_EXP	3.5	2.0	5.7	0.2	0.0	1.2	0.2	0.0	1.1	0.0	0.0	0.7	0.6	0.1	1.8	0.4	0.0	1.4
	KE_Nyando_UNEXP				0.7	0.1	1.9	0.6	0.1	1.8	0.9	0.3	2.2	1.2	0.4	2.6	1.2	0.4	2.5
	Overall Total	**2.4**	**2.0**	**2.9**	**2.7**	**2.2**	**3.2**	**1.8**	**1.5**	**2.2**	**2.5**	**2.1**	**2.9**	**2.5**	**2.1**	**2.9**	**2.4**	**2.1**	**2.8**

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites

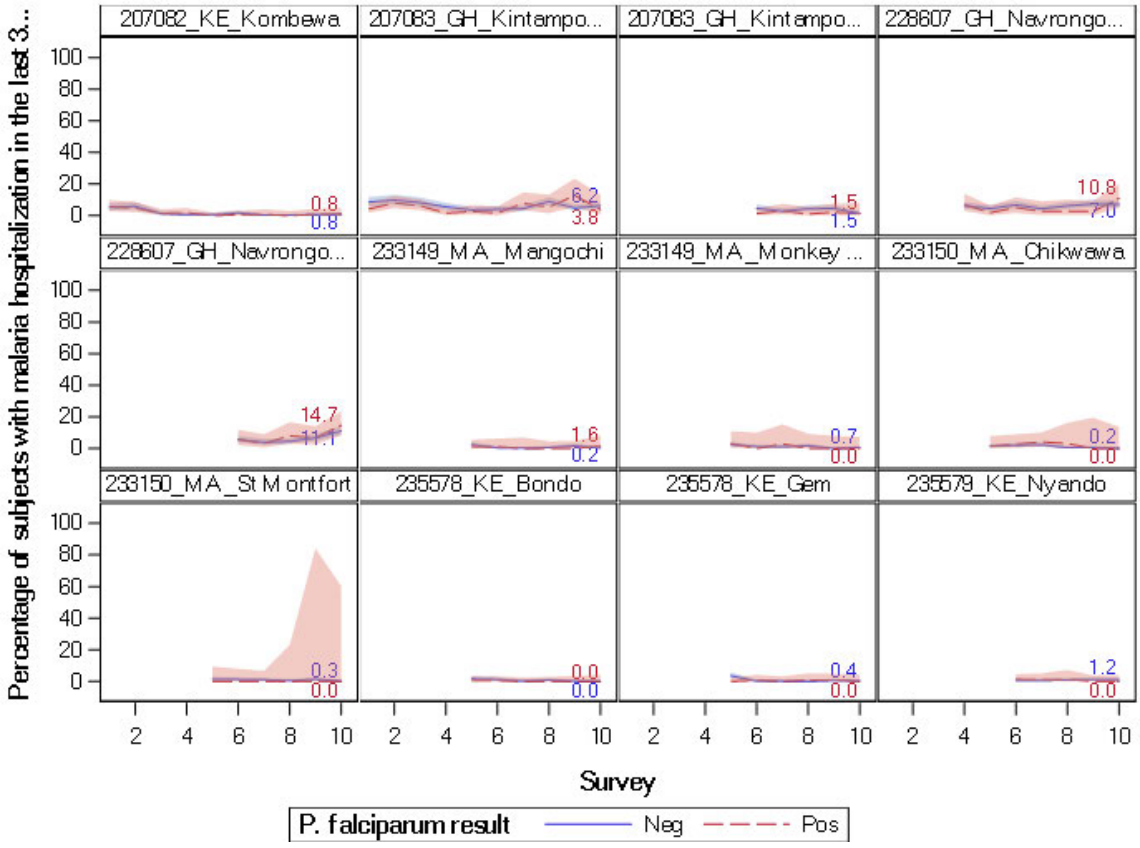
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy

NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy

95% CI = Exact 95% Lower and Upper confidence limits

Source: Table B2_S1 to Table B2_S10

Figure 9 Malaria hospitalization in the last 3 months by center (Ghana, Kenya and Malawi sites only) and survey, according to *P. falciparum* infection status (ATP Cohort)



ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi; Neg = negative; Pos = positive
Shaded area = Exact 95% Lower and Upper confidence limits
Source: Table B2_S1 to Table B2_S10

11.4.2.4. Medical history

11.4.2.4.1. Anti-malarial or any other medication taken in the last 14 days

Overall sites, 16.6% (Survey 1), 16.0% (Survey 2), 19.0% (Survey 3), 22.0% (Survey 4), 24.1% (Survey 5), 17.4% (Survey 6), 10.8% (Survey 7), 10.7% (Survey 8), 14.5% (Survey 9) and 7.2% (Survey 10) of participants had taken anti-malarial or any other medication in the last 14 days before the visit (Table D9.2_S1 to Table D9.2_S10).

Overall sites, in participants taking anti-malarial drugs in the last 14 days, a significantly lower proportion was recorded in PF INF vs. NOT INF participants in Surveys 3 and 4, and a significantly higher proportion was recorded in PF INF vs. NOT INF participants in Survey 5 (Table 26). Results by center are presented in Table 26 and Figure 10.

Details on anti-malarial or any other medication are presented according to *P. falciparum* infection status in Table D9.1_S1 to Table D9.1_S10 for the Total Cohort, and according to parasite density in Table D10.1_S1 to Table D10.1_S10 for the Total Cohort and Table D10.2_S1 to Table D10.2_S10 for the ATP Cohort.

Table 26 Antimalarial drug taken in the past 14 days by center and survey, according to *P. falciparum* infection status (ATP Cohort)

Pf infection status	Study center	Survey 1			Survey 2			Survey 3			Survey 4		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	BF_Nouna	12.2	9.1	15.8	7.0	4.9	9.6	10.5	7.5	14.2	15.6	11.4	20.6
	BF_Sapone	0.7	0.1	2.4	1.6	0.5	3.7	2.1	0.6	5.2	7.8	4.5	12.4
	SN_Niakhar	0.0	0.0	33.6	0.0	0.0	70.8						
	TZ_Korogwe	23.8	14.0	36.2	11.1	1.4	34.7						
	KE_Kombewa_EXP	8.7	5.1	13.5	5.3	2.6	9.5	5.2	2.6	9.1	1.4	0.3	4.1
	GH_Kintampo_EXP	0.5	0.0	2.6	7.1	4.0	11.4	6.2	3.4	10.2	7.0	3.8	11.7
	GH_Navrongo_EXP										29.0	20.4	38.9
	SN_Keur Soce	0.0	0.0	70.8	0.0	0.0	45.9						
	Overall Total	**7.1**	**5.7**	**8.7**	**5.4**	**4.2**	**6.8**	**6.7**	**5.2**	**8.5**	**10.5**	**8.7**	**12.7**
NOT INF	BF_Nouna	19.2	14.0	25.3	12.5	7.0	20.1	26.2	20.8	32.1	12.2	9.0	16.2
	BF_Sapone	2.3	0.9	4.7	5.3	3.0	8.6	3.0	1.5	5.1	16.4	12.9	20.4
	SN_Niakhar	1.0	0.4	2.2	0.0	0.0	0.6						
	TZ_Korogwe	13.2	10.5	16.4	2.7	1.6	4.4						
	KE_Kombewa_EXP	22.6	18.6	27.0	9.8	7.1	13.0	14.0	10.7	17.9	4.9	3.0	7.5
	GH_Kintampo_EXP	3.1	1.6	5.4	16.0	12.5	20.0	17.9	14.1	22.1	15.9	12.5	19.8
	GH_Navrongo_EXP										20.4	17.0	24.2
	SN_Keur Soce	0.0	0.0	0.6	0.0	0.0	0.6						
	Overall Total	**7.5**	**6.6**	**8.5**	**5.0**	**4.2**	**5.8**	**14.0**	**12.2**	**15.9**	**14.4**	**12.9**	**16.0**

Pf infection status	Study center	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	1.1	0.1	3.8	4.3	1.9	8.3	0.7	0.0	4.1	1.6	0.2	5.8	2.4	0.5	6.9	0.8	0.0	4.6
	GH_Kintampo_EXP	8.5	4.6	14.1	5.0	1.9	10.7	0.0	0.0	3.5	4.1	0.8	11.4	15.9	7.9	27.3	1.9	0.0	10.3
	GH_Kintampo_UNEXP				4.5	1.8	9.1	3.0	0.8	7.5	2.0	0.2	7.1	11.0	5.4	19.3	1.5	0.0	8.0
	GH_Navrongo_EXP	26.4	18.4	35.6	27.8	19.2	37.9	14.3	7.4	24.1	21.7	12.7	33.3	16.2	8.7	26.6	14.9	7.7	25.0
	GH_Navrongo_UNEXP				16.0	9.6	24.4	11.6	5.9	19.8	10.7	4.7	19.9	14.6	8.0	23.7	5.3	1.7	11.9
	MA_Mangochi_EXP	85.7	77.2	92.0	8.1	3.3	16.1	2.0	0.0	10.4	0.0	0.0	4.6	1.3	0.0	7.2	1.6	0.0	8.4
	MA_Monkey Bay_UNEXP	87.3	76.5	94.4	8.6	1.8	23.1	0.0	0.0	10.3	5.3	0.6	17.7	0.0	0.0	8.0	0.0	0.0	7.4
	MA_Chikwawa_UNEXP	7.2	2.4	16.1				3.1	0.6	8.8	3.1	0.1	16.2	0.0	0.0	19.5	0.0	0.0	13.7
	MA_St Montfort_EXP	13.2	4.4	28.1				1.9	0.0	10.1	0.0	0.0	23.2	0.0	0.0	84.2	0.0	0.0	60.2
	KE_Bondo_UNEXP	21.5	15.4	28.8	8.9	5.2	14.1	9.4	5.1	15.5	8.7	4.4	15.0	6.7	2.7	13.3	2.3	0.3	8.1
	KE_Gem_EXP	17.1	11.4	24.2	7.6	3.7	13.6	9.6	4.9	16.5	19.8	12.7	28.7	10.9	5.8	18.3	3.4	0.7	9.6
	KE_Nyando_UNEXP				8.5	4.6	14.1	0.9	0.0	5.1	4.1	0.8	11.4	5.3	1.7	12.0	5.6	1.8	12.6
	Overall Total	**24.7**	**22.0**	**27.4**	**9.1**	**7.6**	**10.9**	**5.0**	**3.8**	**6.4**	**7.5**	**5.9**	**9.4**	**8.2**	**6.5**	**10.2**	**3.7**	**2.5**	**5.2**
NOT INF	KE_Kombewa_EXP	3.9	2.2	6.2	6.3	4.1	9.0	3.6	2.1	5.8	3.4	1.9	5.4	2.7	1.5	4.6	1.9	0.9	3.5
	GH_Kintampo_EXP	8.3	5.9	11.2	6.4	4.4	9.0	4.6	3.0	6.9	5.9	4.0	8.3	6.7	4.7	9.2	3.8	2.4	5.8
	GH_Kintampo_UNEXP				9.2	6.7	12.3	6.2	4.2	8.8	7.2	5.1	9.8	11.0	8.4	14.0	0.9	0.3	2.2
	GH_Navrongo_EXP	27.3	23.4	31.4	26.7	22.9	30.8	15.1	12.1	18.5	11.5	8.9	14.5	16.2	13.1	19.6	11.0	8.5	14.0
	GH_Navrongo_UNEXP				15.2	12.1	18.7	9.3	6.9	12.2	7.8	5.7	10.4	10.4	7.9	13.3	5.5	3.7	7.9
	MA_Mangochi_EXP	9.6	7.2	12.6	0.6	0.1	1.7	0.7	0.2	1.9	1.3	0.5	2.7	1.3	0.5	2.7	0.4	0.0	1.3
	MA_Monkey Bay_UNEXP	5.6	3.8	7.9	0.4	0.0	1.3	0.4	0.0	1.3	0.2	0.0	1.0	0.2	0.0	1.0	1.8	0.9	3.3
	MA_Chikwawa_UNEXP	4.5	2.9	6.6				2.9	1.6	4.7	0.9	0.3	2.0	1.0	0.4	2.2	0.5	0.1	1.5
	MA_St Montfort_EXP	1.3	0.5	2.6				1.8	0.9	3.3	0.0	0.0	0.6	0.2	0.0	0.9	0.0	0.0	0.6
	KE_Bondo_UNEXP	27.6	23.5	32.0	11.7	8.8	15.2	9.9	7.3	13.0	10.4	7.8	13.5	5.8	3.9	8.3	3.3	1.9	5.2
	KE_Gem_EXP	30.2	26.0	34.7	12.3	9.4	15.6	12.5	9.7	15.7	14.4	11.4	17.8	12.9	10.0	16.1	7.6	5.5	10.2
	KE_Nyando_UNEXP				10.3	7.6	13.5	7.3	5.2	10.0	12.2	9.6	15.3	8.3	6.0	11.1	6.3	4.3	8.7
	Overall Total	**12.8**	**11.8**	**13.8**	**9.8**	**8.9**	**10.6**	**6.0**	**5.5**	**6.7**	**6.1**	**5.5**	**6.7**	**6.2**	**5.6**	**6.8**	**3.5**	**3.1**	**4.0**

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites

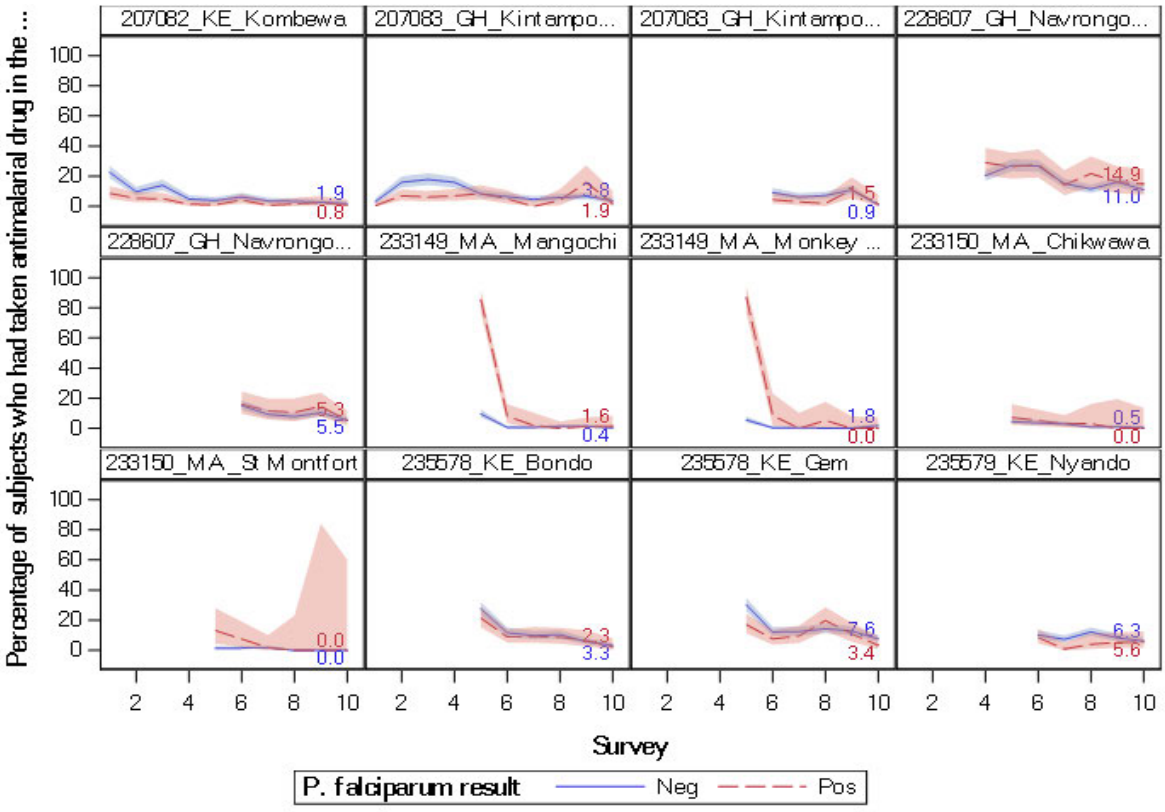
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy

NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy

95% CI = Exact 95% Lower and Upper confidence limits

Source: Table D9.2_S1 to Table D9.2_S10

Figure 10 Antimalarial drug taken in the past 14 days by center (Ghana, Kenya and Malawi sites only) and survey, according to *P. falciparum* infection status (ATP Cohort)



ATP = according to protocol; GH = Ghana; KE = Kenya; MA = Malawi; Neg = negative; Pos = positive
Shaded area = Exact 95% Lower and Upper confidence limits
Source: Table D9.2_S1 to Table D9.2_S10

11.4.2.4.2. Fever at the visit

The proportion of participants with fever measured at the visit was 5.1% (Survey 1), 4.8% (Survey 2), 3.9% (Survey 3), 4.2% (Survey 4), 4.6% (Survey 5), 3.7% (Survey 6), 2.2% (Survey 7), 2.8% (Survey 8), 3.5% (Survey 9) and 2.9% (Survey 10) (Table D7.2_S1 to Table D7.2_S10).

Overall, in all 10 surveys, the proportion of participants with fever measured at the visit was significantly higher in PF INF vs. NOT INF participants, ranging from 6.2% (Survey 3) to 11.7% (Survey 5) and 1.3% (Survey 7) to 3.5% (Survey 1), respectively (Table 27).

Details on fever measured at the visit according to *P. falciparum* infection status are presented in Table D7.1_S1 to Table 7.1_S10 for the Total Cohort, and according to parasite density in Table D8.1_S1 to Table 8.1_S10 for the Total Cohort and Table D8.2_S1 to Table D8.2_S10 for the ATP Cohort.

Table 27 Fever at visit by center and survey, according to *P. falciparum* infection status (ATP Cohort)

Pf infection status	Study center	Survey 1			Survey 2			Survey 3			Survey 4		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	BF_Nouna	7.2	4.9	10.2	6.6	4.5	9.1	5.1	3.1	8.0	8.6	5.4	12.7
	BF_Sapone	4.4	2.3	7.3	7.9	5.2	11.5	6.7	3.6	11.2	7.8	4.5	12.4
	SN_Niakhar	11.1	0.3	48.2	33.3	0.8	90.6						
	TZ_Korogwe	38.1	26.1	51.2	5.6	0.1	27.3						
	KE_Kombewa_EXP	9.2	5.5	14.1	7.9	4.5	12.8	8.5	5.1	13.0	7.1	4.0	11.5
	GH_Kintampo_EXP	10.3	6.6	15.2	10.4	6.6	15.3	5.3	2.8	9.1	4.8	2.2	9.0
	GH_Navrongo_EXP										17.0	10.2	25.8
	SN_Keur Soce	33.3	0.8	90.6	33.3	4.3	77.7						
	Overall Total	**9.1**	**7.5**	**10.9**	**8.0**	**6.5**	**9.6**	**6.2**	**4.8**	**7.9**	**8.2**	**6.6**	**10.2**
NOT INF	BF_Nouna	1.5	0.3	4.3	4.5	1.5	10.1	2.4	0.9	5.2	3.5	1.8	6.0
	BF_Sapone	2.6	1.1	5.1	2.8	1.2	5.5	2.2	1.0	4.2	1.3	0.4	2.9
	SN_Niakhar	2.4	1.3	4.0	1.7	0.8	3.1						
	TZ_Korogwe	2.8	1.6	4.6	0.9	0.3	2.0						
	KE_Kombewa_EXP	3.5	1.9	5.8	1.0	0.3	2.5	3.6	2.0	6.0	2.6	1.2	4.7
	GH_Kintampo_EXP	2.8	1.4	5.0	2.1	0.9	4.0	1.1	0.3	2.7	1.2	0.4	2.8
	GH_Navrongo_EXP										3.2	1.8	5.1
	SN_Keur Soce	7.0	5.1	9.4	10.4	8.1	13.2						
	Overall Total	**3.5**	**2.9**	**4.3**	**3.4**	**2.8**	**4.2**	**2.3**	**1.6**	**3.3**	**2.4**	**1.7**	**3.1**

Pf infection status	Study center	Survey 5			Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	9.6	5.8	14.8	13.5	8.9	19.3	11.2	6.4	17.8	6.5	2.8	12.4	6.5	2.8	12.3	9.3	4.7	16.1
	GH_Kintampo_EXP	7.2	3.6	12.5	13.4	7.9	20.9	3.9	1.1	9.6	14.9	7.7	25.0	9.5	3.6	19.6	7.7	2.1	18.5
	GH_Kintampo_UNEXP				8.4	4.5	13.9	7.5	3.7	13.4	4.0	1.1	10.0	4.4	1.2	10.9	6.0	1.7	14.6
	GH_Navrongo_EXP	12.7	7.1	20.4	18.6	11.4	27.7	10.4	4.6	19.4	8.7	3.3	18.0	27.0	17.4	38.6	17.6	9.7	28.2
	GH_Navrongo_UNEXP				22.6	15.1	31.8	8.4	3.7	15.9	16.0	8.6	26.3	16.9	9.8	26.3	17.9	10.8	27.1
	MA_Mangochi_EXP	9.2	4.3	16.7	7.0	2.6	14.6	5.9	1.2	16.2	7.7	2.9	16.0	13.3	6.6	23.2	17.2	8.9	28.7
	MA_Monkey Bay_UNEXP	9.5	3.6	19.6	2.9	0.1	14.9	2.9	0.1	15.3	7.9	1.7	21.4	6.8	1.4	18.7	14.6	6.1	27.8
	MA_Chikwawa_UNEXP	10.1	4.2	19.8				10.3	5.1	18.1	12.5	3.5	29.0	5.9	0.1	28.7	12.0	2.5	31.2
	MA_St Montfort_EXP	10.5	2.9	24.8				11.3	4.3	23.0	7.1	0.2	33.9	0	0.0	84.2	25.0	0.6	80.6
	KE_Bondo_UNEXP	17.1	11.6	23.9	5.6	2.7	10.0	5.0	2.0	10.1	5.5	2.2	11.0	3.8	1.0	9.5	5.8	1.9	13.0
	KE_Gem_EXP	16.4	10.8	23.5	8.4	4.3	14.5	4.3	1.4	9.9	8.5	4.0	15.5	8.2	3.8	15.0	9.1	4.0	17.1
	KE_Nyando_UNEXP				3.3	1.1	7.5	5.6	2.1	11.8	12.2	5.7	21.8	7.4	3.0	14.7	6.7	2.5	14.1
	Overall Total	**11.7**	**9.8**	**13.9**	**10.4**	**8.7**	**12.2**	**7.3**	**5.9**	**9.0**	**8.8**	**7.0**	**10.8**	**9.8**	**7.9**	**11.9**	**11.1**	**9.0**	**13.5**
NOT INF	KE_Kombewa_EXP	5.6	3.6	8.2	3.6	2.0	5.9	5.6	3.7	8.1	1.9	0.9	3.6	0.4	0.1	1.5	1.5	0.6	3.0
	GH_Kintampo_EXP	1.8	0.8	3.5	2.5	1.3	4.3	1.4	0.6	2.9	1.5	0.7	3.0	3.9	2.4	5.9	2.0	1.0	3.6
	GH_Kintampo_UNEXP				1.3	0.5	2.9	0.9	0.2	2.2	2.4	1.2	4.1	1.0	0.3	2.3	0.6	0.1	1.6
	GH_Navrongo_EXP	3.4	2.0	5.4	3.6	2.1	5.6	1.3	0.5	2.7	2.1	1.0	3.7	3.8	2.3	5.8	2.7	1.5	4.4
	GH_Navrongo_UNEXP				4.0	2.5	6.2	1.4	0.6	2.8	2.7	1.5	4.4	6.1	4.2	8.5	2.6	1.4	4.4
	MA_Mangochi_EXP	1.2	0.4	2.6	1.2	0.4	2.5	0.2	0.0	1.0	0.6	0.1	1.7	2.3	1.2	4.0	1.7	0.8	3.2
	MA_Monkey Bay_UNEXP	2.4	1.3	4.1	0.7	0.2	1.8	0.4	0.0	1.3	0.9	0.3	2.1	1.1	0.4	2.3	2.4	1.3	4.0
	MA_Chikwawa_UNEXP	2.1	1.1	3.8				1.7	0.8	3.2	1.4	0.6	2.8	2.9	1.7	4.6	0.7	0.2	1.8
	MA_St Montfort_EXP	1.3	0.5	2.6				0.4	0.0	1.3	3.1	1.8	4.8	3.2	1.9	4.9	4.8	3.3	6.9
	KE_Bondo_UNEXP	4.6	2.9	7.0	0.7	0.1	2.1	0.4	0.1	1.5	2.1	1.0	3.8	2.4	1.3	4.2	1.6	0.7	3.0
	KE_Gem_EXP	4.2	2.5	6.5	1.5	0.6	3.1	1.8	0.8	3.5	2.2	1.1	3.9	2.0	1.0	3.7	0.8	0.2	2.0
	KE_Nyando_UNEXP				0.7	0.1	1.9	0.4	0.0	1.5	2.1	1.0	3.7	1.6	0.7	3.1	1.4	0.6	2.8
	Overall Total	**2.9**	**2.4**	**3.4**	**2.0**	**1.6**	**2.4**	**1.3**	**1.0**	**1.6**	**1.9**	**1.6**	**2.3**	**2.6**	**2.2**	**3.0**	**1.9**	**1.6**	**2.3**

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites

PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy

NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy

95% CI = Exact 95% Lower and Upper confidence limits

Fever = temperature recorded at visit after axillary conversion ≥ 37.5°C

Source: Table D7.2_S1 to Table D7.2_S10

11.4.2.5. Geographical heterogeneity

Of note, the protocol definition of including a minimum of 10 participants per segment was not respected in 4 segments in 3 sites in Survey 5, 2 segments in 2 sites in Survey 6, 4 segments in 2 sites in Survey 7, 5 segments in 2 sites in Survey 8, 6 segments in 5 sites in Survey 9 and 13 segments in 6 sites in Survey 10 did not respect. Therefore, these results should be interpreted with caution, especially for the prevalence of *P. falciparum* in these segments. Further details on this protocol deviation are provided in Section 11.2.2.

Significant geographical heterogeneity by segment varied across surveys for each center (Table 28). Approximately 600 participants were included in each center, divided across 3 to 14 segments (Table G1_S1 to Table G1_S10). Although random sampling of the study population was done, the number of participants in each segment at each site varied widely and could then influence the heterogeneity test performed.

Additional details on the geographical heterogeneity by segment for the number and surface area of each segment are presented in Table G2_S1 to Table G2_S10 and for the prevalence of *P. falciparum* by segment in Table G3_S1 to Table G3_S10.

Table 28 *P. falciparum* parasitemia occurrence measured by microscopy - heterogeneity among segments according to center and survey (ATP Cohort)

Study center (surveys participating in)	Significant heterogeneity (Surveys 1-10)
BF_Nouna (Surveys 1-4)	Survey 1, p<0.0001; Survey 2, p=0.0184; Survey 4, p=0.0017
BF_Sapone (Surveys 1-4)	Survey 1, p=0.0321; Survey 2, p<0.0001; Survey 3, p=0.0497
SN_Keur Soce (Survey 1-2)	-
SN_Niakhar (Surveys 1-2)	-
TZ_Korogwe (Surveys 1-2)	Survey 1, p=0.0037; Survey 2, p=0.0275
KE_Kombewa_EXP (Surveys 1-10)	Survey 1, p=0.0220; Survey 2, p<0.0001; Survey 3, p=0.0223; Survey 4, p=0.0093; Survey 6, p=0.0005; Survey 8, p=0.0004; Survey 9, p=0.0061; Survey 10, p=0.0075
GH_Kintampo_EXP (Surveys 1-10)	Survey 2, p=0.0065; Survey 3, p=0.0487
GH_Kintampo_UNEXP (Surveys 6-10)	Survey 6, p=0.0478
GH_Navrongo_EXP (Surveys 4-10)	Survey 4, p=0.0278; Survey 8, p=0.0045; Survey 10, p=0.0212
GH_Navrongo_UNEXP (Surveys 6-10)	Survey 7, p=0.0206; Survey 8, p=0.0001; Survey 9, p=0.0006; Survey 10, p=0.0002
MA_Mangochi_EXP (Surveys 5-10)	Survey 5, p<0.0001; Survey 6, p=0.0007; Survey 7, p=0.0169; Survey 8, p=0.0063; Survey 10, p<0.0001
MA_Monkey Bay_UNEXP (Surveys 5-10)	-
MA_Chikwawa_UNEXP(Surveys 5-10)	Survey 5, p=0.0015; Survey 10, p=0.0013
MA_St Montfort_EXP (Surveys 5-10)	Survey 5, p=0.0063
KE_Bondo_UNEXP (Surveys 5-10)	Survey 5, p=0.0001; Survey 6, p<0.0001; Survey 7, p=0.0260; Survey 8, p=0.0046
KE_Gem_EXP (Surveys 5-10)	Survey 5, p=0.0179; Survey 6, p<0.0001; Survey 7, p=0.0046; Survey 8, p=0.0039; Survey 9, p=0.0028; Survey 10, p=0.0009
KE_Nyando_UNEXP (Surveys 6-10)	Survey 6, p=0.0046; Survey 8, p=0.0006; Survey 10, p=0.0176

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
P-value: Cochran's Q test based upon inverse variance weights
Source: Table G4_S1 to Table G4_S10

11.4.2.6. Association between malaria control interventions or risk factors and *P. falciparum* infection

Both malaria prevention measures and risk factors were considered in a multivariable model with center effect adjustment – the variables were selected using a backward selection method. The multivariable model was exploratory; therefore, the results should be interpreted with caution.

The only consistent variable shown to be significant across all 10 surveys was age as a continuous variable, showing a higher risk of *P. falciparum* infection with increasing age.

Details on malaria control interventions and risk factors are presented in Table R1_S1 to Table R1_S10, Table R2_S1 to Table R2_S10, Table R3_S1 to Table R3_S10, Table R4_S1 to Table R4_S10, Table R5_S1 to Table R5_S10, Table R6_S1 to Table R6_S10, and Table R7_S1 to Table R7_S10.

Details on unadjusted ORs for each center are presented in the following tables:
SN Niakhar: Table MCI8A_S1 to Table MCI8A_S2 and Table R9A_S1 to Table R9A_S2
SN Keur Soce: Table MCI8B_S1 to Table MCI8B_S2 and R9B_S1 to Table R9B_S2
TZ Korogwe: Table MCI9A_S1 to Table MCI9A_S2 and R10A_S1 to Table R10A_S2
BF Nouna: Table MCI7A_S1 to Table MCI7A_S4, Table R8A_S1 to Table R8A_S4
BF Sapone: Table MCI7B_S1 to Table MCI7B_S4, Table R8B_S1 to Table R8B_S4
KE Gem EXP: Table MCI10A_S5 to Table MCI10A_S10, Table R11A_S5 to Table R11A_S10
KE Bondo UNEXP: Table MCI10B_S5 to Table MCI10B_S10, Table R11B_S5 to Table R11B_S10
KE Kombewa EXP: Table MCI10C_S1 to Table MCI10C_S10, Table R11C_S1 to Table R11C_S10
KE Nyando UNEXP: Table MCI10D_S6 to Table MCI10D_S10, Table R11D_S6 to Table R11D_S10
GH Kintampo EXP: Table MCI11A_S1 to Table MCI11A_S10, Table R12A_S1 to Table R12A_S10
GH Kintampo UNEXP: Table MCI11B_S6 to Table MCI11B_S10, Table R12B_S6 to Table R12B_S10
GH Navrongo EXP: Table MCI11C_S4 to Table MCI11C_S10, Table R12C_S4 to Table R12C_S10
GH Navrongo UNEXP: Table MCI11D_S6 to Table MCI11D_S10, Table R12D_S6 to Table R12D_S10
MA Mangochi EXP: Table MCI12A_S5 to Table MCI12A_S10, Table R13A_S5 to Table R13A_S10
MA Monkey Bay UNEXP: Table MCI12B_S5 to Table MCI12B_S10, Table R13B_S5 to Table R13B_S10
MA St Montfort EXP: Table MCI12C_S5 to Table MCI12C_S10, Table R13C_S5 to Table R13C_S10
MA Chikwawa UNEXP: Table MCI12D_S5 to Table MCI12D_S10, Table R13D_S5 to Table R13D_S10.

Details on the adjusted logistic regression model are presented in Table MCI14A_S1 to Table MCI14A_S10, Table MCI14B_S1 to Table MCI14B_S10, Table R15A_S1 to Table R15A_S10, Table R15B_S1 to Table R15B_S10, Table R16A_S1 to Table R16A_S10 and Table R16B_S1 to Table R16B_S10.

11.4.3. Results of tertiary objectives/other analyses

Of the participants included in the ATP Cohort, results of tertiary objectives are described below.

11.4.3.1. RTS,S/AS01$_E$ vaccination

In alignment with the MVIP and implementation of RTS,S/AS01$_E$ vaccination, participants were to receive the RTS,S/AS01$_E$ vaccine in exposed sites from Survey 5 onwards. Only 4 participants received the RTS,S/AS01$_E$ vaccine in Survey 5 (Table V2_S5); data are summarized in this section from Survey 6 onwards.

Overall sites, 4.3% (Survey 6), 15.0% (Survey 7), 22.4% (Survey 8), 27.3% (Survey 9) and 38.5% (Survey 10) of participants received at least 1 dose of RTS,S/AS01$_E$ vaccine (Table V2_S6 to Table V2_S10). In exposed sites, the percentage of participants across sites receiving at least 1 dose of RTS,S/AS01$_E$ vaccine increased with each subsequent survey: 0% to 15.0% in Survey 6, 22.3% to 35.7% in Survey 7, 39.8% to 48.9% in Survey 8, 40.7% to 53.0% in Survey 9 and 49.9% to 63.0% in Survey 10.

A significantly lower proportion of participants in the PF INF vs NOT INF group received RTS,S/AS01$_E$ vaccination in Surveys 6-10 (Table 29). This finding is partially attributable to the prevalence of *P. falciparum* being significantly lower in the 6M-4Y vs. 5Y-9Y age group, which is the age group eligible for RTS,S/AS01$_E$ vaccination (Table D12.1_S5 to Table D12.1_S10 [Total Cohort] and Table D12.2_S5 to Table D12.2_S10 [ATP Cohort]).

Results according to RTS,S/AS01$_E$ vaccination status are presented for use of MCIs in Table MCI18_S5 to Table MCI18_S10 and Table MCI21_S5 to MCI21_S10.

Table 29 RTS,S/AS01 vaccination by center and survey, according to *P. falciparum* infection status (Surveys 6-10; ATP Cohort)

Pf infection status	Study center	Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
PF INF	KE_Kombewa_EXP	11.9	7.6	17.4	14.2	8.8	21.3	24.4	17.1	33.0	33.9	25.6	42.9	35.6	27.0	44.9
	GH_Kintampo_EXP	0.8	0.0	4.6	9.7	4.8	17.1	16.2	8.7	26.6	17.5	9.1	29.1	28.8	17.1	43.1
	GH_Kintampo_UNEXP	0.0	0.0	2.4	0.0	0.0	2.7	0.0	0.0	3.7	0.0	0.0	4.0	0.0	0.0	5.4
	GH_Navrongo_EXP	0.0	0.0	3.7	3.9	0.8	11.0	11.6	5.1	21.6	10.8	4.8	20.2	21.6	12.9	32.7
	GH_Navrongo_UNEXP	0.0	0.0	3.4	0.0	0.0	3.8	0.0	0.0	4.8	0.0	0.0	4.1	1.1	0.0	5.7
	MA_Mangochi_EXP	1.2	0.0	6.3	7.8	2.2	18.9	16.7	9.2	26.8	21.3	12.7	32.3	29.7	18.9	42.4
	MA_Monkey Bay_UNEXP	0.0	0.0	10.0	0.0	0.0	10.3	0.0	0.0	9.3	2.3	0.1	12.0	14.6	6.1	27.8
	MA_Chikwawa_UNEXP				0.0	0.0	3.7	0.0	0.0	10.9	0.0	0.0	19.5	4.0	0.1	20.4
	MA_St Montfort_EXP				17.0	8.1	29.8	14.3	1.8	42.8	0.0	0.0	84.2	25.0	0.6	80.6
	KE_Bondo_UNEXP	0.0	0.0	2.0	0.7	0.0	3.9	1.6	0.2	5.6	1.9	0.2	6.7	17.4	10.1	27.1
	KE_Gem_EXP	5.3	2.2	10.7	15.7	9.5	23.6	25.5	17.5	34.9	35.5	26.6	45.1	27.3	18.3	37.8
	KE_Nyando_UNEXP	0.0	0.0	2.4	0.9	0.0	5.1	0.0	0.0	4.9	6.4	2.4	13.4	15.7	8.9	25.0
	Overall Total	**2.5**	**1.7**	**3.5**	**5.7**	**4.4**	**7.2**	**10.3**	**8.4**	**12.5**	**14.1**	**11.9**	**16.5**	**19.1**	**16.5**	**22.0**
NOT INF	KE_Kombewa_EXP	16.4	13.0	20.3	24.7	20.8	28.9	43.8	39.3	48.4	55.3	50.7	59.8	69.7	65.4	73.8
	GH_Kintampo_EXP	9.4	6.9	12.3	29.8	25.8	34.0	46.4	42.1	50.8	54.2	49.9	58.5	62.4	58.2	66.5
	GH_Kintampo_UNEXP	0.0	0.0	0.8	0.0	0.0	0.8	0.2	0.0	1.1	0.0	0.0	0.7	0.6	0.1	1.6
	GH_Navrongo_EXP	0.0	0.0	0.7	32.3	28.3	36.5	53.8	49.4	58.1	58.2	53.8	62.4	65.8	61.5	69.8
	GH_Navrongo_UNEXP	0.0	0.0	0.7	0.0	0.0	0.7	0.0	0.0	0.7	0.0	0.0	0.7	17.2	14.0	20.8
	MA_Mangochi_EXP	7.0	4.9	9.5	30.8	27.0	34.9	44.8	40.5	49.2	50.8	46.4	55.1	52.3	48.0	56.6
	MA_Monkey Bay_UNEXP	0.0	0.0	0.7	0.2	0.0	1.0	0.2	0.0	1.0	2.9	1.7	4.6	15.2	12.3	18.5
	MA_Chikwawa_UNEXP				0.4	0.0	1.4	1.6	0.7	3.0	7.4	5.4	9.8	19.1	15.9	22.5
	MA_St Montfort_EXP				37.5	33.5	41.7	44.7	40.6	48.8	40.8	36.8	44.9	61.4	57.4	65.4
	KE_Bondo_UNEXP	0.0	0.0	0.9	0.9	0.2	2.2	3.5	2.1	5.6	8.8	6.5	11.7	31.5	27.5	35.7
	KE_Gem_EXP	16.8	13.5	20.6	39.7	35.3	44.2	49.8	45.3	54.3	56.9	52.4	61.4	58.0	53.6	62.3
	KE_Nyando_UNEXP	0.0	0.0	0.8	1.4	0.6	2.9	1.5	0.7	2.9	17.2	14.0	20.8	38.9	34.7	43.3
	Overall Total	**4.8**	**4.2**	**5.4**	**16.7**	**15.8**	**17.7**	**24.1**	**23.0**	**25.2**	**29.1**	**28.0**	**30.3**	**40.9**	**39.7**	**42.1**
TOTAL	KE_Kombewa_EXP	15.0	12.2	18.1	22.3	19.1	25.9	39.8	35.9	43.9	50.8	46.8	54.9	63.0	59.0	66.9
	GH_Kintampo_EXP	7.7	5.7	10.1	26.3	22.8	30.1	42.7	38.7	46.7	50.3	46.3	54.4	59.5	55.4	63.5
	GH_Kintampo_UNEXP	0.0	0.0	0.6	0.0	0.0	0.6	0.2	0.0	0.9	0.0	0.0	0.6	0.5	0.1	1.5
	GH_Navrongo_EXP	0.0	0.0	0.6	28.7	25.1	32.5	48.9	44.8	53.0	52.3	48.3	56.4	60.3	56.3	64.3
	GH_Navrongo_UNEXP	0.0	0.0	0.6	0.0	0.0	0.6	0.0	0.0	0.6	0.0	0.0	0.6	14.7	11.9	17.8

Pf infection status	Study center	Survey 6			Survey 7			Survey 8			Survey 9			Survey 10		
		%	95% CI		%	95% CI		%	95% CI		%	95% CI		%	95% CI	
	MA_Mangochi_EXP	6.1	4.4	8.4	28.9	25.3	32.7	41.2	37.2	45.2	47.1	43.0	51.2	49.9	45.8	54.0
	MA_Monkey Bay_UNEXP	0.0	0.0	0.6	0.2	0.0	0.9	0.2	0.0	0.9	2.8	1.7	4.5	15.2	12.4	18.3
	MA_Chikwawa_UNEXP				0.3	0.0	1.2	1.5	0.7	2.8	7.2	5.2	9.5	18.4	15.4	21.8
	MA_St Montfort_EXP				35.7	31.9	39.7	44.0	40.0	48.1	40.7	36.7	44.7	61.2	57.2	65.1
	KE_Bondo_UNEXP	0.0	0.0	0.6	0.8	0.3	1.9	3.1	1.9	4.9	7.6	5.6	10.0	29.5	25.9	33.3
	KE_Gem_EXP	14.3	11.6	17.4	35.1	31.3	39.1	45.5	41.5	49.6	53.0	48.9	57.1	53.5	49.4	57.5
	KE_Nyando_UNEXP	0.0	0.0	0.6	1.3	0.6	2.6	1.3	0.6	2.6	15.5	12.7	18.6	35.5	31.7	39.5
	Overall Total	**4.3**	**3.8**	**4.8**	**15.0**	**14.2**	**15.8**	**22.4**	**21.4**	**23.3**	**27.3**	**26.3**	**28.3**	**38.5**	**37.3**	**39.6**

Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy
95% CI = Exact 95% Lower and Upper confidence limits
Source: Table V2_S6 to Table V2_S10

11.4.3.2. Prevalence of *P. falciparum* measured by NAAT and microscopy

Of note, the prevalence of *P. falciparum* measured by NAAT was not measured in SN Keur Soce in Survey 1.

Overall sites, across surveys, the prevalence of *P. falciparum* measured by NAAT ranged from 18.1% in Survey 10 to 45.9% in Survey 3, and measured by microscopy from 11.2% in Survey 10 to 41.0% in Survey 3 (Table 30).

By center (excluding Keur Soce in Survey 1), across surveys, the prevalence of *P. falciparum* as measured by NAAT ranged from 1.3% in SN Keur Soce (Survey 2) to 76.3% in BF Nouna (Survey 2). The prevalence of *P. falciparum* as measured by microscopy ranged from 0.3% in MA St Montfort (Survey 9) to 81.3% in BF Nouna (Survey 2).

Table 30 *P. falciparum* as measured by NAAT and by microscopy by center and survey (ATP Cohort)

	Study center	Survey 1		Survey 2		Survey 3		Survey 4	
		n	%	n	%	n	%	n	%
NAAT	BF_Nouna	406	69.9	457	76.3	250	41.7	298	49.7
	BF_Sapone	246	57.7	390	65.1	276	46.0	294	49.0
	SN_Niakhar	15	2.7	14	2.3				
	TZ_Korogwe	108	18.0	32	5.3				
	KE_Kombewa_EXP	262	43.7	236	39.4	292	48.7	276	46.0
	GH_Kintampo_EXP	231	40.9	281	46.8	283	47.2	246	41.0
	GH_Navrongo_EXP							177	29.5
	SN_Keur Soce*	-	-	7	1.3				
	Overall Total	**1268**	**38.0**	**1417**	**34.1**	**1101**	**45.9**	**1291**	**43.0**
Microscopy	BF_Nouna	403	66.5	488	81.3	352	58.7	257	42.8
	BF_Sapone	299	49.5	316	52.8	194	32.3	204	34.0
	SN_Niakhar	9	1.5	3	0.5				
	TZ_Korogwe	63	10.5	18	3.0				
	KE_Kombewa_EXP	196	32.7	189	31.6	213	35.6	211	35.2
	GH_Kintampo_EXP	214	35.7	212	35.3	225	37.5	186	31.0
	GH_Navrongo_EXP							100	16.7
	SN_Keur Soce	3	0.5	6	1.0				
	Overall Total	**1187**	**28.2**	**1232**	**29.3**	**984**	**41.0**	**958**	**31.9**

	Study center	Survey 5		Survey 6		Survey 7		Survey 8		Survey 9		Survey 10	
		n	%	n	%	n	%	n	%	n	%	n	%
NAAT	KE_Kombewa_EXP	259	43.2	258	43.0	213	35.5	214	35.7	211	35.2	158	26.3
	GH_Kintampo_EXP	191	31.8	185	30.8	150	25.0	104	17.3	102	17.0	85	14.2
	GH_Kintampo_UNEXP			198	33.0	170	28.3	140	23.3	127	21.2	98	16.3
	GH_Navrongo_EXP	180	30.1	175	29.2	145	24.2	138	23.0	173	28.8	126	21.0
	GH_Navrongo_UNEXP			204	34.0	182	30.3	178	29.7	181	30.2	166	27.7
	MA_Mangochi_EXP	161	27.1	122	20.4	120	20.0	127	21.2	126	21.0	111	18.5
	MA_Monkey Bay_UNEXP	121	20.2	62	10.3	56	9.3	78	13.0	81	13.5	103	17.2
	MA_Chikwawa_UNEXP	119	21.6			130	21.0	40	6.7	43	7.2	38	6.4
	MA_St Montfort_EXP	71	12.6			93	15.2	32	5.4	13	2.2	11	1.8
	KE_Bondo_UNEXP	212	35.1	260	43.6	203	33.7	215	35.5	187	31.0	119	20.7
	KE_Gem_EXP	238	39.8	189	32.3	163	27.0	188	31.0	176	29.3	135	22.4
	KE_Nyando_UNEXP			248	41.3	195	32.5	156	25.7	165	27.5	147	24.5
	Overall Total	**1552**	**29.2**	**1901**	**31.8**	**1820**	**25.1**	**1610**	**22.3**	**1585**	**22.0**	**1297**	**18.1**
Microscopy	KE_Kombewa_EXP	187	31.2	185	30.8	134	22.3	123	20.5	124	20.7	118	19.7
	GH_Kintampo_EXP	153	25.5	119	19.8	103	17.2	74	12.3	63	10.5	52	8.7
	GH_Kintampo_UNEXP			155	25.8	133	22.2	99	16.5	91	15.2	67	11.2
	GH_Navrongo_EXP	110	18.2	97	16.2	77	12.8	69	11.5	74	12.3	74	12.3
	GH_Navrongo_UNEXP			106	17.7	95	15.8	75	12.5	89	14.8	95	15.8
	MA_Mangochi_EXP	98	16.4	86	14.3	51	8.5	78	13.0	75	12.5	64	10.6
	MA_Monkey Bay_UNEXP	63	10.5	35	5.8	34	5.7	38	6.3	44	7.3	48	8.0
	MA_Chikwawa_UNEXP	69	11.8			97	15.6	32	5.3	17	2.8	25	4.2
	MA_St Montfort_EXP	38	6.5			53	8.6	14	2.3	2	0.3	4	0.7
	KE_Bondo_UNEXP	158	25.9	179	29.9	139	23.0	127	21.0	105	17.4	86	14.3
	KE_Gem_EXP	146	24.4	131	22.3	115	19.0	106	17.5	110	18.3	88	14.6
	KE_Nyando_UNEXP			153	25.5	107	17.8	74	12.2	94	15.7	89	14.8
	Overall Total	**1022**	**19.0**	**1246**	**20.8**	**1138**	**15.7**	**909**	**12.6**	**888**	**12.3**	**810**	**11.2**

*Prevalence of *P. falciparum* measured by NAAT was not measured in Keur Soce in Survey 1
Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites; NAAT = Nucleic acid amplification test
Source: Table S7_S1 to Table S7_S10; Table S20_S1 to Table S20_S10

11.4.3.2.1. Concordance in P. falciparum infection measured by NAAT vs. microscopy

Overall sites, across surveys, the proportion of participants detected as positive by NAAT and negative by microscopy ranged from 20.9% in Survey 2 to 46.9% in Survey 9 (Table 31). The proportion of participants measured as negative by NAAT and detected as positive by microscopy ranged from 0.5% in Survey 10 to 12.2% in Survey 3.

By center, across surveys, the proportion of participants detected as positive by NAAT and negative by microscopy ranged from 12.5% in BF Nouna (Survey 2) to 92.3% in MA St Montfort EXP (Survey 9). The proportion of participants measured as negative by NAAT and detected as positive by microscopy ranged from 0% in SN Niakhar (Survey 2), BF Sapone (Survey 3) and GH Navrongo EXP/UNEXP and MA St Montfort EXP all in Survey 10 to 61.3% in BF Nouna (Survey 2).

The concordance in *P. falciparum* prevalence between qualitative results from the 2 methods (NAAT vs. microscopy) reached a significant substantial overall agreement across all 10 surveys, with a κ coefficient ranging from 0.62 (Surveys 8 and 9) to 0.78 (Survey 2). The level of concordance between the 2 methods showed variation by center with a κ coefficient ranging from 0.13 (slight agreement) in MA St Montfort EXP (Survey 9) to 0.85 (almost perfect agreement) in MA Chikwawa UNEXP (Survey 8).

When looking at the concordance between quantitative measures by NAAT and microscopy overall, it is important to note that 32.2% (Survey 1), 29.2% (Survey 2), 35.7% (Survey 3), 49.7% (Survey 4), 51.9% (Survey 5), 41.8% (Survey 6), 60.1% (Survey 7), 65.6% (Survey 8), 62.9% (Survey 9) and 59.3% (Survey 10) of infections categorized as low-density by NAAT were measured as negative by microscopy (Table S26_S1 to Table S26_S10). Additionally, 30.8% (Survey 1), 40.9% (Survey 2), 33.6% (Survey 3), 23.1% (Survey 4), 51.0% (Survey 5), 89.0% (Survey 6), 33.5% (Survey 7), 26.0% (Survey 8), 28.1% (Survey 9) and 22.0% (Survey 10) of infections assessed as medium density by NAAT were categorized as high to very high by microscopy (Table S26_S1 to Table S26_S10). Refer to Section 11.4.3.5 for a summary of slide reading results by survey.

Table 31 Concordance between *P. falciparum* measured by microscopy vs measured by NAAT - by center and survey (ATP Cohort)

Study center	Survey 1				Survey 2				Survey 3				Survey 4			
	NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
BF_Nouna	59	14.5	38	21.7	57	12.5	87	61.3	46	18.4	148	42.3	95	31.9	54	17.9
Kappa coefficient	**0.62 [0.55; 0.69]**				**0.28 [0.19; 0.37]**				**0.37[0.30-0.44]**				**0.50 [0.43; 0.57]**			
BF_Sapone	34	13.8	2	1.1	78	20.0	4	1.9	82	29.7	0	0.0	96	32.7	6	2.0
Kappa coefficient	**0.83 [0.78; 0.88]**				**0.72 [0.67; 0.78]**				**0.72 [0.66-0.77]**				**0.66 [0.60; 0.72]**			
SN_Niakhar	8	53.3	1	0.2	11	78.6	0	0.0								
Kappa coefficient	**0.60 [0.36; 0.84]**				**0.35 [0.06; 0.64]**											
TZ_Korogwe	53	49.1	8	1.6	16	50.0	2	0.4								
Kappa coefficient	**0.59 [0.50; 0.68]**				**0.63 [0.47; 0.78]**											
KE Kombewa_EXP	88	33.6	22	6.5	51	21.6	4	1.1	83	28.4	4	1.3	74	26.8	9	2.8
Kappa coefficient	**0.62 [0.55; 0.68]**				**0.80 [0.75; 0.85]**				**0.71 [0.65-0.76]**				**0.72 [0.66; 0.77]**			
GH_Kintampo_EXP	43	18.6	21	6.3	80	28.5	11	3.4	64	22.6	6	1.9	69	28.0	9	2.5
Kappa coefficient	**0.76 [0.71; 0.82]**				**0.69 [0.63; 0.75]**				**0.76 [0.71-0.81]**				**0.72 [0.66; 0.78]**			
SN_Keur Soce*	-	-	-	-	3	42.9	2	0.4								
Kappa coefficient	**-**				**0.61 [0.30; 0.92]**											
GH_Navrongo_EXP													81	45.8	4	0.9
Kappa coefficient													**0.61 [0.54; 0.68]**			
Total	**285**	**22.5**	**92**	**4.4**	**296**	**20.9**	**110**	**4.0**	**275**	**25.0**	**158**	**12.2**	**415**	**32.1**	**82**	**4.8**
Kappa coefficient	**0.75 [0.73; 0.78]**				**0.78 [0.75; 0.80]**				**0.63 [0.60-0.66]**				**0.65 [0.62; 0.68]**			

Study center	Survey 5				Survey 6				Survey 7				Survey 8				Survey 9				Survey 10			
	NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
KE_Kombewa_EXP	86	33.2	14	4.1	90	34.9	17	5.0	83	39.0	4	1.0	95	44.4	4	1.0	91	43.1	4	1.0	47	29.7	7	1.6
Kappa coefficient	**0.65 [0.59; 0.71]**				**0.62 [0.56; 0.69]**				**0.65 [0.59; 0.72]**				**0.60 [0.54; 0.67]**				**0.62 [0.55; 0.68]**				**0.75 [0.68; 0.81]**			
GH_Kintampo_EXP	43	22.5	5	1.2	67	36.2	1	0.2	50	33.3	3	0.7	31	29.8	1	0.2	48	47.1	9	1.8	36	42.4	3	0.6
Kappa coefficient	**0.81 [0.75; 0.86]**				**0.71 [0.64; 0.77]**				**0.74 [0.67; 0.80]**				**0.79 [0.72; 0.86]**				**0.60 [0.51; 0.69]**				**0.68 [0.59; 0.77]**			
GH_Kintampo_UNEXP					57	28.8	14	3.5	59	34.7	22	5.1	53	37.9	12	2.6	49	38.6	13	2.7	36	36.7	5	1.0
Kappa coefficient					**0.72 [0.66; 0.78]**				**0.64 [0.57; 0.71]**				**0.66 [0.59; 0.74]**				**0.65 [0.58; 0.73]**				**0.71 [0.63; 0.80]**			
GH_Navrongo_EXP	72	40.0	2	0.5	79	45.1	1	0.2	73	50.3	5	1.1	73	52.9	4	0.9	102	59.0	3	0.7	52	41.3	0	0.0
Kappa coefficient	**0.67 [0.60; 0.74]**				**0.63 [0.56; 0.70]**				**0.58 [0.50; 0.66]**				**0.56 [0.48; 0.64]**				**0.49 [0.41; 0.56]**				**0.69 [0.62; 0.77]**			
GH_Navrongo_UNEXP					100	49.0	2	0.5	89	48.9	2	0.5	104	58.4	1	0.2	94	51.9	2	0.5	71	42.8	0	0.0
Kappa coefficient					**0.57 [0.50; 0.64]**				**0.59 [0.51; 0.66]**				**0.50 [0.42; 0.57]**				**0.56 [0.48; 0.63]**				**0.66 [0.59; 0.73]**			
MA_Mangochi_EXP	69	42.9	6	1.4	45	36.9	7	1.5	71	59.2	2	0.4	58	45.7	9	1.9	55	43.7	4	0.8	48	43.2	1	0.2
Kappa coefficient	**0.64 [0.56; 0.71]**				**0.70 [0.62; 0.77]**				**0.52 [0.42; 0.61]**				**0.61 [0.53; 0.69]**				**0.65 [0.57; 0.73]**				**0.68 [0.59; 0.76]**			
MA_Monkey Bay_UNEXP	66	54.5	8	1.7	30	48.4	3	0.6	27	48.2	5	0.9	41	52.6	1	0.2	39	48.1	2	0.4	56	54.4	1	0.2
Kappa coefficient	**0.53 [0.44; 0.62]**				**0.63 [0.52; 0.75]**				**0.62 [0.50; 0.74]**				**0.60 [0.50; 0.71]**				**0.64 [0.54; 0.74]**				**0.58 [0.48; 0.67]**			
MA_Chikwawa_UNEXP	55	46.2	4	0.9					47	36.2	13	2.7	9	22.5	1	0.2	27	62.8	1	0.2	14	36.8	1	0.2
Kappa coefficient	**0.63 [0.54; 0.71]**								**0.68 [0.60; 0.75]**				**0.85 [0.76; 0.94]**				**0.51 [0.36; 0.67]**				**0.75 [0.63; 0.87]**			
MA_St Montfort_EXP	41	57.7	6	1.2					50	53.8	10	1.9	23	71.9	5	0.9	12	92.3	1	0.2	7	63.6	0	0.0
Kappa coefficient	**0.52 [0.40; 0.64]**								**0.54 [0.44; 0.64]**				**0.37 [0.19; 0.55]**				**0.13 [-0.10; 0.36]**				**0.53 [0.22; 0.83]**			
KE_Bondo_UNEXP	60	28.3	5	1.3	91	35.0	10	3.0	74	36.5	10	2.5	92	42.8	4	1.0	86	46.0	4	1.0	41	34.5	3	0.7
Kappa coefficient	**0.75 [0.69; 0.81]**				**0.64 [0.58; 0.70]**				**0.66 [0.60; 0.73]**				**0.62 [0.55; 0.68]**				**0.60 [0.53; 0.67]**				**0.74 [0.66; 0.81]**			
KE_Gem_EXP	99	41.6	7	1.9	62	32.8	3	0.8	67	41.1	19	4.3	86	45.7	4	1.0	68	38.6	2	0.5	54	40.0	7	1.5
Kappa coefficient	**0.60 [0.54; 0.67]**				**0.72 [0.66; 0.78]**				**0.60 [0.53; 0.68]**				**0.61 [0.54; 0.68]**				**0.68 [0.62; 0.75]**				**0.67 [0.59; 0.74]**			
KE_Nyando_UNEXP					97	39.1	2	0.6	91	46.7	3	0.7	86	55.1	4	0.9	72	43.6	1	0.2	59	40.1	1	0.2
Kappa coefficient					**0.64 [0.58; 0.70]**				**0.60 [0.53; 0.66]**				**0.53 [0.45; 0.61]**				**0.65 [0.58; 0.72]**				**0.69 [0.62; 0.76]**			
Total	**591**	**38.1**	**57**	**1.5**	**718**	**37.8**	**60**	**1.5**	**781**	**42.9**	**98**	**1.8**	**751**	**46.6**	**50**	**0.9**	**743**	**46.9**	**46**	**0.8**	**521**	**40.2**	**29**	**0.5**
Kappa coefficient	**0.67 [0.65; 0.69]**				**0.67 [0.65; 0.69]**				**0.63 [0.61; 0.65]**				**0.62 [0.60; 0.64]**				**0.62 [0.60; 0.64]**				**0.70 [0.67; 0.72]**			

*SN_Keur Soce had only QNS (Quantity Not Sufficient) results so this center is not represented on this table produced only on valid NAAT results

Shaded fields represent sites not participating in a specific survey

ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites; NAAT = Nucleic acid amplification test; Micro = microscopy; +ve = positive; -ve = negative

Source: Table S25_S1 to Table S25_S10

11.4.3.3. Gametocyte results

Of note, detection of gametocytes by NAAT was not measured in Keur Soce in Survey 1.

Overall sites, across surveys, gametocytes detected by microscopy ranged from 1.3% in Survey 10 to 6.9% in Survey 1, and measured by NAAT from 12.3% in Survey 10 to 27.4% in Survey 4 (Table 32).

Across all surveys (excluding Keur Soce in Survey 1), gametocytemia detected by microscopy ranged by center from 0% in SN Niakhar (Survey 2), MA Chikwawa (Survey 9 and 10) and MA St Montfort (Survey 9 and 10) to 22.7% in BF Sapone (Survey 1). Gametocytemia measured by NAAT ranged by center from 0.2% in SN Niakhar (Survey 2) to 44.8% in BF Nouna (Survey 2), (on valid results) in participants positive for asexual *P. falciparum* parasites.

The concordance in gametocytemia between NAAT and microscopy reached a significant slight to fair overall agreement across all 10 surveys, with a κ coefficient ranging from 0.05 (Surveys 5 and 10) to 0.30 (Survey 1) (Table 33). The level of concordance between the 2 methods showed variation by center with a κ coefficient ranging from -0.09 (no agreement) in MA Chikwawa UNEXP (Survey 8) to 0.67 (substantial agreement) in SN Keur Soce (Survey 2) (Table 33).

Table 32 Gametocytes as measured by NAAT and by microscopy - by center and survey (ATP Cohort)

	Study center	Survey 1		Survey 2		Survey 3		Survey 4	
		n	%	n	%	n	%	n	%
NAAT	BF_Nouna	205	35.3	268	44.8	130	21.7	209	34.8
	BF_Sapone	145	34.1	229	38.2	148	24.7	177	29.5
	SN_Niakhar	2	0.4	1	0.2				
	TZ_Korogwe	21	3.5	11	1.8				
	KE_Kombewa_EXP	81	13.5	120	20.0	122	20.4	223	37.2
	GH_Kintampo_EXP	94	16.7	134	22.3	174	29.0	141	23.5
	GH_Navrongo_EXP							72	12.0
	SN_Keur Soce	0	0.0	4	0.7				
	Overall Total	**548**	**16.4**	**767**	**18.5**	**574**	**23.9**	**822**	**27.4**
Microscopy	BF_Nouna	96	15.8	77	12.8	35	5.8	56	9.3
	BF_Sapone	137	22.7	109	18.2	52	8.7	54	9.0
	SN_Niakhar	3	0.5	0	0.0				
	TZ_Korogwe	8	1.3	1	0.2				
	KE_Kombewa_EXP	24	4.0	9	1.5	6	1.0	20	3.3
	GH_Kintampo_EXP	18	3.0	32	5.3	51	8.5	38	6.3
	GH_Navrongo_EXP							25	4.2
	SN_Keur Soce	5	0.8	5	0.8				
	Overall Total	**291**	**6.9**	**233**	**5.5**	**144**	**6.0**	**193**	**6.4**

	Study center	Survey 5		Survey 6		Survey 7		Survey 8		Survey 9		Survey 10	
		n	%	n	%	n	%	n	%	n	%	n	%
NAAT	KE_Kombewa_EXP	198	33.0	184	30.7	134	22.3	146	24.3	155	25.8	123	20.5
	GH_Kintampo_EXP	166	27.7	147	24.5	112	18.7	85	14.2	69	11.5	57	9.5
	GH_Kintampo_UNEXP			173	28.8	125	20.8	109	18.2	88	14.7	77	12.8
	GH_Navrongo_EXP	127	21.2	135	22.5	76	12.7	60	10.0	103	17.2	74	12.3
	GH_Navrongo_UNEXP			153	25.5	111	18.5	86	14.3	114	19.0	104	17.4
	MA_Mangochi_EXP	130	21.9	100	16.7	97	16.2	69	11.5	87	14.5	78	13.0
	MA_Monkey Bay_UNEXP	92	15.4	55	9.2	44	7.3	43	7.2	54	9.0	59	9.8
	MA_Chikwawa_UNEXP	96	17.4			98	15.8	30	5.0	27	4.5	20	3.4
	MA_St Montfort_EXP	58	10.3			54	8.8	19	3.2	3	0.5	8	1.3
	KE_Bondo_UNEXP	168	27.8	207	34.7	134	22.2	149	24.6	120	19.9	89	15.5
	KE_Gem_EXP	161	26.9	141	24.1	100	16.6	127	21.0	129	21.5	95	15.8
	KE_Nyando_UNEXP			201	33.5	138	23.0	118	19.5	119	19.8	101	16.8
	Overall Total	**1196**	**22.5**	**1496**	**25.0**	**1223**	**16.9**	**1041**	**14.4**	**1068**	**14.8**	**885**	**12.3**
Microscopy	KE_Kombewa_EXP	34	5.7	24	4.0	23	3.8	24	4.0	21	3.5	13	2.2
	GH_Kintampo_EXP	29	4.8	28	4.7	11	1.8	14	2.3	12	2.0	1	0.2
	GH_Kintampo_UNEXP			24	4.0	18	3.0	16	2.7	11	1.8	3	0.5
	GH_Navrongo_EXP	19	3.1	22	3.7	11	1.8	14	2.3	19	3.2	13	2.2
	GH_Navrongo_UNEXP			23	3.8	19	3.2	14	2.3	27	4.5	17	2.8
	MA_Mangochi_EXP	7	1.2	9	1.5	1	0.2	4	0.7	4	0.7	5	0.8
	MA_Monkey Bay_UNEXP	5	0.8	1	0.2	1	0.2	2	0.3	2	0.3	6	1.0
	MA_Chikwawa_UNEXP	1	0.2			1	0.2	4	0.7	0	0.0	0	0.0
	MA_St Montfort_EXP	1	0.2			5	0.8	2	0.3	0	0.0	0	0.0
	KE_Bondo_UNEXP	26	4.3	41	6.9	22	3.6	20	3.3	27	4.5	11	1.8
	KE_Gem_EXP	16	2.7	16	2.7	16	2.6	18	3.0	40	6.7	13	2.2
	KE_Nyando_UNEXP			19	3.2	2	0.3	3	0.5	11	1.8	9	1.5
	Overall Total	**138**	**2.6**	**207**	**3.5**	**130**	**1.8**	**135**	**1.9**	**174**	**2.4**	**91**	**1.3**

Note: data represent +ve (positive) participants as a % of overall population
Shaded fields represent sites not participating in a specific survey
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites; NAAT = Nucleic acid amplification test
Source: Table S7_S1 to Table S7_S10; Table S20_S1 to Table S20_S10

Table 33 Concordance between *P. falciparum* gametocytemia measured by microscopy vs measured by NAAT - by center and survey (ATP Cohort)

Study center	Survey 1				Survey 2				Survey 3				Survey 4			
	NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
BF_Nouna	139	67.8	20	10.0	199	74.3	7	3.7	100	76.9	4	3.3	157	75.1	0	0.0
Kappa coefficient	**0.22 [0.14; 0.30]**				**0.19 [0.14; 0.25]**				**0.19 [0.11-0.27]**				**0.17 [0.12; 0.21]**			
BF_Sapone	64	44.1	15	15.0	140	61.1	16	9.9	119	80.4	22	17.2	126	71.2	1	0.9
Kappa coefficient	**0.38 [0.27; 0.48]**				**0.26 [0.19; 0.33]**				**0.02 [-0.06-0.11]**				**0.24 [0.17; 0.30]**			
SN_Niakhar	1	50.0	1	7.7	1	100	0	0.0								
Kappa coefficient	**0.42 [-0.24; 1.00]**				**0.00 [0.00; 0.00]**											
TZ_Korogwe	14	66.7	1	1.1	11	100	1	4.8								
Kappa coefficient	**0.42 [0.19; 0.65]**				**-0.06 [-0.17; 0.05]**											
KE_Kombewa_EXP	63	77.8	4	2.2	113	94.2	2	1.7	121	99.2	5	2.9	203	91.0	0	0.0
Kappa coefficient	**0.25 [0.14; 0.36]**				**0.04 [-0.01; 0.09]**				**-0.02 [-0.06-0.01]**				**0.04 [0.02; 0.05]**			
GH_Kintampo_EXP	82	87.2	1	0.7	110	82.1	5	3.4	137	78.7	12	11.0	108	76.6	2	1.9
Kappa coefficient	**0.14 [0.06; 0.22]**				**0.15 [0.08; 0.22]**				**0.08 [0.01-0.16]**				**0.19 [0.12; 0.26]**			
SN_Keur Soce*	-	-	-	-	1	25.0	0	0.0								
Kappa coefficient	-				**0.67 [0.10; 1.00]**											
GH_Navrongo_EXP													50	69.4	2	1.9
Kappa coefficient													**0.32 [0.20; 0.44]**			
Total	363	66.2	42	5.9	575	75.0	31	4.8	477	83.1	43	8.2	644	78.3	5	1.1
Kappa coefficient	**0.30 [0.25; 0.35]**				**0.19 [0.16; 0.22]**				**0.08 [0.05-0.12]**				**0.16 [0.13; 0.19]**			

Study center	Survey 5				Survey 6				Survey 7				Survey 8				Survey 9				Survey 10			
	NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve		NAAT +ve Micro -ve		NAAT -ve Micro +ve	
	N	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
KE_Kombewa_EXP	172	86.9	2	3.3	163	88.6	0	0.0	112	83.6	1	1.3	123	84.2	0	0.0	134	86.5	0	0.0	110	89.4	0	0.0
Kappa coefficient	**0.05 [0.01; 0.09]**				**0.07 [0.04; 0.10]**				**0.12 [0.06; 0.17]**				**0.11 [0.06; 0.15]**				**0.08 [0.04; 0.11]**				**0.05 [0.02; 0.08]**			
GH_Kintampo_EXP	137	82.5	0	0.0	120	81.6	1	2.6	104	92.9	2	5.3	71	83.5	0	0.0	58	84.1	0	0.0	57	100	1	3.6
Kappa coefficient	**0.05 [0.03; 0.08]**				**0.07 [0.03; 0.12]**				**0.01 [-0.04; 0.06]**				**0.07 [0.02; 0.11]**				**0.11 [0.04; 0.18]**				**-0.02 [-0.07; 0.02]**			
GH_Kintampo_UNEXP					151	87.3	0	0.0	107	85.6	0	0.0	96	88.1	1	3.2	79	89.8	0	0.0	74	96.1	0	0.0
Kappa coefficient					**0.04 [0.02; 0.06]**				**0.08 [0.04; 0.12]**				**0.04 [-0.00; 0.09]**				**0.07 [0.02; 0.11]**				**0.02 [-0.00; 0.04]**			
GH_Navrongo_EXP	110	86.6	1	1.9	113	83.7	0	0.0	66	86.8	0	0.0	49	81.7	2	2.6	86	83.5	1	1.4	63	85.1	2	3.8
Kappa coefficient	**0.07 [0.02; 0.12]**				**0.08 [0.04; 0.12]**				**0.13 [0.05; 0.20]**				**0.17 [0.06; 0.29]**				**0.13 [0.06; 0.19]**				**0.09 [0.01; 0.18]**			
GH_Navrongo_UNEXP					130	85.0	0	0.0	92	82.9	0	0.0	72	83.7	0	0.0	89	78.1	0	0.0	91	87.5	3	4.8
Kappa coefficient					**0.08 [0.04; 0.12]**				**0.14 [0.08; 0.20]**				**0.17 [0.09; 0.25]**				**0.17 [0.10; 0.24]**				**0.06 [-0.01; 0.13]**			
MA_Mangochi_EXP	123	94.6	0	0.0	92	92.0	0	0.0	96	99.0	0	0.0	66	95.7	1	1.7	84	96.6	1	2.6	73	93.6	0	0.0
Kappa coefficient	**0.02 [0.00; 0.04]**				**0.03 [0.01; 0.05]**				**0.00 [-0.00; 0.01]**				**0.02 [-0.03; 0.08]**				**0.01 [-0.03; 0.04]**				**0.04 [0.00; 0.07]**			
MA_Monkey Bay_UNEXP	87	94.6	0	0.0	54	98.2	0	0.0	43	97.7	0	0.0	42	97.7	1	2.8	53	98.1	1	3.7	55	93.2	1	2.3
Kappa coefficient	**0.03 [0.00; 0.05]**				**0.00 [-0.00; 0.01]**				**0.01 [-0.01; 0.03]**				**-0.00 [-0.07; 0.06]**				**-0.01 [-0.07; 0.04]**				**0.04 [-0.03; 0.11]**			
MA_Chikwawa_UNEXP	95	99.0	0	0.0					97	99.0	0	0.0	29	96.7	2	20.0	27	100	0	0.0	20	100	0	0.0
Kappa coefficient	**0.00 [-0.00; 0.01]**								**0.01 [-0.00; 0.02]**				**-0.09 [-0.23; 0.06]**				**0.00 [0.00; 0.00]**				**0.00 [0.00; 0.00]**			
MA_St Montfort_EXP	57	98.3	0	0.0					50	92.6	0	0.0	18	94.7	0	0.0	3	100	0	0.0	8	100	0	0.0
Kappa coefficient	**0.01 [-0.01; 0.02]**								**0.06 [0.00; 0.12]**				**0.05 [-0.04; 0.13]**				**0.00 [0.00; 0.00]**				**0.00 [0.00; 0.00]**			
KE_Bondo_UNEXP	143	85.1	1	2.3	167	80.7	1	1.9	114	85.1	1	1.4	129	86.6	0	0.0	96	80.0	1	1.5	78	87.6	0	0.0
Kappa coefficient	**0.06 [0.02; 0.09]**				**0.08 [0.04; 0.12]**				**0.10 [0.04; 0.15]**				**0.09 [0.05; 0.13]**				**0.14 [0.08; 0.21]**				**0.07 [0.02; 0.11]**			
KE_Gem_EXP	145	90.1	0	0.0	127	90.1	2	4.1	86	86.0	1	1.6	109	85.8	0	0.0	90	69.8	1	2.1	83	87.4	0	0.0
Kappa coefficient	**0.07 [0.03; 0.10]**				**0.03 [-0.01; 0.07]**				**0.10 [0.04; 0.16]**				**0.10 [0.05; 0.14]**				**0.18 [0.10; 0.25]**				**0.08 [0.03; 0.13]**			
KE_Nyando_UNEXP					183	91.0	0	0.0	137	99.3	1	1.8	115	97.5	0	0.0	108	90.8	0	0.0	92	91.1	0	0.0
Kappa coefficient					**0.04 [0.02; 0.05]**				**-0.01 [-0.03; 0.02]**				**0.01 [-0.00; 0.03]**				**0.05 [0.02; 0.09]**				**0.06 [0.02; 0.10]**			
Total	**1069**	**89.4**	**4**	**1.1**	**1300**	**86.9**	**4**	**1.0**	**1104**	**90.3**	**6**	**1.0**	**919**	**88.3**	**7**	**1.2**	**907**	**84.9**	**5**	**1.0**	**804**	**90.8**	**7**	**1.7**
Kappa coefficient	**0.05 [0.04; 0.06]**				**0.06 [0.05; 0.07]**				**0.06 [0.05; 0.07]**				**0.08 [0.06; 0.09]**				**0.10 [0.08; 0.11]**				**0.05 [0.03; 0.06]**			

*SN_Keur Soce had only QNS (Quality Not Sufficient) results so this center is not represented on this table produced only on valid NAAT results

Shaded fields represent sites not participating in a specific survey. ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites; NAAT = Nucleic acid amplification test; Micro = microscopy; +ve = positive; -ve = negative. The all-zero rows and/or columns are taking into account for the computation of simple and weighted Kappa tests

Source: Table S27_S1 to Table S27_S10

Additional details on *P. falciparum* infection and gametocyte results measured by NAAT are presented by vaccine eligibility subgroups in Table S21_S1 to Table S21_S10, by RTS,S/AS01$_E$ vaccination status in Table S22_S5 to Table S22_S10 and details on gametocyte results measured by NAAT presented by *P. falciparum* infection status measured by NAAT in Table S23_S1 to Table S23_S10.

Details for *P. falciparum* results measured by microscopy according to gametocyte results are presented in Table S10_S1 to Table S10_S10 and for *P. falciparum* density according to gametocytes results measured by microscopy and NAAT in Table S11_S1 to Table S11_S10 and in Table S24_S1 to Table S24_S10, respectively.

11.4.3.4. Analysis of parasite prevalence trends

The Cochran-Armitage trend test was computed only on centers with results for at least 3 surveys (see Section 10.9.2.2 for further details).

The Cochran-Armitage trend test for site parasite prevalence measured by microscopy was significant for all sites, with the exception of GH Navrongo UNEXP and MA Monkey Bay (Table 34).

Results for the Cochran-Armitage trend test on the RTS,S/AS01$_E$ vaccination history are presented in Table V5.

Table 34 Cochran-Armitage trend test in the parasite prevalence measured by microscopy by center and according to RTS,S/AS01 vaccine eligible or ineligible subgroup (ATP Cohort)

Center	Group	Cochran-Armitage Trend Test	P-value for Trend Test (Two-sided)
BF_Nouna	Eligible	10.283	<0.0001
	Ineligible	3.449	0.0006
	Total	10.579	<0.0001
BF_Sapone	Eligible	8.262	<0.0001
	Ineligible	1.394	0.1633
	Total	7.427	<0.0001
KE_Kombewa_EXP	Eligible	7.690	<0.0001
	Ineligible	5.443	<0.0001
	Total	9.241	<0.0001
GH_Kintampo_EXP	Eligible	15.036	<0.0001
	Ineligible	11.956	<0.0001
	Total	18.800	<0.0001
GH_Kintampo_UNEXP	Eligible	5.997	<0.0001
	Ineligible	4.322	<0.0001
	Total	7.299	<0.0001
GH_Navrongo_EXP	Eligible	3.047	0.0023
	Ineligible	2.897	0.0038
	Total	3.889	0.0001
GH_Navrongo_UNEXP	Eligible	-0.983	0.3257
	Ineligible	2.285	0.0223
	Total	1.003	0.3157

Center	Group	Cochran-Armitage Trend Test	P-value for Trend Test (Two-sided)
MA_Mangochi_EXP	Eligible	3.413	0.0006
	Ineligible	0.149	0.8815
	Total	2.626	0.0086
MA_Monkey Bay_UNEXP	Eligible	0.561	0.5749
	Ineligible	0.600	0.5486
	Total	0.830	0.4067
MA_Chikwawa_UNEXP	Eligible	5.585	<0.0001
	Ineligible	5.180	<0.0001
	Total	7.527	<0.0001
MA_St Montfort_EXP	Eligible	6.437	<0.0001
	Ineligible	4.384	<0.0001
	Total	7.708	<0.0001
KE_Bondo_UNEXP	Eligible	6.331	<0.0001
	Ineligible	3.000	0.0027
	Total	6.884	<0.0001
KE_Gem_EXP	Eligible	4.510	<0.0001
	Ineligible	1.872	0.0612
	Total	4.603	<0.0001
KE_Nyando_UNEXP	Eligible	4.515	<0.0001
	Ineligible	1.896	0.0580
	Total	4.824	<0.0001

Asymptotic test used for Cochran-Armitage Trend test
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
Eligible group = subjects eligible for the RTS,S/AS01 vaccination
Ineligible group = subjects not eligible for the RTS,S/AS01 vaccination
Source: Table T1 (Annex – Report Tables Survey 10)

11.4.3.5. Slide reading results

Across all 10 surveys, 2 slides were available for slide reading in ≥ 99.5% of participants included in the ATP Cohort (Table S1_S1 to Table S1_S10). A third slide reading was needed in < 6% of participants in each survey and a fourth slide reading was conducted for 1 participant in Survey 6 (Table S5_S1 to Table S5_S10).

Per protocol, the preferred methodology for estimating *P. falciparum* parasite density was counting parasites against an assumed 8000 leukocytes / microliter of blood. The method was used in ≥ 99.4% of slide readings in Surveys 1-7 and in 85.4%, 85.1% and 84.9% of participants in Surveys 8, 9 and 10, respectively (Table S3_S1 to Table S3_S10). Slide reading was performed within 1 day of sample collection for 35.1% of participants in Survey 1, 66.0% in Survey 2, 76.3% in Survey 4, 68.3% in Survey 5 and in 83.7% to 97.6% of participants in Survey 3 and Surveys 6-10 (Table S6_S1 to Table S6_S10).

Parasite density was mostly low (< 2500 parasites/μL of blood) overall, with approximately half of participants with low parasite density among positive participants as measured by microscopy (620/1187 (52.2%) Survey 1; 673/1232 (54.6%) Survey 2; 602/984 (61.2%) Survey 3; 521/958 (54.4%) Survey 4; 500/1022 (48.9%) Survey 5; 649/1246 (52.1%) Survey 6; 630/1138 (55.4%) Survey 7; 490/909 (53.9%) Survey 8; 458/888 (51.6%) Survey 9; 422/810 (52.1%) Survey 10) (Table S7_S1 to Table S7_S10). Approximately one-fifth of participants had medium density (2500–9999 parasites/μL) (286/1187 (24.1%) Survey 1; 280/1232 (22.7%) Survey 2; 201/984 (20.4%) Survey 3;

209/958 (21.8%) Survey 4; 233/1022 (22.8%) Survey 5; 285/1246 (22.9%) Survey 6; 215/1138 (18.9%) Survey 7; 172/909 (18.9%) Survey 8; 191/888 (21.5%) Survey 9; 193/810 (23.8%) Survey 10) and one-quarter had high (10 000–19 999 parasites/µL) to very high (≥ 20 000 parasites/µL) density (281/1187 (23.7%) Survey 1; 279/1232 (22.6%) Survey 2; 181/984 (18.4%) Survey 3; 228/958 (23.8%) Survey 4; 288/1022 (28.2%) Survey 5; 312/1246 (25.0%) Survey 6; 293/1138 (25.7%) Survey 7; 247/909 (27.2%) Survey 8; 239/888 (26.9%) Survey 9; 195/810 (24.1%) Survey 10).

The proportion of participants with fever measured at the visit tended to increase with parasite density in all 10 surveys (Table D8.2_S1 to Table D8.2_S10). In addition, a very high parasite density (≥ 20 000 parasites/µL of blood) was more frequently observed in participants with measured fever vs. no fever in each survey (25.1% vs 2.5% Survey 1; 23.5% vs 3.0% Survey 2; 28.7% vs 3.6% Survey 3; 37.0% vs 3.4% Survey 4; 24.5% vs 2.3% Survey 5; 33.6% vs 2.1% Survey 6; 32.9% vs 1.8% Survey 7; 23.0% vs 1.6% Survey 8; 18.4% vs 1.7% Survey 9; 21.2% vs 1.1% vs Survey 10, respectively) (Table S17_S1 to Table S17_S10).

Additional details on parasite density by vaccine eligibility subgroups in Table S8_S1 to Table S8_S10, by RTS,S/AS01$_E$ vaccination status in Table S9_S5 to Table S9_S10, by bednet use in Table S14_S1 to Table S14_S10 and Table S15_S1 to Table S15_S10 and by RDT result in Table S19_S1 to Table S19_S10 and Table S19b_S1 to Table S19b_S10.

11.4.3.6. Rapid diagnostic test results

RDT results for participants included in the ATP Cohort are presented in Table S2_S1 to Table S2_S10. As per protocol, RDT was only performed in participants with measured fever at the visit or reported fever in the last 24 hours or in participants presenting signs/symptoms of clinical malaria at the visit; RDT results restricted to this subgroup are presented in Table S2b_S1 and Table S2b_S3 to Table S2b_S10, and are described below, with the exception of Survey 2 for which this subgroup analysis was not conducted.

Overall sites, across surveys, among participants diagnosed as positive by microscopy (i.e., PF INF), most were also tested positive by RDT (96.8% Survey 1; 90.6% Survey 2; 92.7% Survey 3; 94.5% Survey 4; 94.4% Survey 5; 94.4% Survey 6; 93.4% Survey 7; 92.0% Survey 8; 92.7% Survey 9; 94.5% Survey 10) (Table 35). By center, across surveys, the proportion of RDT-positive participants in the microscopy-positive group ranged from 69.6% in BF Nouna (Survey 3) to 100% in BF Nouna (Survey 1), BF Sapone (Surveys 3 and 4), SN Niakhar (Surveys 1 and 2), SN Keur Soce (Survey 1), GH Kintampo EXP (Surveys 6, 8, 10), GH Kintampo UNEXP (Surveys 6, 7, 8, 10), GH Navrongo EXP (Surveys 6 and 10), GH Navrongo UNEXP (Survey 9), MA Mangochi EXP (Surveys 7 and 10), MA Monkey Bay UNEXP (Surveys 6, 7, 8, 9), MA Chikwawa UNEXP (Surveys 5, 8, 9), MA St Montfort EXP (Surveys 7, 8, 10) and KE Gem EXP (Surveys 7 and 10).

Overall, 27.1% (Survey 1), 24.9% (Survey 2), 42.7% (Survey 3), 33.0% (Survey 4), 31.7% (Survey 5), 30.5% (Survey 6), 28.0% (Survey 7), 23.8% (Survey 8), 16.2% (Survey 9) and 16.5% (Survey 10) of participants negative for *P. falciparum* by microscopy (i.e., NOT INF) had positive RDT results. By center, positive RDT results were found in 0% (SN Niakhar [Survey 2], SN Keur Soce [Surveys 1 and 2], GH Kintampo UNEXP [Survey 10], MA Monkey Bay UNEXP [Surveys 7, 8, 9] and MA St Montfort [Surveys 9 and 10]) to 85.7% (BF Sapone [Survey 1]) of participants testing negative for *P. falciparum* by microscopy.

Table 35 Positive rapid diagnostic test results by center and survey, according to *P. falciparum* infection status (ATP Cohort - restricted to participants with fever*)

Pf infection status	Study center	Survey 1		Survey 2		Survey 3		Survey 4	
		n	%	n	%	n	%	n	%
PF INF	BF_Nouna	140	100	105	82.0	32	69.6	45	84.9
	BF_Sapone	22	91.7	32	94.1	13	100	24	100
	SN_Niakhar	4	100	1	100				
	TZ_Korogwe	35	92.1	5	83.3				
	KE_Kombewa_EXP	119	93.7	136	92.5	137	95.8	149	97.4
	GH_Kintampo_EXP	103	99.0	103	98.1	84	98.8	55	93.2
	SN_Keur Soce	1	100	3	75.0				
	Overall Total	**424**	**96.8**	**385**	**90.6**	**266**	**92.7**	**273**	**94.5**
NOT INF	BF_Nouna	30	76.9	17	56.7	6	24.0	16	32.7
	BF_Sapone	12	85.7	8	47.1	4	40.0	6	42.9
	SN_Niakhar	2	1.5	0	0.0				
	TZ_Korogwe	13	14.0	3	6.8				
	KE_Kombewa_EXP	87	34.1	98	34.6	102	45.3	75	31.6
	GH_Kintampo_EXP	40	47.1	55	38.7	42	41.6	30	35.3
	SN_Keur Soce	0	0.0	0	0.0				
	Overall Total	**184**	**27.1**	**181**	**24.9**	**154**	**42.7**	**127**	**33.0**

Pf infection status	Study center	Survey 5		Survey 6		Survey 7		Survey 8		Survey 9		Survey 10	
		n	%	n	%	n	%	n	%	n	%	n	%
PF INF	KE_Kombewa_EXP	147	98.7	161	95.3	122	92.4	73	92.4	88	88.9	89	89.9
	GH_Kintampo_EXP	43	95.6	37	100	13	92.9	18	100	14	93.3	8	100
	GH_Kintampo_UNEXP			17	100	15	100	12	100	49	86.0	5	100
	GH_Navrongo_EXP	49	94.2	50	100	23	92.0	20	87.0	28	96.6	24	100
	GH_Navrongo_UNEXP			49	98.0	22	95.7	37	97.4	42	100	51	98.1
	MA_Mangochi_EXP	29	87.9	8	72.7	9	100	5	83.3	13	92.9	21	100
	MA_Monkey Bay_UNEXP	21	77.8	6	100	6	100	3	100	4	100	8	88.9
	MA_Chikwawa_UNEXP	18	100			45	91.8	5	100	3	100	8	88.9
	MA_St Montfort_EXP	5	83.3			12	100	3	100	-	-	2	100
	KE_Bondo_UNEXP	87	92.6	60	83.3	44	91.7	37	82.2	33	97.1	22	95.7
	KE_Gem_EXP	57	96.6	26	96.3	30	100	29	90.6	41	97.6	23	100
	KE_Nyando_UNEXP			38	95.0	26	86.7	24	96.0	29	90.6	30	90.9
	Overall Total	**456**	**94.4**	**452**	**94.4**	**367**	**93.4**	**266**	**92.0**	**344**	**92.7**	**291**	**94.5**
NOT INF	KE_Kombewa_EXP	141	44.8	98	26.8	133	29.3	86	32.2	45	16.2	73	19.9
	GH_Kintampo_EXP	11	24.4	25	33.3	8	20.5	5	16.1	6	12.0	6	19.4
	GH_Kintampo_UNEXP			4	23.5	3	25.0	9	20.0	39	14.9	0	0.0
	GH_Navrongo_EXP	26	19.0	34	30.9	22	28.9	11	13.8	23	18.7	9	14.5
	GH_Navrongo_UNEXP			42	34.7	24	25.0	36	30.3	40	26.3	37	24.0
	MA_Mangochi_EXP	13	18.3	2	7.7	3	37.5	4	25.0	5	22.7	9	26.5
	MA_Monkey Bay_UNEXP	14	17.5	4	11.8	0	0.0	0	0.0	0	0.0	4	18.2
	MA_Chikwawa_UNEXP	25	28.7			28	35.4	5	6.8	5	12.2	4	7.5
	MA_St Montfort_EXP	7	12.5			7	13.5	5	5.7	0	0.0	0	0.0
	KE_Bondo_UNEXP	59	31.1	45	40.9	30	35.3	28	26.7	20	19.2	11	15.7
	KE_Gem_EXP	48	46.6	25	39.7	19	32.2	20	29.9	25	28.7	13	18.8
	KE_Nyando_UNEXP			15	34.9	13	19.4	26	28.0	14	9.3	20	11.5
	Overall Total	**344**	**31.7**	**294**	**30.5**	**290**	**28.0**	**235**	**23.8**	**222**	**16.2**	**186**	**16.5**

*Definition for Survey 1: either fever at visit or fever during the last 24 hours; definition for Surveys 3-10: either fever at visit or fever during the last 24 hours or other symptoms/signs of clinical malaria at the time of the visit; Survey 2; subset not analyzed for Survey 2
Shaded fields represent sites not participating in a specific survey
Fields with no data (-) represent no participants with known result for fever as defined above
ATP = according to protocol; BF = Burkina Faso; GH = Ghana; KE = Kenya; MA = Malawi; SN = Senegal; TZ = Tanzania; EXP = exposed sites; UNEXP = unexposed sites
PF_INF = Subjects infected with *P. falciparum* parasitemia measured by microscopy
NOT_INF = Subjects not infected with *P. falciparum* parasitemia measured by microscopy
Source: Table S2b_S1, Table S2b_S3 to Table S2b_S10; Table S2_S2 for Survey 2

11.5. Other analyses

Not applicable.

11.6. Adverse events/adverse reactions

Of the participants included in the Total Cohort, none experienced any SAEs related to the study procedure in any survey (i.e., Surveys 1-10) (Table 1 in Annex – Report Tables Survey 1 to Survey 10).

12. DISCUSSION

12.1. Key results

- Overall sites, *P. falciparum* parasitemia prevalence was highest in Survey 3, after which prevalence decreased with subsequent surveys to Survey 8 and remained at a similar level up to Survey 10. The higher prevalence in Surveys 1-4 reflects the high malaria transmission intensity in the Burkina Faso sites participating in the earlier surveys. Post-RTS,S/AS01$_E$ vaccination, *P. falciparum* prevalence generally decreased over surveys in most centers in Ghana, Kenya and Malawi.
- The observed prevalence of *P. falciparum* measured by microscopy varied by center and by age group. Overall for each survey, and in most centers, the prevalence of *P. falciparum* was significantly lower in the 6M-4Y vs. 5Y-9Y JTEG age groups.

  The prevalence of *P. falciparum* varied across sites. Considering study sites from Ghana, Kenya and Malawi only, the prevalence of *P. falciparum* ranged from 0% in MA St Montfort EXP (Survey 9) to 32.75% in KE Kombewa EXP (Survey 4) in the 6M-4Y JTEG age group, and from 0.99% in MA St Montfort (Survey 10) to 57.50% in GH Kintampo EXP (Survey 1) in the 5Y-9Y JTEG age group.
- Overall in each survey (Survey 6 to Survey 10), the prevalence of *P. falciparum* was higher among the RTS,S/AS01$_E$ unvaccinated compared to vaccinated participants.
- Most participants slept under a bednet the night before the visit, ranging by center from 59.8% in GH Kintampo EXP to 99.7% KE Nyando UNEXP, both in Survey 10. The use of other MCIs was rare and showed variations among centers. Overall, a higher proportion of participants slept under a bednet the night before the visit in the 6M-4Y vs. 5Y-9Y age groups in each survey.
- Overall sites, in all 10 surveys, a significantly higher percentage of participants slept under a bednet the night before the visit when comparing vaccine eligible vs. ineligible subgroups.
- Considering exposed study sites participating pre- and post-vaccination (KE Kombewa EXP, GH Kintampo EXP, GH Navrongo EXP), bednet usage the night before the visit remained high post-vaccination, ranging between 70.2% to 98.3% pre-vaccination and between 59.8% to 99.5% post-vaccination.

- There was no significant difference in the prevalence of *P. falciparum* according to gender across surveys. There was no significant difference in bednet usage according to gender across surveys, with the exception of Survey 2 in which more females than males used bednets.
- Parasite density was low in approximately half, moderate in approximately 20% and high to very high in approximately 25% of *P. falciparum* positive participants measured by microscopy.
- Overall, the prevalence of *P. falciparum* by microscopy was higher in participants with fever vs. no fever measured at the visit in all 10 surveys. Fever measured at the visit tended to be reported more often in infected participants compared to non-infected participants, and observed among participants with a higher parasite density overall and by center.
- Data on care seeking behavior (child taken for treatment for reported fever or malaria in the last 14 days) did not show a clear trend in relation to infection status of the child across surveys. Considering exposed study sites participating pre- and post-vaccination introduction, the percentage of participants seeking anti-malarial or fever treatment in the last 14 days remained similar in pre- and post-RTS,S/AS01$_E$ vaccination periods.
- Overall, the proportion of participants hospitalized for malaria in the last 3 months before the visit was low (≤3.1% across surveys), and was comparable between infected and not infected cohorts. Considering exposed study sites participating pre- and post-vaccination, the percentage of participants hospitalized for malaria in the last 3 months remained similar in pre- and post-RTS,S/AS01$_E$ vaccination periods.
- The prevalence of *P. falciparum* measured by microscopy was lower compared to the results of prevalence obtained by NAAT. However, the concordance between qualitative results from the 2 methods (microscopy vs. NAAT) reached a substantial overall agreement in each survey.
- Overall, across surveys, among participants with fever or malaria symptoms diagnosed as *P. falciparum* positive by microscopy, most were also tested positive by RDT (>90.0%); 16.2% (Survey 9) to 42.7% (Survey 3) of participants negative for *P. falciparum* by microscopy had positive RDT results.
- The proportion of participants positive for *Plasmodium* species other than *P. falciparum* was low across all surveys (≤3.0% *P. malariae*, ≤0.9% *P. ovale*, ≤0.3% *P. vivax*). The highest prevalence for *P. malariae* was measured in BF Nouna (9.5%) and for *P. ovale* in KE Gem EXP (3.0%); *P. vivax* was recorded for 3 participants across study sites/surveys.
- Overall, 69.4% (Survey 1) to 97.2% (Survey 10) of participants were vaccinated with any combination of the DTP vaccine (third dose), and 53.7% (Survey 1) to 89.0% (Survey 5 and Survey 10) of participants had received the measles (first dose) vaccine.

A lower proportion of participants in *P. falciparum* infected compared to not infected cohorts received the third dose of any combination of the DTP vaccine in all 10 surveys. The same trend was not observed for participants receiving the first dose of measles vaccine.

Considering exposed study sites participating pre- and post-vaccination, the proportion of participants who received the third dose of any combination of the DTP vaccine remained high post-RTS,S/AS01$_E$ vaccination. Results by site varied in participants who received the measles (first dose) vaccine.

- Overall, across surveys, gametocytes detected by microscopy were lower than measured by NAAT across surveys. The concordance in gametocytemia between NAAT and microscopy testing methods reached a significant slight to fair overall agreement across all 10 surveys.
- Overall, 4.3% (Survey 6), 15.0% (Survey 7), 22.4% (Survey 8), 27.3% (Survey 9) and 38.5% (Survey 10) of participants received at least 1 dose of RTS,S/AS01$_E$ vaccine. A significantly lower proportion of *P. falciparum* infected vs not infected participants had received RTS,S/AS01$_E$ vaccination in Surveys 6-10. This finding is partially attributable to the prevalence of *P. falciparum* being significantly lower in the 6M-4Y vs. 5Y-9Y age group, which is the age group eligible for RTS,S/AS01$_E$ vaccination.
- Significant geographical heterogeneity by segment was observed across surveys for each center. Approximately 600 participants were included in each center, divided across 3 to 14 segments. Although random sampling of the study population was done, the number of participants in each segment at each site varied widely and could then influence the heterogeneity test performed.

12.2. Limitations

- EPI-MAL-005 was planned to be conducted in sites defined in the EPI-MAL-002 and EPI-MAL-003 protocols. From Survey 5 onwards, in alignment with the MVIP and implementation of RTS,S/AS01$_E$ vaccination, the study sites participating in EPI-MAL-005 were restricted to the 3 countries where the RTS,S/AS01$_E$ vaccine was to be implemented: Ghana, Kenya and Malawi. As a result, the countries participating and number of study sites varied in Surveys 1-4; sites in Burkina Faso, Senegal, and Tanzania were early terminated. In Surveys 5-10, additional sites participated in Ghana and Kenya, and the study was extended to sites in Malawi.
- A minimum of 10 participants per segment was not respected in 4 segments in 3 sites in Survey 5, 2 segments in 2 sites in Survey 6, 4 segments in 2 sites in Survey 7, 5 segments in 2 sites in Survey 8, 6 segments in 5 sites in Survey 9 and 13 segments in 6 sites in Survey 10 did not respect. Consequently, the geographical heterogeneity analysis is difficult to interpret.

- Since some data (i.e., use of bednets and other MCI, care seeking behaviors, malaria prevention measures and risk factors) were collected via questionnaires, these results could be subject to reporting bias from parents/legally acceptable representatives. In addition, it is not easy to generalize bednet use based on the report for 1 night. People tend to over report their usage of bednets, potentially due to the perceived health benefits of these nets and the social pressure to report adherence to recommended practices [Perkins, 2019; Brew, 2020]. Also, MCIs may be targeted to areas with higher parasite prevalence and with variations in coverage within an area, which may confound any observations [Drakeley, 2017].
- Comparison of data by RTS,S/AS01$_E$ vaccination status should be interpreted with caution as eligible participants for vaccination were from the younger JTEG age group. The number of eligible children was low in Survey 5 (start of vaccination), and increased with subsequent surveys. The number and characteristics of vaccinated and unvaccinated participants therefore differs across surveys.
- Most participants were categorized as being in countryside locations (Table R3_S1 to Tables R3_S10), however, as there is no precise definition of the type of 'location' in the protocol, this result may be due to a different interpretation between the centers.
- The multivariable model for the study of malaria prevention measure and risk factors is not stable, due to differing collinearity within the model. Therefore, results are difficult to interpret at the present time.

12.3. Interpretation

- In this study, prevalence of *P. falciparum* was assessed at annual surveys from 2014 to 2024. The prevalence of *P. falciparum* was shown to be significantly lower in the 6M-4Y vs. 5Y-9Y age groups, with prevalence across study sites from Ghana, Kenya and Malawi ranging from 0% to 33% and 1% to 58%, respectively. Results were similar in a study of prevalence across 3 annual surveys (2011-2013) in 6 sub-Saharan African countries, including Ghana, Kenya, Malawi [Drakeley, 2017], in which *P. falciparum* prevalence rates (assessed using microscopy) were lower in the 6M-4Y group compared to the older age group, with the estimated pooled prevalence between 17.9% and 28.9% in the 6M-4Y age group. The prevalence of *P. falciparum* varies across age groups, with young children often experiencing a lower burden. Ochwedo et al. [Ochwedo, 2021] showed that lowest infection rate by microscopy in 2020 (equivalent time to Surveys 5 and 6) in a rural area of western Kenya was among children <5 years (11%) compared with older children.

Prevalence of *P. falciparum* was higher in RTS,S/AS01$_E$ unvaccinated than in vaccinated children. Weekly and end-of-season surveys showed that the prevalence of malaria parasitemia was consistently lower after the administration of RTS,S/AS01 [Syed, 2022]. Also, there was an observed decrease in prevalence in both RTS,S/AS01$_E$ vaccinated and unvaccinated cohorts in the post-vaccination period. The RTS,S/AS01$_E$ vaccine primarily targets the *P. falciparum* parasite. In malaria-endemic settings, by reducing the number of malaria-infected individuals, or mosquitoes, will reduce parasite reservoirs and means of transmission in a community [Ko, 2024]. This can offer some protection to all community members including unvaccinated children, who are at high risk for severe malaria.

- In this study, most participants slept under a bednet the night before the visit, with a higher proportion of younger children than older using bednets. Other MCIs were rarely used, showing variation across centers. In 8 study centers from 6 sub-Saharan African countries from 2011 to 2013, the proportion of children aged 6 months to 5 years who slept under a bednet the night before the visit ranged from 33% to 95% [Drakeley, 2017]. In the WHO sub-Saharan Africa region, the percentage of children aged under 5 years sleeping under an ITN increased between 2000 and 2023, from 3% to 59% [WHO, 2024].
- No differences were observed in the prevalence of *P. falciparum* or in the use of MCIs according to the gender across surveys. In many studies, male children show a slightly higher prevalence of *P. falciparum* infection compared to female children [Kepha, 2016; Topazian, 2020; Awosolu, 2021; Oluwafemi, 2024]. However, this difference can vary depending on factors like age, geographic location, and seasonal variations.

  In many malaria-endemic regions, gender difference is among the reported reasons related to ITN utilization. Findings of surveys on the gender differences in the use of ITNs in settings in Africa found that females are more likely to use ITNs compared to males [Garley, 2013; Sichalwe, 2025]. In the light of these findings it's important to consider a range of factors, including cultural norms, household dynamics, age, household prioritization when net supply is limited, targeted educational campaigns and socioeconomic status, to understand the difference in the bednet usage patterns for both genders [Olapeju, 2018; Sichalwe, 2025].
- In this study, parasite density was low in approximately half of *P. falciparum* positive participants. Malaria parasite density is a crucial indicator of infection severity and response to treatment [WHO, 2016]. A sample with a low parasite density may indicate mild malaria [Antwi-Baffour, 2023]. Parasitemia is high in early infections, lower and less frequent in chronic infections and nil or erratic in the case of subclinical evolution of the disease. Therefore, correct diagnosis can be seriously affected when performed at low parasitemia levels [Desquesnes, 2022].

- The observation of increased *P. falciparum* prevalence in participants with fever, and of more frequent fever in infected participants and those with higher parasite density, is consistent with studies that have shown that children with fever have a significantly higher chance of being infected with malaria compared to those without fever, even after adjusting for factors like age and location [Okiro, 2010]. In regions with malaria, the proportion of reported fever cases that are caused by malaria infection is consistently higher than would be expected by chance, indicating that a significant portion of fevers in these areas are directly linked to malaria parasites, especially in regions with higher transmission intensity. And, as previously discussed, malaria parasite density, as determined by microscopy of blood smears, correlates with fever and other clinical symptoms. Higher parasite densities generally indicate a more severe infection and are associated with a greater likelihood of experiencing fever and other clinical manifestations of malaria [Imwong, 2016].
- No clear trend in care seeking was observed in this study in relation to the infection status of the child. In an MVIP evidence report, seeking treatment for fever or receiving antimalarial treatment was reported to be comparable between the time before and 18-24 months after the start of RTS,S/AS01$_E$ vaccination in Ghana, Malawi, and Kenya, and between implementation and comparison areas [WHO, 2021].
- In this study, hospitalization for malaria was low across surveys. Globally, malaria is a major cause of hospitalization, especially in sub-Saharan Africa. The proportion of malaria cases requiring hospitalization varies depending on factors including age, disease severity, and geographic location history of malaria family size [Workineh, 2018]. In some regions, a significant percentage of all hospital admissions are due to malaria [Deressa, 2004; Kamau, 2022].
- The results of the study were consistent with NAAT being a more sensitive method for *P. falciparum* detection than microscopy. NAATs, particularly PCR, are more effective in identifying low-density infections, including those that are submicroscopic [Syed, 2022; van Eijk, 2023; Tegegn, 2024]. The variation in concordance between microscopy and NAATs for *P. falciparum* detection by center is consistent with the literature with studies reporting 75-84% concordance, with NAATs identifying more positive cases, particularly in asymptomatic or low-density infections [Ahmad, 2021; Zebaze, 2021; Ikegbunam, 2024].
- As previously reported, parasite density was low in approximately half of *P. falciparum* positive participants in this study. Consistent with published studies, gametocyte detection by NAAT generally shows higher sensitivity compared to microscopy, especially for low-density gametocyte infections [Koepfli, 2018]. Microscopy and NAAT show better concordance when gametocyte densities are high. Therefore, NAAT can be a more reliable method than microscopy, especially when dealing with discordant results [Coleman, 2006].

- In this study, a high percentage of participants with fever or malaria symptoms diagnosed as positive by microscopy were also tested positive by RDT (>90% across surveys), and of those negative for *P. falciparum* by microscopy, 16% to 43% across surveys had positive RDT results. The concordance between RDTs and microscopy for malaria diagnosis can vary depending on factors including parasite density, species, and the specific RDT used. While microscopy is the gold standard, RDTs offer a convenient and rapid alternative, particularly in resource-limited settings. Studies have shown that overall concordance is generally good, but sensitivity can be lower in cases of low parasitemia or mixed infections [Osman, 2010; Wu, 2015; Chaudhury, 2021].
- The proportion of participants with Plasmodium species other than *P. falciparum* was low across all surveys. While *P. falciparum* is the most prevalent malaria species, particularly in sub-Saharan Africa, other species like *P. vivax*, *P. malariae*, and *P. ovale* also cause malaria and are important to consider [Oriero, 2020; Nundu, 2021]. *P. vivax* is widely distributed globally and is a significant cause of malaria outside of sub-Saharan Africa. In sub-Saharan Africa, the low prevalence of *P. vivax* is attributed to a high proportion of the population having a Duffy-negative blood group [Price, 2020]. *P. malariae* and *P. ovale* are less common but can be found in various regions in sub-Saharan Africa [Oriero, 2020]. The latter species frequently occur as mixed infections with other parasites, which can lead to underestimation of their true prevalence [Nundu, 2021].
- The RTS,S vaccine is designed to be integrated into the existing EPI, making it convenient to deliver alongside other vaccines [WHO, 2015]. In this study, following initiation of RTS,S/AS01$_E$ vaccination, vaccine coverage in exposed sites increased with each subsequent survey from 0% to 15.0% in Survey 6, 22.3% to 35.7% in Survey 7, 39.8% to 48.9% in Survey 8, 40.7% to 53.0% in Survey 9 and 49.9% to 63.0% in Survey 10. The uptake of the RTS,S/AS01$_E$ malaria vaccine in infants and children did not appear to negatively impact the uptake of other childhood vaccinations (including DTP and measles vaccines) in this study, consistent with findings from the MVIP in pilot areas in Ghana, Kenya, and Malawi [Adjei, 2024].

12.4. Generalizability

The generalizability of the study findings is limited due to the following:

- Data were collected during the post rain season (transmission peak), therefore prevalence estimates should be limited to that time of the year especially in geographies where malaria transmission has a strong seasonal pattern.
- Data were collected from sites from the 3 countries (known for a high burden of *P. falciparum*), therefore caution should be taken when generalizing the findings to other settings.
- Due to the initially low RTS,S/AS01$_E$ vaccine coverage that increased gradually during the post-vaccination period, generalizing the findings to the years post-vaccination is limited.

13. OTHER INFORMATION

Not applicable.

14. CONCLUSION

P. falciparum prevalence varied by age, center, and RTS,S/AS01$_E$ vaccination status, with younger children and vaccinated participants showing lower infection rates. Bednet use was common, especially among younger children, while the use of other preventive measures was limited. No gender differences were observed.

Bednet usage the night before the visit remained high post-RTS,S/AS01$_E$ vaccination periods. Other MCIs were rarely used. Care-seeking behaviors (anti-malarial or fever treatment, hospitalization for malaria) remained similar in pre- and post-RTS,S/AS01$_E$ vaccination periods. DTP/HepB/Hib and measles vaccine administration remained high in post-RTS,S/AS01$_E$ vaccination periods.

Microscopy detected less infection and gametocyte rates compared to NAAT, though both methods showed moderate agreement. Overall, high RTS,S/AS01$_E$ vaccine coverage and the protective impact of vaccination highlight the importance of integrated malaria control and accurate diagnostics.

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APPENDICES

ANNEX 1 LIST OF STAND-ALONE DOCUMENTS

Number	Document reference number	Date	Title
1.	116682	28 Aug 2025	Annex 1: List of stand-alone documents
2.	116682	28 Aug 2025	Annex 2: Glossary of Terms
3.	116682	28 Aug 2025	Annex 3: Trademarks
6.	116682	28 Aug 2025	Annex 4: Report sign-off

ANNEX 2 GLOSSARY OF TERMS

Care seeking behavior:	When and where and at what time a child is taken for treatment for reported fever or malaria in the last 14 days.
Catchment area:	In this study, the catchment area is defined as the area of the HDSS (or equivalent system) study center participating in the EPI-MAL-002 and EPI-MAL-003 studies.
Malaria control interventions:	Any intervention or control measure targeted at reducing malaria transmission or preventing malaria disease. This includes ITNs, LLINs, SMC, IPTi, and ACT.
Malaria prevention measures:	Any individual intervention used to prevent malaria and not specifically recommended by the malaria program. This includes mosquito coils and local herbs.
Vaccine eligible subgroup:	Vaccine eligible subgroup comprises all participants aged less than 6 years and the participants aged more or equal to 6 years who received at least one RTS,S vaccine dose.
Vaccine ineligible subgroup:	Vaccine ineligible subgroup comprises all participants aged more or equal to 6 years except participants who received at least one RTS,S vaccine dose.

ANNEX 3 TRADEMARKS

Trademarks of the GSK group of companies	Generic description
Mosquirix	*Plasmodium falciparum* and hepatitis B vaccine (recombinant, adjuvanted)

Trademarks not owned by the GSK group of companies	Generic description
-	-

ANNEX 4 REPORT SIGN-OFF

Signature Page for 116682 TMF-22131038 v2.0

Reason for signing: Approved	Name: PPD Role: Approver Date of signature: 16-Sep-2025 11:12:40 GMT+0000

Signature Page for TMF-22131038 v2.0

Study Protocol
Sponsor:
GlaxoSmithKline Biologicals
Rue de l'Institut 89, 1330 Rixensart,
Belgium

eTrack study number and Abbreviated Title	116682 (EPI-MALARIA-005 BOD AME)
Date of protocol	Final Version 1: 21 January 2014
Date of protocol amendment	Amendment 1 Final: 21 September 2016 **Amendment 2 Final: 14 September 2018**
Title	Epidemiology study of malaria transmission intensity in sub-Saharan Africa.
Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Co-ordinating author	PPD, Freelance Science Writer for GSK Biologicals
Contributing authors (Amended 14 September 2018)	• PPD, PPD, Global Epidemiology • PPD, ***Clinical Manager Safety Physician*** • PPD, PPD • PPD Clinical Laboratory Sciences-SM Business and Decision Life Sciences for GSK Biologicals • PPD, Global Study Manager, external consultant for GSK Biologicals • PPD, ***Local Delivery Lead*** • PPD, external consultant for GSK Biologicals • PPD, Clinical Manager Safety Physician • PPD, Clinical Immunology Manager • PPD, Study Delivery Lead, ***Synteract®*** for GSK Biologicals • PPD, ***Lead Epidemiologist-Malaria, Aixial for GSK Biologicals***

eTrack study number and Abbreviated Title	116682 (EPI-MALARIA-005 BOD AME)
Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Contributing authors (Amended 14 September 2018)	• PPD, Senior Manager, Epidemiologist, ManiAfriCare for GSK Biologicals • PPD, Study Statistician, 4clinics for GSK Biologicals • PPD, Lead Epidemiologist-Malaria • PPD ***, Senior Lead Epidemiologist-Malaria*** • PPD, Study Data Manager, ***TCS for GSK Biologicals*** • PPD ***, Clinical & Epidemiology Project Lead, DDW Vaccines*** • PPD, PPD • PPD, Clinical Epidemiologist, Bartech for GSK Biologicals • PPD, Global Patent representative • PPD, Oversight Data Manager • PPD, Study Data Manager • PPD ***, Study Statistician***

GSK Biologicals' protocol template for observational studies and interventional studies without administration of medicinal products as described in a research protocol based on the Protocol Document Standard version 14.1.2

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Protocol Amendment 2 Sponsor Signatory Approval

eTrack study number and Abbreviated Title	116682 (EPI-MALARIA-005 BOD AME)
Date of protocol amendment	Amendment 2 Final: 14 September 2018
Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Sponsor signatory	François Roman Clinical & Epidemiology Project Lead, DDW Vaccines

Signature _____

Date _____

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Protocol Amendment 2 Rationale

Amendment number: Amendment 2

Rationale/background for changes:

A delay in the implementation of the RTS,S/AS01$_E$ vaccine in the 3 countries participating in the World Health Organisation (WHO)-led Malaria Vaccine Implementation Programme (MVIP) has resulted in a delay to the start of EPI-MAL-003. As a consequence, EPI-MAL-005, being an ancillary study to EPI-MAL-003, will need to be extended in order to mirror the EPI-MAL-003 timeline. The need for an additional survey is the trigger for the second amendment of this protocol. Additional revisions to the protocol are listed below.

1. The current protocol – protocol amendment 1 - currently details 9 annual surveys with study duration of up to 9 years. The study will include at least 1 further annual survey, lasting for at least 10 years in total. Thus, the longest participating sites will perform the study for at least 10 years meaning 10 surveys, whilst some sites joining later will not perform as many surveys. Protocol text has been revised accordingly.
2. Country and study site participation have changed during the course of the study following WHO recommendations for pilot implementation of RTS,S/AS01$_E$ in settings with moderate-to-high transmission of malaria and WHO Regional Office for Africa selection for the initial introduction of RTS,S/AS01$_E$ in 3 countries (Ghana, Kenya and Malawi) through the MVIP. EPI-MAL-003 study site selection will be performed following Ministries of Health pre-selection and according to WHO guidance in the framework of the MVIP, to include 4 sites in each of the 3 countries selected for the MVIP. Being an ancillary study to EPI-MAL-002 and EPI-MAL-003 studies, EPI-MAL-005 is/will be conducted in study sites conducting EPI-MAL-002 and/or EPI-MAL-003. Clarification on the countries and sites participating in the study has been provided.
3. In response to a Corrective and Preventive Action following a Critical Quality Attributes audit conducted in Kintampo, Ghana, reference to study conduct in accordance with ‘Good Pharmacoepidemiology Practices (GPP) guidelines’ has been added to Section 5.1 ‘Regulatory and ethical considerations, including the informed consent process’ to align with STD-POL-GSKF-408, and additionally protocols EPI-MAL-002 and EPI-MAL-003.
4. Vaccine eligible and ineligible subgroups were defined based on assumptions on the duration of follow-up of the EPI-MAL-005 study and date of vaccine implementation. This amendment primarily documents the extension of the study for at least 1 further survey. Furthermore, the date of implementation of the vaccine has yet to be confirmed. It is therefore not possible to apply these assumptions and the applicable text in Section 7.7.1.2 ‘By vaccine eligible/ineligible subgroup: Statistical analyses for vaccine association adjustments and association between vaccine and transmission’ has been revised.

Protocol Amendment 2 Investigator Agreement

I agree:

- To conduct the study in compliance with this protocol, any mutually agreed future protocol amendments or protocol administrative changes, with the terms of the study agreement and with any other study conduct procedures and/or study conduct documents provided by GlaxoSmithKline (GSK) Biologicals.
- To assume responsibility for the proper conduct of the study at ***the*** site***(s)***. **(Amended 14 September 2018)**
- That I am aware of, and will comply with, 'Good Clinical Practice' (GCP) or other applicable guidelines and all applicable regulatory requirements.
- To ensure that all persons assisting me with the study are adequately informed about study-related duties and functions as described in the protocol.
- To acquire the reference ranges for laboratory tests performed locally and, if required by local regulations, obtain the laboratory's current certification or Quality Assurance procedure manual.
- To ensure that no samples (including serum samples) are retained onsite or elsewhere without the approval of GSK Biologicals and the express written informed consent of the subject and/or the subject's legally acceptable representative.
- To perform no other biological assays on the samples except those described in the protocol or its amendment(s).
- To co-operate with a representative of GSK Biologicals in the monitoring process of the study and in resolution of queries about the data.
- That I have been informed that certain regulatory authorities require the sponsor to obtain and supply, as necessary, details about the investigator's ownership interest in the sponsor, and more generally about his/her financial ties with the sponsor. GSK Biologicals will use and disclose the information solely for the purpose of complying with regulatory requirements.

Hence I:

- Agree to supply GSK Biologicals with any necessary information regarding ownership interest and financial ties (including those of my spouse and dependent children).
- Agree to promptly update this information if any relevant changes occur during the course of the study and for one year following completion of the study.
- Agree that GSK Biologicals may disclose any information it has about such ownership interests and financial ties to regulatory authorities.
- Agree to provide GSK Biologicals with an updated Curriculum Vitae and other documents required by regulatory agencies for this study.

eTrack study number and Abbreviated Title	116682 (EPI-MALARIA-005 BOD AME)
Date of protocol amendment	Amendment 2 Final: 14 September 2018
Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Investigator name	_____
Signature	_____
Date	_____

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Sponsor Information

1. Sponsor

GlaxoSmithKline Biologicals

Rue de l'Institut 89, 1330 Rixensart, Belgium

2. Sponsor Medical Expert for the Study

Refer to the local study contact information document.

3. Sponsor Study Monitor

Refer to the local study contact information document.

4. Study Contact for Reporting of a Serious Adverse Event (SAE)

GSK Biologicals Central Back-up Study Contact for Reporting SAEs: refer to protocol Section 6.3.2.

SYNOPSIS

Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01$_E$ introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Rationale for the study (Amended 14 September 2018)	Following the pivotal Phase III study of the candidate malaria vaccine RTS,S/AS01$_E$ (Malaria-055), two consecutive vaccine safety monitoring studies (EPI-MAL-002 and EPI-MAL-003) will be conducted to monitor incidence rates of meningitis, protocol defined adverse events of ***special*** interest (AESI), and of other adverse events leading to hospitalisation or death, in children. The first study, EPI-MAL-002, is a ***baseline*** surveillance study prior to RTS,S/AS01$_E$ authorisation in the country; the second study, EPI-MAL-003, will more specifically monitor RTS,S/AS01$_E$ safety***, as well as vaccine effectiveness and impact,*** and will only start when RTS,S/AS01$_E$ is authorised ***and implemented*** in the country. The World Health Organi***s***ation's ***(WHO's)*** Strategic Advisory Group of Experts (SAGE) on Immunization and the Malaria Policy Advisory Committee (MPAC) recommended pilot implementations of RTS,S/AS01$_E$ in children of 5–17 months of age, in parts of 3-5 sub-Saharan African countries, administering 3 doses of the vaccine to children aged 5-9 months of age in areas of moderate-to-high transmission of malaria with a fourth dose 15-18 months later. The first vaccine introduction is foreseen in 2018. The secondary endpoints of these studies also include monitoring the incidence of malaria disease as diagnosed during out-patient visits or hospitalisation. Health and Demographic Surveillance System (HDSS) (or equivalent system) sites[1] in countries in ***s***ub-Saharan Africa will participate in these studies, enrolling approximately 30 000 children <5 years of age in EPI-MAL-002 and approximately 45 000 children <5 years in EPI-MAL-003. This epidemiology study (EPI-MAL-005) is planned to run in parallel with these two studies, enrolling from the same HDSS ***(***or equivalent system) populations. The primary objectives of this study are to produce longitudinal estimates of parasite prevalence in humans, and record malaria control measure

[1] ***Throughout the document, the terms of site, cluster and centre are used interchangeably, having the same meaning.***

usage in areas where EPI-MAL-002 and EPI-MAL-003 studies will take place. As requested by WHO/JTEG, parasite prevalence as an indicator of malaria transmission intensity (MTI) may also contribute to the evidence base for vaccine recommendation in different MTI settings. It is expected that RTS,S/AS01$_E$ vaccine introduction through national immunisation systems will lead to a reduction in the incidence of malaria disease in vaccinated subjects in EPI-MAL-003 when compared to baseline rates recorded in EPI-MAL-002. Annual fluctuations in malaria incidence occur as a result of changes in transmission intensity, which may be caused by changes in environmental factors such as rainfall or changes in usage of other malaria control interventions. Therefore, by taking into account these variations in MTI and malaria control intervention coverage, it will be possible to estimate more accurately the vaccine impact on clinical disease during EPI-MAL-003. These data will also allow for an assessment of any association between vaccination and gametocyte carriage in the 0-2 year age group, as an indicator of the potential effect of the vaccine on malaria transmission.

Outside of the controlled setting of a clinical trial, there is the risk that usage of malaria control interventions such as ***indoor*** residual spraying and bednets may change following vaccine introduction. Vaccine introduction may lead to the misperception that other interventions are no longer required or may alter health seeking behaviours for fever, and thus are potential confounders of the effect of the vaccine on clinic-identified malaria and therefore need to be monitored.

Although not yet considered as the gold standard, NAAT-based (nucleic acid amplification test) techniques can detect infections of lower malaria parasite density and quantification of parasitaemia than is achievable by microscopy. Identification of gametocytes by microscopy is inherently challenging, thus their presence is often missed, even by highly trained technicians. Therefore, additional analysis of collected blood samples by NAAT will allow for the detection of lower density parasite infections and will be a more sensitive measure of changes in both parasite and gametocyte prevalence and density, thereby providing greater insight into potential changes upon vaccine implementation. This will also provide comparability of data collected in this study with the technique likely to be favoured in clinical trials in the future.

These data will enable a more complete assessment of the benefits and risks of vaccine introduction, and thereby more insight into the potential vaccine impact in

EPI-MAL-002/-003, by adjusting incidence data for overall changes in transmission and other malaria control intervention coverage, and assist generalisation of results to other populations.

Objectives

Co-Primary

In subjects aged 6 months to <10 years:

- To obtain longitudinal estimates of *P. falciparum* parasite prevalence in order to characterise malaria transmission intensity in a standardised way at centres conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.
- To obtain longitudinal estimates of the use of malaria control interventions in centres conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.

Secondary

In subjects aged 6 months to <10 years:

- To estimate trends in longitudinal estimates of the parasite prevalence of *P. falciparum* by vaccine eligible or ineligible subgroups and overall.
- To obtain longitudinal estimates of the prevalence of *Plasmodium* species other than *P. falciparum*; overall and by age group.
- To estimate longitudinal trends in receipt and timing of the third dose of DTP/HepB/Hib and the first dose of measles EPI vaccines, at around 14 weeks and 9 months of age respectively, as appropriate by country.
- To describe changes in care seeking behaviours for reported fever or malaria in the previous 14 days.
- To assess within-site geographical heterogeneity in malaria transmission intensity.
- To describe individual malaria prevention measures and risk factors for clinical malaria according to the parasite density observed.

Tertiary

In subjects aged 6 months to <10 years:

- To compare asexual and sexual (gametocyte) parasitaemia (qualitative and quantitative-density) in the RTS,S/AS01$_E$ vaccinated and unvaccinated subjects.
- To compare asexual and sexual (gametocyte) parasitaemia (qualitative and semi-quantitative-density) when measured by microscopy or NAAT.

Study design (Amended 14 September 2018)

- Type of design: A multi-centric, epidemiology longitudinal cross-sectional study at centres in ***s***ub-Saharan Africa that are participating in GSK's EPI-MAL-002 and EPI-MAL-003 studies.
- There will be no study vaccine administered in this epidemiology study.
- Study population: Subjects 6 months to <10 years of age.
- Type of study: self-contained
- All medications that may influence malaria parasitaemia within 14 days prior to each survey will be recorded.
- Axillary body temperature of all subjects at the time of the survey will be recorded.
- Biological samples: A capillary blood sample will be obtained for evaluation of malaria infection by blood slide and NAAT. In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours or other symptoms/signs of clinical malaria, a rapid diagnostic test (RDT) will be conducted. If the RDT is positive, treatment will be given according to National guidelines. If a subject for whom no RDT was required is identified as being parasite positive following microscopy, National guidelines should be followed for clinical management of the subject.
- Microscopy and NAAT will be used to evaluate the level of asexual and sexual parasitaemia.
- Serious adverse events (SAEs) associated with the study procedure (capillary blood sampling) will be collected.
- Using ***Geographic Information System (***GIS***)*** to determine geographical variability in MTI locally: Study areas will be mapped by villages using grid referencing. Subjects will be attributed to their village, however, to avoid PII (personally identifiable information); small

villages will be grouped when the number of participants is less than 10, ***so*** that it is not possible to identify one subject from one village. Therefore the study area will be divided into segments with a minimum of 10 subjects by segment regrouping villages by proximity if needed. Villages will be grouped at the time of random sampling of the study population. A map will be drawn showing the location of numbered segments, each numbered with a unique ID code and containing one or more villages. This map will NOT be submitted to GSK, but segments will be reported by their ID code and surface (km^2) and subjects will be attributed to a segment code in the study database.

- Each study site will be requested annually to provide centre specific information about interventions from the malaria control programme in the study area to provide meteorological data for the study site such as rainfall and temperature. The information will be collected in the form of a questionnaire that will be recorded in a separate database to that for subject-specific data.
- Data collection: Electronic Case Report Form (eCRF).
- This study will involve up to ***10*** annual cross sectional surveys during malaria peak transmission ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies***.
- Duration of the study: up to ***10*** years ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies***:
  - Epoch 001: Survey 1 at Year 1
  - Epoch 002: Survey 2 at Year 2
  - Epoch 003: Survey 3 at Year 3
  - Epoch 004: Survey 4 at Year 4
  - Epoch 005: Survey 5 at Year 5.
  - Epoch 006: Survey 6 at Year 6.
  - Epoch 007: Survey 7 at Year 7.
  - Epoch 008: Survey 8 at Year 8.
  - Epoch 009: Survey 9 at Year 9
  - ***Epoch 010: Survey 10 at Year 10***

Synopsis Table 1 Study groups and epochs foreseen in the study (Amended 14 September 2018)

Study Group	Age (Min/Max)	Epochs									
		Epoch 001 Survey 1	Epoch 002 Survey 2	Epoch 003 Survey 3	Epoch 004 Survey 4	Epoch 005 Survey 5	Epoch 006 Survey 6	Epoch 007 Survey 7	Epoch 008 Survey 8	Epoch 009 Survey 9	***Epoch 010 Survey 10***
Study site	6 months / 9 years	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	***600 subjects***

Discussion of study design (Amended 14 September 2018)

Several methods of estimating MTI exist, including entomological inoculation rates (EIR), serological conversion rates (SCR) and blood parasite prevalence. The methodology and interpretation of SCR to classify the intensity of malaria is not commonly used yet, and although the EIR is a standard method, the measure is challenging and interpretation and comparability of setting may be difficult due to vector heterogeneity. Parasite prevalence, although requiring trained staff for slide reading, provides a standardised and relatively easy to implement method to assess MTI in study sites of varied transmission intensity and is therefore the method of choice in this study.

At least 10 annual cross sectional surveys at peak transmission will provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by EPI-MAL-002 and EPI-MAL-003. Malaria transmission is highly seasonal so surveys will be carried out during the course of the rainy season preferably when rains decrease, the period of highest malaria transmission. Annual fluctuations may be seen in all endemic areas and a longitudinal assessment will allow for a better appreciation of the scale and trend of this annual variation. Endemicity is dependent on several environmental factors including climate (rain and temperature), access to malaria care, and use of other malaria control interventions. Therefore, concurrent collection of data on these factors will be important for the interpretation of these study results and evaluation of vaccine impact.

This study will be conducted in parallel to EPI-MAL-002 and EPI-MAL-003 in order to assess parasite prevalence and malaria control measures before and after vaccine introduction.

The age group for enrolment (6 months to <10 years) has been selected in this study as this permits analysis of parasite prevalence according to the WHO definition (2-9 years) and by the JTEG requested age (<5 years).

Number of subjects	Total expected sample size: Per site and by survey is a maximum of 400 subjects aged 6 months to <5 years and a maximum of 200 subjects aged 5 to <10 years.
Endpoints (Amended 14 September 2018)	**Primary** • Occurrence of *P. falciparum* parasitaemia (using microscopy) Criteria/definitions: infection with *P. falciparum* determined using a blood smear slide and determined using microscopy. • Occurrence of malaria control interventions Criteria/definitions: malaria control interventions are mosquito net usage ***(including insecticide-treated nets [ITN] and long lasting insecticidal nets [LLIN]), indoor*** residual spraying ***(IRS)***, seasonal malaria chemoprevention (SMC), intermittent preventative treatment in infants (IPTi), and ACT therapy received within the last 14 days. **Secondary** • Demography and history characteristics Criteria/definitions: gender, age, medical history. • Occurrence of *Plasmodium* species other than *P. falciparum* (using microscopy) Criteria/definitions: infection with *Plasmodium* species other than *P. falciparum* determined using a blood smear slide and microscopy. • Occurrence of uptake and timing of the third dose of DTP/HepB/Hib and the first measles EPI vaccines Criteria/definitions: vaccination record of receipt of dose 3 of the DTP/HepB/Hib and the first dose of the measles EPI vaccines. • Occurrence of anti-malarial therapy Criteria/definitions: any anti-malarial therapy received in the last 14 days. • Occurrence of measured fever Criteria/definitions: any measured fever at time of visit (axillary temperature ≥37.5°C). • Occurrence of reported fever Criteria/definitions: any reported fever occurring in the last 24 hours.

- Occurrence of care seeking behaviour

  Criteria/definitions: occurrence of visits to health providers following reported fever or malaria in the previous 14 days.

- Geo-referencing characteristics

  Criteria/definitions: positioning of the subject's residence will be attributed to a segment with a unique ID from the grid referencing study area map in which the subject resides, where necessary, grouping small geographically proximate villages so that each segment has at least 10 study subjects to avoid PII, and proceeding as far as geographically appropriate.

- Occurrence of individual malaria prevention measures and risk factors

  Criteria/definitions: malaria prevention measures are repellents and local herbs not specifically recommended by the national programme and risk factors are rural/urban area, construction material for the house, floor and roof, type of eaves (open/closed), use of electricity and water source (distance from and type).

Tertiary

- Occurrence of RTS,S/AS01$_E$ vaccine doses

  Criteria/definitions: vaccination record of each dose received of the RTS,S/AS01$_E$ vaccine..

- Occurrence of *P. falciparum* parasitaemia (using NAAT)

  Criteria/definitions: detection of *P. falciparum* on dried blood spot and determined using NAAT.

- Occurrence of sexual *P. falciparum* parasitaemia (using microscopy)

  Criteria/definitions: detection of sexual *P. falciparum* using a blood smear slide and determined using microscopy.

- Occurrence of sexual *P. falciparum* (using NAAT/QT-NASBA)

  Criteria/definitions: detection of sexual *P. falciparum* on dried blood spot and determined using NAAT.

TABLE OF CONTENTS

PAGE

LIST OF TABLES

PAGE

LIST OF FIGURES

PAGE

LIST OF APPENDICES

PAGE

LIST OF ABBREVIATIONS

ACT	Artemisinin-based combination therapy
AESI	Adverse events of ***special*** interest
AMC	Academic Medical Center
ATP	According to protocol
CI	Confidence interval
CSP	Circumsporozoite protein
DTP	Diphtheria, tetanus, pertussis
eCRF	electronic Case Report Form
EIR	Entomological inoculation rates
EPI	Expanded program on immunization
GAPDH	Glyceraldehyde 3-phosphate dehydrogenase
GCP	Good Clinical Practice
GIS	Geographic Information System
GPP	***Good Pharmacoepidemiology Practice***
GSK	GlaxoSmithKline
HDSS	Health and Demographic surveillance system
HBsAg	Hepatitis B surface antigen
HepB	Hepatitis B
Hib	Heamophilus influenza type b
ICF	Informed consent form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IPTi	Intermittent preventative treatment in infants
IPTp	Intermittent preventative treatment in pregnancy

IRB	Institutional Review Board
IRS	Indoor residual spraying
ITN	Insecticide-treated net
JTEG	Joint technical expert group
LAR	Legally acceptable representative
LL	Lower limit
LLIN	***Long lasting insecticidal nets***
MPAC	Malaria Policy Advisory Committee
MTI	Malaria transmission intensity
MVI	PATH-Malaria Vaccine Initiative
MVIP	***Malaria Vaccine Implementation Programme***
NAAT	Nucleic acid amplification test
NC/NT-SAE	Non-communicable and non-traumatic serious adverse events
P. falciparum	*Plasmodium falciparum*
PII	Personally identifiable information
PRAC	Pharmacovigilance Risk Assessment Committee
QT-PCR	Quantitative polymerase chain reaction
QT-NASBA	Quantitative nucleic acid sequence-based amplification
RDT	Rapid diagnostic test
RR	Relative risk
RSE	Relative standard error
RT-PCR	Reverse transcriptase polymerase chain reaction
RTS	Hybrid protein comprising HBs (hepatitis B surface antibody) and CSP portions
RTS,S	Particulate antigen, containing both RTS and HBs proteins
SAE	Serious adverse event

SAGE	Strategic Advisory Group of Experts
SCR	Serological conversion rate
SDV	Source document verification
SMC	Seasonal malaria chemoprevention
SOP	Standard operating procedure
SPM	Study procedures manual
TFL	Tables, figures, listings
UL	Upper limit
WHO	World Health Organisation

(Amended 14 September 2018)

GLOSSARY OF TERMS

Anonymised data:	Information about an individual that GSK or a third party cannot reasonably attribute to the individual, or could only attribute to the individual by expending a disproportionate amount of time, effort or expense (e.g. de-identified or aggregated information). For the purpose of this policy, Key-Coded personally identifiable information shall not be considered Anonymised Information
Child in care:	A child who has been placed under the control or protection of an agency, organisation, institution or entity by the courts, the government or a government body, acting in accordance with powers conferred on them by law or regulation. The definition of a child in care can include a child cared for by foster parents or living in a care home or institution, provided that the arrangement falls within the definition above. The definition of a child in care does not include a child who is adopted or has an appointed legal guardian.
Catchment area:	In this study, the catchment area is defined as the area of the HDSS (or equivalent system) study site participating in the EPI-MAL-002 and EPI-MAL-003 studies.
Care seeking behaviour:	When and where and at what time a child is taken for treatment for reported fever or malaria in the last 14 days.
DTP/HepB/Hib:	This refers to DTP, or DTP-Hep B (tetravalent) or DTP-HepB-Hib (pentavalent).
Eligible:	Qualified for enrolment into the study based upon strict adherence to inclusion/exclusion criteria.
Epidemiological study:	An observational or interventional study without administration of medicinal product(s) as described in a research protocol.
Epoch:	An epoch is a self-contained set of consecutive time points or a single time point from a single protocol. Self-contained means that data collected for all subjects at all time points within that epoch allows to draw a complete conclusion. Typical examples of epochs are retrospective data collection and prospective data collection, etc.
eTrack:	GSK Biologicals' tracking tool for clinical/ epidemiological trials.

Evaluable:	Meeting all eligibility criteria, complying with the procedures defined in the protocol, and, therefore, included in the according-to-protocol (ATP) analysis (see Section 7.3 for details on criteria for evaluability).
First dose measles:	First measles containing vaccine.
Malaria control interventions:	Any intervention or control measure targeted at reducing malaria transmission or preventing malaria disease [World Health Organisation, 2013]. This includes ITN, ***LLIN,*** IRS, SMC, IPTi, ***IPTp*** and ACTs.
Malaria prevention measures:	Any individual intervention used to prevent malaria and not specifically recommended by the malaria program. This includes mosquito coils and local herbs.
Protocol amendment:	The International Conference on Harmonisation (ICH) defines a protocol amendment as: 'A written description of a change(s) to or formal clarification of a protocol.' GSK Biologicals further details this to include a change to an approved protocol that affects the safety of subjects, scope of the investigation, study design, or scientific integrity of the study.
Protocol administrative change:	A protocol administrative change addresses changes to only logistical or administrative aspects of the study. NB Any change that falls under the definition of a protocol amendment (e.g., a change that affects the safety of subjects, scope of the investigation, study design, or scientific integrity of the study) MUST be prepared as an amendment to the protocol.
Self-contained study:	Study with objectives not linked to the data of another study.
Site Monitor:	An individual assigned by the sponsor who is responsible for assuring the proper conduct of epidemiological studies at one or more investigational sites.
Study population:	Sample of population of interest.
Subject:	Term used throughout the protocol to denote an individual who has been contacted in order to participate or participates in the epidemiological study or a person about whom some medical information has been recorded in a database.

Subjects at least 6 months of age:	Six months old is defined as the same day as the date of birth occurring 6 calendar months later (e.g. if born on the 8th January, a child becomes 6 months old on the 8th July).
Subject number:	A unique number identifying a subject, assigned to each subject consenting to participate in the study.
Surveillance:	The ongoing systematic collection, collation, analysis, and interpretation of descriptive epidemiological health data on a specific disease. Surveillance can monitor incidence and/or prevalence, and/or inform about when and where health problems are occurring and who is affected.
Vaccine eligible age:	Vaccine eligible is defined as those subjects that on the basis of age would be eligible for RTS,S/AS01$_E$ vaccination, even if vaccine is unavailable at the time of assessment. The age will depend on the label for RTS,S/AS01$_E$ vaccination in the country. (At the time of study start, there will be no available vaccination with RTS,S/AS01$_E$).
Vaccine ineligible age:	Vaccine ineligible is defined as those subjects that on the basis of age would be ineligible for RTS,S/AS01$_E$ vaccination, regardless of vaccine availability at the time of assessment. The age will depend on the label for RTS,S/AS01$_E$ vaccination in the country.

(Amended 14 September 2018)

1. INTRODUCTION

1.1. Background

GlaxoSmithKline (GSK) Biologicals in partnership with the PATH-Malaria Vaccine Initiative (MVI) is developing a *Plasmodium falciparum* malaria vaccine for routine immunisation of infants and children living in malaria-endemic areas.

GSK Biologicals has formulated the candidate pre-erythrocytic *P. falciparum* malaria vaccine, RTS,S/AS01$_E$, which is currently under evaluation. The vaccine consists of sequences of the circumsporozoite (CS) protein and hepatitis B surface antigen (HBsAg) adjuvanted with AS01 (liposome formulation with MPL and QS21 immunostimulants).

In the pivotal Phase III study (Malaria-055), efficacy of the candidate malaria vaccine RTS,S/AS01$_E$ against first or only episodes of clinical malaria over a follow-up of 12 months in children aged 5-17 months was 55.8% ($p<0.0001$), and in coadministration with DTPwHepB/Hib vaccine at 6, 10 and 14 weeks of age was 31.3% ($p<0.0001$). Phase II and early Phase III data suggest it has an acceptable safety profile when given to young children and infants in co-administration with EPI routine vaccines. Please refer to the current Investigator Brochure for a review of the pre-clinical and clinical studies, and the potential risks and benefits of RTS,S/AS02 and RTS,S/AS01.

1.2. Rationale for the study

Following the pivotal Phase III study of the candidate malaria vaccine RTS,S/AS01$_E$ (Malaria-055), two consecutive vaccine safety monitoring studies (EPI-MAL-002 and EPI-MAL-003) will be conducted to monitor incidence rates of meningitis, protocol defined adverse events of ***special*** interest (AESI), and ***of*** other adverse events leading to hospitalisation ***or*** death***, in children***. The first study, EPI-MAL-002, is a ***baseline*** surveillance study prior to RTS,S/AS01$_E$ authorisation in the country; the second study, EPI-MAL-003, will more specifically monitor RTS,S/AS01$_E$ safety***, as well as vaccine effectiveness and impact,*** and will only start when RTS,S/AS01$_E$ is authorised ***and implemented*** in the country. ***The World Health Organisation's (WHO's) Strategic Advisory Group of Experts (SAGE) on immunization and the Malaria Policy Advisory Committee (MPAC) recommended pilot implementations of RTS,S/AS01$_E$ in children of 5–17 months of age, in parts of 3-5 sub-Saharan African countries, administering 3 doses of the vaccine to children aged 5-9 months of age in areas of moderate-to-high transmission of malaria with a fourth dose 15-18 months later. The first vaccine introduction is foreseen in 2018.*** The secondary endpoints of these studies ***also*** include monitoring the incidence of malaria disease as diagnosed during out-patient visits or hospitalisation. Health and Demographic Surveillance System (HDSS) (or equivalent system) sites[2] in countries in ***s***ub-Saharan Africa will participate in these studies,

[2] ***Throughout the document, the terms of site, cluster and centre are used interchangeably, having the same meaning.***

enrolling approximately 30 000 children <5 years of age in EPI-MAL-002 and approximately 45 000 children <5 years in EPI-MAL-003.

This epidemiology study (EPI-MAL-005) is planned to run in parallel with these two studies, enrolling from the same HDSS (or equivalent system) populations. The primary objectives of this study are to produce longitudinal estimates of parasite prevalence in humans, and record malaria control measure usage in areas where EPI-MAL-002 and EPI-MAL-003 studies will take place. As requested by WHO/JTEG, parasite prevalence as an indicator of malaria transmission intensity (MTI) may also contribute to the evidence base for vaccine recommendation in different MTI settings. It is expected that RTS,S/AS01$_E$ vaccine introduction through national immunisation systems will lead to a reduction in the incidence of malaria disease in vaccinated subjects in EPI-MAL-003 when compared to baseline rates recorded in EPI-MAL-002. Annual fluctuations in malaria incidence occur as a result of changes in transmission intensity, which may be caused by changes in environmental factors such as rainfall or changes in usage of other malaria control interventions. Therefore, by taking into account these variations in MTI and malaria control intervention coverage, it will be possible to estimate more accurately the vaccine impact on clinical disease during EPI-MAL-003. These data will also allow for an assessment of any association between vaccination and gametocyte carriage in the 0-2 year age group, as an indicator of the potential effect of the vaccine on malaria transmission.

Outside of the controlled setting of a clinical trial, there is the risk that usage of malaria control interventions such as ***indoor*** residual spraying and bednets may change following vaccine introduction. Vaccine introduction may lead to the misperception that other interventions are no longer required or may alter health seeking behaviours for fever, and thus are potential confounders of the effect of the vaccine on clinic-identified malaria and therefore need to be monitored.

Although not yet considered as the gold standard, NAAT-based (nucleic acid amplification test) techniques can detect infections of lower malaria parasite density and give more accurate quantification of parasitaemia than is achievable by microscopy. Identification of gametocytes by microscopy is inherently challenging, thus their presence is often missed, even by highly trained technicians. Therefore, additional analysis of collected blood samples by NAAT will allow for the detection of lower density parasite infections and will be a more sensitive measure of changes in both parasite and gametocyte prevalence and density, thereby providing greater insight into potential changes upon vaccine implementation. This will also provide comparability of data collected in this study with the technique likely to be favoured in clinical trials in the future.

These data will enable a more complete assessment of the benefits and risks of vaccine introduction, and thereby more insight into the potential vaccine impact in EPI-MAL-002/-003, by adjusting incidence data for overall changes in transmission and other malaria control intervention coverage, and assist generalisation of results to other populations.

(Amended 14 September 2018)

2. OBJECTIVES

2.1. Co-Primary objectives

In subjects aged 6 months to <10 years:

- To obtain longitudinal estimates of *P. falciparum* parasite prevalence in order to characterise malaria transmission intensity in a standardised way at centres conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.
- To obtain longitudinal estimates of the use of malaria control interventions in centres conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.

Refer to Section 7.1.1 for the definition of the primary endpoints.

2.2. Secondary objectives

In subjects aged 6 months to <10 years:

- To estimate trends in longitudinal estimates of the parasite prevalence of *P. falciparum* by vaccine eligible or ineligible subgroups and overall.
- To obtain longitudinal estimates of the prevalence of *Plasmodium* species other than *P. falciparum*; overall and by age group.
- To estimate longitudinal trends in receipt and timing of the third dose of DTP/HepB/Hib and the first dose of measles EPI vaccines, at around 14 weeks and 9 months of age respectively, as appropriate by country.
- To describe changes in care seeking behaviours for reported fever or malaria in the previous 14 days.
- To assess within-site geographical heterogeneity in malaria transmission intensity.
- To describe individual malaria prevention measures and risk factors for clinical malaria according to the parasite density observed.

Refer to Section 7.1.2 for the definition of the secondary endpoints.

2.3. Tertiary objectives

In subjects aged 6 months to <10 years:

- To compare asexual and sexual (gametocyte) parasitaemia (qualitative and quantitative-density) in the RTS,S/AS01$_E$ vaccinated and unvaccinated subjects.
- To compare asexual and sexual (gametocyte) parasitaemia (qualitative and semi-quantitative-density) when measured by microscopy or NAAT.

Refer to Section 7.1.3 for the definition of the tertiary endpoints.

3. STUDY DESIGN OVERVIEW

Protocol waivers or exemptions are not allowed with the exception of immediate safety concerns. Therefore, adherence to the study design requirements, including those specified in the outline of study procedures (Section 5.4), are essential and required for study conduct.

- Type of design: A multi-centric, epidemiology longitudinal cross-sectional study at centres in ***s***ub-Saharan Africa that are participating in GSK's EPI-MAL-002 and EPI-MAL-003 studies.
- There will be no study vaccine administered in this epidemiology study.
- Study population: Subjects 6 months to <10 years of age.
- Type of study: self-contained
- All medications that may influence malaria parasitaemia within 14 days prior to each survey will be recorded.
- Axillary body temperature of all subjects at the time of the survey will be recorded.
- Biological Samples: A capillary blood sample will be obtained for evaluation of malaria infection by blood slide and NAAT. In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours or other symptoms/signs of clinical malaria, a rapid diagnostic test (RDT) will be conducted. If the RDT is positive, treatment will be given according to National guidelines. If a subject for whom no RDT was required is identified as being parasite positive following microscopy, National guidelines should be followed for clinical management of the subject.
- Microscopy and NAAT will be used to evaluate the level of asexual and sexual parasitaemia.
- Serious adverse events (SAEs) associated with the study procedure (capillary blood sampling) will be collected.
- Using Geographic Information System (GIS) to determine geographical variability in MTI locally: Study areas will be mapped by villages using grid referencing. Subjects will be attributed to their village, however, to avoid PII (personally identifiable information), small villages will be grouped when the number of participants is less than 10, ***so*** that it is not possible to identify one subject from one village. Therefore the study area will be divided into segments with a minimum of 10 subjects by segment regrouping villages by proximity if needed. Villages will be grouped at the time of random sampling of the study population. A map will be drawn showing the location of numbered segments, each numbered with a unique ID code and containing one or more villages. This map will NOT be submitted to GSK, but segments will be reported by their ID code and surface (km^2) and subjects will be attributed to a segment code in the study database.
- Each study site will be requested annually to provide centre specific information about interventions from the malaria control program in the study area and, if facilities are available, to provide meteorological data for the study site such as

rainfall and temperature. The information will be collected in the form of a questionnaire that will be recorded in a separate database to that for subject-specific data.

- Data collection: Electronic Case Report Form (eCRF).
- This study will involve up to ***10*** annual cross sectional surveys during malaria peak transmission ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies***.
- Duration of the study: up to ***10*** years ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies:***
  - Epoch 001: Survey 1 at Year 1
  - Epoch 002: Survey 2 at Year 2
  - Epoch 003: Survey 3 at Year 3
  - Epoch 004: Survey 4 at Year 4
  - Epoch 005: Survey 5 at Year 5.
  - Epoch 006: Survey 6 at Year 6.
  - Epoch 007: Survey 7 at Year 7.
  - Epoch 008: Survey 8 at Year 8.
  - Epoch 009: Survey 9 at Year 9
  - ***Epoch 010: Survey 10 at Year 10***

(Amended 14 September 2018)

Table 1 Study groups and epochs foreseen in the study (Amended 14 September 2018)

Study Group	Age (Min/Max)	Epochs									
		Epoch 001 Survey 1	Epoch 002 Survey 2	Epoch 003 Survey 3	Epoch 004 Survey 4	Epoch 005 Survey 5	Epoch 006 Survey 6	Epoch 007 Survey 7	Epoch 008 Survey 8	Epoch 009 Survey 9	*Epoch 010 Survey 10*
Study site	6 months / 9 years	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	***600 subjects***

3.1. Discussion of study design

Several methods of estimating MTI exist, including entomological inoculation rates (EIR), serological conversion rates (SCR) and blood parasite prevalence. The methodology and interpretation of SCR to classify the intensity of malaria is not commonly used yet, and although the EIR is a standard method, the measure is challenging and interpretation and comparability of setting may be difficult due to vector heterogeneity. Parasite prevalence, although requiring trained staff for slide reading, provides a standardised and relatively easy to implement method to assess MTI in study sites of varied transmission intensity and is therefore the method of choice in this study.

At least 10 annual cross sectional surveys at peak transmission will provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by EPI-MAL-002 and EPI-MAL-003. Malaria transmission is highly seasonal so surveys will be carried out during the course of the rainy season preferably when rains decrease, the period of highest malaria transmission. Annual fluctuations may be seen in all endemic areas and a longitudinal assessment will allow for a better appreciation of the scale and trend of this annual variation. Endemicity is dependent on several environmental factors including climate (rain and temperature), access to malaria care, and use of other malaria control interventions. Therefore, concurrent collection of data on these factors will be important for the interpretation of these study results and evaluation of vaccine impact.
(Amended 14 September 2018)

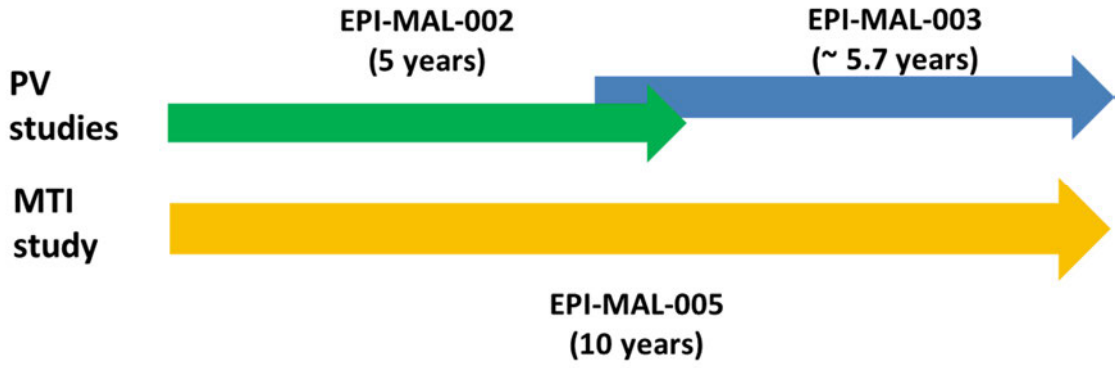
This study will be conducted in parallel to EPI-MAL-002 and EPI-MAL-003 in order to assess parasite prevalence and malaria control measures before and after vaccine introduction.

The age group for enrolment (6 months to <10 years) has been selected in this study as this permits analysis of parasite prevalence according to the WHO definition [WHO, 1963] (2-9 years) and by the JTEG requested age (<5 years).

4. STUDY POPULATION

4.1. Number of subjects / centres

Subjects 6 months to <10 years of age ***living*** in HDSS (or equivalent system) catchment areas ***of*** the sites participating in the EPI-MAL-002 and EPI-MAL-003 studies ***are eligible for enrolment*** (see Section 4.1.1). Subjects ***already*** enrolled in EPI-MAL-002 and EPI-MAL-003 are eligible for participation in this study.



(Amended 14 September 2018)

Each study site will enroll approximately 600 subjects per survey. These subjects will be selected at random from the HDSS (or equivalent system) population listings prepared at each site. The selection process will be repeated every year meaning that the subjects will be different in each cross-sectional survey except if they are re-selected in a subsequent survey by chance. The population listings generated from the demographic surveillance

will allow for sampling of the required subjects according to stratification by age group as follows (all subject numbers are approximately plus or minus 5 children):

- 60 children aged 6 months to <1 year
- 120 children aged 1 year
- 120 children aged 2 years
- 50 children aged 3 years
- 50 children aged 4 years
- 40 children aged 5 years
- 40 children aged 6 years
- 40 children aged 7 years
- 40 children aged 8 years
- 40 children aged 9 years

Therefore, the total expected sample size per site and by survey is a maximum of 400 subjects aged 6 months to <5 years and a maximum of 200 subjects aged 5 to <10 years. Refer to Section 7.2 for a detailed description of the criteria used in the estimation of sample size.

4.1.1. Recruitment of study centres / investigators

The ancillary EPI-MAL-005 study will be conducted in sites defined in the EPI-MAL-002 and EPI-MAL-003 protocols. At the time of original protocol finalisation, ***identified study sites were located*** in Burkina Faso, Ghana, ***Kenya,*** Senegal, ***and*** Tanzania.

Following the WHO's SAGE on immunization and the MPAC recommendations of pilot implementations of RTS,S/AS01$_E$ in 3-5 distinct settings in sub-Saharan Africa restricted to moderate-to-high transmission of malaria, ***site selection in some of the initially chosen EPI-MAL-002, EPI-MAL-003 and EPI-MAL-005 study sites located in low endemicity settings (i.e. in Senegal and Tanzania) had to be terminated. In April 2017, the WHO Regional Office for Africa announced that the RTS,S/AS01$_E$ vaccine will be first introduced in 3 countries (Ghana, Kenya and Malawi) through the Malaria Vaccine Implementation Programme (MVIP). Selection of the clusters that are/will participate in GSK's baseline, Phase IV and ancillary studies (i.e. EPI-MAL-002, EPI-MAL-003 and EPI-MAL-005, respectively), being fully embedded in the MVIP, depends on the cluster identification process led by the Ministries of Health according to WHO guidance. They have been, or will be, selected as follows:***

- ***Sites have been, or will be, selected from the 3 countries where the RTS,S/AS01$_E$ vaccine will be implemented (Ghana, Kenya and Malawi). Burkina Faso sites that started EPI-MAL-005 will early terminate the conduct of the study following Survey 4; data from these sites will be presented in the interim report planned following Survey 5.***

- ***As currently planned in the MVIP and according to WHO guidance, 4 study sites (corresponding to 4 clusters of the MVIP) in each of the 3 countries selected for the RTS,S/AS01$_E$ pilot implementation programme (12 study sites/clusters in total) are planned to be part of EPI-MAL-005.***
- ***Of note, all study sites are submitted to a comprehensive scientific and operational study site assessment conducted by GSK, which will determine study feasibility in those sites.***

In summary, selection of sites will be performed in EPI-MAL-002 and EPI-MAL-003 studies following Ministries of Health pre-selection and according to WHO guidance, to include 4 sites in each of the 3 countries selected for the MVIP. EPI-MAL-005 is/will be conducted in study sites conducting EPI-MAL-002 and/or EPI-MAL-003.

(Amended 14 September 2018)

4.1.2. Sampling methods

All participating centres will have a HDSS (or equivalent system) in place. In general, any variation in sampling procedure should follow as closely as possible the Guidelines of the [Roll Back Malaria Monitoring and Evaluation Reference Group, 2005]. The following steps serve as an example of a sampling method.

1. Generate a list from the HDSS (or equivalent system) database of all children aged 6 months to <10 years.
2. Order the list of subjects by age, then by village within each age category.
3. Divide the total number of children for each age category by the sample needed in that age category, including 10% or more, according to local variations, extra to reflect non-response/refusal. This gives the size of the sequence for that age category (e.g. every xth subject, where x=total number of children for age category/number to be selected in the age category).
4. If the sequence (x) is 20 for example, select randomly a first subject among the 20 first subjects.
5. From this subject, pick every 20th subject until the end of that age category.
6. Repeat steps 3-5 for each age category.

If a subject is not found during the study team visit (e.g. possible migration, hospitalisation, …) three attempts should be made to reach the subject at home to minimise sampling bias, before the subject's enrolment is abandoned. It is likely there will be some non-response as a result of migration or refusal by the parents/LAR and this has been taken into account in the sample size calculation.

The household of each randomly selected subject should be visited by a study team that will be able to carry out the protocol procedures in field conditions e.g. informed consent form (ICF) procedure, blood sample collection, questionnaire administration and data recording. In order to enable logistically feasible, but methodologically rigorous, sampling the field team should work their way through the sampling at their own discretion in a way that minimises travel to and between sampling points, e.g. in order of proximity of subjects or geographical sequence.

Each study site will enrol approximately 600 subjects per survey. To allow for 10% non-response 660 subjects should therefore be randomly selected from the HDSS (or equivalent system) database distributed over all age categories as described in Section 4.1. In order to meet enrolment timelines, the sampling scheme could be implemented in the following fashion: 3 survey teams, each comprising two individuals, can be in the field 5 days per week for a period of 8 weeks. Each day in the field, a minimum of 5 subjects should be visited per team. Therefore, over the course of the 8 weeks, a minimum of 600 visits can be made. Though more time may be required if large numbers of subjects require repeat visits, teams may achieve more visits per day than proposed here if subjects are in close proximity or in the same household.

4.2. Inclusion criteria for enrolment

Deviations from inclusion criteria are not allowed because they can potentially jeopardise the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol is essential.

All subjects must satisfy ALL the following criteria at study entry:

- Subjects' whose parent(s)/Legally Acceptable Representative(s) [LAR(s)], in the opinion of the investigator, can and will comply with the requirements of the protocol.
- A male or female 6 months to <10 years of age at the time of survey.
- Signed informed consent or thumbprinted and witnessed informed consent obtained from the parent(s)/LAR(s) of the child.

4.3. Exclusion criteria for enrolment

Deviations from exclusion criteria are not allowed because they can potentially jeopardise the scientific integrity of the study, regulatory acceptability or subject safety. Therefore, adherence to the criteria as specified in the protocol is essential.

The following criteria should be checked at the time of study entry. If ANY exclusion criterion applies, the subject must not be included in the study:

- Child in care

  Please refer to the glossary of terms for the definition of child in care.
- Current active participation in any trial involving administration of an investigational malaria vaccine or malaria drug.

5. CONDUCT OF THE STUDY

5.1. Regulatory and ethical considerations, including the informed consent process

The study will be conducted in accordance with the ICH Guideline for Good Clinical Practice (GCP)***, Guidelines for Good Pharmacoepidemiology Practices (GPP) [ISPE, 2015]***, other applicable guidelines, all applicable subject privacy requirements and the guiding principles of the Declaration of Helsinki.
(Amended 14 September 2018)

The study has been designed and will be conducted in accordance with the ICH Harmonised Tripartite Guideline for clinical investigation of medicinal products in the paediatric population (ICH E11) and all other applicable ethical guidelines.

GSK will obtain favourable opinion/approval to conduct the study prior to a site initiating the study in that country or will document that neither a favourable opinion nor an approval to conduct the study is needed.

Conduct of the study includes, but is not limited to, the following:

- Institutional Review Board (IRB)/Independent Ethics Committee (IEC) review and favourable opinion/approval of study protocol and any subsequent amendments.
- Subject's parent(s)/LAR(s) informed consent and subject informed assent, as appropriate.
- Investigator reporting requirements as stated in the protocol.

GSK Biologicals will provide full details of the above procedures to the investigator, either verbally, in writing, or both.

Freely given and written or thumbprinted informed consent must be obtained from each subject's parent(s)/LAR(s) or the impartial witness and subject informed assent, as appropriate, prior to participation in the study.

GSK Biologicals will prepare a model Informed Consent Form (ICF) which will embody the applicable ICH GCP or other applicable guidelines, and GSK Biologicals required elements. While it is strongly recommended that this model ICF be followed as closely as possible, the informed consent requirements given in this document are not intended to pre-empt any local regulations which require additional information to be disclosed for informed consent to be legally effective. Clinical judgement, local regulations and requirements should guide the final structure and content of the local version of the ICF.

The investigator has the final responsibility for the final presentation of the ICF, respecting the mandatory requirements of local regulations. The ICF generated by the investigator with the assistance of the sponsor's representative must be acceptable to GSK Biologicals and be approved (along with the protocol, and any other necessary documentation) by the IRB/IEC.

5.2. Subject identification

Subject numbers will be assigned sequentially to subjects consenting to participate/to be included in the study, according to the range of subject numbers allocated to each study centre.

5.3. General study aspects

Supplementary study conduct information not mandated to be present in this protocol is provided in the accompanying Study Procedures Manual (SPM). The SPM provides the investigator and the site personnel with administrative and detailed technical information that does not impact the safety of the subjects.

5.4. Outline of study procedures

Table 2 details study procedures to be conducted during the study.

Table 2 List of study procedures to be conducted at each survey visit (Amended 14 September 2018)

Epoch	**Epoch 001**	**Epoch 002**	**Epoch 003**	**Epoch 004**	**Epoch 005**	**Epoch 006**	**Epoch 007**	**Epoch 008**	**Epoch 009**	***Epoch 010***
Study Group[1]	**Survey 1**	**Survey 2**	**Survey 3**	**Survey 4**	**Survey 5**	**Survey 6**	**Survey 7**	**Survey 8**	**Survey 9**	***Survey 10***
Timepoint	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	***Year 10***
Informed consent	●	●	●	●	●	●	●	●	●	●
Check inclusion/exclusion criteria	●	●	●	●	●	●	●	●	●	●
Record demographic details	●	●	●	●	●	●	●	●	●	●
Record subject's vaccination status[2]	●	●	●	●	●	●	●	●	●	●
Record any anti-malarial medication or other medication received within the previous 14 days	●	●	●	●	●	●	●	●	●	●
Record relevant medical history (hospitalisation, reported fever, and care seeking behaviour)	●	●	●	●	●	●	●	●	●	●
Record axillary body temperature	●	●	●	●	●	●	●	●	●	●
Record malaria control measures used in the household	●	●	●	●	●	●	●	●	●	●
Record malaria prevention and risk factors	●	●	●	●	●	●	●	●	●	●
Take capillary blood sample[3]	●	●	●	●	●	●	●	●	●	●
Assessment of RDT[4]	●	●	●	●	●	●	●	●	●	●
Study conclusion	●	●	●	●	●	●	●	●	●	●

Footnotes to Table 2:

● is used to indicate a study procedure that requires documentation in the individual eCRF

[1] New sites will join the study after survey 3, depending on when they are included in EPI-MAL-002/-003. The total surveys at these new sites will therefore be less than ***10***.

[2] RTS,S/AS01 and 3rd dose DTP/HepB/Hib and first dose measles EPI vaccinations, only

[3] Capillary blood sample for determination of parasite prevalence (blood slides and NAAT by filter paper)

[4] In the event of measured fever at time of visit (axillary temperature ≥37.5°C) or fever reported in last 24 hours or other symptoms/signs of clinical malaria, a rapid diagnostic test (RDT) will be conducted using capillary blood sample taken for blood slide preparation.

Table 3 List of study procedures to be conducted during survey (Amended 14 September 2018)

Epoch	Epoch 001	Epoch 002	Epoch 003	Epoch 004	Epoch 005	Epoch 006	Epoch 007	Epoch 008	Epoch 009	*Epoch 010*
Study Group	**Survey 1**	**Survey 2**	**Survey 3**	**Survey 4**	**Survey 5**	**Survey 6**	**Survey 7**	**Survey 8**	**Survey 9**	***Survey 10***
Timepoint	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	***Year 10***
Site specific information collection - Meteorological data[1]	●	●	●	●	●	●	●	●	●	●
Site specific information collection – Malaria Control Programme	●	●	●	●	●	●	●	●	●	●

● is used to indicate a study procedure that requires documentation in the individual eCRF.
[1] Availability of meteorological data will be based on the site having the weather station. All sites received weather stations either post Survey 1 or 2 or at study start for the new sites.

5.5. Detailed description of study procedures to be conducted at each survey visit

5.5.1. Check inclusion and exclusion criteria

Check all applicable inclusion and exclusion criteria as described in Sections 4.2 and 4.3 before enrolment.

5.5.2. Informed consent

The signed/witnessed/thumbprinted informed consent of the subject's parent(s)/LAR(s) must be obtained before study participation. The signed informed assent of a subject below the age of consent (i.e., minor) should be obtained in addition to the signed informed consent by his/her parent(s)/LAR(s) according to local rules and regulations. Refer to Section 5.1 for the requirements on how to obtain informed consent and assent, as appropriate.

5.5.3. Collect demographic data

Record demographic data (date of birth, gender) and study area identification in the subject's eCRF.

5.5.4. Check and record medications/vaccinations

Record RTS,S/AS01$_E$ (all doses) and other vaccinations (i.e. 3rd dose DTP/HepB/Hib and first dose measles EPI vaccinations) administered, including dates. The vaccination status will be recorded in the eCRF.

Record use of any anti-malarial or any other medication within 14 days prior to study visit. Data to be verified from health card or medical prescription document.

5.5.5. Check and record relevant medical history

Record details of relevant medical history in the eCRF:

- Obtain reported history of temperature within the last 24 hours by interview
- Obtain details for hospitalisation for malaria within the last 3 months by interview and/or review of subject's health card
- Obtain details of visits to health provider for fever or malaria treatment in the previous 14 days by interview and/or review of subject's health card.

5.5.6. Assessment of body temperature

The following information must be recorded in the eCRF:

- Axillary temperature as measured by a digital thermometer at the time of the survey.

5.5.7. Collect data on malaria control interventions

Record the following malaria control measures in the subject's eCRF:

- ***Indoor r***esidual spraying ***(IRS)***, mosquito net usage ***(including insecticide-treated nets [ITN] and long lasting insecticidal nets [LLIN])***, seasonal malaria chemoprevention (SMC), intermittent preventive treatment in infants (IPTi), and all anti-malaria therapy received within the last 14 days.
  (Amended 14 September 2018)

5.5.8. Collect data on malaria prevention measures and risk factors

Record the following information in the subject's eCRF:

- Repellents and local herbs used, rural/urban area, construction material for the house, floor, and roof, type of eaves (open/closed), use of electricity, and water source (distance from and type).

5.5.9. Capillary blood sampling

A capillary blood sample collected by finger/heel prick, will be taken during the study visit for the assessment of parasitaemia (see Section 5.6.2). The following biological samples will be taken at each survey visit:

- Blood for asexual and sexual (gametocyte) microscopy (2 slides, approximately 2 drops on each microscope slide).

  Preparation of microscopic slides in the field or at the laboratory is at the discretion of the study site staff. For microscopic slide preparation in the field, approximately 2 drops of blood will be applied directly on each microscopy slide. For microscopic slide preparation in the laboratory, the blood sample will be collected in provided microtubes for transport to the laboratory.

- Blood for asexual and sexual (gametocyte) NAATs (approximately 2 drops on filter paper).

In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in last 24 hours or other symptoms/signs of clinical malaria, a RDT will also be conducted using the capillary blood sample

Refer to the Module on Biospecimen Management in the SPM for general handling of blood samples.

5.5.10. Site specific information collection

Centre specific information about meteorological data such as rainfall, temperature and humidity, if available, will be collected by questionnaire and recorded in a separate database to that for subject-specific data. All sites received weather stations either post Survey 1 or 2 or at study start for the new sites.

Centre specific information about interventions from the malaria control programme in the study area, such as bednet usage ***(including ITN and LLIN)***, IRS, ACT, SMC, IPTp and IPTi, will be collected by questionnaire and recorded in a separate database to that for subject-specific data.
(Amended 14 September 2018)

5.5.11. Recording of SAEs

Capillary blood sampling is the only invasive procedure involved in this study. SAEs related to this procedure will be recorded.

- Refer to Section 6.2 for procedures for the investigator to record SAEs. Refer to Section 6.3 for guidelines on how to submit SAE reports to GSK Biologicals.
- The subjects' parent(s)/LAR(s) will be instructed to contact the investigator immediately should the subjects manifest any signs or symptoms they perceive as serious.

5.5.12. Study conclusion

The investigator will:

- Review all the data collected to ensure accuracy and completeness
- Complete the Study Conclusion screen in the eCRF.

5.6. Biological sample handling and analysis

Please refer to the SPM for details of biospecimen management (handling, storage and shipment).

Samples will not be labelled with information that directly identifies the subjects but will be coded with the identification number for the subject (subject number).

- Collected samples will be used for protocol mandated research. In addition, these samples may be used to perform research related to the improvement, development and quality assurance of the laboratory tests described in this protocol. This may include the management of the quality of these tests, the maintenance or improvement of these tests, the development of new test methods, as well as making sure that new tests are comparable to previous methods and work reliably.
- It is also possible that future findings may make it desirable to use the samples acquired in this study for future research, not described in this protocol. Therefore, all subjects in countries where this is allowed will be invited to give another specific consent when signing the Informed Consent Form to allow GSK or a contracted partner to use the samples for future research including development of tests and their quality assurance. Future research will be subject to the laws and regulations in the respective countries and will only be performed once an independent Ethics Committee or Review Board has approved this research.

Information on further investigations and their rationale can be obtained from GSK Biologicals.

Any sample testing will be done in line with the consent of the subject's parent(s)/LAR(s).

Refer also to the Investigator Agreement, where it is noted that the investigator cannot perform any other biological assays except those described in the protocol or its amendment(s).

Collected samples will be stored for a maximum of 20 years (counting from when the last subject performed the last study visit/contact), unless local rules, regulations or guidelines require different timeframes or different procedures, which will then be in line with the subject consent. These extra requirements need to be communicated formally to and discussed and agreed with GSK Biologicals.

5.6.1. Use of specified study materials

When materials are provided by GSK Biologicals, it is MANDATORY that all samples (including serum samples) be collected and stored exclusively using those materials in the appropriate manner. The use of other materials could result in the exclusion of the subject from the ATP analysis (See Section 7.3 for the definition of study cohorts/data sets to be analysed). The investigator must ensure that his/her personnel and the laboratory(ies) under his/her supervision comply with this requirement. However, when GSK Biologicals does not provide material for collecting and storing samples, appropriate materials from the investigator's site must be used. Refer to the Module on Clinical Trial Supplies in the SPM.

5.6.2. Biological samples

Table 4 Biological samples

Sample type	Quantity	Timepoint
Whole blood	Approximately 1 drop (RDT assessment)*	Survey Visit
Whole blood	Approximately 4 drops; 1 drop for the thin smear and up to 3 drops for the thick smear (merozoite and gametocyte microscopy assessment)	Survey Visit
Whole blood	2 to 3 drops; filter paper collection (parasite and gametocyte NAAT assessment)	Survey Visit

RDT = Rapid Diagnostic Test
NAAT = Nucleic Acid Amplification Test
*In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in last 24 hours or other symptoms/signs of clinical malaria.

5.6.3. Laboratory assays

Please refer to APPENDIX A for a detailed description of the assays performed in the study. Please refer to APPENDIX B for the address of the clinical laboratories used for sample analysis.

In the event of fever measured at time of visit (axillary temperature ≥37.5°C) or reported fever in last 24 hours or other symptoms/signs of clinical malaria, a RDT will be conducted. The clinical management of subjects presenting with malaria as identified by RDT or microscopy will follow National guidelines. Subjects will receive appropriate care according to standard clinical practice.

All blood slides with thick and thin smears will be made in duplicate. One slide with thick and thin smears will be sent for storage to a GSK dedicated laboratory facility and the remaining slide will be stored at the study site. For each slide, parasitaemia will be determined independently by two readers and in the case of non-concordance an additional read by a third independent reader will be carried out. Since there will be no full blood count performed in the study subjects the used methodology for the determination of *P. falciparum* asexual parasite density may be based on an assumed white cell count of 8000/µL. Please refer to APPENDIX A for a description of other methodologies for the determination of *P. falciparum* asexual parasite density.

CCI [redacted]

CCI

The GSK Biologicals' clinical laboratories have established a Quality System supported by procedures. The activities of GSK Biologicals' clinical laboratories are audited regularly for quality assessment by an internal (sponsor-dependent) but laboratory-independent Quality Department.

6. SAFETY

The procedure of capillary blood sampling will be performed once at the survey visit. Only SAEs related to the blood sampling procedure that occur in temporal association with the procedure will be recorded (up to 7 days after the survey visit).

The investigator or site staff is/are responsible during the study for the detection and documentation of events meeting the criteria and definition of a SAE as provided in this protocol.

Each subject's parent(s)/ LAR(s) will be instructed to contact the investigator immediately should the subject manifest any signs or symptoms they perceive as serious.

6.1. Safety definitions

6.1.1. Definition of a serious adverse event

An SAE is any untoward medical occurrence that:

a. Results in death,

b. Is life-threatening,

   NB: The term 'life-threatening' in the definition of 'serious' refers to an event in which the subject was at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, had it been more severe.

c. Requires hospitalisation or prolongation of an existing hospitalisation,

   NB: In general, hospitalisation signifies that the subject has been admitted at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or in an out-patient setting.

   Complications that occur during hospitalisation are also considered AEs. If a complication prolongs hospitalisation or fulfils any other serious criteria, the event will also be considered serious. When in doubt as to whether 'hospitalisation' occurred or was necessary, the AE should be considered serious.

   Hospitalisation for elective treatment of a pre-existing condition (known or diagnosed prior to informed consent signature) that did not worsen from baseline is NOT considered an SAE.

d. Results in disability/incapacity,

   NB: The term disability means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhoea, influenza like illness, and accidental trauma (e.g., sprained ankle) which may interfere or prevent everyday life functions but do not constitute a substantial disruption.

   Medical or scientific judgement should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the subject or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation.

6.2. Detecting and recording SAEs

6.2.1. Time periods for detecting and recording SAEs

In order to fulfil international reporting obligations, SAEs that are related to study participation (i.e., protocol-mandated procedures, invasive tests, a change from existing therapy) will be collected and recorded from the time the subject consents to participate in the study/study start until she/he is discharged from the study.

6.2.2. Evaluation of SAEs

6.2.2.1. Active questioning to detect SAEs

When an SAE occurs, it is the responsibility of the investigator to review all documentation (e.g., hospital progress notes, laboratory and diagnostics reports) relative to the event. The investigator will then record all relevant information regarding the SAE in the eCRF. The investigator is not allowed to send photocopies of the subject's medical records to GSK Biologicals instead of appropriately completing the eCRF. However, there may be instances when copies of medical records for certain cases are requested by GSK Biologicals. In this instance, all subject identifiers will be blinded on the copies of the medical records prior to submission to GSK Biologicals.

The investigator will attempt to establish a diagnosis pertaining to the event based on signs, symptoms, and/ or other clinical information. In such cases, the diagnosis should be documented as the SAE and not the individual signs/symptoms.

6.2.2.2. Assessment of the intensity of SAEs

The investigator will assess the maximum intensity that occurred over the duration of the event for all SAEs recorded during the study. The assessment will be based on the investigator's clinical judgement.

The intensity should be assigned to one of the following categories:

1 (mild)	=	An SAE which is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
2 (moderate)	=	An SAE which is sufficiently discomforting to interfere with normal everyday activities.
3 (severe)	=	An SAE which prevents normal, everyday activities (in a young child, such an AE would, for example, prevent attendance at school/ kindergarten/ a day-care centre and would cause the parent(s)/ LAR(s) to seek medical advice.)

An event is defined as 'serious' when it meets one of the pre-defined outcomes as described in Section 6.1.1.

6.2.2.3. Assessment of causality

The investigator should assess the causality of each SAE. The investigator will use clinical judgement to determine the relationship between the SAEs and study participation. Alternative causes, such as natural history of the underlying diseases, other concomitant therapy and other risk factors will be considered and investigated.

There may be situations when a SAE has occurred and the investigator has minimal information to include in the initial report to GSK Biologicals. However it is very important that the investigator always makes an assessment of causality for every event prior to submission of the SAE report to GSK Biologicals. The investigator may change his/her opinion of causality in light of follow-up information and update the SAE information accordingly.

If an event meets the criteria to be considered as 'serious' (see Section 6.1.1), additional examinations/tests will be performed by the investigator in order to determine ALL possibly contributing factors to each SAE.

Possibly contributing factors include:

- Medical history.
- Concomitant medication.
- Protocol required procedure.
- Other procedure not required by the protocol.
- Other cause (specify).

6.2.2.4. Assessment of outcomes

The investigator will assess the outcome of all SAEs recorded during the study as:

- Recovered/ resolved.
- Recovering/ resolving.
- Not recovered/ not resolved.
- Recovered with sequelae/ resolved with sequelae.
- Fatal.

6.3. Reporting of SAEs

6.3.1. Prompt reporting of SAEs related to study participation to GSK

SAEs that occur in the time period defined in Section 6.2.1 will be reported promptly to GSK within the timeframes described in Table 6 once the investigator determines that the event meets the protocol definition of an SAE.

Table 6 Timeframes for submitting SAEs related to study participation to GSK

Type of event	Initial reports		Follow-up of relevant information on a previous report	
	Timeframe	Documents	Timeframe	Documents
SAEs related to study participation	24 hours*	Electronic SAE report	24 hours*	Electronic SAE report

* Timeframe allowed after receipt or awareness of the information.

6.3.2. Contact information for reporting SAEs to GSK

Study Contact for Reporting SAEs
Refer to the local study contact information document.
Back-up Study Contact for Reporting SAEs
24/24 hour and 7/7 day availability: GSK Biologicals Clinical Safety & Pharmacovigilance Email: RIX.CT-Safety-Vac@gsk.com Fax: +32 2 656 51 16 or +32 2 656 80 09

6.3.3. Completion and transmission of SAEs reports related to study participation to GSK

Once an investigator becomes aware that an SAE has occurred in a study subject, the investigator (or designee) must complete the information in the electronic Expedited Adverse Event Report WITHIN 24 HOURS. The report will always be completed as thoroughly as possible with all available details of the event. Even if the investigator does not have all information regarding an SAE, the report should still be completed within 24 hours. Once additional information is received, the report should be updated WITHIN 24 HOURS.

The investigator will always provide an assessment of causality at the time of the initial report.

6.3.3.1. Back-up system in case the electronic reporting system does not work

If the electronic reporting system does not work, the investigator (or designee) must complete, then date and sign a paper Expedited Adverse Event Report and fax it to the GSK Biologicals Clinical Safety and Pharmacovigilance department within 24 hours.

This back-up system should only be used if the electronic reporting system is not working and NOT if the system is slow. As soon as the electronic reporting system is working again, the investigator (or designee) must complete the electronic Expedited Adverse Event Report within 24 hours. The final valid information for regulatory reporting will be the information reported through the electronic reporting system.

6.3.4. Updating of SAE information after freezing of the subject's eCRF

When additional SAE information is received after freezing of the subject's eCRF, new or updated information should be recorded on a paper Expedited Adverse Event Report, with all changes signed and dated by the investigator. The updated report should be faxed to the GSK Biologicals Clinical Safety and Pharmacovigilance department or to the Study Contact for Reporting SAEs (see the Sponsor Information) within the designated reporting time frames specified in Table 6.

6.3.5. Regulatory reporting requirements for SAEs

The investigator will promptly report all SAEs to GSK Biologicals in accordance with the procedures detailed in Section 6.3.1. GSK Biologicals has a legal responsibility to promptly notify, as appropriate, both the local regulatory authority and other regulatory agencies about the safety of a product under epidemiological investigation. Prompt notification of SAEs by the investigator to the Study Contact for Reporting SAEs is essential so that legal obligations and ethical responsibilities towards the safety of other subjects are met.

6.4. Follow-up of SAEs

6.4.1. Follow-up during the study

After the initial SAE report, the investigator is required to proactively follow each subject and provide further relevant information on the subject's condition to GSK Biologicals (within 24 hours for SAEs, refer to Table 6).

All SAEs documented at a previous visit/ contact and recorded as not recovered/ not resolved or recovering/ resolving will be reviewed at subsequent visits/ contacts until the end of the study.

6.4.1.1. Follow-up after the subject is discharged from the study

The investigator will follow-up subjects:

- With SAEs until the event has resolved, subsided, stabilised, disappeared, or until the event is otherwise explained, or the subject is lost to follow-up.

If the investigator receives additional relevant information on a previously reported SAE, he/ she will provide this information to GSK Biologicals using a paper Expedited Adverse Event Report.

GSK Biologicals may request that the investigator performs or arranges for the conduct of additional clinical examinations/ tests and/ or evaluations to elucidate as fully as possible the nature and/ or causality of the SAE. The investigator is obliged to assist. If a subject dies during participation in the study or during a recognised follow-up period, GSK Biologicals will be provided with any available post-mortem findings, including histopathology.

7. STATISTICAL METHODS

7.1. Endpoints

7.1.1. Primary endpoints

Primary

- Occurrence of *P. falciparum* parasitaemia (using microscopy)

  Criteria/definitions: infection with *P. falciparum* determined using a blood smear slide and determined using microscopy.

- Occurrence of malaria control interventions

  Criteria/definitions: malaria control interventions are mosquito net usage ***(including insecticide-treated nets [ITN] and long lasting insecticidal nets [LLIN]), indoor*** residual spraying ***(IRS)***, seasonal malaria chemoprevention (SMC), intermittent preventative treatment in infants (IPTi), and ACT therapy received within the last 14 days.

(Amended 14 September 2018)

7.1.2. Secondary endpoints

Secondary

- Demography and history characteristics

  Criteria/definitions: gender, age, medical history.

- Occurrence of *Plasmodium* species other than *P. falciparum* (using microscopy)

  Criteria/definitions: infection with *Plasmodium* species other than *P. falciparum* determined using a blood smear slide and microscopy.

- Occurrence of uptake and timing of the third dose of DTP/HepB/Hib and the first measles EPI vaccines

  Criteria/definitions: vaccination record of receipt of dose 3 of the DTP/HepB/Hib and the first dose of the measles EPI vaccines.

- Occurrence of anti-malarial therapy

  Criteria/definitions: any anti-malarial therapy received in the last 14 days.

- Occurrence of measured fever

  Criteria/definitions: any measured fever at time of visit (axillary temperature ≥37.5°C).

- Occurrence of reported fever

  Criteria/definitions: any reported fever occurring in the last 24 hours.

- Occurrence of care seeking behaviour

  Criteria/definitions: occurrence of visits to health providers following reported fever or malaria in the previous 14 days.

- Geo-referencing characteristics

  Criteria/definitions: positioning of the subject's residence will be attributed to a segment with a unique ID from the grid referencing study area map in which the subject resides, where necessary, grouping small geographically proximate villages so that each segment has at least 10 study subjects to avoid PII, and proceeding as far as geographically appropriate.

- Occurrence of individual malaria prevention measures and risk factors

  Criteria/definitions: malaria prevention measures are repellents and local herbs not specifically recommended by the national programme and risk factors are rural/urban area, construction material for the house, floor and roof, type of eaves (open/closed), use of electricity and water source (distance from and type).

7.1.3. Tertiary endpoints

- Occurrence of RTS,S/AS01$_E$ vaccine doses

  Criteria/definitions: vaccination record of each dose received of the RTS,S/AS01$_E$ vaccine..

- Occurrence of *P. falciparum* parasitaemia (using NAAT)

  Criteria/definitions: detection of *P. falciparum* on dried blood spot and determined using NAAT.

- Occurrence of sexual *P. falciparum* parasitaemia (using microscopy)

  Criteria/definitions: detection of sexual *P. falciparum* using a blood smear slide and determined using microscopy.

- Occurrence of sexual *P. falciparum* (using NAAT/QT-NASBA)

  Criteria/definitions: detection of sexual *P. falciparum* on dried blood spot and determined using NAAT.

7.2. Determination of sample size

In this study, sample sizes have been designed to ensure sufficiently narrow confidence intervals (CIs) around centre-wise parasite prevalence estimates (with a maximum residual standard error [RSE] of 0.25) according to the WHO definition [WHO, 1963] (2-9 years) and to the JTEG requested age (<5 years).

Moreover, when these estimates are used to adjust vaccine clinical malaria estimates from EPI-MAL-002/-003 for annual fluctuations in MTI and control measure use, a sufficient level of precision for the vaccine ineligible subgroup is maintained. In addition, the ability to detect longitudinal trends in parasite prevalence has been considered in these sample size calculations.

7.2.1. Children aged 6 months to <5 years

The sample size is computed for each centre separately and is considered for the point estimate of prevalence of infection among children aged at least 6 months and less than 5 years during one cross-sectional survey.

The effective sample size is computed to obtain an estimation of the prevalence of infection with a relative standard error equal to a maximum of 0.25.

Given that the expected sample size should be greater than 100, CI limits are computed using the approximated 95% CI.

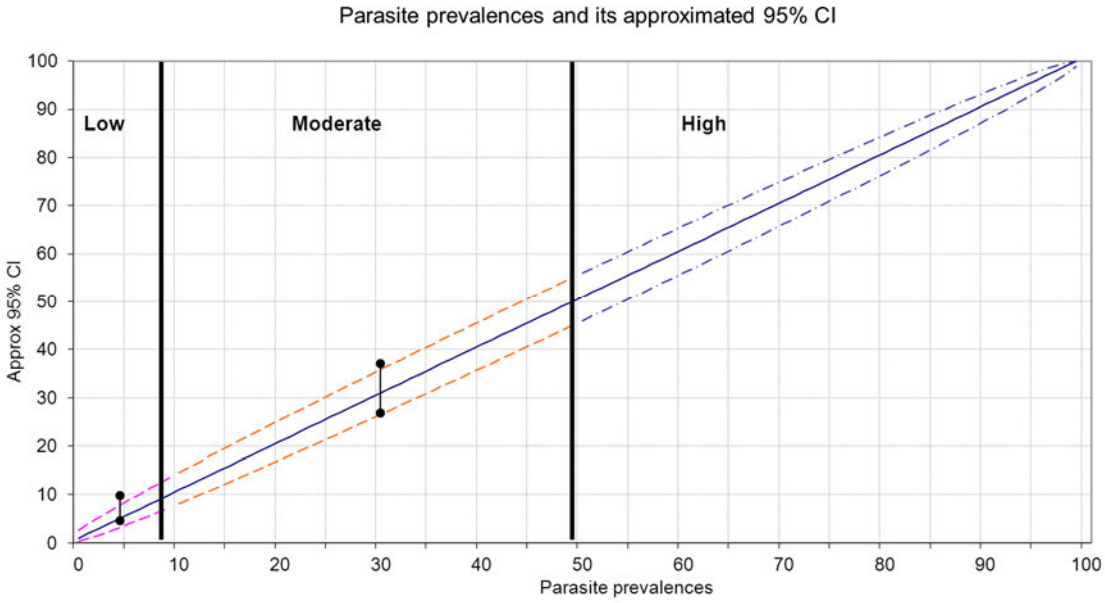
In Table 7 values of the CI limits are computed for several expected parasite prevalences in function of effective sample sizes equal to 100, 200, 300, 400, 600 and 1000 subjects. To meet the criteria of precision defined above, the effective sample sizes are 400 eligible subjects. Indeed, for an expected parasite prevalence of 5%, the RSE is equal to 0.23 (= half-width of CI / 2*p) (shaded values in Table 7).

Table 7 Approximated 95% CI limits around different values of observed parasite prevalence computed in function of several sample sizes

Sample size	Approx. 95% CI	Expected parasite prevalence										
		5	10	20	25	30	40	50	60	70	80	90
100	LL (%)	1.9	5.2	12.9	17.1	21.5	30.5	39.9	49.7	59.9	70.6	82.0
	UL (%)	11.8	18.0	29.4	34.8	40.1	50.3	60.1	69.5	78.5	87.1	94.8
200	LL (%)	2.6	6.4	14.8	19.3	23.8	33.2	42.9	52.8	63.1	73.6	84.8
	UL (%)	9.3	15.2	26.4	31.7	36.9	47.2	57.1	66.8	76.2	85.2	93.6
300	LL (%)	2.9	7.0	15.7	20.3	24.9	34.5	44.2	54.2	64.4	74.9	85.9
	UL (%)	8.3	14.1	25.1	30.4	35.6	45.8	55.8	65.5	75.1	84.3	93.0
400	LL (%)	3.2	7.3	16.3	20.9	25.6	35.2	45.0	55.0	65.2	75.7	86.5
	UL (%)	7.7	13.5	24.3	29.6	34.8	45.0	55.0	64.8	74.4	83.7	92.7
600	LL (%)	3.5	7.8	16.9	21.6	26.4	36.1	45.9	55.9	66.1	76.5	87.2
	UL (%)	7.1	12.8	23.5	28.7	33.9	44.1	54.1	63.9	73.6	83.1	92.2
1000	LL (%)	3.8	8.2	17.6	22.4	27.2	37.0	46.9	56.9	67.0	77.4	87.9
	UL (%)	6.6	12.1	22.6	27.8	33.0	43.1	53.1	63.0	72.8	82.4	91.8

In Figure 1, precision around expected parasite prevalence is illustrated taking into account the defined sample size. For example, for an expected parasite prevalence of 7%, the lower and upper limits of the approximated 95% CI are equal to 4.8% and 10.1%, respectively. For an expected parasite prevalence of 31%, the limits are 25.9% and 36.6%, respectively.

Figure 1 Illustration of the lower (LL) and upper (UL) limits of the approximated 95%CI built around observed parasite prevalences for a sample of 400 subjects



Study sites are in different endemicity classes, so a sample of 400 subjects in this age class will allow for suitable confidence limits around parasite prevalence estimates for sites within each of the endemicity classes.
(Amended 14 September 2018)

Note that with the sampling strategy using the proposed stratification by age (Section 4.1.2), 400 eligible subjects aged at least 6 months and less than 5 years will be recruited.

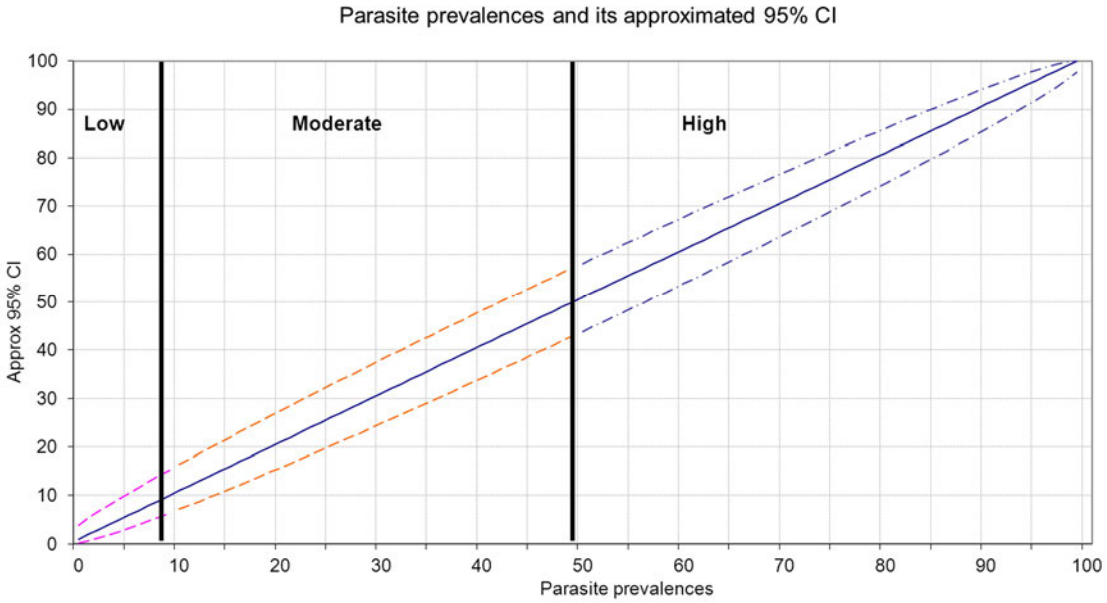
7.2.2. Children aged 2 to <10 years

Based on the defined recruitment scheme (see Section 4.1.1), the sample size of children aged 2 to <10 years will be approximately equal to the number of eligible subjects aged 0-5 years; ensuring the adequate precision for this age group. Indeed, following the recruitment scheme explained in Section 4.1.1, 420 subjects would be aged between 2 to <10 years.

7.2.3. Children aged 5 to <10 years

Concerning children aged at least 5 years and less than 10 years, the effective sample size is computed to obtain an estimation of the prevalence of infection with a relative standard error equal to a maximum of 0.35. Therefore, the sample size will be approximately 200 eligible subjects (see Figure 2).

Figure 2 Illustration of the lower (LL) and upper (UL) limits of the approximated 95%CI built around observed parasite prevalences for a sample of 200 subjects



Since the precision of 0.25 was adequate and determined for the WHO (children aged 6 months to <5 years) and JTEG (children aged 2 to <10 years) definitions, the sample size for the subgroup of children 5-9 years was fixed at 200 which gives a relative standard error equal to a maximum of 0.35. In addition, it is anticipated that children in this older age group are more likely to be at school and it may take longer to recruit this age group with subsequent logistics and financial implications.

7.3. Cohorts for Analyses

7.3.1. Total cohort

The Total cohort will include all subjects enrolled in the study.

All the information for these subjects will be collected in the eCRF (after receiving signed informed consent).

7.3.2. According-To-Protocol cohort

The According to Protocol (ATP) cohort will include all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom at least one laboratory result of the blood sample is available.

A detailed, comprehensive list of reasons for elimination from ATP analyses will be established at the time of data cleaning.

7.4. Derived and transformed data

- Age in the study will be computed as the difference between the date of informed consent and the date of birth. The age will be expressed in the following groups: 0.5 to <3 years, 3 to <5 years, 5 to <10 years.
- The fever status will be derived from the axillary temperature measured at the time of the visit. The value 'Yes' will be given if the temperature is ≥37.5°C.
- The parasite density will be grouped into the following classes:
  - Low: <2500 parasites/ µL
  - Medium: 2500 – 9999 parasites/ µL
  - High: 10000 – 19999 parasites/ µL
  - Very high: ≥20000 parasites/ µL

  In the case of two positive slides readings, the parasites density (parasites/µL) at the subject level will be defined as the geometric mean of both (those positive) slide reading values if the subject status is defined as positive. In the case of three positive slide readings, the two closest readings will be selected to calculate the geometric mean. In the case of negative parasite status, the density will be recorded as missing.

7.5. Analysis of demographics

The number of subjects enrolled as well as the number excluded from the ATP analyses will be presented. Demographic characteristics (age and gender) will be summarised using descriptive statistics.

Centre specific data regarding the malaria control programme will be summarised for each site and cross-surveys separately.

7.6. Analysis of primary objectives

The parasite prevalence will be estimated as the proportion of subjects infected divided by the number of subjects tested. All CIs will be two-sided 95% CIs computed using the exact method, calculated from Proc StatXact [Clopper, 1934]. The estimates of parasite prevalence will be done each year and for each site separately.

The estimates of the use of malaria control measures will be estimated the same way; as the proportions of subjects using malaria control measures divided by the number of subjects for which this information is available.

7.7. Analysis of secondary objectives

7.7.1. Trends in parasite prevalence

7.7.1.1. Overall

First the trends in parasite prevalence between each cross-sectional malariometric surveys will be tested using the Cochran-Armitage trend test [Agresti, 1990]. This hypothesis test will be performed on the parasite prevalence computed on the independent samples of subjects in each survey separately within each site.

7.7.1.2. By vaccine eligible/ineligible subgroup: Statistical analyses for vaccine association adjustments and association between vaccine and transmission

For the analysis of association between RTS,S/AS01$_E$ vaccine and transmission, two subgroups must be considered:

- Vaccine eligible subgroup (see glossary of terms for definition). This subgroup will be used to assess the association between vaccination and transmission intensity, assuming a constant MTI in unvaccinated subjects (which will be measured using the second subgroup).
- Vaccine ineligible subgroup (see glossary of terms for definition). Due to the fact that the main reservoir of malaria is in the population between 5-20 years old (based on data collected in parallel [Epi-Mal-001 study] to the pivotal efficacy Phase III trial, not published) and MTI will be assessed for ***approximately 5*** years following the introduction of the vaccine, it will be assumed that there will be negligible herd immunity effect. Therefore, this subgroup will be used to detect any annual fluctuation (control group). If there is any herd effect, then the vaccine effect will be an underestimate.

(Amended 14 September 2018)

7.7.1.2.1. Annual fluctuations: vaccine ineligible subgroup

Once the cross-surveys are collected, the independent samples of subjects in each survey will be tested and assessed using a Chi-square statistic to test the significance of the differences among the parasite prevalences in each survey; meaning annual fluctuations.

If a significant difference is detected, further analyses will be done to characterise the difference(s).

Two methods will be then used. The first method is by two-by-two comparison between each cross-survey result. The advantage is identification of non-linear variations. The disadvantage is that longitudinal aspects of all surveys are not taken into consideration.

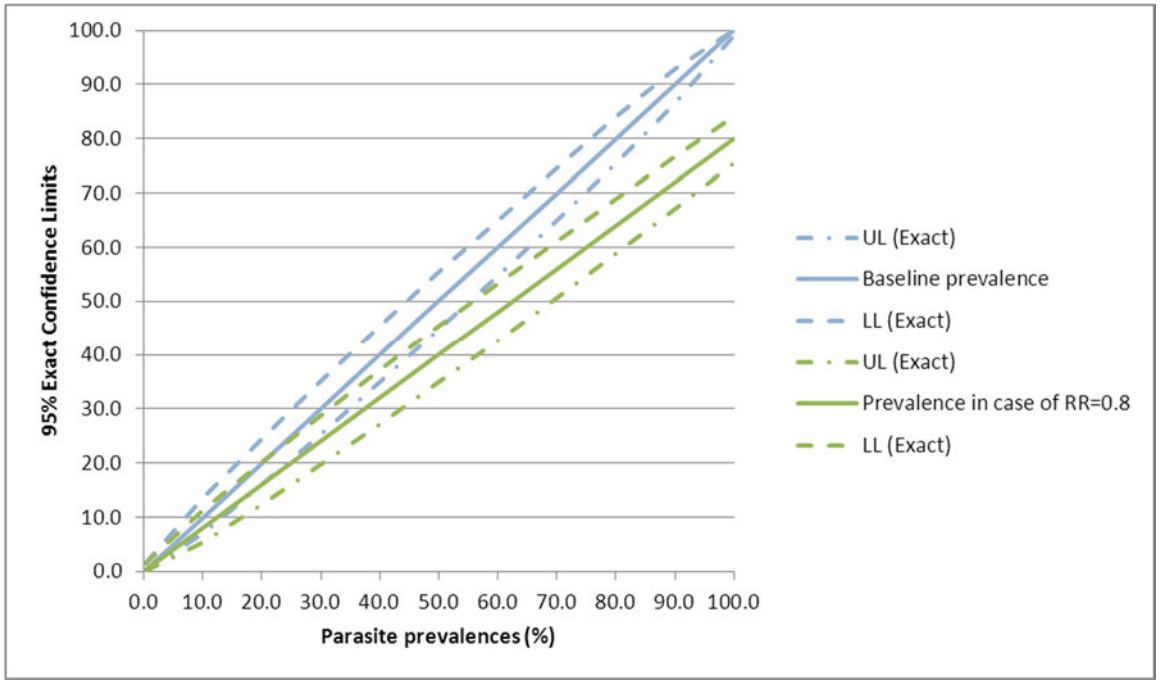
As shown in Table 8 and in Figure 3, a relative risk (RR) of one year of the study to another equal to 0.8 and 0.6 could be detected for a baseline prevalence greater than 60% and 20%, respectively. Note; these statements are based on non-overlapping CIs.

Table 8 Power estimation to detect a certain RR (from 0.1 to 0.9) depending on different baseline prevalences (from 0.1 to 0.9) with a sample size of 360 subjects

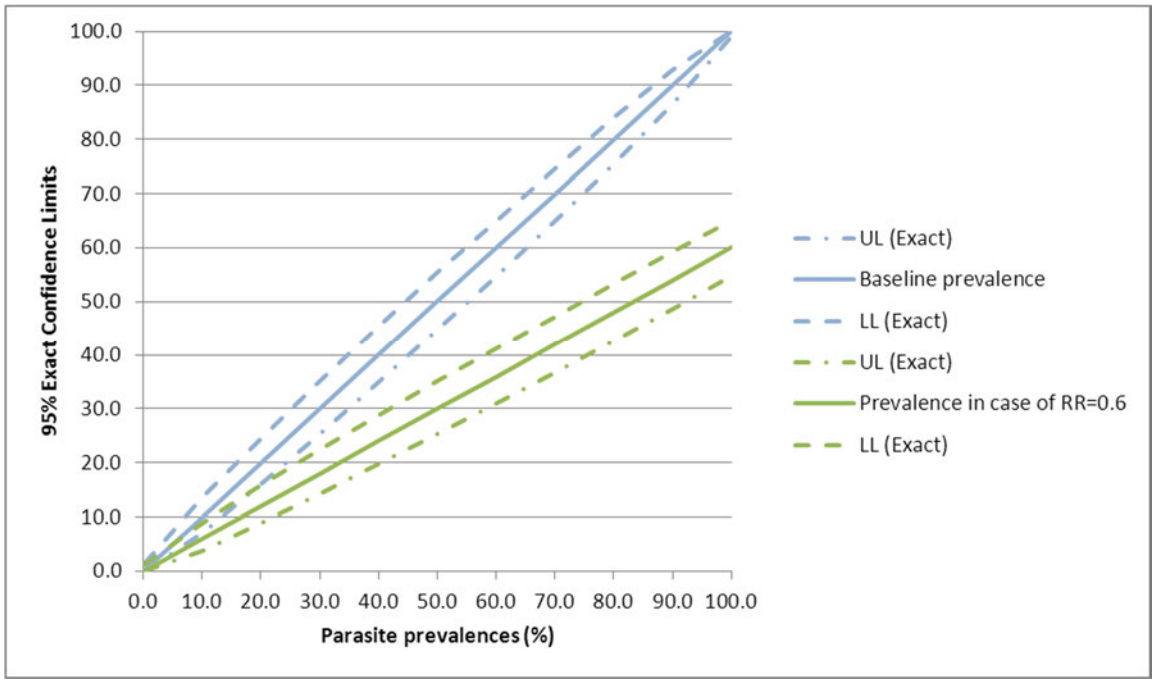
	Relative Risk								
Baseline	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**
0.1	1	1	0.97	0.89	*0.72*	*0.51*	*0.3*	*0.15*	*0.07*
0.2	1	1	1	1	0.97	0.83	*0.57*	*0.29*	*0.1*
0.3	1	1	1	1	1	0.97	0.79	*0.44*	*0.14*
0.4	1	1	1	1	1	1	0.93	*0.61*	*0.2*
0.5	1	1	1	1	1	1	0.98	*0.77*	*0.27*
0.6	1	1	1	1	1	1	1	0.9	*0.37*
0.7	1	1	1	1	1	1	1	0.97	*0.51*
0.8	1	1	1	1	1	1	1	1	*0.71*
0.9	1	1	1	1	1	1	1	1	0.93

Figure 3 Illustration of the lower (LL) and upper (UL) limits of the exact 95% CI built around both compared prevalences with a sample size of 360 subjects

a. based on a RR of 0.8



b. based on a RR of 0.6

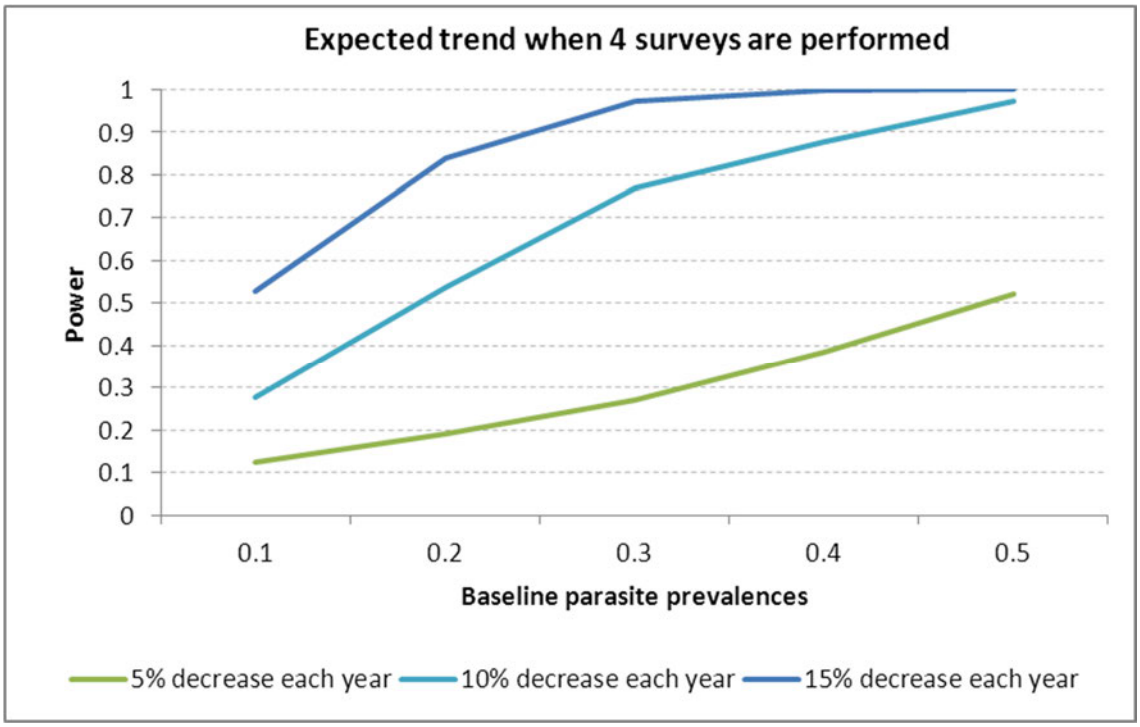


The second method is to perform a Cochran linear hypothesis trend test in which all longitudinal estimations will be used to detect a linear trend. However, only linear trends could be detected. As shown in Figure 4, a 5% decrease could not be detected if the baseline incidence is smaller than 50%. Based on 4 surveys, and a threshold of 90% power, a 10% decrease could be detected for a baseline incidence higher than or equal to 40% and a 15% decrease could be detected for a baseline incidence higher than or equal to~25%. The power improves with an increased number of surveys.

Table 9 Power estimation to detect a certain RR (from 0.1 to 0.9) depending on different baseline prevalence with a sample size of 240 subjects

	Relative Risk								
Baseline	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**
0.1	0.99	0.96	0.88	*0.73*	*0.55*	*0.36*	*0.22*	*0.12*	*0.06*
0.2	1	1	1	0.97	0.87	*0.67*	*0.42*	*0.21*	*0.08*
0.3	1	1	1	1	0.98	0.87	*0.62*	*0.32*	*0.11*
0.4	1	1	1	1	1	0.97	0.79	*0.45*	*0.14*
0.5	1	1	1	1	1	0.99	0.92	*0.6*	*0.19*
0.6	1	1	1	1	1	1	0.98	*0.75*	*0.26*
0.7	1	1	1	1	1	1	1	0.89	*0.37*
0.8	1	1	1	1	1	1	1	0.98	*0.54*
0.9	1	1	1	1	1	1	1	1	0.8

Figure 4 Illustration of the power to detect a trend using the Cochran trend test, and based on a sample size of 360 subjects and an assumed decrease each year of 5%, 10% or 15%

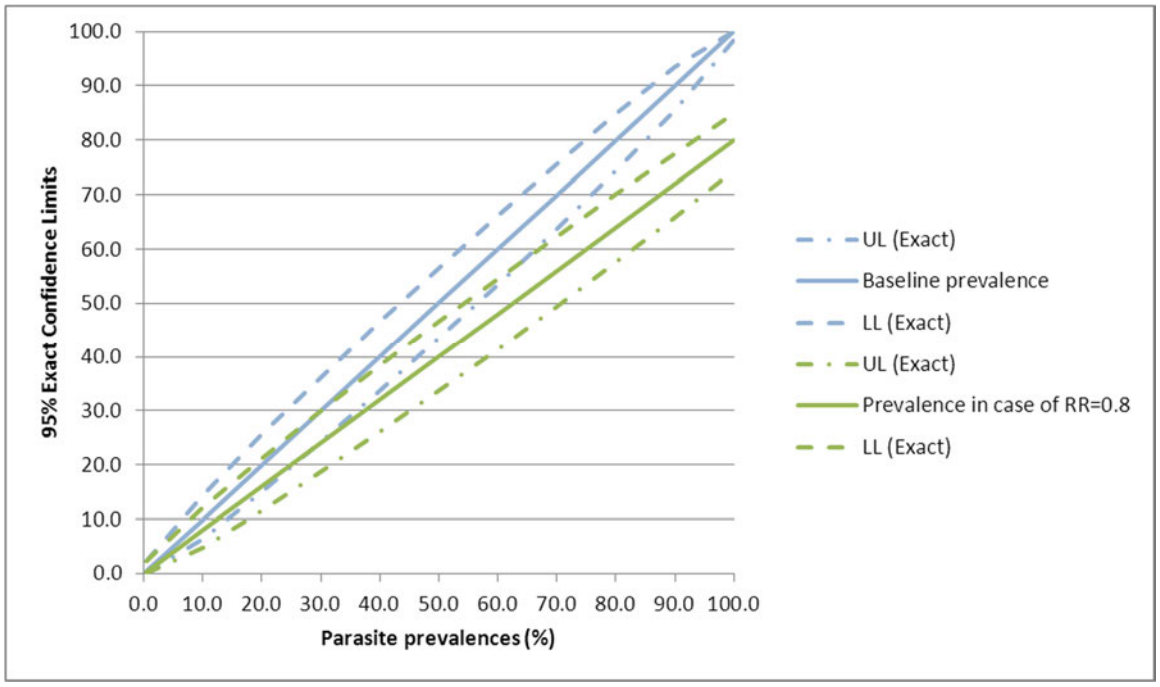


7.7.1.2.2. Association between vaccine and parasite prevalence: vaccine eligible subgroup

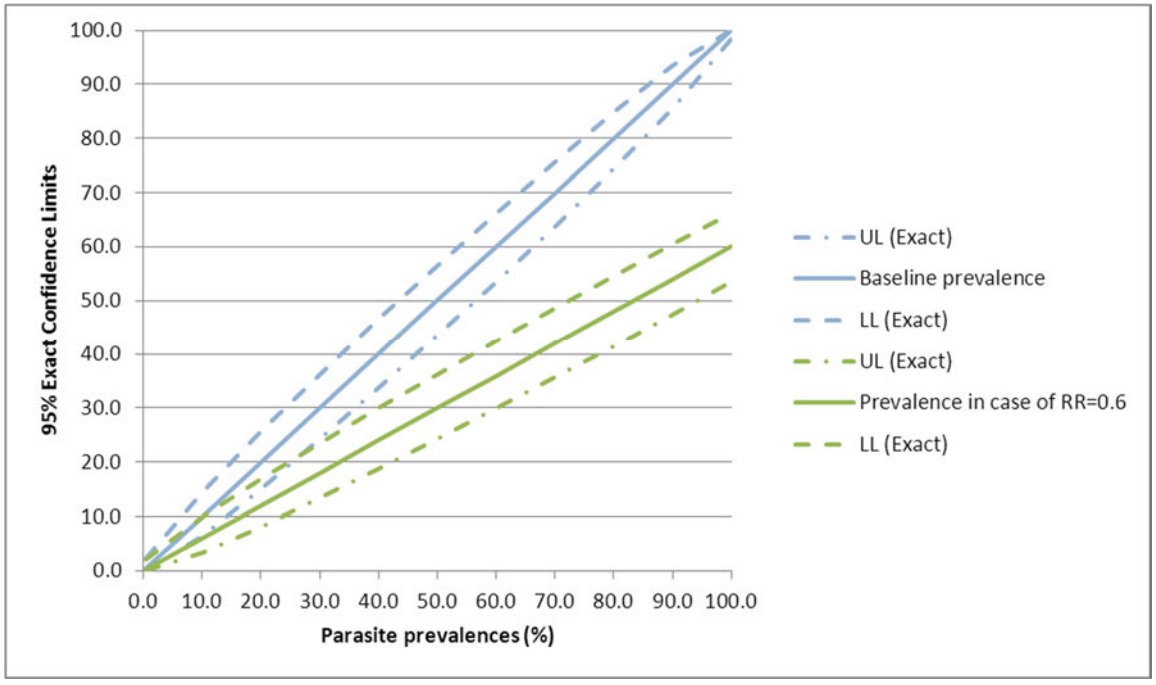
Using the same first methodology for the vaccine ineligible subgroup (Section 7.7.1.2.1), a statistically significant difference could be detected for a RR of 0.8 and 0.6 at a baseline prevalence greater than 70% and 30%, respectively, as shown in Figure 5 or in Table 9.

Figure 5 Illustration of the lower (LL) and upper (UL) limits of the exact 95% CI built around both compared prevalences with a sample size of 240 subjects

a. based on a RR of 0.8



b. based on a RR of 0.6



7.7.2. Other prevalences and proportions

The parasite prevalence and the estimates of the use of malaria control measures will be estimated by age group as defined in Section 7.4.

The prevalence of *Plasmodium* species other than *P. falciparum* will be estimated as the proportion of subjects infected divided by the number of subjects tested.

Prevalence for each segment will be estimated using the following criteria for level of endemicity: 'high' ≥ 60%, 'moderate' 20%-59%, and 'low' <20% relating to the proportion of infected children in each segment [Snow, 1997; Omumbo, 1998].

The proportion of subjects having received the third dose of DTP/HepB/Hib and the first dose of measles EPI vaccine will be estimated as the ratio of the subjects having received the third dose of DTP/HepB/Hib and the first dose of measles EPI vaccine divided by the number of subjects who should have received the third dose of DTP/pentavalent and the first dose of measles EPI (i.e. 14 weeks and 9 months of age, respectively). Moreover, among the subjects having received the third dose of DTP/HepB/Hib and the first dose of measles EPI vaccine, the proportions of subjects having received them on time, in advance and with delay will be estimated.

The care seeking behaviours will be described as the proportions of subjects having received care among all subjects with reported fever or malaria in the previous 14 days by the place they sought for care.

The prevalence of gametocyte presence will be estimated as the proportion of subjects infected divided by the number of subjects tested.

The parasite and gametocyte prevalences will also be estimated separately for microscopy and NAAT results.

7.7.3. Within-site geographical heterogeneity and risk factors

To assess within-site geographical heterogeneity, the parasite prevalence will be estimated separately in each village, grouping villages where necessary. Moreover, these geo-referencing characteristics will be part of the risk factor analysis described hereafter.

To describe the risk factors for malaria, a multivariable logistic regression will be used with all potential confounding variables.

7.8. Analysis of tertiary objectives

The comparisons of asexual and sexual (gametocyte) parasitaemia measured by microscopy and NAAT will be done using Cohen's Kappa coefficient. The hypothesis test will be done per centre, and overall.

7.9. Interpretation of analyses

Comparative analyses will be descriptive with the aim to characterise the difference between groups in the endpoint(s) related to the objective(s). These descriptive analyses should not be interpreted.

7.10. Conduct of analyses

Any deviation(s) or change(s) from the original statistical plan outlined in this protocol will be described and justified in the final study report.

7.10.1. Sequence of analyses

The analysis will be performed in each epoch, on as clean as possible data for the initial epochs and on clean data for the final epoch. The objective assessing trends will be analysed only at the final epoch. The other objectives will be analysed at all epochs.

All analyses, apart from the trend analyses, will be done for each epoch by centre and by classes of age (6 months to <5 years versus 5 to <10 years and 6 months to <3 years versus 3 to <10 years), and by year for the age group 6 months to <5 years. They will be detailed in the Statistical Analysis Plan (SAP) and the Tables, Figures, Listings (TFL) before the analysis. Statistical reports will be written after each epoch. A clinical report will be written after Surveys 2 and 5 and an integrated report will be written at the end of the study.

7.10.2. Statistical considerations for interim analyses

Only descriptive analyses and estimations of point estimate prevalence will be computed for each interim analysis. These analyses will be descriptive only. Therefore no adjustment of type I error is needed.

Concerning the sample size required for each interim analysis, please refer to Section 7.2.

8. ADMINISTRATIVE MATTERS

To comply with ICH GCP or other applicable guidelines administrative obligations relating to data collection, monitoring, archiving data, audits, confidentiality, ownership and publications must be met.

8.1. Electronic Case Report Form instructions

A validated GSK defined electronic data collection tool will be used as the method for data collection.

In all cases, subject initials will not be collected nor transmitted to GSK. Subject data necessary for analysis and reporting will be entered/transmitted into a validated database or data system. Clinical data management will be performed in accordance with applicable GSK standards and data cleaning procedures.

While completed eCRFs are reviewed by a GSK Biologicals' Site Monitor at the study site, omissions or inconsistencies detected by subsequent eCRF review may necessitate clarification or correction of omissions or inconsistencies with documentation and approval by the investigator or appropriately qualified designee. In all cases, the investigator remains accountable for the study data.

Once the database is archived and the clinical study report is complete and approved by all parties, each participating investigator will be provided with a CD-ROM of the final version of the data generated at his/her investigational site.

8.2. Study monitoring by GSK Biologicals

GSK will monitor the study to verify that, amongst others, the:

- Data are authentic, accurate, and complete.
- Safety and rights of subjects are being protected.
- Study is conducted in accordance with the currently approved protocol, any other study agreements, GCP and all applicable regulatory requirements.

The investigator and the head of the medical institution (where applicable) agrees to allow the monitor direct access to all relevant documents.

The investigator must ensure provision of reasonable time, space and qualified personnel for monitoring visits.

Direct access to all study-site related and source data is mandatory for the purpose of monitoring review. The monitor will perform an eCRF review and a Source Document Verification (SDV). By SDV we understand verifying eCRF entries by comparing them with the source data that will be made available by the investigator for this purpose.

The Source Documentation Agreement Form describes the source data for the different data in the eCRF. This document should be completed and signed by the site monitor and investigator and should be filed in the monitor's and investigator's study file. Any data item for which the eCRF will serve as the source must be identified, agreed and documented in the source documentation agreement form.

For eCRF, the monitor will mark completed and approved screens at each visit.

Upon completion or premature discontinuation of the study, the monitor will conduct site closure activities with the investigator or site staff, as appropriate, in accordance with applicable regulations, GCP, and GSK procedures.

8.3. Record retention

Following closure of the study, the investigator must maintain all site study records (except for those required by local regulations to be maintained elsewhere) in a safe and secure location. The records must be easily accessible, when needed (e.g., audit or inspection), and must be available for review in conjunction with assessment of the facility, supporting systems, and staff. Where permitted by applicable laws/regulations or

institutional policy, some or all of these records can be maintained in a validated format other than hard copy (e.g., microfiche, scanned, electronic); however, caution needs to be exercised before such action is taken. The investigator must ensure that all reproductions are legible and are a true and accurate copy of the original and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the investigator must ensure that an acceptable back-up of the reproductions exists and that there is an acceptable quality control procedure in place for making these reproductions.

GSK will inform the investigator/institution of the time period for retaining these records to comply with all applicable regulatory requirements. However, the investigator/institution should seek the written approval of the sponsor before proceeding with the disposal of these records. The minimum retention time will meet the strictest standard applicable to a particular site, as dictated by ICH GCP or other applicable guidelines, any institutional requirements or applicable laws or regulations, or GSK standards/procedures; otherwise, the minimum retention period will default to 15 years.

The investigator/institution must notify GSK of any changes in the archival arrangements, including, but not limited to, archival at an off-site facility and transfer of ownership of the records in the event the investigator leaves the site.

8.4. Quality assurance

To ensure compliance with GCP or other applicable guidelines and all applicable regulatory requirements, GSK may conduct a quality assurance audit. Regulatory agencies may also conduct a regulatory inspection of this study. Such audits/inspections can occur at any time during or after completion of the study. If an audit or inspection occurs, the investigator and institution agree to allow the auditor/inspector direct access to all relevant documents and to allocate his/her time and the time of his/her staff to the auditor/inspector to discuss findings and any relevant issues.

8.5. Posting of information on publicly available registers and publication policy

Study information from this protocol will be posted on public registers before enrolment of subjects begins.

Interventional studies that do not evaluate vaccines/products are progressed for publication in the scientific literature when the results provide important scientific or medical knowledge.

8.6. Provision of study results to investigators

Where required by applicable regulatory requirements, an investigator signatory will be identified for the approval of the study report. The investigator will be provided reasonable access to statistical tables, figures, and relevant reports and will have the opportunity to review the complete study results at a GSK Biologicals site or other mutually-agreed location.

GSK Biologicals will also provide the investigator with the full summary of the study results. The investigator is encouraged to share the summary results with the study subjects, as appropriate.

9. COUNTRY SPECIFIC REQUIREMENTS

Not applicable.

10. REFERENCES

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(Amended 14 September 2018)

APPENDIX A LABORATORY ASSAYS - DETERMINATION OF PARASITAEMIA BY MICROSCOPY

Slide reading methodology

All slide readers will be required to demonstrate proficiency at "Competent" level or above as documented by certification/training records [World Health Organization, 2009].

For further details of the reading methodology described, refer to the WHO Basic Malaria Microscopy Learners Guide [World Health Organization, 1991].

Slide preparation and assessing parasite presence

Slide preparation: During subject visits, capillary blood samples are used to produce two slides per subject containing both a thick and thin blood smear per slide. The thin film is produced from one small blood drop in the centre of the slide. Using the edge of a second, clean slide, firmly spread the single drop of blood across the sample slide. The thick film is produced from 3 larger drops of blood approximately 1cm away from the thin film. The drops should be joined and spread using the corner of the spreader to become a circular thick film of approximately 1cm diameter.

Thick film examination: A 100-field examination of the thick film should be conducted to assess presence of parasites and species.

Negative result: 100 fields free of parasites are read before a slide is declared negative.

Positive result: If parasites are present within reading of 100 fields, the slide is positive. Positive slides are examined for a further 100 fields to ensure all species present are detected.

Parasite density counting against assumed 8000 leukocytes per microlitre

In this method of estimating parasite density, it is assumed that there are 8000 leukocytes per microlitre of blood.

Step 1: Use 2 tally counters, one to count parasites and the other to count leukocytes.

a. If upon counting 200 leukocytes, 10 or more parasites have been counted, the results can be recorded as the parasites per 200 leukocytes.

b. If upon counting 200 leukocytes, 9 or fewer parasites have been recorded, the reader should continue counting until 500 leukocytes have been counted and the number of parasites per 500 leukocytes can be recorded.

Step 2: Convert the number of parasites relative to leukocyte count to an estimated number of parasites per microlitre:

$$\frac{\text{number of parasites x 8000}}{\text{number of leukocytes}} = \text{parasites per microlitre}$$

For example, if 20 parasites were observed upon counting 500 leukocytes, it would give an estimated 320 parasites per microlitre.

It should be noted that the count should be by species, and counts for *P. falciparum* should be made for both gametocytes and asexual parasites.

Criteria for concordance for double reading of slides

All slides will be read twice, by two independent readers to quantify the *P. falciparum* parasite presence and density. If slides are judged to be discordant, a third independent read will be organised in the following cases:

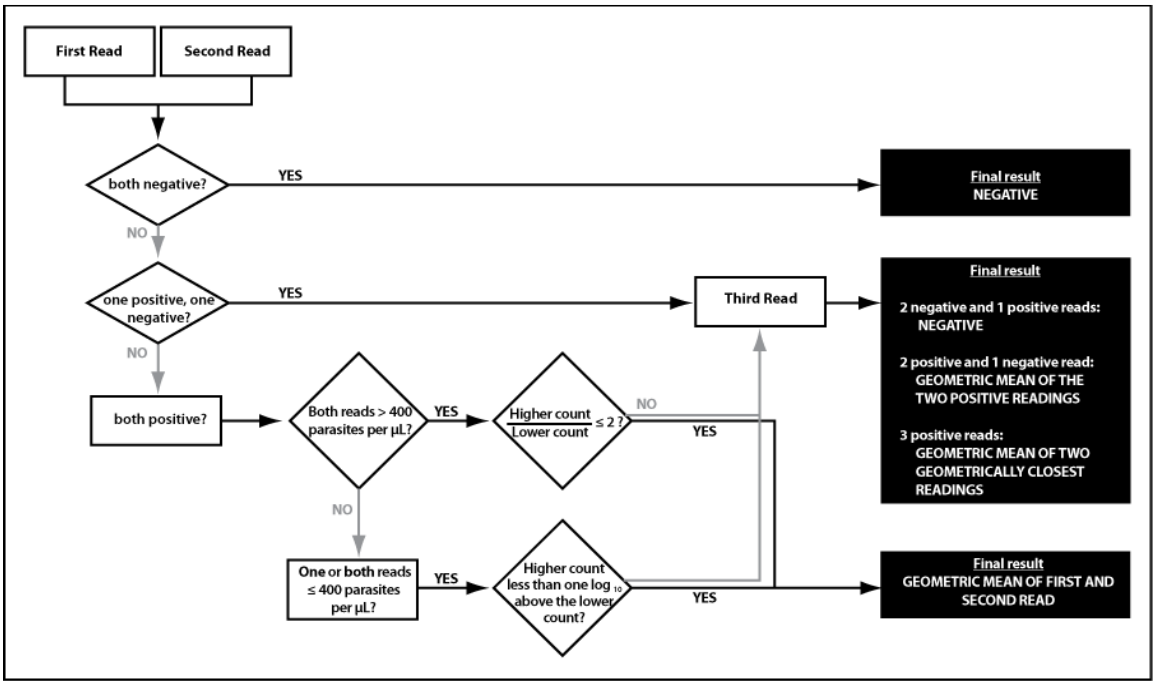
- The result from one reader is negative and the one of the other is positive.
- For high and medium positive parasitaemia results (blood parasitaemia >400/μL), the higher count divided by the lower count is >2.
- For low parasitaemia (blood parasitaemia ≤400/μL), the highest reading density is more than one $\log_{10}$ higher than the lowest reading.
- If parasitaemia result is high or medium in one slide and the result from the other slide reading is low, i.e. one is >400/μL and the other is ≤400/μL, criterion (C) will be applied.

Determination of final result

If there are two concordant results the final result is the geometric mean of the two readings.

If the first two readings are discordant then the final result will follow the following principles:

- For cases of positive/negative discrepancy (A), the majority decision will be adopted. If the decision is positive, the final result will be the geometrical mean of the two positives.
- For cases of three positive reads (B and C), the final result will be the geometric mean of the two geometrically closest readings.



Identification of *Plasmodium* species

Positive parasitaemia identified on any thick blood film must always be identified to species. This will be done on thin blood film except in case of low parasitaemia.

Archiving of blood slides

Two blood slides are taken, one for reading and archiving at the centres; the second one will be archived centrally at a GSK dedicated laboratory facility.

CCI

[redacted]

CCI

APPENDIX B CLINICAL LABORATORIES

Table 10 Outsourced laboratories

Laboratory	Address
Academic Medical Center (AMC) Laboratory for clinical parasitology, L1-247 Department of Medical Microbiology	Meibergdreef 9 1105 AZ Amsterdam The Netherlands

APPENDIX C AMENDMENTS AND ADMINISTRATIVE CHANGES TO THE PROTOCOL

GlaxoSmithKline Biologicals Vaccine Value & Health Science (VVHS) Protocol Amendment 1	
eTrack study number and Abbreviated Title	116682 (EPI-MALARIA-005 BOD AME)
Amendment number:	Amendment 1
Amendment date:	21 September 2016
Co-ordinating author:	PPD, XPE Pharma & Sciences for GSK Biologicals

1. Risk Management Plan requirement for follow-up extension in EPI-MAL-003 study. EPI-MAL-005 study is conducted in parallel with the EPI-MAL-002 and EPI-MAL-003 studies, and therefore with the extension of EPI-MAL-003, there is need to extend the EPI-MAL-005 study which provides useful data to compare the EPI-MAL-002 and EPI-MAL-003 studies. EPI-MAL-005 study has been extended by four years to nine years.
2. New sites selected for the EPI-MAL-002 and EPI-MAL-003 studies will be included in this study. In addition, World Health Organisation (WHO) proposed the use of RTS,S/AS01$_E$ in moderate to high malaria transmission settings. Due to WHO's proposal, the two sites in Senegal and one site in Tanzania will no longer be participating in this study after Survey 2 because the malaria transmission in these countries is low.
3. The study design was updated to indicate that there is an overlap of EPI-MAL-002 and EPI-MAL-003 with no break.
4. The word "interventional" was removed from the detailed title of the study because this word is no longer in the detailed title of EPI-MAL-002.
5. The tertiary objectives wording has been updated. *P. falciparum* gametocyte NASBA assay was initially expected to be semi-quantitative, but during the method optimisation the assay was more variable than expected. Therefore the test will only be considered as qualitative.
6. The name and address of the laboratory where the NAAT tests will be performed were updated because the activities and projects of laboratory have been transferred to the Academic Medical Centre in Amsterdam.
7. The sample size wording has been updated to reflect the true reason for the limited sample size in children 5-9 years to reach a relative standard error equal to a maximum of 0.35 based on the Pharmacovigilance Risk Assessment Committee (PRAC)'s recommendation.

8.	The quantity of blood needed for asexual and sexual (gametocyte) assessment and parasite and gametocyte NAAT assessment has been updated.
9.	The criteria for when the rapid diagnostic test will be done has been updated from not only for fever > 37.5°C, but also for subjects with other symptoms/signs of clinical malaria.

Amended text has been included in *bold italics* and deleted text in ~~strikethrough~~ in the following sections:

Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two ~~interventional~~ studies pre- and post RTS,S/AS***01E*** introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Co-ordinating author	PPD, Freelance Science Writer for GSK Biologicals
Contributing authors	• PPD, ~~Project Statistician~~ ***Lead Epidemiologist-Malaria*** • PPD, ***Oversight Data Manager, Business and Decision Life Sciences for GSK Biologicals*** • PPD Study Data Manager • PPD, ***Clinical Laboratory Sciences***-SM, external consultant for GSK Biologicals • PPD, ***Study Delivery Lead***, ***SynteractHCR Benelux NV*** for GSK Biologicals • PPD, ***Study Statistician, 4clinics for GSK Biologicals*** • PPD, ***Senior Manager, Epidemiologist, ManiAfriCare for GSK Biologicals*** • PPD, ~~WHO Fellow, Malaria Team~~ ***Clinical Epidemiologist, Bartech for GSK Biologicals*** • PPD, ***Senior Local Delivery Lead*** • PPD, ***Global Patent representative***

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Protocol *Amendment 1* Sponsor Signatory Approval

Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two ~~interventional~~ studies pre- and post RTS,S/AS***01$_E$*** introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Sponsor signatory	~~Laurence Baril, Head, Global Epidemiology~~ ***François Roman, Clinical & Epidemiology Project Lead, DDW Vaccines***

SYNOPSIS

Detailed Title	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS***01$_E$*** introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
Rationale for the study	Following the pivotal Phase III study of the candidate malaria vaccine RTS,S/AS01$_E$ (Malaria-055), two consecutive vaccine safety monitoring studies (EPI-MAL-002 and EPI-MAL-003) will be conducted to monitor incidence rates of ***meningitis,*** protocol defined adverse events of specific interest (***AESI*****,** ***and*** ~~non-communicable and non-traumatic serious~~ ***of other adverse events*** ~~(NC/NT-SAE).~~***leading to hospitalisation or death, in children***. The first study, EPI-MAL-002, is a surveillance study prior to RTS,S/AS***01$_E$*** authorisation in the country; the second study, EPI-MAL-003, will more specifically monitor RTS,S/ AS0***1$_E$*** safety and will only start when RTS,S/AS0***1$_E$*** is registered and authorised in the country. ***The*** ~~planned age range for licensure of~~ ***World Health Organization's Strategic Advisory Group of Experts (SAGE) on Immunization and the Malaria Policy Advisory Committee (MPAC) recommended pilot implementations of RTS,S/AS01$_E$*** ~~candidate~~ ***in children of 5–17 months of age, in parts of 3-5 sub-Saharan African (SSA) countries, administering 3 doses of the vaccine*** ~~is in~~ ***to children*** ~~from 6 weeks~~ ***aged 5-9 months of age*** ~~to less than18 months~~.***in areas of moderate-to-high transmission of malaria with a fourth dose 15-18 months later. The first vaccine introduction is foreseen in 2018.*** The secondary endpoints of these studies ***also*** include monitoring the incidence of malaria disease as diagnosed during out-patient visits or hospitalisation. Up to

seven ***Health and*** Demographic Surveillance System (~~DSS~~ ***H***DSS) (***or equivalent system)*** sites in ~~five~~ countries in Sub-Saharan Africa will participate in these studies, enrolling approximately ~~40~~***3***0 000 children <~~3~~***5*** years of age in ~~each study~~ ***EPI-MAL-002 and approximately 45 000 children <5 years in EPI-MAL-003.***

This epidemiology study (EPI-MAL-005) is planned to run in parallel with these two studies, enrolling from the same ~~DSS~~ ***H***DSS ***or (equivalent system)*** populations.

Although not yet ***considered as the*** ~~global~~ ***gold*** standard, NAAT-based (nucleic acid amplification test) techniques can detect infections of lower malaria parasite density and ~~give more accurate~~ quantification of parasitaemia than is achievable by microscopy. Identification of gametocytes by microscopy is inherently challenging, thus their presence is often missed, even by highly trained technicians. Therefore, additional analysis of collected blood samples by NAAT will allow for the detection of lower density parasite infections and will be a more sensitive measure of changes in ***both*** parasite and gametocyte prevalence and density, thereby providing greater insight into potential changes upon vaccine implementation.

Objectives

Secondary

- To estimate longitudinal trends in receipt and timing of the third dose of DTP***/HepB/Hib*** ~~pentavalent~~ and the first dose of measles EPI vaccines, at around 14 weeks and 9 months of age respectively, as appropriate by country.

Tertiary

- To compare asexual and sexual (gametocyte) parasitaemia (qualitative- and ***semi***-quantitative-density) when measured by microscopy or NAAT.

Study design

- Biological samples: A capillary blood sample will be obtained for evaluation of malaria infection by blood slide and NAAT. In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours ***or other symptoms/signs of clinical malaria,*** a rapid diagnostic test (RDT) will be conducted. If the RDT is positive, treatment will be given according to National guidelines. If a subject for whom no RDT was required is identified as being parasite positive following microscopy, National guidelines should be followed for clinical management of the subject.

- Each study site will be requested annually to provide centre specific information about interventions from the malaria control programme in the study area ~~and, if facilities are available,~~ to provide meteorological data for the study site such as rainfall and temperature. The information will be collected in the form of a questionnaire that will be recorded in a separate database to that for subject-specific data.
- This study will involve up to ~~5~~***9*** annual cross sectional surveys during malaria peak transmission.
- Duration of the study: up to ~~5~~***9*** years

  ~~NOTE: surveys may not be in consecutive years and the total will then be less than 5.~~

  – ***Epoch 006: Survey 6 at Year 6.***

  – ***Epoch 007: Survey 7 at Year 7.***

  – ***Epoch 008: Survey 8 at Year 8.***

  – ***Epoch 009: Survey 9 at Year 9***

Synopsis Table 1 Study groups and epochs foreseen in the study

Study Group	Age (Min/ Max)	~~No of sites~~	~~Total no of subjects~~	~~Total no of subjects/site~~	Epochs								
					Epoch 001 Survey 1	Epoch 002 Survey 2	Epoch 003 Survey 3	Epoch 004 Survey 4	Epoch 005 Survey 5	***Epoch 006 Survey 6***	***Epoch 007*** Survey 7	***Epoch 008*** Survey 8	***Epoch 009*** Survey 9
~~Total~~ ***Study site***	6 months / 9 years	~~7~~	~~2100~~	~~3000~~	~~420060~~ 0 subjects	~~4200~~ 600 subjects	~~420060~~ 0 subjects	~~4200~~ 600 subjects	~~420060~~ 0 subjects	***600 subjects***	***600 subjects***	***600 subjects***	***600 subjects***

Discussion of study design

Nine ~~Up to 5~~ annual cross sectional surveys at peak transmission will provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by EPI-MAL-002 and EPI-MAL-003. Malaria transmission is highly seasonal so surveys will be carried out ~~at the end~~ ***during the course*** of the rainy season ***preferably when rains decrease***, the period of highest malaria transmission.

Number of subjects	Total expected sample size: ~~14000 subjects aged 6 months to <5 years and 7000 subjects aged 5 to <10 years.~~ ***Per site and by survey is a maximum of 400 subjects aged 6 months to <5 years and a maximum of 200 subjects aged 5 to <10 years.***
Endpoints	**Secondary** • Occurrence of uptake and timing of the third dose of DTP***/HepB/Hib*** ~~pentavalent~~ and the first measles EPI vaccines Criteria/definitions: vaccination record of receipt of dose 3 of the DTP***/HepB/Hib*** ~~pentavalent~~ and the first dose measles EPI vaccines.

LIST OF ABBREVIATIONS

AMC	***Academic Medical Center***
eCRF	~~Electronic case report form~~ ***electronic Case Report Form***
GCP	Good ~~clinical practice~~ ***Clinical Practice***
GIS	***Geographic Information System***
HDSS	***Health and*** Demographic surveillance system
HepB	***Hepatitis B***
Hib	***Heamophilus influenza type b***
~~KIT~~	~~Koninklijk Instituut voor de Tropen (Royal Tropical Institute)~~
MPAC	***Malaria Policy Advisory Committee***
PRAC	***Pharmacovigilance Risk Assessment Committee***
SAGE	***Strategic Advisory Group of Experts***
WHO	***World Health Organisation***

GLOSSARY OF TERMS

Catchment area:	In this study, the catchment area is defined as the area of the ***H***DSS (***or equivalent system)*** study site participating in the EPI-MAL-002 and EPI-MAL-003 studies.
DTP/HepB/Hib	***This refers to DTP, or DTP-Hep B (tetravalent) or DTP-HepB-Hib (pentavalent).***
First dose measles	***First measles containing vaccine.***

1 INTRODUCTION

1.1 Background

GSK Biologicals has formulated the candidate pre-erythrocytic *P. falciparum* malaria vaccine, RTS,S/AS***01E***, which is currently under evaluation. The vaccine consists of sequences of the circumsporozoite (CS) protein and hepatitis B surface antigen (HBsAg) adjuvanted with AS01 (liposome formulation with MPL and QS21 immunostimulants).

In the pivotal Phase III study (Malaria-055), efficacy of the candidate malaria vaccine RTS,S/AS01***E*** against first or only episodes of clinical malaria over a follow-up of 12 months in children aged 5-17 months was 55.8% (p<0.0001), and in coadministration with DTPwHepB/Hib vaccine at 6, 10 and 14 weeks of age was 31.3% (p<0.0001).

1.2 Rationale for the study

Following the pivotal Phase III study of the candidate malaria vaccine RTS,S/AS01***E*** (Malaria-055), two consecutive vaccine safety monitoring studies (EPI-MAL-002 and EPI-MAL-003) will be conducted to monitor incidence rates of ***meningitis,*** protocol defined adverse events of ~~specific~~ ***special*** interest (AESI) and ~~non-communicable and non-traumatic serious~~ ***other adverse events*** ~~(NC/NT-SAE).~~***leading to hospitalisations and death***. The first study, EPI-MAL-002, is a surveillance study prior to RTS,S/AS***01E*** authorisation in the country; the second study, EPI-MAL-003, will more specifically monitor RTS,S/AS***01E*** safety and will only start when RTS,S/AS***01E*** is registered and authorised in the country. The planned age range for licensure of the RTS,S/AS01$_E$ candidate vaccine is in children from 6 weeks of age to less than18 months. The secondary endpoints of these studies include monitoring the incidence of malaria disease as diagnosed during out-patient visits or hospitalisation. Up to seven ***Health and*** Demographic Surveillance System (***H***DSS) (***or equivalent system)*** sites in ~~five~~ ***different*** countries in Sub-Saharan Africa will participate in these studies, enrolling approximately ~~40~~***3***0 000 children <~~3~~***5*** years of age in ~~each study~~ ***EPI-MAL-002 and approximately 45 000 children <5 years in EPI-MAL-003.***

This epidemiology study (EPI-MAL-005) is planned to run in parallel with these two studies, enrolling from the same ***H***DSS (***or equivalent system)*** populations.

Although not ***yet considered as*** the ~~global~~ ***gold*** standard, NAAT-based (nucleic acid amplification test) techniques can detect infections of lower malaria parasite density and give more accurate quantification of parasitaemia than is achievable by microscopy. Identification of gametocytes by microscopy is inherently challenging, thus their presence is often missed, even by highly trained technicians. Therefore, additional analysis of collected blood samples by NAAT will allow for the detection of lower density parasite infections and will be a more sensitive measure of changes in ***both*** parasite and gametocyte prevalence and density, thereby providing greater insight into potential changes upon vaccine implementation. This will also provide comparability of data collected in this study with the technique likely to be favoured in clinical trials in the future.

2 OBJECTIVES

2.2 Secondary objectives

- To estimate longitudinal trends in receipt and timing of the third dose of DTP***/HepB/Hib*** ~~pentavalent~~ and the first dose of measles EPI vaccines, at around 14 weeks and 9 months of age respectively, as appropriate by country.

2.3 Tertiary objectives

- To compare asexual and sexual (gametocyte) parasitaemia (qualitative and ***semi-***quantitative-density) ***when measured by microscopy or NAAT*** in the RTS,S/AS01E vaccinated and unvaccinated subjects.
- To compare asexual and sexual (gametocyte) parasitaemia (qualitative- and ***semi-***quantitative-density) when measured by microscopy or NAAT.

3 STUDY DESIGN OVERVIEW

- Biological Samples: A capillary blood sample will be obtained for evaluation of malaria infection by blood slide and NAAT. In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours ***or other symptoms/signs of clinical malaria,*** a rapid diagnostic test (RDT) will be conducted. If the RDT is positive, treatment will be given according to National guidelines. If a subject for whom no RDT was required is identified as being parasite positive following microscopy, National guidelines should be followed for clinical management of the subject.

Using ***Geographic Information System*** (GIS) to determine geographical variability in MTI locally: Study areas will be mapped by villages using grid referencing.

- This study will involve up to ~~5~~***9*** annual cross sectional surveys during malaria peak transmission.
- Duration of the study: up to ~~5~~***9*** years

  ~~NOTE: surveys may not be in consecutive years and the total will then be less than 5.~~

  - ***Epoch 006: Survey 6 at Year 6.***
  - ***Epoch 007: Survey 7 at Year 7.***
  - ***Epoch 008: Survey 8 at Year 8.***
  - ***Epoch 009: Survey 9 at Year 9***

Table 1 Study groups and epochs foreseen in the study

Study Group	Age (Min/Max)	~~No of sites~~	~~Total no of subjects~~	~~Total no of subjects/site~~	Epochs								
					Epoch 001 Survey 1	Epoch 002 Survey 2	Epoch 003 Survey 3	Epoch 004 Survey 4	Epoch 005 Survey 5	***Epoch 006 Survey 6***	***Epoch 007*** Survey 7	***Epoch 008*** Survey 8	***Epoch 009*** Survey 9
~~Total~~ ***Study site***	6 months / 9 years	~~7~~	~~2100~~	~~3000~~	~~420060~~ 0 subjects	~~4200~~ 600 subjects	~~420060~~ 0 subjects	~~4200~~ 600 subjects	~~420060~~ 0 subjects	***600 subjects***	***600 subjects***	***600 subjects***	***600 subjects***

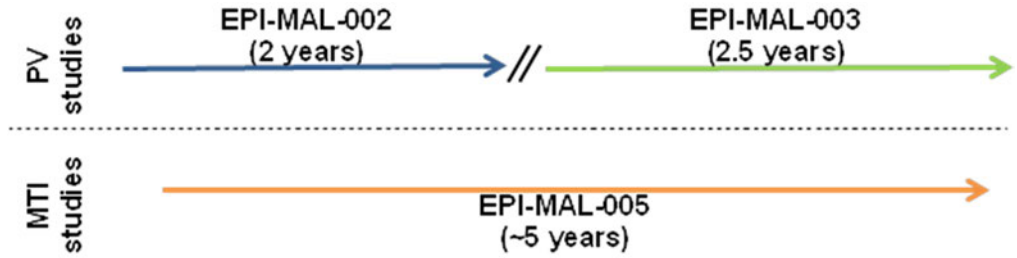
3.1 Discussion of study design

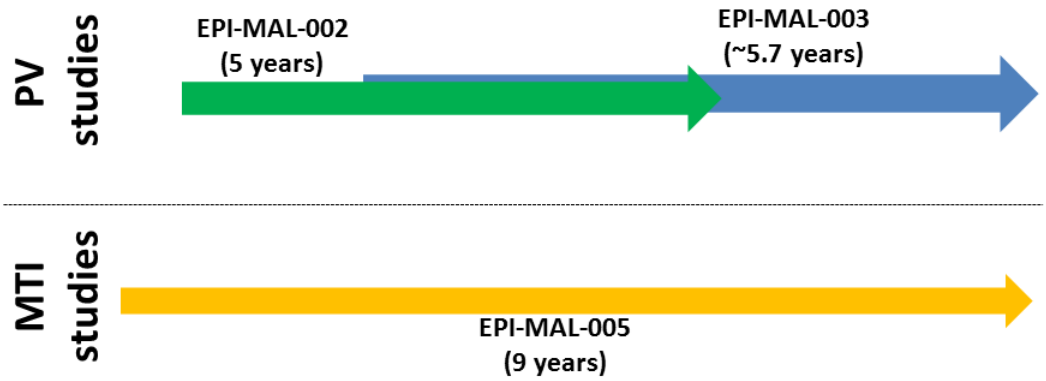
~~Up to 5~~ ***Nine*** annual cross sectional surveys at peak transmission will provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by EPI-MAL-002 and EPI-MAL-003. Malaria transmission is highly seasonal so surveys will be carried out ~~at~~ ***during the*** ~~end~~ ***course of the rainy season preferably when rains decrease***, the period of highest malaria transmission.

4 STUDY POPULATION

4.1 Number of subjects/ centres

Subjects 6 months to <10 years of age will be enrolled in ***H***DSS (***or equivalent system)*** catchment areas at the sites participating in the EPI-MAL-002 and EPI-MAL-003 studies of the candidate malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa. Up to ~~7~~ ***seven*** ***H***DSS (***or equivalent system)*** sites ~~will~~ ***are planned to*** participate in this study (see Section 4.1.1). Subjects enrolled in EPI-MAL-002 and EPI-MAL-003 are eligible for participation in this study.





Each study site will enroll approximately 600 subjects per survey. ***These subjects will be selected at random from the HDSS (or equivalent system) population listings prepared at each site. The selection process will be repeated every year meaning that the subjects will be different in each cross-sectional survey except if they are re-selected in a subsequent survey by chance***. ***The*** population ***listings*** generated from the demographic surveillance will allow for sampling of the required subjects according to stratification by age group as follows (all subject numbers are approximately plus or minus 5 children):

Therefore, the total expected sample size ~~over 5 surveys~~ ***per site and by survey is a maximum of*** ~~14000~~ ***400 subjects aged 6 months to <5 years and a maximum of*** ~~7000~~ ***200 subjects aged 5 to <10 years***, ~~calculated as follows:~~

- ~~Subjects aged 6 months to <5 years: max 5 study years x 7 sites x 400 subjects = max 14000 subjects~~
- ~~Subjects aged 5 to <10 years: max 5 study years x 7 sites x 200 subjects = max 7000 subjects.~~

4.1.1 Recruitment of study centres/ investigators

All ***H***DSS ***(or equivalent system)*** study sites participating in EPI-MAL-002 and EPI-MAL-003 will be approached with regard to participation in this epidemiological study. At the time of ***original*** protocol finalisation, these comprised ~~centres~~ ***sites*** in Burkina Faso, Ghana, Senegal, Tanzania, and Kenya ~~(APPENDIX A).~~

The study sites will be revised after survey 2. Following the World Health Organization (WHO)'s Strategic Advisory Group of Experts (SAGE) on Immunization and the Malaria Policy Advisory Committee (MPAC) recommendations of pilot implementations of RTS,S/AS01$_E$ in 3-5 distinct settings in sub-Saharan Africa (SSA) restricted to moderate-to-high transmission of malaria, other settings in SSA with moderate-to-high transmission of malaria might be added to the already defined EPI-MAL-002 and EPI-MAL-003 study sites. These new sites will also be added to the EPI-MAL-005 study.

The study sites in Senegal and Tanzania with low malaria transmission will no longer participate in the study after Survey 2.

4.1.2 Sampling methods

All participating centres will have a ***H***DSS ***(or equivalent system)*** in place. In general, any variation in sampling procedure should follow as closely as possible the Guidelines of the Roll Back Malaria Monitoring and Evaluation Reference Group [2005]. The following steps serve as an example of a sampling method.

1. Generate a list from the ***H***DSS ***(or equivalent system)*** database of all children aged 6 months to <10 years.

Each study site will enrol approximately 600 subjects per survey. To allow for 10% non-response 660 subjects should therefore be randomly selected from the ***H***DSS ***(or equivalent system)*** database distributed over all age categories as described in Section 4.1.

5.4 Outline of study procedures

Table 2 details study procedures to be conducted during the study.

Table 2 List of study procedures to be conducted at each survey visit

Epoch	**Epoch 001**	**Epoch 002**	**Epoch 003**	**Epoch 004**	**Epoch 005**	***Epoch 006***	***Epoch 007***	***Epoch 008***	***Epoch 009***
Study Group[1]	**Survey 1**	**Survey 2**	**Survey 3**	**Survey 4**	**Survey 5**	***Survey 6***	***Survey 7***	***Survey 8***	***Survey 9***
Timepoint	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	***Year 6***	***Year 7***	***Year 8***	***Year 9***
Informed consent	●	●	●	●	●	●	●	●	●
Check inclusion/exclusion criteria	●	●	●	●	●	●	●	●	●
Record demographic details	●	●	●	●	●	●	●	●	●
Record subject's vaccination status[2]	●	●	●	●	●	●	●	●	●
Record any anti-malarial medication or other medication received within the previous 14 days	●	●	●	●	●	●	●	●	●
Record relevant medical history (hospitalisation, reported fever, and care seeking behaviour)	●	●	●	●	●	●	●	●	●
Record axillary body temperature	●	●	●	●	●	●	●	●	●
Record malaria control measures used in the household	●	●	●	●	●	●	●	●	●
Record malaria prevention and risk factors	●	●	●	●	●	●	●	●	●
Take capillary blood sample ~~(up to 500 µL)~~[3]	●	●	●	●	●	●	●	●	●
Assessment of RDT[4]	●	●	●	●	●	●	●	●	●
Study conclusion	●	●	●	●	●	●	●	●	●

● is used to indicate a study procedure that requires documentation in the individual eCRF.

1. ***The new sites will join the study after survey 3, depending on when they are included in EPI-MAL 002/ 003. The total surveys at these new sites will therefore be less than 9***~~. Surveys may not be in consecutive years and the total will then be less than 5~~
2. RTS,S/AS01 and 3rd dose DTP/***HepB/Hib*** and first dose measles EPI vaccinations, only
3. Capillary blood sample for determination of parasite prevalence (blood slides and NAAT by filter paper)
4. ~~Only~~ In the event of measured fever at time of visit (axillary temperature ≥37.5°C) or fever reported in last 24 hours ***or other symptoms/signs of clinical malaria***, a rapid diagnostic test (RDT) will be conducted using capillary blood sample taken for blood slide preparation.

Table 3 List of study procedures to be conducted during survey

Epoch	Epoch 001	Epoch 002	Epoch 003	Epoch 004	Epoch 005	*Epoch 006*	*Epoch 007*	*Epoch 008*	*Epoch 009*
Study Group[1]	Survey 1	Survey 2	Survey 3	Survey 4	Survey 5	*Survey 6*	*Survey 7*	*Survey 8*	*Survey 9*
Timepoint	Year 1	Year 2	Year 3	Year 4	Year 5	*Year 6*	*Year 7*	*Year 8*	*Year 9*
Site specific information collection - Meteorological data ~~(if available)~~ [1]	●	●	●	●	●	●	●	●	●
Site specific information collection – Malaria Control Programme	●	●	●	●	●	●	●	●	●

● is used to indicate a study procedure that requires documentation in the individual eCRF.
~~Surveys may not be in consecutive years and the total will then be less than 5.~~ Availability of meteorological data will be based on the site having the weather station. All sites received weather stations either post Survey 1 or 2.

5.5.4 Check and record medications/vaccinations

Record RTS,S/AS01*E* (all doses) and other vaccinations (i.e. 3rd dose DTP***/HepB/Hib*** ~~pentavalent~~ and first dose measles EPI vaccinations) administered, including dates. The vaccination status will be recorded in the eCRF.

5.5.7 Collect data on malaria control interventions

Record the following malaria control measures in the subject's eCRF:

- Residual spraying, mosquito net usage, seasonal malaria chemoprevention (SMC), intermittent ~~preventative~~ ***preventive*** treatment in infants (IPTi), and ~~ACT~~ ***all anti-malaria*** therapy received within the last 14 days.

5.5.9 Capillary blood sampling

A capillary blood sample ~~(up to 500µL),~~ collected by finger/heel prick, will be taken during the study visit for the assessment of parasitaemia (see Section 5.6.2). The following biological samples will be taken at each survey visit:

- Blood for asexual and sexual (gametocyte) microscopy (2 slides ~~[up to 4 slides might be prepared according to study site standard operating procedures (SOPs)].~~ approximately 2 drops on each microscope slide).

In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in last 24 hours ***or other symptoms/signs of clinical malaria***, a RDT will also be conducted using the capillary blood sample.

5.5.10 Site specific information collection

All sites received a weather station either post Survey 1 or Survey 2.

5.6 Biological sample handling and analysis

- It is also possible that future findings may make it desirable to use the samples acquired in this study for future research, not described in this protocol. Therefore, all subjects in countries where this is allowed ***when signing the Informed Consent Form*** will be invited to give another specific consent to allow GSK or a contracted partner ***to*** use the samples for future research including development of tests and their quality assurance.

5.6.2 Biological samples

Table 4 Biological samples

Sample type	Quantity	~~Sample volume (max)~~	Timepoint
Whole blood	Approximately 1 drop (RDT assessment)*	~~0.06~~	Survey Visit
Whole blood	Approximately 4 drops; ***1 drop for the thin smear and up to 3 drops for the thick smear*** ~~up to 2 drops on each microscope slide~~ (merozoite and gametocyte microscopy assessment)	~~0.24 mL~~	Survey Visit
Whole blood	~~Approximately~~ 2 ***to 3*** drops; filter paper collection parasite and gametocyte NAAT assessment)	~~0.12 mL~~	Survey Visit

RDT = Rapid Diagnostic Test
NAAT = Nucleic Acid Amplification Test
*~~Only in~~ In the event of measured fever at time of visit (axillary temperature ≥37.5°C) or reported fever in last 24 hours ***or other symptoms/signs of clinical malaria.***

5.6.3 Laboratory assays

Please refer to ~~APPENDIX B~~ ***APPENDIX A*** for a detailed description of the assays performed in the study. Please refer to ~~APPENDIX C~~ ***APPENDIX B*** for the address of the clinical laboratories used for sample analysis.

In the event of fever measured at time of visit (axillary temperature ≥37.5°C) or reported fever in last 24 hours ***or other symptoms/signs of clinical malaria***, a RDT will be conducted. The clinical management of subjects presenting with malaria as identified by RDT or microscopy will follow National guidelines. Subjects will receive appropriate care according to standard clinical practice.

All blood slides with thick and thin smears will be made in duplicate. ~~In the study sites where study site SOPs require the preparation of separate thin and thick smears, up to 4 blood slides might be prepared.~~ One slide with thick and thin smears, ~~or two slides with separate thick and thin smears,~~ will be sent for storage to a GSK dedicated laboratory facility and the remaining slide~~(s)~~ will be stored at the study site. For each slide, parasitaemia will be determined independently by two readers and in the case of non-concordance an additional read by a third independent reader will be carried out. Since there will be no full blood count performed in the study subjects the used methodology for the determination of *P. falciparum* asexual parasite density may be based on an assumed white cell count of 8000/µL. Please refer to ~~APPENDIX B~~ ***APPENDIX A*** for a description of other methodologies for the determination ***of*** *P. falciparum* asexual parasite density.

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[redacted]

7.1.2 Secondary endpoints

- Occurrence of uptake and timing of the third dose of DTP***/HepB/Hib*** ~~pentavalent~~ and the first measles EPI vaccines

  Criteria/definitions: vaccination record of receipt of dose 3 of the DTP***/HepB/Hib*** ~~pentavalent~~ and the first dose ***of the*** measles EPI vaccines.

7.2.3 Children aged 5 to < 10 years

Since the precision of 0.25 was adequate and determined for the WHO (children aged 6 months to <5 years) and JTEG (children aged 2 to <10 years) definitions, the sample size for the subgroup of children 5-9 years was fixed at 200 which gives a relative standard error equal to a maximum of 0.35. In addition, it is anticipated that children in this older age group are more likely to be at school and it may take longer to recruit this age group with subsequent logistics and financial implications.

7.7.1.1 Overall

First the trends in parasite prevalence between each cross-sectional malariometric surveys will be tested using the Cochran-Armitage trend test [Agresti, 1990]. This hypothesis test will be performed on the parasite prevalence ***computed on the independent samples of subjects in each survey,*** within each site separately.

7.7.1.2.1 Annual fluctuations: vaccine ineligible subgroup

Once the cross-surveys are collected, the independent samples of subjects in each survey will be ***tested and*** assessed using a Chi-square statistic to test the significance of the differences among the parasite prevalences in each survey; meaning annual fluctuations.

7.7.2 Other prevalences and proportions

Prevalence ~~estimate~~ for each segment will be estimated using the following criteria for level of endemicity: ‘high’ ≥ 60%, ‘moderate’ 20%-59%, and ‘low’ <20% relating to the proportion of infected children in each segment [Snow 1997; Omumbo 1998].

The proportion of subjects having received the third dose of DTP/***HepB/Hib*** ~~pentavalent~~ and the first dose of measles EPI vaccine will be estimated as the ratio of the subjects having received the third dose of DTP/***HepB/Hib*** ~~pentavalent~~ and the first dose of

measles EPI vaccine divided by the number of subjects who should have received the third dose of DTP/pentavalent and the first dose of measles EPI (i.e. 14 weeks and 9 months of age, respectively). Moreover, among the subjects having received the third dose of DTP/***HepB/Hib*** ~~pentavalent~~ and the first dose of measles EPI vaccine, the proportions of subjects having received them on time, in advance and with delay will be estimated.

7.8 Analysis of tertiary objectives

The comparisons of asexual and sexual (gametocyte) parasitaemia measured by microscopy and NAAT will be done using ***Cohen's Kappa coefficient*** ~~Fisher's exact test~~. The hypothesis test will be done per centre, and overall. ~~No correction for multiple testing will be done.~~

7.10.1 Sequence of analyses

Statistical reports will be written after each epoch. A clinical report will be written ***after*** ~~each epoch by GSK~~ ***Surveys 2 and 5 and an integrated report will be written at the end of the study.***

~~APPENDIX A STUDY SITES~~

~~PI Last Name~~	~~PI First Name~~	~~Country- Study Site~~	~~Location~~
~~Owusu-Agyei~~	~~Seth~~	~~GHANA - KINTAMPO~~	~~Kintampo Health Research Centre~~ Kintampo GHANA
~~Otieno~~	~~Walter~~	~~KENYA - KOMBEWA~~	~~Walter Reed Project - Kombewa Clinical Research Centre~~ Opposite Kisumu West District Hospital Kisumu Bondo Road Kisumu KENYA
~~Lusingu~~	~~John~~	~~TANZANIA - KOROGWE~~	~~Joint Malaria Programme (JMP)~~ Korogwe District Hospital, New Laboratory Building, Korogwe, Tanga TANZANIA
~~Gaye~~	~~Omar~~	~~SENEGAL – KEUR SOCE~~	~~Centre de Recherche de Keur Socé~~ ~~Departement de Parasitologie~~ Faculté de Médecine Université Cheikh Anta Diop, Dakar SENEGAL
~~Sokhna~~	~~Cheikh S~~	~~SENEGAL - NIAKHAR~~	~~UMR 198 URMITE~~ ~~Unite de Recherche sur les Maladies Infectieuses et Tropicales Emergentes~~ Campus commun IRD-UCAD de Hann BP 1386 CP 18524 Dakar SENEGAL
~~Bienvenu Sirima~~	~~Sodiomon~~	~~BURKINA FASO - SAPONE~~	~~Centre National de recherche et de Formation sur le paludisme (CNRFP)~~ 01 BP 2208 Ouagadougou 01 BURKINA FASO
~~Sie~~	~~Ali~~	~~BURKINA FASO - NOUNA~~	~~Centre de Recherche en Santé de Nouna,~~ ~~PO BOX 02 Nouna~~ ~~BURKINA FASO~~

APPENDIX A

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[redacted]

APPENDIX ~~C~~ ***B*** CLINICAL LABORATORIES

Table 10 Outsourced laboratories

Laboratory	Address
Koninklijk Instituut voor de Tropen (KIT) (Royal Tropical Institute) ***Academic Medical Center (AMC)*** Laboratory for clinical parasitology, L1-247 Department of Medical Microbiology	Meibergdreef 39 ***9*** 1105 AZ Amsterdam The Netherlands

GlaxoSmithKline Biologicals SA

Vaccines R & D

Protocol Amendment 2

eTrack study number and Abbreviated Title	116682 (EPI-MALARIA-005 BOD AME)
Amendment number:	Amendment 2
Amendment date:	14 September 2018
Co-ordinating author:	PPD, Freelance Science Writer for GSK Biologicals

Rationale/background for changes:

A delay in the implementation of the RTS,S/AS01$_E$ vaccine in the 3 countries participating in the World Health Organisation (WHO)-led Malaria Vaccine Implementation Programme (MVIP) has resulted in a delay to the start of EPI-MAL-003. As a consequence, EPI-MAL-005, being an ancillary study to EPI-MAL-003, will need to be extended in order to mirror the EPI-MAL-003 timeline. The need for an additional survey is the trigger for the second amendment of this protocol. Additional revisions to the protocol are listed below.

1. The current protocol – protocol amendment 1 - currently details 9 annual surveys with study duration of up to 9 years. The study will include at least 1 further annual survey, lasting for at least 10 years in total. Thus, the longest participating sites will perform the study for at least 10 years meaning 10 surveys, whilst some sites joining later will not perform as many surveys. Protocol text has been revised accordingly.
2. Country and study site participation have changed during the course of the study following WHO recommendations for pilot implementation of RTS,S/AS01$_E$ in settings with moderate-to-high transmission of malaria and WHO Regional Office for Africa selection for the initial introduction of RTS,S/AS01$_E$ in 3 countries (Ghana, Kenya and Malawi) through the MVIP. EPI-MAL-003 study site selection will be performed following Ministries of Health pre-selection and according to WHO guidance in the framework of the MVIP, to include 4 sites in each of the 3 countries selected for the MVIP. Being an ancillary study to EPI-MAL-002 and EPI-MAL-003 studies, EPI-MAL-005 is/will be conducted in study sites conducting EPI-MAL-002 and/or EPI-MAL-003. Clarification on the countries and sites participating in the study has been provided.
3. In response to a Corrective and Preventive Action following a Critical Quality Attributes audit conducted in Kintampo, Ghana, reference to study conduct in accordance with ‘Good Pharmacoepidemiology Practices (GPP) guidelines’ has been added to Section 5.1 ‘Regulatory and ethical considerations, including the informed consent process’ to align with STD-POL-GSKF-408, and additionally protocols EPI-MAL-002 and EPI-MAL-003.

4.	Vaccine eligible and ineligible subgroups were defined based on assumptions on the duration of follow-up of the EPI-MAL-005 study and date of vaccine implementation. This amendment primarily documents the extension of the study for at least 1 further survey. Furthermore, the date of implementation of the vaccine has yet to be confirmed. It is therefore not possible to apply these assumptions and the applicable text in Section 7.7.1.2 'By vaccine eligible/ineligible subgroup: Statistical analyses for vaccine association adjustments and association between vaccine and transmission' has been revised.

Amended text has been included in *bold italics* and deleted text in ~~strikethrough~~ in the following sections:

Contributing authors

- ……
- PPD **, *Clinical Manager Safety Physician***
- PPD , PPD ~~Senior Manager, Global Study Management~~
- PPD ~~/~~ PPD , Clinical Laboratory Sciences-SM Business and Decision Life Sciences ~~/ external consultant~~ for GSK Biologicals
- ……..
- PPD **, *Local Delivery Lead***
- PPD , external consultant for GSK Biologicals
- …….
- PPD , Study Delivery Lead, ~~SynteractHCR Benelux NV~~ ***Synteract®*** for GSK Biologicals
- PPD **, *Lead Epidemiologist-Malaria, Aixial for GSK Biologicals***
- ……..
- PPD **, *Senior Lead Epidemiologist-Malaria***
- PPD , Study Data Manager, ***TCS for GSK Biologicals***
- PPD **, *Clinical & Epidemiology Project Lead, DDW Vaccines***
- PPD , ~~Senior Local Delivery Lead~~ PPD
- ……
- PPD , Oversight Data Manager~~, Business and Decision Life Sciences for GSK Biologicals~~
- PPD ~~and~~ PPD Study Data Manager
- PPD **, *Study Statistician***

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Protocol Amendment 2 Investigator Agreement

I agree:

- ……..
- To assume responsibility for the proper conduct of the study at ~~this~~ ***the*** site***(s)***.

SYNOPSIS

Rationale for the study

Following the pivotal Phase III study of the candidate malaria vaccine RTS,S/AS01$_E$ (Malaria-055), two consecutive vaccine safety monitoring studies (EPI-MAL-002 and EPI-MAL-003) will be conducted to monitor incidence rates of meningitis, protocol defined adverse events of ~~specific~~ ***specific*** interest (AESI), and of other adverse events leading to hospitalisation or death, in children. The first study, EPI-MAL-002, is a ***baseline*** surveillance study prior to RTS,S/AS01$_E$ authorisation in the country; the second study, EPI-MAL-003, will more specifically monitor RTS,S/AS01$_E$ safety***, as well as vaccine effectiveness and impact,*** and will only start when RTS,S/AS01$_E$ is ~~registered and~~ authorised ***and implemented*** in the country. The World Health Organi~~sz~~ation's ***(WHO's)*** Strategic Advisory Group of Experts (SAGE) on Immunization and the Malaria Policy Advisory Committee (MPAC) recommended pilot implementations of RTS,S/AS01$_E$ in children of 5–17 months of age, in parts of 3-5 sub-Saharan African ~~(SSA)~~ countries, administering 3 doses of the vaccine to children aged 5-9 months of age in areas of moderate-to-high transmission of malaria with a fourth dose 15-18 months later. The first vaccine introduction is foreseen in 2018. The secondary endpoints of these studies also include monitoring the incidence of malaria disease as diagnosed during out-patient visits or hospitalisation. ~~Up to seven~~ Health and Demographic Surveillance System (HDSS) (or equivalent system) sites*[1]* in countries in ~~S~~*s*ub-Saharan Africa will participate in these studies, enrolling approximately 30 000 children <5 years of age in EPI-MAL-002 and approximately 45 000 children <5 years in EPI-MAL-003.

This epidemiology study (EPI-MAL-005) is planned to run in parallel with these two studies, enrolling from the same HDSS ***(***or ~~(~~equivalent system) populations. The primary objectives of this study are to produce longitudinal estimates of parasite

prevalence in humans, and record malaria control measure usage in areas where EPI-MAL-002 and EPI-MAL-003 studies will take place.……..

Outside of the controlled setting of a clinical trial, there is the risk that usage of malaria control interventions such as ***indoor*** residual spraying and bednets may change following vaccine introduction. ……

*[1] **Throughout the document, the terms of site, cluster and centre are used interchangeably, having the same meaning.***

Study design

- Type of design: A multi-centric, epidemiology longitudinal cross-sectional study at centres in ~~S~~***s***ub-Saharan Africa that are participating in GSK's EPI-MAL-002 and EPI-MAL-003 studies.
- …….
- Using ***Geographic Information System (***GIS***)*** to determine geographical variability in MTI locally: Study areas will be mapped by villages using grid referencing. Subjects will be attributed to their village, however, to avoid PII (personally identifiable information); small villages will be grouped when the number of participants is less than 10, ~~such~~ ***so*** that it is not possible to identify one subject from one village. ……..
- ……
- This study will involve up to ~~9~~ ***10*** annual cross sectional surveys during malaria peak transmission ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies***.
- Duration of the study: up to ~~9~~ ***10*** years ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies***:
  - ……..
  - ***Epoch 010: Survey 10 at Year 10***

Synopsis Table 1 Study groups and epochs foreseen in the study

Study Group	Age (Min/Max)	Epochs									
		Epoch 001 Survey 1	Epoch 002 Survey 2	Epoch 003 Survey 3	Epoch 004 Survey 4	Epoch 005 Survey 5	Epoch 006 Survey 6	Epoch 007 Survey 7	Epoch 008 Survey 8	Epoch 009 Survey 9	*Epoch 010 Survey 10*
Study site	6 months / 9 years	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	***600 subjects***

Discussion of study design	……. ~~Nine~~ ***At least 10*** annual cross sectional surveys at peak transmission will provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by EPI-MAL-002 and EPI-MAL-003. ……
Endpoints	**Primary** • Occurrence of *P. falciparum* parasitaemia (using microscopy) Criteria/definitions: infection with *P. falciparum* determined using a blood smear slide and determined using microscopy. • Occurrence of malaria control interventions Criteria/definitions: malaria control interventions are mosquito net usage ***(including insecticide-treated nets [ITN] and long lasting insecticidal nets [LLIN]), indoor*** residual spraying ***(IRS)***, seasonal malaria chemoprevention (SMC), intermittent preventative treatment in infants (IPTi), and ACT therapy received within the last 14 days.

LIST OF ABBREVIATIONS

AESI	Adverse events of ~~specific~~ ***special*** interest
GPP	***Good Pharmacoepidemiology Practice***
LLIN	***Long lasting insecticidal nets***
MVIP	***Malaria Vaccine Implementation Programme***

GLOSSARY OF TERMS

Malaria control interventions:	Any intervention or control measure targeted at reducing malaria transmission or preventing malaria disease [World Health Organisation, 2013]. This includes ITN, ***LLIN,*** IRS, SMC, IPTi, ***IPTp*** and ACTs.

1.2 Rationale for the study

Following the pivotal Phase III study of the candidate malaria vaccine RTS,S/AS01$_E$ (Malaria-055), two consecutive vaccine safety monitoring studies (EPI-MAL-002 and EPI-MAL-003) will be conducted to monitor incidence rates of meningitis, protocol defined adverse events of ~~special~~ ***specific*** interest (AESI), and ***of*** other adverse events leading to hospitalisation~~s and~~ ***or*** death***, in children***. The first study, EPI-MAL-002, is a ***baseline*** surveillance study prior to RTS,S/AS01$_E$ authorisation in the country; the second study, EPI-MAL-003, will more specifically monitor RTS,S/AS01$_E$ safety***, as well as vaccine effectiveness and impact,*** and will only start when RTS,S/AS01$_E$ is ~~registered and~~ authorised ***and implemented*** in the country. ***The World Health Organisation's (WHO's) Strategic Advisory Group of Experts (SAGE) on immunization and the Malaria Policy Advisory Committee (MPAC) recommended pilot implementations of RTS,S/AS01$_E$ in children of 5–17 months of age, in parts of 3-5 sub-Saharan African ~~(SSA)~~ countries, administering 3 doses of the vaccine to children aged 5-9 months of age in areas of moderate-to-high transmission of malaria with a fourth dose 15-18 months later. The first vaccine introduction is foreseen in 2018.*** ~~The planned age range for licensure of the RTS,S/AS01$_E$ candidate vaccine is in children from 6 weeks of age to less than18 months.~~ The secondary endpoints of these studies ***also*** include monitoring the incidence of malaria disease as diagnosed during out-patient visits or hospitalisation. ~~Up to seven~~ Health and Demographic Surveillance System (HDSS) (or equivalent system) sites[2] in ~~different~~ countries in ~~S~~***s***ub-Saharan Africa will participate in these studies, enrolling approximately 30 000 children <5 years of age in EPI-MAL-002 and approximately 45 000 children <5 years in EPI-MAL-003.

……..

Outside of the controlled setting of a clinical trial, there is the risk that usage of malaria control interventions such as ***indoor*** residual spraying and bednets may change following vaccine introduction. …….

[2] Throughout the document, the terms of site, cluster and centre are used interchangeably, having the same meaning.

3. STUDY DESIGN OVERVIEW

……

- Type of design: A multi-centric, epidemiology longitudinal cross-sectional study at centres in ~~S~~***s***ub-Saharan Africa that are participating in GSK's EPI-MAL-002 and EPI-MAL-003 studies.
- …….
- Using Geographic Information System (GIS) to determine geographical variability in MTI locally: Study areas will be mapped by villages using grid referencing. Subjects will be attributed to their village, however, to avoid PII (personally identifiable information), small villages will be grouped when the number of participants is less than 10, ~~such~~ ***so*** that it is not possible to identify one subject from one village. ….

- ……
- This study will involve up to ~~9~~ ***10*** annual cross sectional surveys during malaria peak transmission ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies***.
- Duration of the study: up to ~~9~~ ***10*** years ***with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies:***
  - ……
  - ***Epoch 010: Survey 10 at Year 10***

Table 1 Study groups and epochs foreseen in the study

Study Group	Age (Min/Max)	Epochs									
		Epoch 001 Survey 1	Epoch 002 Survey 2	Epoch 003 Survey 3	Epoch 004 Survey 4	Epoch 005 Survey 5	Epoch 006 Survey 6	Epoch 007 Survey 7	Epoch 008 Survey 8	Epoch 009 Survey 9	***Epoch 010 Survey 10***
Study site	6 months / 9 years	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	600 subjects	***600 subjects***

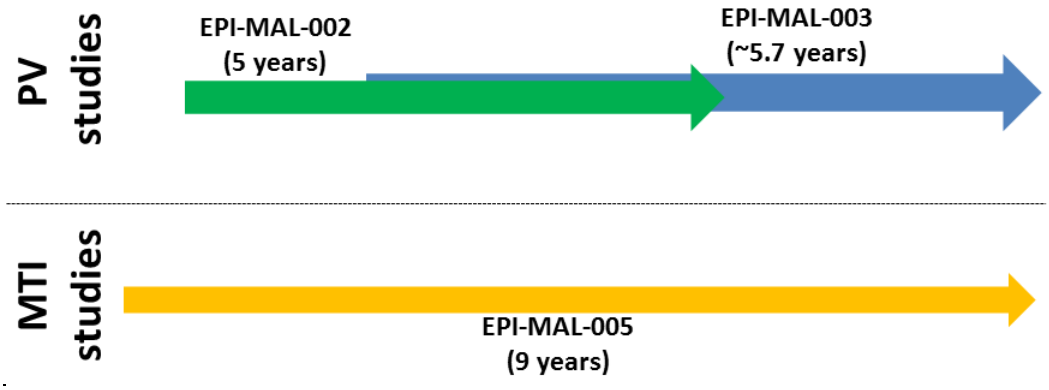
3.1. Discussion of study design

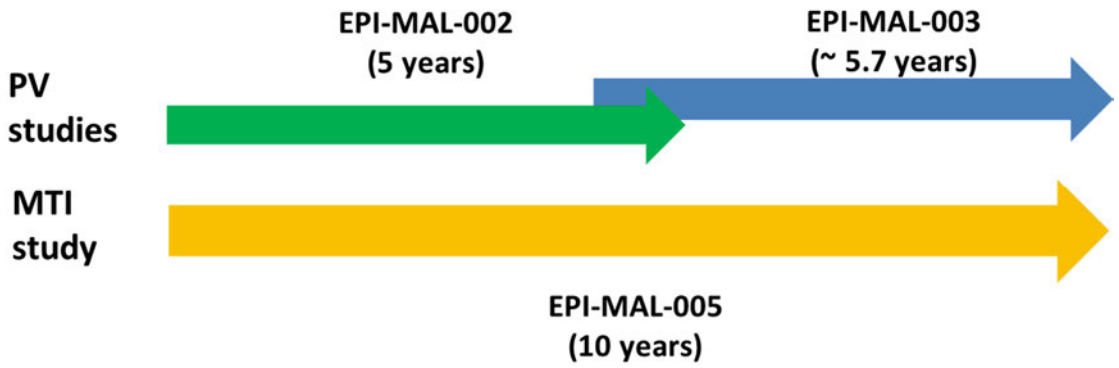
……..

~~Nine~~ ***At least 10*** annual cross sectional surveys at peak transmission will provide point estimates of parasite prevalence and subsequently a longitudinal assessment of the level of endemicity in each area covered by EPI-MAL-002 and EPI-MAL-003. …….

4.1. Number of subjects/ centres

Subjects 6 months to <10 years of age ~~will be enrolled~~ ***living*** in HDSS (or equivalent system) catchment areas ~~at~~ ***of*** the sites participating in the EPI-MAL-002 and EPI-MAL-003 studies ~~of the candidate malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa~~ ***are eligible for enrolment***~~. Up to seven HDSS (or equivalent system) sites are planned to participate in this study~~ (see Section 4.1.1). Subjects ***already*** enrolled in EPI-MAL-002 and EPI-MAL-003 are eligible for participation in this study.





4.1.1 Recruitment of study centres / investigators

~~All HDSS (or equivalent system) study sites participating in EPI-MAL-002 and EPI-MAL-003 will be approached with regard to participation in this epidemiological study.~~ ***The ancillary EPI-MAL-005 study will be conducted in sites defined in the EPI-MAL-002 and EPI-MAL-003 protocols.*** At the time of original protocol finalisation, ***identified study sites were located*** ~~these comprised sites~~ in Burkina Faso, Ghana, ***Kenya,*** Senegal, ***and*** Tanzania~~, and Kenya~~.

~~The study sites will be revised after survey 2.~~ Following the ~~World Health Organization (~~WHO~~)~~'s ~~Strategic Advisory Group of Experts (~~SAGE~~)~~ on immunization and the ~~Malaria Policy Advisory Committee (~~MPAC~~)~~ recommendations of pilot implementations of RTS,S/AS01$_E$ in 3-5 distinct settings in sub-Saharan Africa ~~(SSA)~~ restricted to moderate-to-high transmission of malaria, ~~other settings in SSA with moderate-to-high transmission of malaria might be added to the already defined EPI-MAL-002 and EPI-MAL-003 study sites. These new sites will also be added to the EPI-MAL-005 study.~~ ***site selection in some of the initially chosen EPI-MAL-002, EPI-MAL-003 and EPI-MAL-005 study sites located in low endemicity settings (i.e. in Senegal and Tanzania) had to be terminated. In April 2017, the WHO Regional Office for Africa announced that the RTS,S/AS01$_E$ vaccine will be first introduced in 3 countries (Ghana, Kenya and Malawi) through the Malaria Vaccine Implementation Programme (MVIP). Selection of the clusters that are/will participate in GSK's baseline, Phase IV and ancillary studies (i.e. EPI-MAL-002, EPI-MAL-003 and EPI-MAL-005, respectively), being fully embedded in the MVIP, depends on the cluster identification process led by the Ministries of Health according to WHO guidance. They have been, or will be, selected as follows:***

- ***Sites have been, or will be, selected from the 3 countries where the RTS,S/AS01$_E$ vaccine will be implemented (Ghana, Kenya and Malawi). Burkina Faso sites that started EPI-MAL-005 will early terminate the conduct of the study following Survey 4; data from these sites will be presented in the interim report planned following Survey 5.***
- ***As currently planned in the MVIP and according to WHO guidance, 4 study sites (corresponding to 4 clusters of the MVIP) in each of the 3 countries selected for the RTS,S/AS01$_E$ pilot implementation programme (12 study sites/clusters in total) are planned to be part of EPI-MAL-005.***

- ***Of note, all study sites are submitted to a comprehensive scientific and operational study site assessment conducted by GSK, which will determine study feasibility in those sites.***

~~The study sites in Senegal and Tanzania with low malaria transmission will no longer participate in the study after Survey 2.~~

In summary, selection of sites will be performed in EPI-MAL-002 and EPI-MAL-003 studies following Ministries of Health pre-selection and according to WHO guidance, to include 4 sites in each of the 3 countries selected for the MVIP. EPI-MAL-005 is/will be conducted in study sites conducting EPI-MAL-002 and/or EPI-MAL-003.

5.1. Regulatory and ethical considerations, including the informed consent process

The study will be conducted in accordance with the ICH Guideline for Good Clinical Practice (GCP)***, Guidelines for Good Pharmacoepidemiology Practices (GPP) [ISPE, 2015]***, ~~or~~ other applicable guidelines, all applicable subject privacy requirements and the guiding principles of the Declaration of Helsinki.

5.4. Outline of study procedures

Table 2 List of study procedures to be conducted at each survey visit

Epoch	**Epoch 001**	**Epoch 002**	**Epoch 003**	**Epoch 004**	**Epoch 005**	**Epoch 006**	**Epoch 007**	**Epoch 008**	**Epoch 009**	***Epoch 010***
Study Group[1]	**Survey 1**	**Survey 2**	**Survey 3**	**Survey 4**	**Survey 5**	**Survey 6**	**Survey 7**	**Survey 8**	**Survey 9**	***Survey 10***
Timepoint	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	***Year 10***
Informed consent	●	●	●	●	●	●	●	●	●	●
Check inclusion/exclusion criteria	●	●	●	●	●	●	●	●	●	●
Record demographic details	●	●	●	●	●	●	●	●	●	●
Record subject's vaccination status[2]	●	●	●	●	●	●	●	●	●	●
Record any anti-malarial medication or other medication received within the previous 14 days	●	●	●	●	●	●	●	●	●	●
Record relevant medical history (hospitalisation, reported fever, and care seeking behaviour)	●	●	●	●	●	●	●	●	●	●
Record axillary body temperature	●	●	●	●	●	●	●	●	●	●
Record malaria control measures used in the household	●	●	●	●	●	●	●	●	●	●
Record malaria prevention and risk factors	●	●	●	●	●	●	●	●	●	●
Take capillary blood sample[3]	●	●	●	●	●	●	●	●	●	●

Epoch	**Epoch 001**	**Epoch 002**	**Epoch 003**	**Epoch 004**	**Epoch 005**	**Epoch 006**	**Epoch 007**	**Epoch 008**	**Epoch 009**	***Epoch 010***
Study Group[1]	**Survey 1**	**Survey 2**	**Survey 3**	**Survey 4**	**Survey 5**	**Survey 6**	**Survey 7**	**Survey 8**	**Survey 9**	***Survey 10***
Timepoint	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	***Year 10***
Assessment of RDT[4]	●	●	●	●	●	●	●	●	●	●
Study conclusion	●	●	●	●	●	●	●	●	●	●

Footnotes to Table 2:

● is used to indicate a study procedure that requires documentation in the individual eCRF

[1] ~~The n~~New sites will join the study after survey 3, depending on when they are included in EPI-MAL-002/-003. The total surveys at these new sites will therefore be less than ~~9~~***10***.

[2] RTS,S/AS01 and 3rd dose DTP/HepB/Hib and first dose measles EPI vaccinations, only

[3] Capillary blood sample for determination of parasite prevalence (blood slides and NAAT by filter paper)

[4] In the event of measured fever at time of visit (axillary temperature ≥37.5°C) or fever reported in last 24 hours or other symptoms/signs of clinical malaria, a rapid diagnostic test (RDT) will be conducted using capillary blood sample taken for blood slide preparation.

Table 3 List of study procedures to be conducted during survey

Epoch	**Epoch 001**	**Epoch 002**	**Epoch 003**	**Epoch 004**	**Epoch 005**	**Epoch 006**	**Epoch 007**	**Epoch 008**	**Epoch 009**	***Epoch 010***
Study Group	**Survey 1**	**Survey 2**	**Survey 3**	**Survey 4**	**Survey 5**	**Survey 6**	**Survey 7**	**Survey 8**	**Survey 9**	***Survey 10***
Timepoint	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	***Year 10***
Site specific information collection - Meteorological data [1]	●	●	●	●	●	●	●	●	●	●
Site specific information collection – Malaria Control Programme	●	●	●	●	●	●	●	●	●	●

● is used to indicate a study procedure that requires documentation in the individual eCRF.

[1] Availability of meteorological data will be based on the site having the weather station. All sites received weather stations either post Survey 1 or 2 or at study start for the new sites.

5.5.7. Collect data on malaria control interventions

Record the following malaria control measures in the subject's eCRF:

- ***Indoor*** ~~R~~***r***esidual spraying ***(IRS)***, mosquito net usage ***(including insecticide-treated nets [ITN] and long lasting insecticidal nets [LLIN])***, seasonal malaria chemoprevention (SMC), intermittent preventive treatment in infants (IPTi), and all anti-malaria therapy received within the last 14 days.

5.5.10. Site specific information collection

…….

Centre specific information about interventions from the malaria control programme in the study area, such as bednet usage ***(including ITN and LLIN)***, IRS, ~~RDT,~~ ACT, SMC, IPTp and IPTi, will be collected by questionnaire and recorded in a separate database to that for subject-specific data.

7.1.1. Primary endpoints

- Occurrence of *P. falciparum* parasitaemia (using microscopy)

  Criteria/definitions: infection with *P. falciparum* determined using a blood smear slide and determined using microscopy.

- Occurrence of malaria control interventions

  Criteria/definitions: malaria control interventions are mosquito net usage ***(including insecticide-treated nets [ITN] and long lasting insecticidal nets [LLIN]), indoor*** residual spraying ***(IRS)***, seasonal malaria chemoprevention (SMC), intermittent preventative treatment in infants (IPTi), and ACT therapy received within the last 14 days.

7.2.1 Children aged 6 months to <5 years

…….

~~Up to seven centres will take part in this study.~~ ~~These~~ ~~centres~~ ***Study sites*** are in different endemicity classes, so a sample of 400 subjects in this age class will allow for suitable confidence limits around parasite prevalence estimates for sites within each of the endemicity classes.

7.7.1.2. By vaccine eligible/ineligible subgroup: Statistical analyses for vaccine association adjustments and association between vaccine and transmission

For the analysis of association between RTS,S/AS01$_E$ vaccine and transmission, two subgroups must be considered:

- Vaccine eligible subgroup (see glossary of terms for definition). ~~After introduction of the vaccine, there will be a catch-up for children less than 18 months old. Taking into account the 18 months of follow-up for the vaccine safety study, the oldest children vaccinated who could potentially be enrolled could be 3.5 years old.~~ This subgroup will be used to assess the association between vaccination and transmission intensity, assuming a constant MTI in unvaccinated subjects (which will be measured using the second subgroup)..

- Vaccine ineligible subgroup (see glossary of terms for definition). Due to the fact that the main reservoir of malaria is in the population between 5-20 years old (based on data collected in parallel [Epi-Mal-001 study] to the pivotal efficacy Phase III trial, not published) and MTI will be assessed for ~~up to 2~~ ***approximately 5*** years following the introduction of the vaccine, it will be assumed that there will be negligible herd immunity effect. Therefore, this subgroup will be used to detect any annual fluctuation (control group). If there is any herd effect, then the vaccine effect will be an underestimate.

~~Assuming a sample size of 600 subjects per centre, and per survey, and a similar sample size of children aged 0 to <5 years (JTEG-requested age and MTI reference for RTS,S/AS01 vaccine efficacy by research centre-transmission intensity, pending Phase III data) and 2 to <10 years (WHO definition [WHO, 1963]); and trying to maximize the sample size of the 0-2 year subgroup, it is expected to have 240 subjects in the vaccine eligible subgroup and 360 subjects in the vaccine ineligible subgroup.~~

10. REFERENCES

International Society for Pharmacoepidemiology (ISPE). Guidelines for Good Pharmacoepidemiology Practices (GPP). Rev 3 (June 2015). http://www.pharmacoepi.org/resources/guidelines_08027.cfm; 2015. Accessed 14 June 2017.

Statistical Analysis Plan

Study alias & e-track number(s): 116682 (EPI-MALARIA-005 BOD AME)

Detailed Title:	An epidemiology study to assess *Plasmodium falciparum* parasite prevalence and malaria control measures in catchment areas of two studies pre- and post RTS,S/AS introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa.
SAP Version:	***Amendment 2 Final***
SAP Date:	***08APR2020***
Scope:	All data pertaining to the above study

Statistical Analysis Plan

Study alias & e-track number(s): 116682 (EPI-MALARIA-005 BOD AME)

TABLE OF CONTENTS

PAGE

Statistical Analysis Plan	
Study alias & e-track number(s): 116682 (EPI-MALARIA-005 BOD AME)	

The SAP is divided into 2 parts:

- first part detailing the analyses to be performed (current document)
- second part: annexe (called TFL) describing the flow and format of tables, figures and listings to be annexed to the SR.

LIST OF ABBREVIATIONS

ACT	Artemisinin-based combination therapy
ATP	According to protocol
CI	Confidence interval
CTRS	Clinical Trial Registry
eCRF	Electronic case report form
GEE	Generalized estimating equations
GSK	GlaxoSmithKline
ICF	Informed consent form
IPTi	Intermittent preventative treatment in infants
IRS	Indoor residual spray
JTEG	Joint technical expert group
LL	Lower limit
LSAF	Life Science Analytics Framework
NAAT	Nucleic acid amplification test
OR	Odds Ratio
P. falciparum	*Plasmodium falciparum*
P. vivax, P. malariae, P. ovale	*Plasmodium vivax, Plasmodium malariae, Plasmodium Ovale*
PII	Personally identifiable information
QT-NASBA	Quantitative nucleic acid sequence-based amplification
QT-PCR	Quantitative polymerase chain reaction
RDT	Rapid diagnostic test
RTS	Hybrid protein comprising HBs (hepatitis B surface antibody) and CSP portions
RTS,S	Particulate antigen, containing both RTS and HBs proteins
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SAR	Statistical Analysis Report
SD	Standard Deviation
SMC	Seasonal malaria chemoprevention
TFL	Tables, Figures and Listings
UL	Upper limit
WHO	World Health Organization

Statistical Analysis Plan	
Study alias & e-track number(s): 116682 (EPI-MALARIA-005 BOD AME)	

1. DOCUMENT HISTORY

Date	Version	Description
22-SEP-2015	Final	
19-DEC-2016	Amendment 1	• Cohen's Kappa coefficient added for the comparison between microscopy and NAAT (tertiary objective) • Precisions added regarding the age derivation • Update following protocol amendment 1 (from 5 surveys to 9 surveys)
08-APR-2020	***Amendment 2***	• ***Update following protocol amendment 2:*** ○ ***The study is extended from 9 surveys to 10 surveys*** ○ ***Changes in sites participating according to sites enrolled in EPI-MAL-002 and EPI-MAL-003 studies.*** ○ ***Update the definition of vaccine eligible/ineligible subgroup based on assumptions on the duration of the EPI-MAL-005 study and dates of RTS,S vaccine implementation start.*** • ***Update of computation rules to manage discrepancies detected during the first surveys and already mentioned in previous SAR.*** • ***Additional analyses to support the EPI-MAL-003 study analysis and interpretation.*** ○ ***Demographic tables and endpoints from primary objectives will be analysed by gender, JTEG age group, vaccine eligible group and RTS,S vaccine group.*** ○ ***Adaptation of the trends analysis due to the update of the sites and the extension of the study.*** ○ ***Details of the dataset that will be incorporated into analyses from EPI-MAL-002 and EPI-MAL-003 studies are removed and will be further detailed in their respective SAPs.***

Statistical Analysis Plan	
Study alias & e-track number(s): 116682 (EPI-MALARIA-005 BOD AME)	

2. STUDY DESIGN

2.1. Study design overview

- ***Type of design: A multi-centric, epidemiology longitudinal cross-sectional study at centres in sub-Saharan Africa that are participating in GSK's EPI-MAL-002 and EPI-MAL-003 studies.***
- ***There will be no study vaccine administered in this epidemiology study.***
- ***Study population: Subjects 6 months to <10 years of age.***
- ***Type of study: self-contained***
- ***All medications that may influence malaria parasitaemia within 14 days prior to each survey will be recorded.***
- ***Axillary body temperature of all subjects at the time of the survey will be recorded.***
- ***Biological Samples: A capillary blood sample will be obtained for evaluation of malaria infection by blood slide and NAAT. In the event of measured fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours or other symptoms/signs of clinical malaria, a rapid diagnostic test (RDT) will be conducted. If the RDT is positive, treatment will be given according to National guidelines. If a subject for whom no RDT was required is identified as being parasite positive following microscopy, National guidelines should be followed for clinical management of the subject.***
- ***Microscopy and NAAT will be used to evaluate the level of asexual and sexual parasitaemia.***
- ***Serious adverse events (SAEs) associated with the study procedure (capillary blood sampling) will be collected.***
- ***Using Geographic Information System (GIS) to determine geographical variability in MTI locally: Study areas will be mapped by villages using grid referencing. Subjects will be attributed to their village, however, to avoid PII (personally identifiable information), small villages will be grouped when the number of participants is less than 10, so that it is not possible to identify one subject from one village. Therefore the study area will be divided into segments with a minimum of 10 subjects by segment regrouping villages by proximity if needed. Villages will be grouped at the time of random sampling of the study population. A map will be drawn showing the location of numbered segments, each numbered with a unique ID code and containing one or more villages. This map will NOT be submitted to GSK, but segments will be reported by their ID code and surface (km^2) and subjects will be attributed to a segment code in the study database.***

- ***Each study site will be requested annually to provide centre specific information about interventions from the malaria control program in the study area and, if facilities are available, to provide meteorological data for the study site such as rainfall and temperature. The information will be collected in the form of a questionnaire that will be recorded in a separate database to that for subject-specific data.***
- ***Data collection: Electronic Case Report Form (eCRF).***
- ***This study will involve up to 10 annual cross-sectional surveys during malaria peak transmission with possible further extension, dependent on the duration of the EPI-MAL-002 and EPI-MAL-003 studies.***

2.2. Study groups

The following group names will be used for the statistical analyses:

Group order in tables	Group label in tables	Group definition for footnote
P. falciparum infection status measured by microscopy		
1	PF_INF	Subjects infected by *P. falciparum* parasitemia*
2	NOT_INF	Subjects not infected by *P. falciparum* parasitemia
3	UNK	Unknown
P. falciparum infection status measured by NAAT		
1	PF_INF_NAAT	Subjects infected by *P. falciparum* parasitemia*
2	NOT_INF_NAAT	Subjects not infected by *P. falciparum* parasitemia
3	UNK_NAAT	Unknown
Age classes according JTEG definition [years]		
1	0.5-4Y	6 months – 4 years at ICF date
2	5-9Y	5 – 9 years at ICF date
3	UNK	Unknown
Age classes according WHO definition [years]		
1	0.5-1Y	6 months – 1 year at ICF date
2	2-9Y	2 – 9 years at ICF date
3	UNK	Unknown
Vaccine eligible age group		
1	Eligible	Vaccine eligible age group*
2	Ineligible	Vaccine ineligible age group*
RTS,S/AS01$_E$ vaccination status		
1	Vaccinated	Children vaccinated with RTS,S/AS01$_E$ malaria vaccine*
2	Unvaccinated	Children unvaccinated with RTS,S/AS01$_E$ malaria vaccine*
Parasites density group measured by microscopy		
1	Low	Low : < 2500 parasites/ µl
2	Medium	Medium : 2500 – 9999 parasites/ µl
3	High	High : 10000 – 19999 parasites/ µl
4	Vhigh	Very high : >= 20000 parasites/ µl
5	Neg	Negative
Parasites density group measured by NAAT		
1	Low_NAAT	Low : < 1000 parasites/ µl
2	Medium_NAAT	Medium : 1000 – 10000 parasites/ µl
3	High_NAAT	High : > 10000 parasites/ µl
5	Neg_NAAT	Negative

* see section 7.4

Tables will, in general, be displayed by centre according to *P. falciparum* infection status and age classes. When it will not be the case (e.g. for some demographic tables), it will be explicitly mentioned.

According to the sites finally participating in the EPI-MAL-002 and EPI-MAL-003 studies, the following study sites names will be used for the statistical analyses:

Site n°	Vaccine exposed status	Group label used in tables	Country	Districts (eCRF denomination - Demography)
Study site				
207078	Unexposed	207078_BF_Nouna	Burkina Faso	Nouna
207079	Unexposed	207079_BF_Sapone	Burkina Faso	Sapone
207083	Exposed	207083_GH_Kintampo_EXP	Ghana	Kintampo North, Kintampo South, Nkoranza North and Techiman North
207083	Unexposed	207083_GH_Kintampo_UNEXP	Ghana	Nkoranza South and Techiman South
228607	Exposed	228607_GH_Navrongo_EXP	Ghana	Kassena-Nankana West and East
228607	Unexposed	228607_GH_Navrongo_UNEXP	Ghana	Builsa North and South
235578	Exposed	235578_KE_Gem	Kenya	Gem (Siaya)
235578	Unexposed	235578_KE_Bondo	Kenya	Bondo (Siaya)
207082	Exposed	207082_KE_Kombewa	Kenya	Kombewa
235579	Unexposed	235579_KE_Nyando	Kenya	Nyando
233149	Exposed	233149_MA_Mangochi	Malawi	Exposed Malawi 1
233149	Unexposed	233149_MA_Monkey Bay	Malawi	Unexposed Malawi 1
233150	Exposed	233150_MA_St Monfort	Malawi	Exposed Malawi 2
233150	Unexposed	233150_MA_Chikwawa	Malawi	Unexposed Malawi 2
207080	Unexposed	207080_SN_Niakhar	Senegal	Niakhar
207084	Unexposed	207084_SN_Keur Soce	Senegal	Keur Soce
207081	Unexposed	207081_TZ_Korogwe	Tanzania	Korogwe

The Senegal and Tanzania sites for which participation in the study was early terminated, were included in Survey 1 and Survey 2 only.

The Burkina Faso sites for which participation in the study was early terminated, were included in Survey 1 to Survey 4 only.

3. OBJECTIVES

As per protocol.

3.1. Co-Primary objectives

In subjects aged ≥6 months and <10 years:

- To obtain longitudinal estimates of *P. falciparum* parasite prevalence in order to characterise malaria transmission intensity in a standardised way at centres conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.

- To obtain longitudinal estimates of the use of malaria control interventions in centres conducting the EPI-MAL-002 and EPI-MAL-003 studies before and after the introduction of the malaria vaccine RTS,S/AS01$_E$ in sub-Saharan Africa.

3.2. Secondary objectives

In subjects aged ≥6 months and <10 years:

- To estimate trends in longitudinal estimates of the parasite prevalence of *P. falciparum* by vaccine eligible or ineligible subgroups and overall.
- To obtain longitudinal estimates of the prevalence of *Plasmodium* species other than *P. falciparum*; overall and by age group.
- To estimate longitudinal trends in receipt and timing of the third dose of DTP/ HepB/Hib and the first dose of measles EPI vaccines, at around 14 weeks and 9 months of age respectively, as appropriate by country.
- To describe changes in care seeking behaviours for reported fever or malaria in the previous 14 days.
- To assess within-site geographical heterogeneity in malaria transmission intensity.
- To describe individual malaria prevention measures and risk factors for clinical malaria according to the parasite density observed.

3.3. Tertiary objectives

In subjects aged ≥6 months and <10 years:

- To compare asexual and sexual (gametocyte) parasitaemia (qualitative- and quantitative-density) in the RTS,S/AS01$_E$ vaccinated and unvaccinated subjects.
- To compare asexual and sexual gametocyte parasitaemia (qualitative- and semi-quantitative-density) when measured by microscopy or NAAT.

4. ENDPOINTS

As per protocol.

4.1. Primary endpoints

- Occurrence of *P. falciparum* parasitaemia (using microscopy).

  Criteria/definitions: infection determined using a blood smear slide and determined using microscopy.

- Occurrence of malaria control interventions.

  Criteria/definitions: malaria control measures are mosquito net usage ***(including insecticide-treated nets [ITN] and long-lasting insecticidal nets [LLIN]), indoor***, residual spraying ***(IRS),*** seasonal malaria chemoprevention (SMC), intermittent preventative treatment in infants (IPTi), and ACT therapy received within the last 14 days.

4.2. Secondary endpoints

- Demography and history characteristics

  Criteria/definitions: gender, age, medical history.

- Occurrence of *Plasmodium* species other than *P. falciparum* (using microscopy)

  Criteria/definitions: infection with *Plasmodium* species other than *P. falciparum* determined using a blood smear slide and microscopy.

- Occurrence of uptake and timing of the third dose of DTP/HepB/Hib and the first measles EPI vaccines

  Criteria/definitions: vaccination record of receipt of dose 3 of the DTP/HepB/Hib and the first dose of the measles EPI vaccines.

- Occurrence of anti-malarial therapy

  Criteria/definitions: any anti-malarial therapy received in the last 14 days.

- Occurrence of measured fever

  Criteria/definitions: any measured fever at time of visit (axillary temperature ≥37.5°C).

- Occurrence of reported fever

  Criteria/definitions: any reported fever occurring in the last 24 hours.

- Occurrence of care seeking behaviour

  Criteria/definitions: occurrence of visits to health providers following reported fever or malaria in the previous 14 days.

- Geo-referencing characteristics

  Criteria/definitions: positioning of the subject's residence will be attributed to a segment with a unique ID from the grid referencing study area map in which the subject resides, where necessary, grouping small geographically proximate villages so that each segment has at least 10 study subjects to avoid PII, and proceeding as far as geographically appropriate.

- Occurrence of individual malaria prevention measures and risk factors

  Criteria/definitions: malaria prevention measures are repellents and local herbs not specifically recommended by the national programme and risk factors are rural/urban area, construction material for the house, floor and roof, type of eaves (open/closed), use of electricity and water source (distance from and type).

4.3. Tertiary endpoints

- Occurrence of RTS,S/AS01$_E$ vaccine doses

  Criteria/definitions: vaccination record of each dose received of the RTS,S/AS01$_E$ vaccine.

- Occurrence of *P. falciparum* parasitaemia (using NAAT)

  Criteria/definitions: detection of *P. falciparum* on dried blood spot and determined using NAAT.

- Occurrence of *P. falciparum* parasitaemia (using microscopy)

  Criteria/definitions: detection of *P. falciparum* using a blood smear slide and determined using microscopy.

- Occurrence of sexual *P. falciparum* (using NAAT/QT-NASBA)

  Criteria/definitions: detection of *P. falciparum* on dried blood spot and determined using NAAT.

5. STUDY POPULATION

As per protocol.

As a reminder, the Total cohort will include all subjects enrolled in the study. All the information for these subjects will be collected in the eCRF (after receiving signed informed consent).

The According to Protocol (ATP) cohort will include all evaluable subjects (i.e. those meeting all eligibility criteria, complying with the procedures defined in the protocol, with no elimination criteria during the study) for whom at least one laboratory result of the blood sample is available.

A detailed, comprehensive list of reasons for elimination from ATP analyses will be established at the time of data cleaning and the following elimination codes will be used.

Cohort	Elimination codes	Eli Type*
Total cohort	900	MA
ATP cohort	2010 (inclusion/exclusion criteria) and 2500 (no slides reading available)	MA

*Internal GSK database code for type of elimination code

6. STATISTICAL METHODS

As per protocol. SAS version 9.2 ***or above*** will be used for statistical analysis.

Continuous variables will be described with number of non-missing observations, mean, standard deviation (SD), median, minimum and maximum and number of missing observations. Categorical variables will be described with frequency tables; absolute numbers and percentages for each level will be given. For some categorical variables 95% confidence intervals (CIs) will also be presented.

All the analyses concerning objectives will be performed on the ATP cohort.

The analysis will be done also on the Total cohort only if we have more than 5% of eliminated subjects; except for the demography where all the tables will be performed for both cohorts.

6.1. Demography, medical history and fever

The number of subjects enrolled as well as the number excluded from the ATP analysis will be presented.

The distribution of subjects by centre will be tabulated according to *P. falciparum* infection status ***measured by microscopy*** and by both JTEG and WHO age classification.

Demographic characteristics (age at Informed Consent date, gender, previous enrolment) will be summarized by *P. falciparum* infection status ***measured by microscopy*** and overall, according to vaccine eligible status (see section 7.4.2) ***and RTS,S/AS01$_E$ vaccination status (see section 7.4.3 – only for the surveys starting after the introduction of the vaccine)***, using descriptive statistics.

Fever in the last 24 hours, fever at the visit, antimalarial or any other medication taken in the past 14 days will be tabulated by centre, and overall according to *P. falciparum* infection status and parasite density ***measured by microscopy***.

6.2. Analysis of parasite prevalence

The analysis of co-primary objective regarding the *P. falciparum* parasitemia prevalence (defined in section 7.4.5) will be done for each centre separately and by age group (WHO and JTEG) and annual age, according to vaccine eligible status (see section 7.4.2), or RTS,S/AS01$_E$ vaccination status (see section 7.4.3 – only for the surveys starting after the introduction of the vaccine) ***and by gender***. The pooled prevalence estimate will be computed considering the centre as random effect (as detailed in section 7.5). The heterogeneity among centres will be tested using Cochran's Q test based upon inverse variance weights.

This analysis of prevalence will be performed on the ATP cohort.

6.3. Analysis of Malaria control interventions

The bednet history information (sleeping under a mosquito net night before visit, new net, pierced or impregnated bednet, and how many holes) will be tabulated by centre, and overall according to *P. falciparum* infection status and parasite density ***measured by microscopy***, ***gender, vaccine eligible status (see section 7.4.2), RTS,S/AS01$_E$ vaccination status (see section 7.4.3 – only for the surveys starting after the introduction of the vaccine) and JTEG age group***.

The analysis of co-primary objective regarding the use of malaria control interventions will be done by computing the proportions of subjects using malaria control interventions among the subjects for which this information is available by centre and overall according to *P. falciparum* infection status and parasite density ***measured by microscopy*** and according to ***gender***, vaccine eligible status (see section 7.4.2), ***RTS,S/AS01$_E$ vaccination status (see section 7.4.3 – only for the surveys starting after the introduction of the vaccine) and JTEG age group***.

The CIs will be computed using the exact method.

Odds Ratio (OR) (unadjusted and adjusted) will be computed (see section ***7.6***).

This analysis will be performed on the ATP cohort

6.4. Analysis of parasite prevalence trends

The analysis of trends of parasitemia prevalence ***measured by microscopy*** (defined in section 7.7) will be performed only for the final analysis (i.e. at the last cross sectional-

surveys), and in the ATP cohort. It will be done for each centre separately and according to vaccine eligible status (see section 7.4.2).

We will compute the *P. falciparum* parasitemia prevalence (defined in section 7.4.5) for each centre separately by survey year. And the pooled prevalence estimate will be computed considering the centre as random effect (as detailed in section 7.5).

Graphs will be performed to summarize the *P. falciparum* parasitemia prevalence according to vaccine eligible status (***see section 7.4.2)*** and survey year, by centre.

6.5. Slide reading results

The analysis of slide readings (availability of slide readings, Malaria RDT results, slide methodology used, filter paper collection, number of days between date of slide reading and collection date) will be performed on the ATP cohort and will be done at the subject level (as defined in section ***7.4.4***) overall and by centre ***according to P. falciparum infection status measured by microscopy***.

6.5.1. Microscopy

6.5.1.1. Descriptive analysis

The analyses of *P. falciparum* and gametocytes will be performed using descriptive statistics for each centre separately and overall and according vaccine eligible status (see section 7.4.2) and RTS,S/AS01$_E$ vaccination status (***see section 7.4.3 – only for the surveys starting after the introduction of the vaccine).*** The density of *P. falciparum* parasitemia and gametocytes will ***also*** be evaluated.

The analyses regarding the prevalence of *Plasmodium* species other than *P. falciparum* will be done according to *P. falciparum* infection status measured by microscopy and vaccine eligible status (***see section 7.4.2)***.

The distribution of *P. falciparum* ***and density measured by microscopy*** (with CIs) will be summarized for each centre separately and overall according to bednet use, and according to fever at the visit.

The results of *P. falciparum* ***and density measured by microscopy*** will also be computed according to the gametocytes results and the malaria RDT.

6.5.1.2. Comparison analysis

The Fisher exact test will be used to perform the comparison, by RTS,S/AS01$_E$ vaccination status, of *P. falciparum* results measured by microscopy (see section 7.8).

6.5.2. NAAT results

6.5.2.1. Descriptive analysis

The analyses of *P. falciparum* and gametocytes will be performed using descriptive statistics for each centre separately and overall and according to vaccine eligible status (see section 7.4.2) and RTS,S/AS01$_E$ vaccination status ***(see section 7.4.3 – only for the surveys starting after the introduction of the vaccine).***

The results of *P. falciparum* ***measured by NAAT*** will also be computed according to the gametocytes results ***measured by NAAT***.

6.5.2.2. Comparison analysis

The Fisher exact test will be used to perform the comparison, by RTS,S/AS01$_E$ vaccination status, of *P. falciparum* results measured by NAAT (see section 7.8).

6.5.3. Comparison between microscopy and NAAT

The comparison of the *P. falciparum* ***results and density*** and gametocytes results measured by microscopy and by NAAT will be performed using the Cohen's Kappa coefficient [Cohen, 1960].

Simple Kappa coefficient will be used to compare the 2x2 contingency tables for the qualitative results (Positive/Negative, see section 7.4.4 for the details of categories).

For semi-quantitative results (see section 7.4.4 for the details of categories), simple and weighted Kappa coefficients will be used to compare the 4x4 contingency tables. The categories High : 10000 – 19999 parasites/ µl and Very high : >= 20000 parasites/ µl for the ***microscopy*** results will be pooled for this analysis.

The extent of the concordance will be assessed using the Landis and Koch scale [Landis, 1977]:

Kappa	Interpretation
0–0.20	Slight agreement
0.21–0.40	Fair agreement
0.41–0.60	Moderate agreement
0.61–0.80	Substantial agreement
0.81–1	Almost perfect agreement

6.6. Vaccination history

The vaccination history (which vaccine and age at vaccination) about DTP, Pentavalent, Measles and RTS,S/AS01$_E$ will be summarized overall and by *P. falciparum* infection status ***measured by microscopy*** using descriptive statistics.

6.7. Change in care seeking behaviours

The malaria or fever treatment taken in the past 14 days ***and details (where, when and at what time was the subject taken for treatment)***, and the malaria hospitalization will be displayed by centre, and overall according to *P. falciparum* infection status ***measured by microscopy***.

6.8. Geographical heterogeneity

The distribution of subjects by segment will be tabulated according to *P. falciparum* infection status ***measured by microscopy***.

Characteristics of segment will be summarized overall using descriptive statistics.

The analysis the *P. falciparum* parasitemia prevalence ***measured by microscopy*** (defined in section 7.4.5) will be done for each segment separately according to the centre. The heterogeneity among segment by centre will be tested using Cochran's Q test based upon inverse variance weights.

6.9. Malaria risk factors

The analysis of malaria risk factors will be performed on the ATP cohort.

The output tables for malaria risk factors (number of subjects in the same house, localisation, house information) will be done by centre and overall according to *P. falciparum* infection status and parasite density ***measured by microscopy***. OR will be computed (see section ***7.6***).

6.10. Malaria control programme at centre level

The centre specific data regarding the malaria control program will be summarized in the data listings by centre and by survey.

6.11. Analysis of SAEs related to study procedure

SAEs reported during the entire study will be tabulated per centre and overall according to *P. falciparum* infection status ***measured by microscopy*** for the Total cohort.

6.12. Output dataset

Annual fluctuations in malaria incidence occur as a result of changes in transmission intensity, which may be caused by changes in environmental factors such as rainfall or changes in usage of other malaria control interventions (use of bednets for example). Therefore, by taking into account these variations in MTI and malaria control intervention coverage, more accurate estimations of the vaccine impact on malaria disease diagnosed by RDT and/or microscopy during EPI-MAL-003 will be possible. Those estimations will be used as covariates in the models, as described in the protocol of the EPI-MAL-003.

EPI-MAL-005 is planned to run in parallel with EPI-MAL-002 and EPI-MAL-003 and will assess the following parameters: prevalence of *P. falciparum* parasitaemia, use of malaria control interventions, changes in environmental factors such as rainfall, changes in health care seeking behaviour, within-site geographical heterogeneity in MTI and individual malaria prevention measures and risk factors for malaria. Compliance with DTP-based, measles and RTS,S/AS01$_E$ vaccines will also be collected.

In order to adjust the comparison, and the estimation of the vaccine impact, an output dataset of the EPI-MAL-005 results will be built so that they could be included as covariates in the EPI-MAL-003 ***and EPI-MAL-002*** models. This dataset will consist of aggregated results by centre, and by survey. These aggregated results will ***be explicitly listed in the appendices of the SAP of the EPI-MAL-003 and Epi-MAL-002 studies with the explanation of the models used***.

7. STATISTICAL CALCULATIONS

7.1. Methodology for computing CI

All CI will be two sided 95% CI.

The exact 95% CIs for a proportion within a group will be calculated from Proc StatXact [Clopper, 1934].

The asymptotic 95% CIs for a mean within a group will be calculated.

7.2. Number of decimals

The following decimal description will be used for the analyses.

Parameters	Number of decimal digits
% of count, including LL & UL of CI	1
p-value	***4***
Minimum, maximum, range	Number of decimals in the raw data
Mean, median	Number of decimals in the raw data +1
SD	Number of decimals in the raw data +2

LL = Lower Limit UL = Upper Limit CI = Confidence Interval
SD = Standard deviation

7.3. Handling missing data

No data handling will be performed in case of missing data.

7.4. Derived and transformed data

7.4.1. Age

The age will be computed as the difference between the informed consent date and the date of birth or taken directly as reported in the CRF if the date of birth is unavailable. The age will be categorized according to the JTEG definition: 0.5-4, 5-9 years and WHO definition: 0.5-1, 2-9 years.

When the age is derived from the informed consent date and the date of birth, it could be possible that the date of birth will not be a full date. When the date will be only a year, it will be read as "*30JUNyyyy"* (except for the year of the survey – given that it is known per inclusion criteria the subject is at least 6 months old). When the date will be a month and a year, it will be read as "*15mmmyyyy"*. For these cases, the minimum age of the infant must be 6 months.

The continuous variable 'Age at IC [years]' is computed based on number of days/365.25.

7.4.1.1. Age at vaccination

The age at vaccination will be computed as the difference between the vaccination date and the date of birth.

It could be possible that the date of vaccination will not be a full date. When the date will be a month and a year, it will be read as "15mmmyyyy" except if the age becomes negative or is equal to zero, ***in which the date of birth will be used***. When the date of vaccination will be only a year, the age at vaccination will not be derived.

If 3 different dates for the DTP/HepB/Hib vaccine are entered, the last date of vaccination is selected as the date of the third dose of DTP/HepB/Hib.

7.4.2. Definition of vaccine eligible/ineligible age group

The vaccine eligible age group is defined as those subjects that on the basis of age would be eligible for RTS,S/AS01$_E$ vaccination, even if vaccine is unavailable at the time of assessment. The age will depend on the label for RTS,S/AS01$_E$ vaccination in the country. (At the time of study start, there will be no available vaccination with RTS,S/AS01$_E$).

The vaccine ineligible age group is defined as those subjects that on the basis of age would be ineligible for RTS,S/AS01$_E$ vaccination, regardless of vaccine availability at the time of assessment. The age will depend on the label for RTS,S/AS01$_E$ vaccination in the country.

The cut-off age between both subgroups will be equal to the maximum age at ***the last survey*** for a child to be able to receive a RTS,S/AS01$_E$ vaccine dose.

After introduction of the RTS,S/AS01$_E$ vaccine in 2019 and based on Country MoH eligibility guidelines, the definition of vaccine eligible/ineligible group is defined as :

- ***RTS,S/AS01$_E$ vaccine ineligible group: regroup all subjects aged more or equal to 6 years except subjects who received at least one RTS,S vaccine dose.***
- ***RTS,S/AS01$_E$ vaccine eligible group: regroup all subjects aged less than 6 years and the subjects aged more or equal to 6 years who received at least one RTS,S vaccine dose.***

7.4.3. Definition of RTS,S/ AS01$_E$ vaccination status

The vaccinated group is defined as those subjects who received at least one dose of the RTS,S/AS01$_E$ vaccine.

The unvaccinated group is defined as those subjects who received no dose of the RTS,S/AS01$_E$ vaccine.

The vaccination status will be determined only for the surveys/centres starting after the introduction of the vaccine.

Note: some vaccinated subjects were able to take part in clinical studies of the RTS,S/AS01$_E$ vaccine during phase III, so these subjects were vaccinated before the introduction of the vaccine.

7.4.4. Definition of a subject infected by a parasite – Slide reading parasitemia results at subject level

7.4.4.1. Microscopy

A subject is defined as infected by a specified parasite (*P. falciparum*, *P. malariae*, *P. vivax*, *P. ovale*) if at least two of his blood slide readings are positive for the corresponding parasite. Results of slide readings at subject level will be missing if all slide reading results are missing.

A subject is defined with presence of gametocytes when detected in at least one slide. It will be missing if all slide readings have missing information regarding the presence of Gametocytes.

The parasite density (parasites/µl) at the subject level is defined as the geometric mean of both (those positive) slide readings values if the subject's status is defined as positive. In the case of three positive slide readings, the two closest readings will be selected to calculate the geometric mean. In the case of negative parasite status, the density will be missing. If there are 3 values for one subject that have the same 'gap' between the lowest and the medium readings and between the medium and highest readings, the 2 greatest values (corresponding to the worst situation) are taken.

The parasites density will be categorized according to the following classes:

- Negative
- Low : < 2500 parasites/ µl
- Medium : 2500 – 9999 parasites/ µl
- High : 10000 – 19999 parasites/ µl
- Very high : >= 20000 parasites/ µl

For the concordances analyses the parasites density will be categorized according to the following classes:

- Negative
- Low : < 2500 parasites/ µl
- Medium : 2500 – 9999 parasites/ µl
- High and Very high : >=10000 parasites/ µl

The gametocytes density (units/ µl) at the subject level is defined as the geometric mean of positive slide readings values if the subject status is defined as positive. It will be missing otherwise.

7.4.4.2. NAAT

By the NAAT method, a subject is defined as infected by the *P. falciparum* or defined with presence of gametocytes if the NAAT reading is positive. Results of slide readings at subject level will be missing if the result is Not Done or Not Received.

The parasites density will be categorized according to the following classes:

- Negative
- Low : < 1000 parasites/ µl
- Medium : 1000 – 10000 parasites/ µl
- High : > 10000 parasites/ µl

7.4.5. Parasite prevalence

The parasite prevalence will be estimated as the proportion of subjects infected divided by the number of subjects tested. These parasites will be estimated using microscopy testing (primary and secondary analyses) and using NAAT (tertiary analyses). The CIs will be computed using the exact method.

7.4.6. Fever at the study visit

The status of fever at the study visit will be derived from the body temperature (axillary temperature). The value 'Yes' will be given if the temperature is ≥37.5°C.

When the route of t° is missing, it will be considered to be the axillary route. If the route is rectal (or tympanic with rectal conversion), then the conversion in axillary will be done, by subtracting 0.5°C (T°_Axil = T°_Rectal – 0.5).

7.4.7. Other medication

A variable 'Other medication over 14 days prior to study visit' will be derived from the eCRF if a subject was administered with a drug which was not reported as an antimalarial drug.

7.4.8. Vaccination

The vaccines DTP, Tetravalent and Pentavalent will be regrouped in one category and called 'DTP/HepB/Hib' as for the EPI-MAL-002 study.

The variable "Tradename of the vaccine" will be used to determine which vaccine is attributed to the subjects. As this variable is a free text variable, an excel file with the correct description of the vaccine was implemented by the epidemiologist.

7.5. Prevalence over all sites

The proportion of occurrence of the *P. falciparum* parasitemia over all sites will be computed based on the proportions observed in each centre. Centres will be treated as clusters and the estimates (with 95%CI) will be computed using generalized estimating equations (GEE) in order to take the correlation between subjects from each study/country into account. The GEE will be fitted using the SAS procedure GENMOD [Boos, 1992) and Rotnitzky, 1990], assuming an exchangeable correlation matrix.

7.6. Modelling of risk factors and malaria control interventions

CCI [redacted]

The potential risk factors and malaria control interventions collected will be considered.

The list of these variables can be found in the TFL. Note that some categories could be grouped at the time of the analysis in case of low representativeness.

A first table will summarise the effect of each risk factor and malaria control interventions individually on the proportion of positive episodes using unadjusted OR (with its 95% CI).

To describe the nature of the relationship between the dependent variable (probability of being *P. falciparum* positive ***measured by microscopy***) and possible explanatory variables, a multiple logistic regression model will be used. Using the Backward selection strategy (with P-value of 0.05 to stay in the model – SLSTAY = 0.05) and the method of Maximum Likelihood to estimate the parameters, the final regression equation will identify the number of possible significant risk factors. Finally, the equation will be

$$Logit(P_i) = Log\left(\frac{P_i}{1-P_i}\right) = \alpha + \sum_j \beta_j X_j$$

where

P_i = probability for a subject to be infected

X_j = significant risk factors

A second table will give the details for the estimated coefficient, the adjusted OR, and the associated p-value ***by using the variable site as cluster***.

The adjusted analysis will be done on one hand for risk factors and for malaria control interventions separately and on the other hand for all variables as a whole.

For the adjusted model, the variables depending on another variable will be adapted to avoid introducing missing values in the model :

- ***If the variable "Antimalarial or any other medication within 14 days prior the study visit" = No, then the value for the variables "Antimalarial drug" and "Other medication over 14 days prior the study visit" is assigned to No.***
- ***If the variable "Indoor residual spray used in past 12 months to spray interior walls of this part of the house" = No, then the value for the variable "Use of indoor residual spray – number of months age" = No Residual Spray.***
- ***If the variable "subject sleep under a mosquito net last night" = No, then the value for the variables "new net (less than 1 year)" "Impregnated Bednet" and "Pierced/torn Bednet" = No Mosquito Net.***
- ***If the variable "Pierced/torn Bednet" = No, then the value for the variable "Number of holes" = No Pierced Bednet.***
- ***The categories of the variable "Use of indoor residual spray – number of months ago" will be regrouped to:***
  - 1-2 months
  - 3-4 months
  - > 4 months
  - No Residual Spray.

7.7. Parasitemia prevalence trends

To determine if a parasitemia prevalence trends may exist across the surveys, a Cochran-Armitage trend test is computed.

As some sites were early terminated during the study and others started after the RTS,S/AS01$_E$ vaccine introduction, the Cochran-Armitage trend test will be computed only on centres with results for at least 3 surveys.

The Cochran-Armitage test is a method of directing chi squared tests toward narrow alternatives. The test is sensitive to the linearity between response variable and experimental variables and detects trends. [Cochran, 1954, Armitage, 1955].

To compute the OR of Survey year according to vaccine eligible status (***see section 7.4.2)*** and for each ***site***, a simple logistic regression model will be used (see section 7.6).

The survey's reference category will be the first survey of the centre.

7.8. Fisher exact test

The comparisons of proportions for categorical variables will be done with Exact Fisher test. The *p*-values less than 0.05 will be used as an indicator that a difference between the two groups compared may exist. However since *p*-values will not be adjusted for multiplicity comparisons, they will have to be interpreted with caution.

7.9. Rapid Diagnostic Test (RDT)

According to protocol, an RDT is performed when the subject has fever at the time of the visit (axillary temperature ≥37.5°C) or fever reported in the last 24 hours or, after amendment 1 of the protocol, other symptoms/signs of clinical malaria. However, several protocol deviations were detected during the first surveys concerning the RDT use, i.e., some centres performed an RDT on non-eligible subjects.
Due to this deviation, additional tables will be computed on the RDT results restricted to subjects with fever at first surveys and to subjects with fever or symptoms/signs of clinical malaria at surveys following amendment 1 of the protocol.

7.10. Malaria risk factors adaptation

An inconsistency was identified during the analysis of survey 2 between the 2 nested variables "What are the main types of windows in the house?" and "Are there nets on the main windows of the house?" (household questionnaire).

For most of the subjects living in a house with "no window", the category "Nets not present" was ticked for the nested variable describing net characteristics.

As a priori living in a house with "no window" could be considered as a protective factor when living in a house with "Nets not present" could be considered as a risk factor for malaria; the team decided to attribute to all subjects living in a house with 'No Window' the value 'Other' for the variable describing net characteristics.

8. CONDUCT OF ANALYSES

8.1. Sequence of analyses

10 analyses will be performed ***with possible further extension, depending on the duration of the EPI-MAL-002 and EPI-MAL-003 studies.***

Description	Analysis ID	TFL short title

	(*LSAF* sub-folder)	
Information collected in the first annual cross sectional survey	ANALYSIS_E1_02	Cross Survey 1
Information collected in the second annual cross sectional survey	ANALYSIS_E1_03	Cross Survey 2
Information collected in the third annual cross sectional survey	ANALYSIS_E1_04	Cross Survey 3
Information collected in the fourth annual cross sectional survey	ANALYSIS_E1_05	Cross Survey 4
Information collected in the fifth annual cross sectional survey	ANALYSIS_E1_07	Cross Survey 5
Information collected in the sixth annual cross sectional survey	ANALYSIS_E1_08	Cross Survey 6
Information collected in the seventh annual cross sectional survey	ANALYSIS_E1_09	Cross Survey 7
Information collected in the eighth annual cross sectional survey	ANALYSIS_E1_10	Cross Survey 8
Information collected in the ninth annual cross sectional survey	***ANALYSIS_E1_11***	***Cross Survey 9***
Information collected in the ***tenth*** annual cross sectional survey and trend analysis over the ***10*** years.	ANALYSIS_E1_01	Cross Survey ***10*** and Trend analysis
Dataset on EPI-MAL-005 results used as covariates in EPI-MAL-002 analyses	***ANALYSIS_E1_12***	***NA***
Dataset on EPI-MAL-005 results used as covariates in EPI-MAL-003 analyses	***ANALYSIS_E1_13***	***NA***

The analysis ID associated in Life Science Analytics Framework (LSAF) could be updated according the needs of the study.

The tables or graphs that will be performed only in the last survey are clearly identified in the TFL.

8.2. Statistical considerations for interim analyses

Not applicable

9. CHANGES FROM PLANNED ANALYSES

CCI

[redacted]

10. REFERENCES

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Annotated Study Book for Study Design: p116682

Study Design Version: 6.0

Sponsor: GlaxoSmithKline

Protocol: EPI-MALARIA-005 (116682)

Generic Drug Name: Not applicable

Epidemiology study of malaria transmission intensity in sub-Saharan Africa

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May 8, 2021 2:52PM

p116682: SCREENING (Screening) [frmSCREENING]		
SCREENING [sctSCR]		
1.	Initials: *[hidden]* [Initials]	[txtScrSINIT] *A3*
2.* ✔	Please tick box to confirm CRF creation:	[itmCRF_FLG] *[A:Y]* ☐
Key: [*] = Item is required [✔] = Source verification required Note: Source verification critical settings made in InForm will override any settings made in Central Designer.		

p116682: ENROLLMENT (Enrollment) [frmENROLLMENT]

ENROLLMENT [sctENROLLMENT]

1.* ✔	Subject Number: [Subj Nr]	[itmPID] N9

Key: [*] = Item is required [✔] = Source verification required
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p116682: SUBJECT IDENTIFICATION (Subject Identification) [frmPATIENTIDENTIFICATION]

SUBJECT IDENTIFICATION [sctPATIENTIDENTIFICATION]

1.* ✔	Subject Number: [Subj Nr]	[*itmPID* : *GENHIST_DATA.PID;PID_SCHD.ITMPID;VIS_INFO_DATA.PID*] *N9*

Key: [*] = Item is required [✔] = Source verification required
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p116682: DEMOGRAPHY (Demography) [frmDEMOGRAPHY]

DEMOGRAPHY [sctDEMOGRAPHY]

1.* ✔	Date of Birth:	[cmpDOB_RAW] [itmDOB_RAW : DEMOG_DATA.DOB_RAW] (MM/DD/YYYY) Date of birth: Req/Unk / Req/Unk / Req/Unk (2003-2025) [itmAGE_MON : DEMOG_DATA.AGE_SP] OR Age N2 [itmAGE_UNIT : DEMOG_DATA.AGE_UNIT] [A:M] Months [A:Y] Years
2.	Date of Birth for OCEANS (DO NOT delete) *[hidden]*	[itmBIRTHDT_HID] (MM/DD/YYYY) NReq / NReq / NReq (2003-2025)
3.* ✔	Gender: [Gender]	[itmSEX : DEMOG_DATA.SEX] [A:M] Male [A:F] Female
4.	Weight for OCEANS (Do not delete) *[hidden]*	[itmWEIGHT_HID] xxxx.
5.* ✔	To which segment in the study area does the subject belong? [To which segment in the study area does the subject belong?]	[itmSEGMNTID2 : DEMOG_DATA.SEGMNTID] N8
6.* ✔	Does the study participant live in a RTS,S exposed or unexposed cluster? [Does the study participant live in a RTS,S exposed or unexposed cluster?]	[itmCLUSTER : DEMOG_DATA.CLUSTR] [A:EC] Exposed Cluster Please select district/sub-county/Cluster: [itmEXPCLUSTER : DEMOG_DATA.EXPCLST] [clDISTGHANAEX] [A:UC] Unexposed Cluster Please select district/sub-county/Cluster: [itmUNEXPCLUSTER : DEMOG_DATA.UNEXCLST] [clDISTGHANAUNEX]
7.* ✔	To which survey subject is enrolled ? [To which survey subject is enrolled :]	[itmSURVEYNB : DEMOG_DATA.SURVEY_NB] [A:1] Survey 1 or 2 [A:3] Survey 3 [A:4] Survey 4 [A:5] Survey 5 [A:6] Survey 6 [A:7] Survey 7 [A:8] Survey 8 [A:9] Survey 9 [A:10] Survey 10 [A:11] Survey 11 [A:OTH] Other

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

Codelist Values Tables: DEMOGRAPHY

Codelist RefName	Codelist Data Type	Subset	Label	Code	Codelist Item RefName	Data Variable RefName
clDISTGHANAEX	String		Kintampo North	KN	KintampoNorth	itmEXPCLUSTER
			Kintampo South	KS	KintampoSouth	
			Techiman North	TN	TechimanNorth	
			Nkoranza North	NN	NkoranzaNorth	
			Kasena Nankana West	KNW	KasenaNankanaWest	
			Kasena Nankana Municipal	KNM	KasenaNankanaMunicipal	
			Kombewa	KMB	Kombewa	
			Gem	GEM	Gem	
			Exposed Malawi 1	EM1	ExposedMalawi1	
			Exposed Malawi 2	EM2	ExposedMalawi2	

clDISTGHANAUNEX	String		Techiman South	TS	citmTECHSOUTH	itmUNEXPCLUSTER
			Nkoranza South	NS	citmNKORSOUTH	
			Builsa North	BN	citmBUILNORTH	
			Builsa South	BS	citmBUILSOUTH	
			Nyando	NYN	citmNYANDO	
			Rarieda	RAR	citmRARIEDA	
			Unexposed Malawi 1	UM1	citmUM1	
			Unexposed Malawi 2	UM2	citmUM2	
			Nouna	NOU	citmNOUNA	
			Sapone	SAP	citmSAPONE	
			Bondo	BON	citmBONDO	

p116682: INFORMED CONSENT (IC) [frmINFORMEDCONSENTRRA]

DATE OF VISIT [sctDATEOFVISIT]

1.* ✔	Date of visit: [Date of visit:]	[*itmACTRDATE* : *ACTDATES_DATA.ACTRDATE*] **(MM/DD/YYYY)** Req ___ / Req ___ / Req ___ (2013-2021)

INFORMED CONSENT [sctINFORMEDCONSENT]

I certify that Informed Consent has been obtained prior to any study procedure.

2.* ✔	Informed Consent Date: [IC date]	[*itmCONS_DAT* : *CONSENT_DATA.CONS_DAT*] **(MM/DD/YYYY)** Req ___ / Req ___ / Req ___ (2013-2024)
3.* ✔	Did the subject agree that her/his biological samples(s) may be used by GSK Biologicals for further research that is NOT RELATED to the disease(s) under study? [Did the subject agree that her/his biological samples(s) may be used by GSK Biologicals for further research that is NOT RELATED to the disease(s) under study?]	[*itmCONS_LAB_Q4* : *CONS_LAB_DATA.CONSLABA*] *[A:Y]* Yes *[A:N]* No *[A:NA]* Not applicable
4.	Informed consent section number *[hidden]* [Section number]	[itmINF_NB1_HID] *N10*
5.* ✔	Subject's Parent(s)/ legally acceptable representativeâ€™s consent to process subject's personal information. [Subject's Parent(s)/ legally acceptable representativeâ€™s consent to process subject's personal information.]	[cmpINFO] [*itmSTUDY_INFO* : *CONSENT_DATA.STDYINFO*] We, subjectâ€™s Parent(s)/ legally acceptable representatives, consent to GSK, Study Staff, and others accessing and using subjectâ€™s medical and personal information for the study as described in the form. *[N:1]* Yes *[N:0]* No [*itmRESEARCH_INFO* : *CONSENT_DATA.RESEARCH*] We, subjectâ€™s Parent(s)/ legally acceptable representatives, consent to GSK, Study Staff, and others accessing and using subjectâ€™s medical and personal information for further research, once the study is complete. *[N:1]* Yes *[N:0]* No

Key: [*] = Item is required [✔] = Source verification required
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p116682: ELIGIBILITY CHECK (Eligibility) [frmELIGIBILITYCHECK]

ELIGIBILITY CHECK [sctELIGIBILITYCHECK]

1.* ✔	Did the subject meet all the entry criteria? [Eligible]	[*itmELIGIBIL* : *ELISHEET_DATA.ELIGIBIL*] *[A:Y]* ☐ Yes *[A:N]* ☐ [cmpINCL_EXCL_CRITERIA] No -> Tick all boxes corresponding to violations of any inclusion/exclusion criteria. Do not enter the subject into the study if he/she failed any of the inclusion or exclusion criteria below. [*itmINCL_CRITERIA* : *ELIGIBIL_DATA.CRIT_NR*] **INCLUSION CRITERIA** All subjects must satisfy ALL the following criteria at study entry: *[A:1]* ☐ Subjects whose parent(s)/Legally Acceptable Representative(s) [LAR(s)], in the opinion of the investigator, can and will comply with the requirements of the protocol *[A:2]* ☐ A male or female 6 months to <10 years of age at the time of survey. *[A:3]* ☐ Signed informed consent or thumb-printed and witnessed informed consent obtained from the parent(s)/LAR(s) of the child. [*itmEXCL_CRITERIA* : *ELIGIBIL_DATA.CRIT_NR*] **EXCLUSION CRITERIA** The following criteria should be checked at the time of study entry. If ANY exclusion criterion applies, the subject must not be included in the study: *[A:4]* ☐ Child in care *[A:6]* ☐ Current active participation in any trial involving administration of an investigational malaria vaccine or malaria drug.
2.	Eligibility section number *[hidden]* [Section number]	[itmELI_NB1_HID] *N10*

Key: [*] = Item is required [✔] = Source verification required
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p116682: PREVIOUSPART (Previous Part) [frmPREVIOUSPART]

Previous Enrolled [sctPREVPART]

1.* ✔	Has subject been enrolled previously in this study? [Has subject been enrolled previously in this study?]	[*itmPREVPART* : *PREVINFO_DATA.PRENRLYN*] *[A:Y]* ☐ [*itmSubjNo* : *PREVINFO_DATA.PR_PID*] Yes --> previous subject number: *N9* *[A:N]* ☐ No

Key: [*] = Item is required [✔] = Source verification required
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p116682: MEDICAL HISTORY (Med Hist) [frmMEDICALHISTORY]

MEDICAL HISTORY [sctMEDICALHISTORY]

1.* ✔	Has the subject been ill with a fever in the last 24 hours? [Has the subject been ill with a fever in the last 24 hours?]	[itmFEVER : MED_HOSP_DATA.FEVER] [A:N] No [A:Y] [itmFEVERDY : MED_HOSP_DATA.FEVERDY] Yes ---->How many days ago did the fever start A2
2.* ✔	What is the subjectâ€™s body temperature now? [What is the subjectâ€™s body temperature now?]	[cmpTEMPERATURE_VS] [itmVS_TEMP : VS_DATA.VSORRES] xxx.x ° C [itmTEMP_ROUTE : VS_DATA.VSLOC] Route [A:A] Axillary [A:O] Oral [A:R] Rectal [A:T] [itmCONVRSN : VS_DATA.CONVRSN] Tympanic (not recommended) Conversion: [A:T] none (or unknown) [A:TO] oral conversion [A:TR] rectal conversion
3.	Unit: *[hidden]*	[itmTEMP_UNIT_HID : VS_DATA.VSORRESU] [clVSORRESU]
4.	VSTEST *[hidden]*	[itmVSTEST_HID : VS_DATA.VSTEST] [clVSTEST]
5.	VSTESTCD *[hidden]*	[itmVSTESTCD_HID : VS_DATA.VSTESTCD] [clVSTESTCD]
6.* ✔	Does the subject have any other signs/symptoms of Malaria at the time of visit?	[itmMAL_SIGNSYMP : MED_HOSP_DATA.SYMP_YN] [A:Y] Yes [A:N] No
7.* ✔	Was the subject treated for fever or malaria in the last 14 days? [Was the subject treated for fever or malaria in the last 14 days?]	[itmMAL_FLG : MED_HOSP_DATA.MAL_FLG] [A:Y] [itmTRETMNT : MED_HOSP_DATA.TRTMENT] Yes, Where was the subject taken for treatment? [N:1] Home [N:2] Drug Seller [N:3] Pharmacy [N:4] Private Clinic [N:5] Health Centre [N:6] Hospital [N:99] [itmOTHERSPECIFY : MED_HOSP_DATA.OTH_TYP] Other A255 [itmTRTMNT_TAKEN : MED_HOSP_DATA.TRMNTTKN] When was the subject taken for treatment? [N:1] Onset [N:2] Subject Did Not Improve [N:3] Subject Got Worse [N:4] [itmOTHER_TRT : MED_HOSP_DATA.OTH_TAKN] Other A128 [itmTIME_TAKEN : MED_HOSP_DATA.TIME_TKN] What time was the subject taken for treatment? [N:1] Same Day [N:2] Next Day [N:3] Two Days Later [N:4] More Than Two Days Later [A:N] No

ADDITIONAL DETAILS [sctADDITIONALDETAILS]

8.* ✔	Was the subject hospitalized in the last 3 months due to Malaria? [Was the subject hospitalized in the last 3 months due to Malaria?]	[*itmSUBJHOSP : MED_HOSP_DATA.HOSP_MAL*] *[A:N]* No *[A:Y]* Yes
9.* ✔	Did the subject sleep last night under a mosquito net?	[*itmSUBJSLEEP : MED_HOSP_DATA.MOS_NET*] *[A:N]* No *[A:Y]* [cmpSUBJSLEEP] Yes [*itmBEDNETNEW : MED_HOSP_DATA.NT_NEW*] ---> Bednet -> New (less than 1 year) *[A:N]* No *[A:Y]* Yes [*itmBEDNETIMP : MED_HOSP_DATA.NT_IMPR*] -> Bednet -> Impregnated (dipped in liquid to repel mosquitos after purchase) *[A:N]* No *[A:Y]* Yes [*itmBEDNETPIRCD : MED_HOSP_DATA.NT_PIERC*] -> Bednet -> Pierced/torn (holes big enough to let one finger go through) *[A:N]* No *[A:Y]* [*itmNUMHOL : MED_HOSP_DATA.NB_HOLES*] Yes, ---> How many holes of that size ? *[A:1]* < 5 *[A:2]* >= 5

Key: [*] = Item is required [✔] = Source verification required
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Codelist Values Tables: MEDICAL HISTORY

Codelist RefName	Codelist Data Type	Subset	Label	Code	Codelist Item RefName	Data Variable RefName
clVSORRESU	String		beats per minute	BPM	citmBPM	itmTEMP_UNIT_HID
			breaths per minute	BRTH	citmBRTH	
			Celsius	CE	citmCE	
			Fahrenheit	FA	citmFAR	
			feet	FT	citmFT	
			inches	IN	citmINCH	
			kg	KG	citmKG	
			ounces	OZ	citmOZ	
			pounds	LB	citmLB	
			cm	CM	citmCM	
			mmHg	MMHG	citmMMHG	
			grams	G	citmGRAM	
clVSTEST	String		Diastolic Blood Pressure	DIASTOLIC BLOOD PRESSURE	citmDIASTOLICBLOODPRESSURE	itmVSTEST_HID
			Heart Rate	HEART RATE	citmHEARTRATE	
			Height	HEIGHT	citmHEIGHT	
			Mid Upper Arm Circumference	MUAC	citmMUAC	
			Respiratory Rate	RESPIRATORY RATE	citmRESPIRATORYRATE	
			Systolic Blood Pressure	SYSTOLIC BLOOD PRESSURE	citmSYSTOLICBLOODPRESSURE	
			Temperature	TEMPERATURE	citmTEMPERATURE	
			Weight	WEIGHT	citmWEIGHT	
			Cranial Perimeter	CRANIAL PERIMETER	citmCRANIALPERIMETER	
			Apgar Score	APGAR SCORE	citmAPGARSCORE	
clVSTESTCD	String		DIABP	DBP	citmDBP	itmVSTESTCD_HID
			HEART RATE	HR	citmHR	

			HEIGHT	HE	citmHEI	
			MUAC	MUAC	citmMUAC2	
			RESP RATE	RR	citmRESPR	
			SYSBP	SBP	citmSBP	
			TEMP	TE	citmTEMP	
			WEIGHT	WE	citmWEIGHT2	
			CRANIAL PERIMETER	CRP	citmCRP	
			APGAR SCORE	APGAR	citmAPGAR	

p116682: HOUSEHOLD QUESTIONNAIRE (MAIN) (HQ Main Question.) [frmHQMAIN]

HOUSEHOLD QUESTIONNAIRE(MAIN) [sctHQMAIN]

1.* ✔	Was the household questionnaire completed for another subject enrolled in the study and living in the same part of the house as this subject [Was the household questionnaire completed for another subject enrolled in the study and living in the same part of the house as this subject]	[*itmCOMPLETE* : *HOUSHLDA_DATA.COMPLETE*] *[A:Y]* ☐ [*itmSUBJNUM* : *HOUSHLDA_DATA.SUBJNUM*] Yes --> Do not complete the household questionnaire for this subject, only record the subject number for whom the questionnaire was already completed and go to sample collection *N9* *[A:N]* ☐ No

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p116682: HOUSEHOLD QUESTIONNAIRE - MALARIA RISK FACTORS (HQ-Malaria Risk Factors) [frmHQ_MALARIARISKFACTORS]

MALERIA RISK FACTORS [sctMALERIARISKFACTORS]

1.* ✔	How many persons in total are living in the same part of the house as this subject? [How many persons in total are living in the same part of the house as this subject?]	[itmPERS_NB : HOUSHLDB_DATA.PERS_NBR] N2
2.* ✔	How many persons living in the same part of the house as this subject are enrolled in this study? [How many persons living in the same part of the house as this subject are enrolled in this study?]	[itmENRO_NB : HOUSHLDB_DATA.ENRO_NB] N1
3.* ✔	Where is the house situated? [Where is the house situated?]	[itmSITUATIO : HOUSHLDB_DATA.SITUATD] [A:R] Rural area [A:SR] Semi- Rural Area [A:U] Urban area
4.* ✔	Please specify the type of location [Please specify the type of location]	[itmLOCATION : HOUSHLDB_DATA.LOCATION] [A:LC] Large city (>1 mil. habitants) [A:SC] Small city (>50 000 and < 1mil. habitants) [A:T] Town (>10 000 and < 50 000 habitants) [A:CS] Countryside (<10 000 habitants)
5.* ✔	What is the main material used for construction of walls of the house? [What is the main material used for construction of walls of the house?]	[itmMAT_WALL : HOUSHLDB_DATA.WALLS] [A:01] Mud [A:02] Brick [A:03] Cement/ Plaster [A:04] Cement /Paint [A:05] Clay [A:99] [itmSPECIFY_W : HOUSHLDB_DATA.SP_WALLS] Others, Specify A128
6.* ✔	What is the main material used for construction of roof of the house? [What is the main material used for construction of roof of the house?]	[itmMAT_ROOF : HOUSHLDB_DATA.ROOF] [A:12] Grass/ Palm [A:13] Iron sheet [A:14] Tiles [A:15] Clay [A:99] [itmSPECIFY_R : HOUSHLDB_DATA.SP_ROOF] Others,Specify A128
7.* ✔	What is the main material used for construction of floor of the house? [What is the main material used for construction of floor of the house?]	[itmMAT_FLOOR : HOUSHLDB_DATA.FLOOR] [A:01] Natural floor (earth, sand, dung) [A:02] Rudimentary floor (wood planks, palm, bamboo) [A:03] Parquet, polished wood [A:04] Vinyl or asphalt strips [A:05] Ceramic tiles [A:06] Cement [A:07] Carpet [A:08] Clay [A:99] [itmSPECIFY_F : HOUSHLDB_DATA.SP_FLOOR] Others, Specify A128
8.* ✔	What are the main types of windows in the house? [What are the main types of windows in the house?]	[itmMAT_WINDOW : HOUSHLDB_DATA.WINDOWS] [A:O] Open [A:C] Closed [A:PO] Partially open [A:NW] No Windows [A:99] [itmSPECIFY_WD : HOUSHLDB_DATA.SP_WD] Others,Specify A128
9.* ✔	Are there nets on the main windows of the house? [Are there nets on the main windows of the house?]	[itmMAT_NET : HOUSHLDB_DATA.NETS] [A:PA] Nets present on all windows [A:PS] Nets present on some windows [A:NP] Nets not present [A:99] [itmSPECIFY_N : HOUSHLDB_DATA.SP_NETS]

		Others, Specify A128
10.* ✔	What is the main source of drinking water for this part of the house? [What is the main source of drinking water for this part of the house?]	[itmWATER_SOU : HOUSHLDB_DATA.WATR_SRC] [A:CW] Closed water source (piped water, tube well, dug well, protected well) [A:OW] [itmWTRSRC : HOUSHLDB_DATA.SRC_DIST] Open water source (unprotected well, spring water, rainwater, tanker truck, surface water), Is the open source in the compound? [A:Y] Yes [A:N] No
11.* ✔	Does this part of the house have electricity? [Does this part of the house have electricity?]	[itmELECTRIC : HOUSHLDB_DATA.ELECTRIC] [A:N] No [A:Y] Yes
12.* ✔	Were any of the following used in this part of the house over last week (last 7 days)? [Were any of the following used in this part of the house over last week (last 7 days)?]	[itmMOSQ_REPL : HOUSHLDB_DATA.MOSQ_RPL] [A:01] Mosquito coils [A:02] Insecticide sprays (e.g. DOOM) [A:03] Commercial Repellents [A:04] Traditional repellents [A:05] None
13.* ✔	Was indoor residual spray used in past 12 months to spray interior walls of this part of the house? [Was indoor residual spray used in past 12 months to spray interior walls of this part of the house?]	[itmRE_SPRAY : HOUSHLDB_DATA.RE_SPRAY] [A:N] No [A:Y] [itmMONTH_SP : HOUSHLDB_DATA.MONTH_SP] Yes, -->If yes, please specify how many months ago was house sprayed N2

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: SAMPLE COLLECTION (Sample collection) [frmSAMPLECOLLECTION]

MALARIA RAPID DIAGNOSTIC TEST [sctRAPIDDIAGNOSTICTEST]

1.* ✔	Was the sample taken for the RDT? [Was the sample taken for the RDT?]	[itmRDTSPL : LABSHEET_DATA.SAMPTAKE] [A:N] No [A:Y] Yes, Please complete the date of collection if different from the visit date
2. ✔	Date of collection [Date of collection]	[itmDATECOLLDT : LABSHEET_DATA.SAMPRDAT] (MM/DD/YYYY) Req / Req / Req (2014-2025)
3.* ✔	Was the Malaria Rapid Diagnosis Test performed? [Was the Malaria Rapid Diagnosis Test performed?]	[itmRAPID_FLG : SMPLCOLL_DATA.RAPD_FLG] [A:N] [itmFEVER_FLG : SMPLCOLL_DATA.FEVR_FLG] No --> [A:0] No reported fever [A:99] [itmSPECIFY_FEVER : SMPLCOLL_DATA.SPECIFY] Other, Specify A128 [A:Y] [itmRESULT : SMPLCOLL_DATA.RESULT] Yes --> Please record the result: [A:NEG] Negative [A:POS] Positive [A:INT] Indeterminate

SLIDE READINGS RESULTS [sctSLIDEREADINGSRESULTS]

4.* ✔	Was sample taken for slide reading? [Was sample taken for slide reading?]	[itmSLIDE_READ : LABSHEET_DATA.SAMPTAKE] [A:N] [itmREASON : SLIDE_S_DATA.REASON] No --->Reason A20 [A:Y] [itmSLDAVAL : SLIDE_S_DATA.SLD_NBR] Yes --> Please complete the following. [A:1] Only one [A:2] Two [itmDATECOLLDT1 : LABSHEET_DATA.SAMPRDAT] (MM/DD/YYYY) Please complete the date of collection if different from the visit date Req / Req / Req (2014-2025)
5.* ✔	Please specify the Slide Tracking number of the slide	[cmpSLIDE_TRACK_NBR] [itmSLIDETRACK_NBR : SLIDE_S_DATA.SLDTRKNB] Subject Number N9 [itmTRACK_NO : SLIDE_S_DATA.TRCK_NO] Tracking Number N2

	Slide Reading	Slide Reading Date	P Ovale	P Vivax	P Malaria	P Falciparum Result	P Falciparum parasites	P Falciparum Presence of Gametocytes	P Falciparum units/Î¼l	Readers' Code
6. ✔										

SLIDE READINGS RESULTS DETAILS Entry [sctRESULTSDETAILS]

6.1 ✔	Slide Reading *[read-only]* [Slide Reading]	[itmSLIDENB : SLIDE_M_DATA.SLIDENB] N10
6.2* ✔	Slide Reading Date [Slide Reading Date]	[itmSLIDE_READ_DT : SLIDE_M_DATA.SLDRD_DT] (MM/DD/YYYY) Req / Req / Req (2014-2025)
6.3* ✔	P Ovale [P Ovale]	[itmPOVALERESULT : SLIDE_M_DATA.POVALE] [A:NEG] Negative [A:POS] Positive
6.4* ✔	P Vivax [P Vivax]	[itmPVIVAXRESULT : SLIDE_M_DATA.PVIVAX] [A:NEG] Negative [A:POS] Positive
6.5* ✔	P Malaria [P Malaria]	[itmPMALARIARESULT : SLIDE_M_DATA.PMALARIA] [A:NEG] Negative [A:POS] Positive
6.6* ✔	P Falciparum Result	[itmPFALCIPARUMRESULT : SLIDE_M_DATA.PFALCIP] [A:NEG] Negative

	[P Falciparum Result]	[A:POS] Positive
6.7 ✔	P Falciparum parasites /Î¼l [P Falciparum parasites]	[itmPFALCIPARUMPARASITES : SLIDE_M_DATA.PF_CONC] N7
6.8* ✔	P Falciparum Presence of Gametocytes [P Falciparum Presence of Gametocytes]	[itmGAMETOCYTES : SLIDE_M_DATA.GAMETOCY] [A:Y] Yes [A:N] No
6.9 ✔	P Falciparum Gametocytes units/Î¼l [P Falciparum units/Î¼l]	[itmGAMETOCYTESUNITS : SLIDE_M_DATA.GA_CONC] N7
6.10* ✔	Readers' Code [Readers' Code]	[READ_CODE : SLIDE_M_DATA.READCODE] A5
SLIDE METHODOLOGY USED [sctSLIDEMETHODOLOGYUSED]		
7.* ✔	Please confirm the method used for the slide reading: [Method used for the slide reading:]	[itmMETHODOL : SMPLCOLL_DATA.METHODOL] [A:WCC] Using an assumed white cell count of 8000 Âµl [A:OTH] [itmMETHOD_OTH : SMPLCOLL_DATA.METHOD_OTH] Other, please explain: A128
8.* ✔	Was Slide shipped to GSK? [Was Slide shipped to GSK?]	[itmSHIPGSK : SMPLCOLL_DATA.SHIPGSK] [A:N] No [A:Y] Yes
9.	For GSK: *[hidden]* [Reconciled]	[itmRECONCIL_HID : SMPLCOLL_DATA.RECONCIL] [A:0] 0 - Lost in transit [A:1] 1 - Lost in site [A:2] 2 - Lost in GSK [A:3] 3 - Scrapped
FILTER PAPER COLLECTION [sctFILTCOLL]		
10.* ✔	Was the filter paper with 2-3 blood spots prepared? [Was the filter paper with 2-3 blood spots prepared?]	[itmfltpapr : LABSHEET_DATA.SAMPTAKE] [A:N] No [A:Y] Yes, Please complete the date of collection if different from the visit date
11. ✔	Date of collection [Date of collection]	[itmDATECOLLDT : LABSHEET_DATA.SAMPRDAT] **(MM/DD/YYYY)** Req / Req / Req (2014-2025)
12.* ✔	Was the filter paper shipped to the laboratory? [Was the filter paper shipped to the laboratory?]	[itmFILTERSHP : SMPLCOLL_DATA.FILTRSHP] [A:N] No [A:Y] Yes
13.	For GSK: *[hidden]* [Reconciled]	[itmRECONCIL_HID : SMPLCOLL_DATA.RECONCIL] [A:0] 0 - Lost in transit [A:1] 1 - Lost in site [A:2] 2 - Lost in GSK [A:3] 3 - Scrapped

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: INFORMED CONSENT (IC_V2) [frmINFORMEDCONSENTRRA_V2]

DATE OF VISIT [sctDATEOFVISIT_V2]

1.*	Date of Visit [Date of Visit]	[*itmACTRDATE_V2* : *ACTDATES_DATA.ACTRDATE*] **(MM/DD/YYYY)** Req ___ / Req ___ / Req ____ (2019-2030)

INFORMED CONSENT [sctINFORMEDCONSENT_V2]

I certify that Inform Consent has been obtained prior to any study procedure.

2.* ✔	Local informed consent version number	[*itmINF_NB_V2* : *CONSENT_DATA.DSSPID*] *A128*
3.* ✔	Informed consent date	[*itmCONS_DAT_V2* : *CONSENT_DATA.CONS_DAT*] **(MM/DD/YYYY)** Req ___ / Req ___ / Req ____ (2019-2030)
4.* ✔	Please indicate if the subject's **samples and coded data** can be used for further research **related to this study vaccine / disease** once the study is complete	[*itmCONS_LAB_REL* : *CONS_LAB_DATA.CONSLABA*] *[A:Y]* Yes *[A:N]* No *[A:NA]* Unknown/Answer not available
5.* ✔	Please indicate if the subject's **samples and coded data** can be used for further research **NOT related to this study vaccine / disease** once the study is complete	[*itmCONS_LAB_NREL* : *CONS_LAB_DATA.CONSLABA*] *[A:Y]* Yes *[A:N]* No *[A:NA]* Unknown/Answer not available

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: LOG STATUS (Log Status) [frmLOG_STATUS_FLG]

CONCOMITANT VACCINATION [sctCONC_VACC_FLG]

1.* ✔	Did the subject receive 3rd dose of DTP/Pentavalent vaccine, 1st dose of Measles vaccine and atleast one dose of RTS,S vaccine [Did the subject receive 3rd dose of DTP/Pentavalent vaccine, 1st dose of Measles vaccine and atleast one dose of RTS,S vaccine]	[*itmCONCFLG* : *CVSHEET_DATA.CV_FLAG*] *[A:Y]* ☐ Yes --> Please complete the corresponding page *[A:N]* ☐ No

MEDICATION [sctMED_FLG]

2.* ✔	Was the subject administered any antimalarial or any other medication within 14 days prior to study visit [Was the subject administered any antimalarial or any other medication within 14 days prior to study visit]	[*itmMD_FLG* : *MDSHEET_DATA.MD_FLAG*] *[A:Y]* ☐ Yes --> Please complete the corresponding page *[A:N]* ☐ No

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: MEDICATION (Medication) - Repeating Form [CONMEDS_CR]

#	Drug Name	Antimalarial drug	Medical indication:	Total daily dose	Route	Start date	End date
1							

MEDICATION [sctCM]

1.* ✔	Drug name: [Drug Name]	[CMTERM : MEDIC_DATA.TRADNAME] A100
2.* ✔	Antimalarial drug	[itmANTIDRUG : MEDIC_DATA.ANTIDRUG] [A:N] No [A:Y] Yes
3.	Modified reported term *[hidden]*	[CMMODIFY : MEDIC_DATA.GSK_MOD] A100
4.	GSK Drug synonym *[hidden]*	[CMDRGSYN] A100
5.	GSK Drug Collection code *[hidden]*	[CMDRGCOL : MEDIC_DATA.GSK_COD] A10
6.	Failed coding *[hidden]*	[calCM_FAILED] A10
7.* ✔	Medical indication:	[cmpMEDINDIC] [itmMEDINDIC : MEDIC_DATA.MEDINDIC] A80 [itmCHRON_CK : MEDIC_DATA.CHRON_CK] Chronic use [A:Y]
8.* ✔	Total daily dose: [Total daily dose]	[cmpTOTDDOSE] [itmMED_DOSE : MEDIC_DATA.MED_DOSE] Dose: A20 [itmMED_UNIT : MEDIC_DATA.MED_UNIT] Unit: A20
9.* ✔	Route: [Route]	[itmMED_ROUT : MEDIC_DATA.MED_ROUT] [clMEDROUT_MED]
10.* ✔	Start date: [Start date]	[itmSRDAT : MEDIC_DATA.MEDSRDAT] **(MM/DD/YYYY)** Req/Unk / Req/Unk / Req/Unk (2000-2025)
11.* ✔	End date: or tick box if continuing at the end of the study [End date]	[cmpMEDERDAT] [itmERDAT : MEDIC_DATA.MEDERDAT] **(MM/DD/YYYY)** Req/Unk / Req/Unk / Req/Unk (2000-2025) [itmCONT_END : MEDIC_DATA.CONT_END] Continuing at the end of the study [A:Y]
12.	For GSK - MON: *[hidden]* [For GSK - MON]	[itmMD_TRANS : MEDIC_DATA.MD_TRANS] A60
13.	Drug name: Generic name is preferred but trade name is preferred in case of multi-component drugs *[hidden]* [Drug name]	[CMCOMPARE] A100
14.	Drug name:	[CMMODCOMPARE]

	Generic name is preferred but trade name is preferred in case of multi-component drugs *[hidden]* [Drug name]	*A100*

Key: [*] = Item is required [✔] = Source verification required
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Codelist Values Tables: MEDICATION

Codelist RefName	Codelist Data Type	Subset	Label	Code	Codelist Item RefName	Data Variable RefName
clMEDROUT_MED	String		Inhalation	IH	citmINHALATION_1	itmMED_ROUT
			Intraarticular	IR	citmINTRAARTICULAR	
			Intradermal	ID	citmINTRADERMAL_1	
			Intramuscular	IM	citmINTRAMUSCULAR_1	
			Intranasal	IN	citmINTRANASAL_1	
			Intravenous	IV	citmINTRAVENOUS_1	
			Oral	PO	citmPORAL_1	
			Parenteral	PE	citmPARENTERAL_1	
			Rectal	PR	citmPRECTAL_1	
			Subcutaneous	SC	citmSUBCUTANEOUS_1	
			Sublingual	SL	citmSUBLINGUAL_1	
			Topical	TO	citmTOPICAL_1	
			Transdermal	TD	citmTRANSDERMAL_1	
			Vaginal	VA	citmVAGINAL_1	
			Other	OTH	citmOTHER_OTH_1	
			Unknown	UNK	citmUNK_1	

p116682: CONCOMITANT VACCINATION (Concomitant vaccination) - Repeating Form [frmCONC_VACCINATION]

#	Which vaccine did the subject receive?	VACCINE DETAILS
1		

VACCINE TYPE [sctVAC_TYP]

1.	Which vaccine did the subject receive? *[read-only]* [Which vaccine did the subject receive?]	[*itmVAC_TYP* : *VACC_CON_DATA.VACC_TYP*] *[A:1]* DTP (3rd Dose) *[A:2]* Pentavalent (3rd Dose) *[A:3]* Measles (1st Dose) *[A:4]* RTS,S

	Vaccine name	Route	Date of administration
2. ✔			

VACCINE DETAILS Entry [sctVAC_DET]

2.1	Vaccine name: (Trade name is preferred) *[read-only]* [Vaccine name]	[*itmCVACC_TRADNAME* : *VACC_CON_DATA.TRADNAME*] *A60*
2.2	Route: *[read-only]* [Route]	[*itmCVACC_ROUTE* : *VACC_CON_DATA.MED_ROUT*] *[A:IH]* Inhalation *[A:ID]* Intradermal *[A:IM]* Intramuscular *[A:IN]* Intranasal *[A:IV]* Intravenous *[A:PO]* Oral *[A:PE]* Parenteral *[A:SC]* Subcutaneous *[A:SL]* Sublingual *[A:TD]* Transdermal *[A:OTH]* [*itmPLSPCFY* : *VACC_CON_DATA.OTHER*] Other --> Please specify *A250* *[A:UNK]* Unknown
2.3	Date of administration: *[read-only]* [Date of administration]	[*itmCVACC_RDAT* : *VACC_CON_DATA.MEDSRDAT*] **(MM/DD/YYYY)** Req/Unk / Req/Unk / Req/Unk (2003-2025)
2.4	For GSK - MON: *[hidden]* [For GSK - MON]	[*itmMON_TRANS* : *VACC_CON_DATA.MD_TRANS*] *A60*
2.5	For GSK - DM: *[hidden]* [For GSK - DM]	[*itmGSK_MOD_HID* : *VACC_CON_DATA.GSK_MOD*] *A60*

Key: [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: CONCOMITANT VACCINATION V2 (Concomitant vaccination V2) [frmCONC_VACCINATION_V2]

	Which vaccine did the subject receive?	Vaccine name	Route	Date of administration
1. ✔				

VACCINE DETAILS Entry [sctVAC_DET_V2]

1.1* ✔	Type of vaccine [Which vaccine did the subject receive?]	[*itmVAC_TYP_V2* : *VACC_CON_DATA.VACC_TYP*] *[A:1]* ☐ DTP (3rd Dose) *[A:5]* ☐ Tetravalent (3rd Dose) *[A:2]* ☐ Pentavalent (3rd Dose) *[A:3]* ☐ Measles (1st Dose) *[A:4]* ☐ RTS,S *[A:OTH]* ☐ Other
1.2* ✔	Vaccine name: (Trade name is preferred) [Vaccine name]	[*itmCVACC_TRADNAME_V2* : *VACC_CON_DATA.TRADNAME*] *A60*
1.3* ✔	Route: [Route]	[*itmCVACC_ROUTE_V2* : *VACC_CON_DATA.MED_ROUT*] *[A:IH]* ☐ Inhalation *[A:ID]* ☐ Intradermal *[A:IM]* ☐ Intramuscular *[A:IN]* ☐ Intranasal *[A:IV]* ☐ Intravenous *[A:PO]* ☐ Oral *[A:PE]* ☐ Parenteral *[A:SC]* ☐ Subcutaneous *[A:SL]* ☐ Sublingual *[A:TD]* ☐ Transdermal *[A:OTH]* ☐ [*itmPLSPCFY_V2* : *VACC_CON_DATA.OTHER*] Other --> Please specify *A250* *[A:UNK]* ☐ Unknown
1.4* ✔	Date of administration: [Date of administration]	[*itmCVACC_RDAT_V2* : *VACC_CON_DATA.MEDSRDAT*] **(MM/DD/YYYY)** ☐ Req/Unk ☐ / ☐ Req/Unk ☐ / ☐ Req/Unk ☐ (2003-2025)
1.5	For GSK - MON: *[hidden]* [For GSK - MON]	[*itmMON_TRANS_V2* : *VACC_CON_DATA.MD_TRANS*] *A60*
1.6	For GSK - DM: *[hidden]* [For GSK - DM]	[*itmGSK_MOD_V2_HID* : *VACC_CON_DATA.GSK_MOD*] *A60*

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: OCCURRENCE OF EXPEDITED ADVERSE EVENTS (SAE Flag) [frmSAE_FLG]

OCCURRENCE OF EXPEDITED ADVERSE EVENTS [sctSAE_FLG]

1.* ✔	Did the subject experience any SAE following the capillary blood sample collection ? [Did the subject experienced any SAE following the capillary blood sample collection ?]	[*itmSAE_FLG* : *AESHEET_DATA.AE_FLAG*] *[A:Y]* ☐ Yes -> Please remember to complete a Expedited Adverse Event Report *[A:N]* ☐ No

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: EXPEDITED ADVERSE EVENT (Expedited Adverse Events) - Repeating Form [AE_SER_CR]

#	Expedited ADVERSE EVENT Report No.	SERIOUS ADVERSE EVENT	Specify the reason for considering this event as SAE.	RELEVANT CONCOMITANT/TREATMENT MEDICATIONS/VACCINATIONS	RELEVANT MEDICAL CONDITIONS/RISK FACTORS	RELEVANT DIAGNOSTIC RESULTS	Relevant diagnostic results not noted on the left columns	General narrative comments
1								

If you wish to record a new SAE please determine if the new SAE is clinically or temporally related to an SAE previously entered on this form.
If yes, record the details below using the 'Add Entry' button in this form.
If not clinically or temporally related, create a new SAE form for this subject by clicking on the 'New' button at the top of the page.
Do not record pre and post randomization events on the same form.

EXPEDITED ADVERSE EVENT REPORT NO. [sctSAE_REPORT_NO]

1. ✔	Expedited ADVERSE EVENT Report No. *[read-only]* [Expedited ADVERSE EVENT Report No.]	[*itmSAE_NB* : *SAE_DATA.SAE_NB*] *N2*
2.	Start date of SAE (minimum date from sctSAE) *[hidden]* [Start date if SAE (minimum date from sctSAE)]	[itmSAE_STRT] **(MM/DD/YYYY)** NReq / NReq / NReq (2000-2025)
3.	Stop date of SAE (maximum date from sctSAE) *[hidden]* [Stop date of SAE (maximum date from sctSAE)]	[itmSAE_STOP] **(MM/DD/YYYY)** NReq / NReq / NReq (2000-2025)

TYPE OF REPORT [sctSAE_TOR]

4.	Initial Report *[hidden]* [Initial Report]	[chkSAE] *[A:1]* Initial
5.	Follow-Up Report *[hidden]* [Follow-Up Report]	[chkFU] *[A:2]* Follow-Up

RANDOMIZATION [sctSAE_RAND]

6.	Did the event occur after initiation of investigational product(s)? *[hidden]* [Did SAE occur after initiation of study medication?]	[*rdcSAERAND* : *SAE_DATA.SAE_RAND*] *[A:Y]* Yes *[A:N]* No

	No.	Event	Start date and time	Outcome / End date and time	Maximum Intensity	Did the subject withdraw from study due to this event?	Was the AE caused by activities related to study procedure?	Medically attended visit
7. ✔								

SERIOUS ADVERSE EVENT Entry [sctSAE]

Use the 'Add Entry' button to enter details of the SAE. For additional SAEs that are clinically or temporally related (e.g., SAEs that occur during the same hospitalization) use the 'Add Entry' button to create a new row for entry of the additional SAE. Enter ONE event per row.

7.1	No. *[read-only]* [No.]	[*AESEQ* : *AE_DATA.AESEQ;OC_SAEDT_DATA.AESEQ;SAE_DATA.AESEQ*] *N5*
7.2* ✔	Event : Diagnosis only (if known), otherwise sign/symptom [Event]	[*AETERM* : *AE_DATA.AE_DESC*] *A100*
7.3	Serious? *[hidden]* [Serious?]	[*itmAESER* : *AE_DATA.AE_SER*] *[A:3]* Serious *[A:1]* Non-Serious
7.4	Potential immune mediated disease (pIMD)? *[hidden]*	[*itmPIMD* : *AE_DATA.P_IMD*] *[A:1]* pIMD *[A:2]* Non pIMD
7.5	MedDRA synonym *[hidden]*	[AEMEDSYN] *A100*
7.6	MedDRA lower level term code *[hidden]*	[*AELLTCD* : *AE_DATA.MD_CODE*] *A10*

7.7	Failed coding *[hidden]*	[calAE_FAILED] *A10*
7.8*	Start date and time Hr:Min (00:00-23:59) [Start date and time]	[***AESTDTTM*** : ***AE_DATA.AE_SRDAT***] **(MM/DD/YYYY hh:mm)** Req/Unk / Req/Unk / Req (2000-2025) NReq : NReq *24-hour clock*
7.9*	Outcome / End date and time Hr:Min (00:23-59) [Outcome / End date and time]	[***AEOUTCD1*** : ***AE_DATA.OUTCOME***] *[A:1]* [***AEENDTTM1*** : ***AE_DATA.AE_ERDAT***] **(MM/DD/YYYY hh:mm)** Recovered/resolved, provide End date and time Req/Unk / Req/Unk / Req/Unk (2000-2025) NReq : NReq *24-hour clock* *[A:2]* Recovering/resolving *[A:3]* Not recovered/not resolved *[A:4]* [***AEENDTTM2*** : ***AE_DATA.AE_ERDAT***] **(MM/DD/YYYY hh:mm)** Recovered/resolved with sequelae, provide End date and time Req/Unk / Req/Unk / Req/Unk (2000-2025) NReq : NReq *24-hour clock* *[A:5]* [***AEENDTTM3*** : ***AE_DATA.AE_ERDAT***] **(MM/DD/YYYY hh:mm)** Fatal, record Date and time of Death Req/Unk / Req/Unk / Req/Unk (2000-2025) NReq : NReq *24-hour clock*
7.10*	Maximum Intensity **Record maximum intensity throughout duration of event** [Maximum Intensity]	[***AESEVCD*** : ***AE_DATA.AE_INTEN***] *[A:1]* Mild *[A:2]* Moderate *[A:3]* Severe *[A:X]* Not applicable
7.11	Intensity at onset of event **Record intensity at the onset of the event** *[hidden]* [Intensity at onset of event]	[ADSEVCD] *[A:1]* Mild *[A:2]* Moderate *[A:3]* Severe *[A:X]* Not applicable
7.12	Maximum Grade **Record maximum grade throughout duration of event** *[hidden]* [Maximum Grade]	[AETOXCD] *[A:1]* Grade 1 *[A:2]* Grade 2 *[A:3]* Grade 3 *[A:4]* Grade 4 *[A:5]* Grade 5
7.13	Grade at onset of event **Record grade at the onset of the event** *[hidden]* [Grade at onset of event]	[ADTOXCD] *[A:1]* Grade 1 *[A:2]* Grade 2 *[A:3]* Grade 3 *[A:4]* Grade 4 *[A:5]* Grade 5
7.14	Maximum Grade or Intensity **Record maximum grade or intensity throughout duration of event** *[hidden]* [Maximum Grade or Intensity]	[AETXHVCD] *[A:1]* Mild or Grade 1 *[A:2]* Moderate or Grade 2 *[A:3]* Severe or Grade 3 *[A:4]* Grade 4 *[A:X]* Not applicable
7.15	Grade or Intensity at onset of event **Record grade or intensity at the onset of the event** *[hidden]* [Grade or Intensity at onset of event]	[ADTXHVCD] *[A:1]* Mild or Grade 1 *[A:2]* Moderate or Grade 2 *[A:3]* Severe or Grade 3 *[A:4]* Grade 4 *[A:X]* Not applicable
7.16	Action taken with investigational product(s) as a result of the event: *[hidden]* [Action taken with investigational product(s) as a result of the event]	[***AEACTRCD*** : ***OC_SAE_DATA.SAE_ACT***] *[A:1]* Investigational product(s) withdrawn

		[A:4] ☐ Dose not changed *[A:5]* ☐ Dose delayed *[A:X]* ☐ Not applicable
7.17	Modified term ***Do not query this item. it is not displayed for sites.*** *[hidden]* [Modified term]	[***AEMODIFY*** : ***AE_DATA.MD_MOD***] *A100*
7.18*	Did the subject withdraw from study due to this event? [Did the subject withdraw from study due to this event?]	[***AEWD*** : ***OC_SAE_DATA.WITHDRAW***] *[A:Y]* ☐ Yes *[A:N]* ☐ No
7.19	Is there a reasonable possibility that the event may have been caused by the investigational product(s)? ***Use best judgment at initial entry. May be amended when additional information becomes available.*** *[hidden]* [Is there a reasonable possibility that the event may have been caused by the investigational product(s)?]	[***AEREL*** : ***AE_DATA.CAUSAL***] *[A:N]* ☐ No *[A:Y]* ☐ Yes
7.20	Duration of AE if < 24 hours *[hidden]* [Duration of AE if < 24 hours]	[cmpAEDUR] [AEDURHR] *0 <= N2 <= 23* Hr(s) [AEDURMIN] *0 <= N2 <= 59* Min(s)
7.21	Time to Onset Since Last Dose *[hidden]* [Time to Onset]	[cmpAEONLDS] [AEONLDSH] Hr(s) *0 <= N2 <= 23* [AEONLDSM] Min(s) *0 <= N2 <= 59*
7.22*	Was the AE caused by activities related to study procedure? [Was the AE caused by activities related to study procedure?]	[***rdcAESREL*** : ***OC_SAE_DATA.REL_PART***] *[A:Y]* ☐ Yes *[A:N]* ☐ No
7.23	Was the event serious? *[hidden]* [Was the event serious?]	[AESER] *[A:Y]* ☐ Yes *[A:N]* ☐ No
7.24	Related Investigational Product *[hidden]* [Related Investigational Product]	[txtAERDG] *A80*
7.25	AE description: Diagnosis only (if known), otherwise sign/symptom *[hidden]* [AE description]	[AECOMPARE] *A100*
7.26	AE description: Diagnosis only (if known), otherwise sign/symptom *[hidden]* [AE description]	[AEMODCOMPARE] *A100*
7.27	Yes, select appropriate investigational product(s) *[hidden]* [Investigational product(s)]	[AERDGCD] *[A:X]* ☐ [enter protocol specific IP definition 1] *[A:Y]* ☐ [enter protocol specific IP definition 2] *[A:Z]* ☐ [enter protocol specific IP definition 3]
7.28	SAEEmailFlag *[hidden]* [SAEEmailFlag]	[txtSAEEmailFlag] *A6*
7.29* ✔	Medically attended visit: [Medically attended visit]	[***itmMED_TYPE*** : ***AE_DATA.MED_TYPE***] *[A:ER]* ☐ Emergency Room *[A:HO]* ☐ Hospitalisation *[A:MD]* ☐ Medical Personnel *[A:NO]* ☐ None
7.30	Narrative include clinical *[hidden]*	[itmNARRATIVEINCLUDECLINICAL] *A255*

[sctEMERGENT]

8.	Sequence Number *[hidden]* [Sequence Number]	[AESEQ2] *N5*
9.	AE description: Diagnosis only (if known), otherwise sign/symptom *[hidden]*	[AETERM_1] *A100*
10.	Start Date and Time of event segment Hr:Min (00:00-23:59) *[hidden]* [Start Date of event segment]	[ADSTDTTM] **(MM/DD/YYYY hh:mm)** Req / Req / Req (2000-2025) NReq : NReq *24-hour clock*
11.	Intensity of event segment *[hidden]* [Intensity of event segment]	[ADSEVCD1] *[A:1]* Mild *[A:2]* Moderate *[A:3]* Severe
12.	Grade of event segment *[hidden]* [Grade of event segment]	[ADTOXCD2] *[A:1]* Grade 1 *[A:2]* Grade 2 *[A:3]* Grade 3 *[A:4]* Grade 4 *[A:5]* Grade 5
13.	Grade or Intensity of event segment *[hidden]* [Grade or Intensity of event segment]	[ADTXHVCD2] *[A:1]* Mild or Grade 1 *[A:2]* Moderate or Grade 2 *[A:3]* Severe or Grade 3 *[A:4]* Grade 4 *[A:5]* Grade 5

SERIOUSNESS [sctSAE_SER]

14.* ✔	Specify the reason for considering this event as SAE. (Tick all that apply) [Specify the reason for considering this event as SAE.]	[*chkAESER* : *SAE_DATA.SER_CRIT*] *[A:A]* Results in death *[A:B]* Is life-threatening (subject was at risk of death at time of event) *[A:C]* Requires hospitalisation or prolongation of hospitalisation (Provide admission and discharge date(s) in narrative) *[A:D]* Results in disability/incapacity (substantial / permanent) *[A:E]* Congenital anomaly/birth defect (in offspring of subject) *[A:F]* Other, specify within general narrative comment

	Drug Name	Total daily dose	Route	Start Date	End date	Medical Indication	Drug type
15. ✔							

RELEVANT CONCOMITANT/TREATMENT MEDICATIONS/VACCINATIONS Entry [sctSAE_CM]

Use the 'Add Entry' button to enter details of any medication/vaccine that may help to explain the SAE, may have caused the SAE or was used to treat the SAE. Ensure each concomitant vaccination or medication recorded in this section is also recorded in the corresponding form located in the LOGS section of the eCRF.

15.1	CM Sequence Number *[hidden]* [CM Sequence Number]	[txtSAECMSEQ] *A4*
15.2* ✔	Drug name: [Drug Name]	[*CMTERM* : *OC_CMVAC_DATA.TRADNAME*] *A100*
15.3	Modified reported term *[hidden]* [Modified reported term]	[*txtCMMODIFY* : *OC_CMVAC_DATA.GSK_MOD*] *A100*

15.4 ✔	Total daily dose: [Total daily dose]	[cmpSAECMDOS] [txtSAECMDOS] Dose: xxxxxxxxx. [*pdcCMUNIT* : *OC_CMMED_DATA.MED_UNIT*] Unit: [*clCMUNITSAE*]
15.5	Frequency *[hidden]* [Frequency]	[pdcSAECMFRQ] [*clSAECMFRQ*]
15.6*	Route [Route]	[*pdcCMROUTCD* : *OC_CMVAC_DATA.MED_ROUT;SAE_DATA.CT_ROUTE*] [*clMEDROUT_MEDSAE*]
15.7*	Start Date [Start Date]	[*dtmSAECMSTD* : *OC_CMVAC_DATA.MEDSRDAT;SAE_DATA.CT_STRT*] **(MM/DD/YYYY)** NReq/Unk / NReq/Unk / NReq/Unk (2000-2025)
15.8 ✔	End date: or tick box if continuing at the end of the study [End date]	[cmpSAECMEND] [dtmSAECMEND] **(MM/DD/YYYY)** NReq/Unk / NReq/Unk / NReq/Unk (2000-2025) [rdcSAECMONG] Continuing at the end of the study A1
15.9	Medical indication *Enter a medical diagnosis not description* [Medical Indication]	[txtCMIND] A50
15.10	Modified reported term *[hidden]* [Modified reported term]	[txtCMINDMODIFY] A100
15.11*	Drug type: [Drug type]	[*pdcCMDRGTYP* : *OC_CMVAC_DATA.DRUG_TYP;SAE_DATA.CT_TYP*] [*clDRUGTYP*]
15.12	CM COMPARE (Hidden) *[hidden]* [CM COMPARE (Hidden)]	[txtCMCOMPARE] A100
15.13	CMIN COMPARE (Hidden) *[hidden]* [CMIN COMPARE (Hidden)]	[txtCMINCOMPARE] A100

	Condition	Start date	Continuing at time of SAE?
16. ✔			

RELEVANT MEDICAL CONDITIONS/RISK FACTORS Entry [sctSAE_MHX]

Use the 'Add Entry' button to enter each past or current medical disorder, allergy or surgery that may be RELEVANT to the SAE. Enter a diagnosis, not description. Relevant family or social history shoud be described in the 'General Narrative Comments' at the bottom of this form. Ensure each medical condition/risk factor recorded in this section is also recorded in the General Medical History form located at the beginning of the eCRF.

16.1	MHx Sequence Number *[hidden]* [MHx Sequence Number]	[txtMHXSEQ] A4
16.2*	Condition ***Enter a medical diagnosis not description.*** [Condition]	[*txtSAEMHTRM* : *OC_MDCON_DATA.CON_DESC;SAE_DATA.MH_COND*] A100
16.3	Modified reported term *[hidden]* [Modified reported term]	[*txtSAEMHMODIFY* : *OC_MDCON_DATA.MD_MOD*] A100
16.4*	Start date: [Start date]	[*dtmMHSTDTM* : *OC_MDCON_DATA.MCSTR_DT;SAE_DATA.MH_STRT*] **(MM/DD/YYYY)** Req/Unk / Req/Unk / Req/Unk (2000-2025)

16.5*	Continuing at time of SAE? [Continuing at time of SAE?]	[*rdcMHCONT* : *OC_MDCON_DATA.CONT_SAE*] *[A:Y]* Yes *[A:N]* [*dtmMHLSTOC* : *OC_MDCON_DATA.MCEND_DT;SAE_DATA.MH_END*] **(MM/DD/YYYY)** No, specify end date or date of last occurrence Req/Unk / Req/Unk / Req/Unk (2000-2025) *[A:U]* Unknown, no information available
16.6	SAE MHX COmpare (Hidden) *[hidden]* [SAE MHX COmpare (Hidden)]	[txtMHXCOMPARE] *A100*

	Test name	Test date	Test result	Test units	Normal low range	Normal high range
17. ✔						

RELEVANT DIAGNOSTIC RESULTS Entry [sctSAE_LAB]

Use the 'Add Entry' button to enter details of relevant tests or procedures carried out to diagnose or confirm the SAE or rule out other diagnoses

17.1	Lab Sequence Number *[hidden]* [Lab Sequence Number]	[txtSAELBSEQ] *A4*
17.2*	Test name [Test name]	[*pdcLBTST* : *OC_LABRS_DATA.LAB_NAME;SAE_DATA.DIAG_NAME*] *[clSAELBTST]*
17.3*	Test date [Test date]	[*dtmLABDTM* : *OC_LABRS_DATA.LAB_DT;SAE_DATA.DIAG_STRT*] **(MM/DD/YYYY)** Req/Unk / Req/Unk / Req (2000-2025)
17.4*	Test result [Test result]	[*txtLABRES* : *OC_LABRS_DATA.LAB_RES*] *A12*
17.5*	Test units [Test units]	[*txtLABUNIT* : *OC_LABRS_DATA.LAB_U*] *A12*
17.6*	Normal low range [Normal low range]	[*txtLABNLR* : *OC_LABRS_DATA.LAB_L;SAE_DATA.DIAG_LOW*] *xxxxxxxxx.xx*
17.7*	Normal high range [Normal high range]	[*txtLABNHR* : *OC_LABRS_DATA.LAB_H;SAE_DATA.DIAG_HIGH*] *xxxxxxxxx.xx*

[sctSAE_LABTXT]

18.	Enter here only the diagnostic results that could not be entered in the above grid, including procedure such as ECG, X rays, etc and tests on stool, CSF etc. Also provide dates. [Relevant diagnostic results not noted on the left columns]	[cmpLABTEXT] [*txtLABTEXT* : *OC_LABRS_DATA.LAB_DET*] *A1000* [*txtLABTEXT1* : *OC_LABRS_DATA.LABTEXT1*] *A1000*

[sctSAE_IP]

19.	If investigational product(s) were stopped temporarily, did the reported event(s) recur after investigational products were restarted? *[hidden]* [If investigational product(s) were stopped temporarily, did the reported event(s) recur after investigation products were restarted?]	[rdcSAEIP] *[A:N]* No *[A:Y]* Yes *[A:U]* Unknown at this time *[A:X]* Not applicable

GENERAL NARRATIVE COMMENTS [sctSAE_COM]

Provide a clear (this narrative will be provided to regulatory authorities) and brief chronological description (with dates) of the clinical course of the event including:
- Associated signs and symptoms
- Clinical evolution (hospitalisation, outcome, description of sequelae if any, autopsy results, etc.)
- Non-drug treatment such as surgery
- Other information useful for the medical assessment of the case (e.g. reason for diagnosis if not obvious or if diagnosis changed)
- Relevant additional risk factors including family or social history (negative sentence can also be helpful)
- Possible cause(s) of the event
- Rationale for relationship when SAE is possibly related to study product, concomitant product or study procedure, etc.

Complete a new box only when the previous one is full.

20.* General narrative comments

[cmpNARRATIVE]

[*txtSAECOMM : OC_SAEDT_DATA.SAECOMM*]

A1000

[*txtSAECOMM1 : OC_SAEDT_DATA.SAECOMM1*]

A1000

[*txtSAECOMM2 : OC_SAEDT_DATA.SAECOMM2*]

A1000

[*txtSAECOMM3 : OC_SAEDT_DATA.SAECOMM3*]

A1000

NON CLINICAL [sctSAE_NC]		
21.	Send incomplete SAE data to GSK Safety *[hidden]* [Send incomplete SAE data to GSK Safety]	[***chkSENDI*** **:** ***OC_SAFAD_DATA.REQDLOAD***] *[A:3]* ☐ Incomplete SAE
22.	Receipt by GSK date *[hidden]* [Receipt by GSK date]	[***dtmSAEDTM*** **:** ***AE_DATA.DTMSAEDTM;OC_SAFAD_DATA.LSTULOAD***] **(MM/DD/YYYY hh:mm)** ☐ Req ☐ / ☐ Req ☐ / ☐ Req ☐ (2000-2025) ☐ Req ☐ : ☐ Req ☐ *24-hour clock*
23.	Was the event serious? *[hidden]* [Was the event serious?]	[AESER] *[A:Y]* ☐ Yes *[A:N]* ☐ No
24.	Sequence Number *[hidden]* [Sequence Number]	[AESEQ1] *N5*
25.	Version Number *[hidden]* [Version Number]	[txtSAEVERSION] *A4*
26.	Case ID *[hidden]* [Case ID]	[***txtSAEID*** **:** ***OC_SAFAD_DATA.OCEAN_ID***] *A20*
27.	Randomisation Number *[hidden]* [Randomisation Number]	[txtSAERNDNO] *A255*
28.	OCEANS Code *[hidden]* [OCEANS Code]	[***txtOCEANSCD*** **:** ***SAE_DATA.CASE_ID***] *A13*
29.	eMail flag *[hidden]*	[calSAEEmailFlag] *A6*
30.	Message sender identifier *[hidden]* [mssgsendid]	[itmMESSAGESENDERIDENTIFIER] *A128*
31.	Study Type *[hidden]* [Study Type]	[itmSAESTUDYTPE] *A128*

32.	Modification datetime *[hidden]*	[itmMOD_DATE] **(MM/DD/YYYY hh:mm:ss)** NReq / NReq / NReq (2000-2025) NReq : NReq : NReq *24-hour clock*

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

Codelist Values Tables: EXPEDITED ADVERSE EVENT

Codelist RefName	Codelist Data Type	Subset	Label	Code	Codelist Item RefName	Data Variable RefName
clCMUNITSAE	String		ACTU	ACTU	clCMUNIT_ACTU	pdcCMUNIT
			AMP	AMP	clCMUNIT_AMP	
			application(s)	AP	clCMUNIT_AP	
			BT	BT	clCMUNIT_BT	
			capsule	CAP	clCMUNIT_CAP	
			Cubic centimeter	CC	clCMUNIT_CC	
			MBecquerel	16	citmCMUNIT_MBQ	
			Variable dose	VA	citmCMUNIT_VA	
			blister	BLS	citmCMUNIT_BLS	
			caplet(s)	CAPL	citmCMUNIT_CAPL	
			cg	CG	citmCMUNIT_CG	
			drop(s)	31	citmCMUNIT_DROP	
			elisa unit	EU	citmCMUNIT_EU	
			g/L	GML	citmCMUNIT_GML	
			g/M2	GM/M2	citmCMUNIT_GMM2	
			g/kg	GM/KG	citmCMUNIT_GMKG	
			grain	GR	citmCMUNIT_GR	
			gram(s)	2	citmCMUNIT_G	
			inch	INCH	citmCMUNIT_INCH	
			injection	INJ	citmCMUNIT_INJ	
			iu	25	citmCMUNIT_IU	
			iu x 10**3	26	citmCMUNIT_IU3	
			iu x 10**6	27	citmCMUNIT_IU6	
			liter	11	citmCMUNIT_L	
			lozenge	LOZ	citmCMUNIT_LOZ	
			mCi	19	citmCMUNIT_MCI	
			mEq	29	citmCMUNIT_MEQ	
			mcg	4	citmCMUNIT_MCG	
			mcg/mg	MCG/MG	citmCMUNIT_MCGMG	
			Megaunits (million units)	MEGU	citmCMUNIT_MEGU	
			mg	3	citmCMUNIT_MG	
			mg/kg	7	citmCMUNIT_MGK	
			mg/m2	9	citmCMUNIT_MGM2	
			mg/min	MGM	citmCMUNIT_MGM	

			mg/ml	MGML	citmCMUNIT_MGML		
			micro unit	MCRU	citmCMUNIT_MCU		
			ml	12	citmCMUNIT_ML		
			ml/hr	MLH	citmCMUNIT_MLH		
			mm	MM	citmCMUNIT_MM		
			mmol	23	citmCMUNIT_MMOL		
			nebule(s)	NEB	citmCMUNIT_NEB		
			ng	5	citmCMUNIT_NG		
			ng/kg	NGK	citmCMUNIT_NGK		
			ounce	OZ	citmCMUNIT_OZ		
			patch	PAT	citmCMUNIT_PAT		
			percent	30	citmCMUNIT_PCT		
			puff(s)	PUFF	citmCMUNIT_PUFF		
			sachet	SAC	citmCMUNIT_SAC		
			spray	SPR	citmCMUNIT_SPR		
			suppository	SUP	citmCMUNIT_SUP		
			tablespoon	TBS	citmCMUNIT_TBS		
			tablet	TAB	citmCMUNIT_TAB		
			teaspoon	TSP	citmCMUNIT_TSP		
			uBecquerel	14	citmCMUNIT_UBQ		
			ugk	8	citmCMUNIT_UGK		
			umol	24	citmCMUNIT_UMOL		
			unit	UNT	citmCMUNIT_UNT		
			unknown	U	citmCMUNIT_U		
			vial(s)	VIA	citmCMUNIT_VIA		
clSAECMFRQ	String		2 times per week	2W	clSAECMFRQ_2W	pdcSAECMFRQ	
			3 times per week	3W	clSAECMFRQ_3W		
			4 times per week	4W	clSAECMFRQ_4W		
			5 times per day	5D	clSAECMFRQ_5D		
			5 times per week	5W	clSAECMFRQ_5W		
			AC	AC	clSAECMFRQ_AC		
			BID	2D	clSAECMFRQ_2D		
			Continuous infusion	CO	clSAECMFRQ_CO		
			Every 2 weeks	FO	clSAECMFRQ_F		
			Every 3 weeks	Q3W	clSAECMFRQ_Q3W		
			Every 3 months	Q3M	clSAECMFRQ_Q3M		
			Every other day	AD	clSAECMFRQ_AD		
			Once a month	MO	clSAECMFRQ_MO		
			Once a week	WE	clSAECMFRQ_WE		
			Once daily	1D	clSAECMFRQ_1D		
			Once only	1S	clSAECMFRQ_1S		
			PC	PC	clSAECMFRQ_PC		

			PRN	PRN	clSAECMFRQ_PRN	
			Q2H	12D	clSAECMFRQ_Q2H	
			Q3D	Q3D	clSAECMFRQ_Q3D	
			Q4D	Q4D	clSAECMFRQ_Q4D	
			Q4H	6D	clSAECMFRQ_Q4H	
			QAM	1M	clSAECMFRQ_QAM	
			QH	24D	clSAECMFRQ_QH	
			QID	4D	clSAECMFRQ_QID	
			QPM	1N	clSAECMFRQ_QPM	
			TID	3D	clSAECMFRQ_TID	
clMEDROUT_MEDSAE	String		Inhalation	055	citmINHALATION_SAE	pdcCMROUTCD
			Intraarticular	014	citmINTRAARTICULAR_SAE	
			Intradermal	023	citmINTRADERMAL_SAE	
			Intramuscular	030	citmINTRAMUSCULAR_SAE	
			Intranasal	045	citmINTRANASAL_SAE	
			Intravenous	042	citmINTRAVENOUS_SAE	
			Oral	048	citmPORAL_SAE	
			Parenteral	051	citmPARENTERAL_SAE	
			Rectal	054	citmPRECTAL_SAE	
			Subcutaneous	058	citmSUBCUTANEOUS_SAE	
			Sublingual	060	citmSUBLINGUAL_SAE	
			Topical	061	citmTOPICAL_SAE	
			Transdermal	062	citmTRANSDERMAL_SAE	
			Vaginal	067	citmVAGINAL_SAE	
			Other	050	citmOTHER_SAE	
			Unknown	065	citmUNK_SAE	
clDRUGTYP	String		Concomitant	2	citmDRUGTYP_01	pdcCMDRGTYP
			Treatment	T	citmDRUGTYP_02	
			Cause of AE	1	citmDRUGTYP_03	
clSAELBTST	String		Activated partial thromboplastin time	Activated partial thromboplastin time	citmSAELBTST01	pdcLBTST
			Alanine aminotransferase	Alanine Amino Transferase	citmSAELBTST79	
			Albumin	Albumin	citmSAELBTST02	
			Alkaline phosphatase	Alkaline phosphatase	citmSAELBTST03	
			Amylase	Amylase	citmSAELBTST04	
			Aspartate Amino Transferase	Aspartate Amino Transferase	citmSAELBTST80	
			Band Neutrophil count	Band Neutrophil count	citmSAELBTST81	
			Base Excess	Base Excess	citmSAELBTST82	
			Basophils	Basophils	citmSAELBTST05	
			Bicarbonate	Bicarbonate	citmSAELBTST06	
			Bilirubin	Bilirubin	citmSAELBTST07	
			Bilirubin direct	Bilirubin direct	citmSAELBTST08	
			Bilirubin total	Bilirubin total	citmSAELBTST09	

Blood glucose	Blood glucose	citmSAELBTST83
Blood myoglobin	Blood myoglobin	SAELBTST10
Blood pH	Blood pH	SAELBTST11
Blood pressure	Blood pressure	SAELBTST12
Blood urea nitrogen	Blood urea nitrogen	SAELBTST13
Body temperature	Body temperature	SAELBTST14
Calcium	Calcium	SAELBTST15
Carbone dioxide	Carbone dioxide	SAELBTST84
CD4 lymphocytes	CD4 lymphocytes	SAELBTST16
CD8 lymphocytes	CD8 lymphocytes	SAELBTST17
Chloride	Chloride	SAELBTST18
Cholesterol total	Cholesterol total	SAELBTST19
C-reactive protein	C-reactive protein	SAELBTST20
Creatine	Creatine	SAELBTST21
Creatine phosphokinase	Creatine phosphokinase	SAELBTST22
Creatine phosphokinase MB	Creatine phosphokinase MB	SAELBTST23
Creatinine	Creatinine	SAELBTST24
Creatinine clearance	Creatinine clearance	SAELBTST25
Diastolic blood pressure	Diastolic blood pressure	SAELBTST26
Eosinophils	Eosinophils	SAELBTST27
Erythrocyte sedimentation rate	Erythrocyte sedimentation rate	SAELBTST28
Fasting blood glucose	Fasting blood glucose	SAELBTST29
FEV 1	FEV 1	SAELBTST30
Gamma-glutamyltransferase	Gamma-glutamyltransferase	SAELBTST31_1
Granulocyte count	Granulocyte count	SAELBTST85_1
HbA1c	HbA1c	SAELBTST34_1
HBV-DNA decreased	HBV-DNA decreased	SAELBTST35_1
HBV-DNA increased	HBV-DNA increased	SAELBTST36_1
Heart rate	Heart rate	SAELBTST37_1
Hematocrit	Hematocrit	SAELBTST38_1
Hemoglobin	Hemoglobin	SAELBTST39_1
High density lipoprotein	High density lipoprotein	SAELBTST40_1
HIV viral load	HIV viral load	SAELBTST41_1
INR	INR	SAELBTST42_1
International normalized ratio	International normalized ratio	SAELBTST88_1
Lactate dehydrogenase	Lactate dehydrogenase	SAELBTST43_1
Lipase	Lipase	SAELBTST44_1
Low density lipoprotein	Low density lipoprotein	SAELBTST45_1
Lymphocytes	Lymphocytes	SAELBTST46_1
Magnesium	Magnesium	SAELBTST47_1
Mean cell hemoglobin concentration	Mean cell hemoglobin concentration	SAELBTST48_1
Mean corpuscular hemoglobin	Mean corpuscular hemoglobin	SAELBTST49_1

			Mean corpuscular volume	Mean corpuscular volume	SAELBTST50_1	
			Mean Platelet Volume	Mean Platelet Volume	SAELBTST89_1	
			Monocytes	Monocytes	SAELBTST51_1	
			Myoglobin urine	Myoglobin urine	SAELBTST90_1	
			Neutrophils	Neutrophils	SAELBTST52_1	
			Oxygen saturation	Oxygen saturation	SAELBTST53_1	
			pCO2	pCO2	SAELBTST54_1	
			pH	pH	SAELBTST55_1	
			pH urine	pH urine	SAELBTST91_1	
			Phosphate	Phosphate	SAELBTST56_1	
			Platelet count	Platelet count	SAELBTST57_1	
			pO2	pO2	SAELBTST58_1	
			Polymerase Chain Reaction	Polymerase Chain Reaction	SAELBTST92_1	
			Polymorphonuclear Count	Polymorphonuclear Count	SAELBTST93_1	
			Potassium	Potassium	SAELBTST59_1	
			Protein total	Protein total	SAELBTST60_1	
			Prothrombin time	Prothrombin time	SAELBTST61_1	
			Red blood cell count	Red blood cell count	SAELBTST62_1	
			Red Cell Distribution Width	Red Cell Distribution Width	SAELBTST94_1	
			Respiratory rate	Respiratory rate	SAELBTST63_1	
			Reticulocyte count	Reticulocyte count	SAELBTST64_1	
			Segmented Neutrophil Count	Segmented Neutrophil Count	SAELBTST95_1	
			Serum glucose	Serum glucose	SAELBTST65_1	
			Serum uric acid	Serum uric acid	SAELBTST66_1	
			Sodium	Sodium	SAELBTST67_1	
			Systolic blood pressure	Systolic blood pressure	SAELBTST68_1	
			Thrombin time	Thrombin time	SAELBTST69_1	
			Total lung capacity	Total lung capacity	SAELBTST70_1	
			Triglycerides	Triglycerides	SAELBTST71_1	
			Troponin	Troponin	SAELBTST72_1	
			Troponin I	Troponin I	SAELBTST73_1	
			Troponin T	Troponin T	SAELBTST74_1	
			Urine myoglobin	Urine myoglobin	SAELBTST75_1	
			Urine pH	Urine pH	SAELBTST76_1	
			Vital capacity	Vital capacity	SAELBTST77_1	
			White blood cell count	White blood cell count	SAELBTST78_1	

p116682: STUDY CONCLUSION (Study Conclusion) [frmSTUDYCONCLUSION]

STUDY CONCLUSION [sctSTUDYCONCLUSION]

LAST INFORMATION

1.* ✔	Is the date of last contact or date when the last information was collected on the subjectâ€™s condition same as the date of SURVEY VISIT? [Is the date of last contact or date when the last information was collected on the subjectâ€™s condition same as the date of SURVEY VISIT?]	[*itmDATE_FLG* : *CONCLUS_DATA.DATE_FLG*] *[A:N]* [*itmLC_RDAT* : *CONCLUS_DATA.LC_RDAT*] **(MM/DD/YYYY)** No -->Please complete the date Req / Req / Req (2000-2025) *[A:Y]* Yes
2.	For Data Managers or Monitors only: Tick or untick this box to require the investigator to re-sign the case book *By ticking or unticking this box you are evoking a change to this form back to an unsigned state. This should be done when significant changes (e.g. those that require medical opinion or other significants situation) occur after the original signature. If the box is already ticked upon arrival on this form, unticking and submitting it accomplishes the same task as ticking and submitting it; that is, the signature will be validated in both [hidden]*	[INVSIG2] *[A:1]* 1
3. ✔	In case subjectâ€™s parent(s)/ legally acceptable representatives freely expressed objection for the use of subjectâ€™s personal information, please tick box.	[*itmINFO* : *CONCLUS_DATA.INFO*] *[A:Y]*

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: INVESTIGATOR SIGNATURE (Investigator signature) [INVSIGN_CR]

INVESTIGATOR SIGNATURE [sctINVSIGN]

1.* ✔	Is this casebook ready to sign? If not, click on the **RETURN** button below	[INVSIGN] *[A:Y]* ☐ Ready to sign
2.	For Data Managers or Monitors only: Tick or untick this box to require the investigator to re-sign the case book *By ticking or unticking this box you are evoking a change to this form back to an unsigned state. This should be done when significant changes (e.g. those that require medical opinion or other significants situation) occur after the original signature. If the box is already ticked upon arrival on this form, unticking and submitting it accomplishes the same task as ticking and submitting it; that is, the signature will be validated in both [hidden]*	[INVSIG2] *[A:1]* ☐ 1

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: SAMPLE RETENTION PERIOD (Sample Retention Period) - Repeating Form [frmUHS]

#	Please check GSK Biologicals sample storage period specified in the ICF in use at your centre.	Date at which the new ICF version was first signed by a Subject / Subjectâ€™s parents / Legally Acceptable Representatives in your centre :
1		

1.	SRP form version *[hidden]* [SRP form version]	[itmUHS_NB_HID] *N10*
SAMPLE STORAGE PERIOD [sctUHS_PERIOD]		
2.* ✔	Please check GSK Biologicals sample storage period specified in the ICF in use at your centre. [Please check GSK Biologicals sample storage period specified in the ICF in use at your centre.]	[***itmPERIOD*** : ***SRP_DATA.PERIOD***] *[A:20]* For a maximum of 20 years *[A:9]* [***itmPERIODSP*** : ***SRP_DATA.PERIODSP***] Other, please specify: *A200*
IF NEW VERSION OF SRP [sctUHS_DATE]		
Complete and submit a new Sample Retention Period Form for each change in the ICF that affects the retention period of samples.		
3. ✔	Date at which the new ICF version was first signed by a Subject / Subjectâ€™s parents / Legally Acceptable Representatives in your centre : [Date at which the new ICF version was first signed by a Subject / Subjectâ€™s parents / Legally Acceptable Representatives in your centre :]	[***itmUHS_DATE*** : ***SRP_DATA.SRP_DATE***] **(MM/DD/YYYY)** NReq / NReq / NReq (2003-2025)

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: SEGMENT IDENTIFICATION (Segment Identification) [frmSEGMENTIDENTIFICATION]

SEGMENTS [sctSegments]

1.* ✔	How many segments are there in this center ? [SEGMENTS]	[*itmSegments* : *SEGMENT_DATA.SEGEMTNS*] *[clSegCenter]*
2.* ✔	Is the study area defined as an RTS,S exposed or unexposed cluster? [Is the study area defined as an RTS,S exposed or unexposed cluster?]	[*itmCLUSTER_SEG* : *SEGMENT_DATA.CLUSTR*] *[A:EC]* Exposed Cluster Please select district/sub-county/Cluster: [*itmEXPCLUSTER_SI* : *SEGMENT_DATA.EXPCLST*] *[clDISTGHANAEX_SI]* *[A:UC]* Unexposed Cluster Please select district/sub-county/Cluster: [*itmUNEXPCLUSTER_SI* : *SEGMENT_DATA.UNEXCLST*] *[clDISTGHANAUNEX_SI]*

	Segment ID	Surface area (km2)
3. ✔		

SEGMENT DETAILS Entry [sctSEGMENTID]

3.1* ✔	Segment ID [Segment ID]	[*itmSEGMNTID1* : *SEGMENT_DATA.SEGMNT_ID*] *A8*
3.2* ✔	Surface area [Surface area (km2)]	[*itmSURFACE* : *SEGMENT_DATA.AREA*] *xxxxxxxxxxx.xx*

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

Codelist Values Tables: SEGMENT IDENTIFICATION

Codelist RefName	Codelist Data Type	Subset	Label	Code	Codelist Item RefName	Data Variable RefName
clSegCenter	String		1	1	citmSegCenter1	itmSegments
			2	2	citmSegCenter2	
			3	3	citmSegCenter3	
			4	4	citmSegCenter4	
			5	5	citmSegCenter5	
			6	6	citmSegCenter6	
			7	7	citmSegCenter7	
			8	8	citmSegCenter8	
			9	9	citmSegCenter9	
			10	10	citmSegCenter10	
			11	11	citmSegCenter11	
			12	12	citmSegCenter12	
			13	13	citmSegCenter13	
			14	14	citmSegCenter14	
			15	15	citmSegCenter15	
			16	16	citmSegCenter16	
			17	17	citmSegCenter17	
			18	18	citmSegCenter18	
			19	19	citmSegCenter19	

			20	20	citmSegCenter20	
			21	21	citmSegCenter21	
			22	22	citmSegCenter22	
			23	23	citmSegCenter23	
			24	24	citmSegCenter24	
			25	25	citmSegCenter25	
clDISTGHANAEX_SI	String		Kintampo exposed	KE	citmKINTEXPO1	itmEXPCLUSTER_SI
			Kasena Nankana	KN	citmKESENANANAK1	
			Kombewa	KMB	citmKOMBEWA1	
			Gem	GEM	citmGEM1	
			Exposed Malawi 1	EM1	citmEXPOMAL11	
			Exposed Malawi 2	EM2	citmEXPOMAL21	
clDISTGHANAUNEX_SI	String		Kintampo unexposed	KU	citmKINTAMPOUNE1	itmUNEXPCLUSTER_SI
			Builsa	BU	citmBUILSA1	
			Nyando	NY	citmNYANDO1	
			Rarieda	RAR	citmRARIEDA1	
			Unexposed Malawi 1	UM1	citmUM11	
			Unexposed Malawi 2	UM2	citmUM21	
			Nouna	NOU	citmNOUNA1	
			Sapone	SAP	citmSAPONE1	
			Bondo	BON	citmBONDO	

p116682: QUESTIONNAIRE (Ques Pg 1) [frmQUESTIONNAIREPART1]

MALARIA CONTROL PROGRAM QUESTIONNAIRE [sctMALERIACONTROLPROGRAMQUESTIONAIRE]

1.* ✔	Month and year of survey completion [Month and year of survey completion]	[itmSURVYCOMP : MAINQUES_DATA.SURV_DT] NReq / NReq (2003-2025)
2.* ✔	Has the questionnaire been completed for this survey? [Has the questionnaire been completed for this survey?]	[itmCOMPLETED : MAINQUES_DATA.COMPLTED] [A:Y] Yes [A:N] [itmOTH_SP : MAINQUES_DATA.SPECIFY] No, Please Specify A128

METEOROLOGICAL DATA [sctMETEOROLOGICAL]

3.* ✔	Are there source of data about temperature available in the study area? [Are there source of data about temperature available in the study area?]	[itmTEMP_FLG : METROLG_DATA.TEMP_FLG] [A:N] No [A:Y] Yes --> Please complete the Temperature Details below
4.* ✔	Are there source of data about rain available in the study area? [Are there source of data about rain available in the study area?]	[itmRAIN_FLG : METROLG_DATA.RAIN_FLG] [A:N] No [A:Y] Yes --> Please complete the Rain Details below
5.* ✔	Are there source of data about humiditiy available in the study area? [Are there source of data about humiditiy available in the study area?]	[itmHUMIDITY_FLG : METROLG_DATA.HUM_FLG] [A:N] No [A:Y] Yes --> Please complete the Humidity Details below

Average Monthly Temperature for the month

6. ✔

TEMPERATURE DETAILS Entry [sctTEMPERATURE]

6.1* ✔	Average Monthly Temperature for the month [Average Monthly Temperature for the month]	[cmpTEMP] [itmTRHDT : METROLG_DATA.MONAVG1] [itmTEMP : METROLG_DATA.TE_VOLUM] Req / Req (2003-2025) -->Temp(°C) xxxx.x

Average Volume of Rain for the month

7. ✔

RAIN DETAILS Entry [sctRAIN]

7.1* ✔	Average Volume of Rain for the month [Average Volume of Rain for the month]	[cmpRAIN] [itmTRHDT : METROLG_DATA.MONAVG2] [itmRTEMP : METROLG_DATA.RN_VOLUM] Req / Req (2003-2025) --> Rain xxxx.x

Average Monthly Humidity for the month

8. ✔

HUMIDITY DETAILS Entry [sctHUMIDITY]

8.1* ✔	Average Monthly Humidity for the month [Average Monthly Humidity for the month]	[cmpHUMIDITY] [itmTRHDT : METROLG_DATA.MONAVG3] [itmHTEMP : METROLG_DATA.HM_VOLUM] Req / Req (2003-2025) --> Humidity(%) xxxx.x

BED NETS [sctBEDNETS]

9.* ✔	Are bed nets used as a prevention measure in the study area? [Are bed nets used as a prevention measure in the study area?]	[itmPREVENTION : MAINQUES_DATA.PREVTN] [A:N] No [A:Y] [itmTYPEBEDNET : MAINQUES_DATA.TYPE_NET] Yes,-->Please Specify Type of Bed net [A:ITN] [itmINDUITN_DT : MAINQUES_DATA.INRDC_DT] (MM/DD/YYYY) ITN (Insecticide Treated Nets) Introduction date Req/Unk / Req/Unk / Req/Unk (2003-2025) [A:LLTN] [itmINDULLTN_DT : MAINQUES_DATA.INLLTNDT] (MM/DD/YYYY) LLIN (Long Lasting Insecticidal Nets) Introduction date Req/Unk / Req/Unk / Req/Unk (2003-2025)

		[A:OTH] [cmpOTHER] Others, [*itmOTH_SP_1* : *MAINQUES_DATA.OTH_SP_1*] Please Specify *A128* [*itmINDU_DT_2* : *MAINQUES_DATA.INDU_DT*] **(MM/DD/YYYY)** Introduction date Req/Unk / Req/Unk / Req/Unk (2003-2025)

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: QUESTIONNAIRE PART2 (Ques Pg 2) [frmQUESTIONNAIREPART2]

BEDNET DETAILS: ITN [sctBEDNETDETAILS_ITN]

1.* ✔ Policy requirement
Target population

[*itmTARGETPOPULATION_ITN* : *BEDITN_DATA.TAR_POP*]

[A:1] ☐ [cmpDIST_REPLACE_INFANTS]
Infants < 1 year [*itmDISTRIBUTION* : *BEDITN_DATA.DISTR_1*]
Bednet distributed *[A:0]* ☐ for free
[A:1] ☐ with charge
[*itmREPLACEMENTPERIOD_1* : *BEDITN_DATA.REPLM_1*]
Replacement period *[A:0]* ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:2] ☐ [cmpDIST_REPLACE_CHD1T5YR]
Children >= 1 and < 5 years [*itmDISTRIBUTION_2* : *BEDITN_DATA.DISTR_2*]
Bednet distributed *[A:0]* ☐ for free
[A:1] ☐ with charge
[*itmREPLACEMENTPERIOD_2* : *BEDITN_DATA.REPLM_2*]
Replacement period *[A:0]* ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:3] ☐ [cmpDIST_REPLACE_CHD5YR]
Children >= 5 years [*itmDISTRIBUTION_3* : *BEDITN_DATA.DISTR_3*]
Bednet distributed *[A:0]* ☐ for free
[A:1] ☐ with charge
[*itmREPLACEMENTPERIOD_3* : *BEDITN_DATA.REPLM_3*]
Replacement period *[A:0]* ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:4] ☐ [cmpDIST_REPLACE_PRG]
Pregnant women [*itmDISTRIBUTION_4* : *BEDITN_DATA.DISTR_4*]
Bednet distributed *[A:0]* ☐ for free
[A:1] ☐ with charge
[*itmREPLACEMENTPERIOD_4* : *BEDITN_DATA.REPLM_4*]
Replacement period *[A:0]* ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:5] ☐ [cmpDIST_REPLACE_ADU]
All adults (Except pregnant women) [*itmDISTRIBUTION_5* : *BEDITN_DATA.DISTR_5*]
Bednet distributed *[A:0]* ☐ for free
[A:1] ☐ with charge
[*itmREPLACEMENTPERIOD_5* : *BEDITN_DATA.REPLM_5*]
Replacement period *[A:0]* ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:6] ☐ [cmpDIST_REPLACE_OTH]
Others [*itmSPECIFY_NET* : *BEDITN_DATA.OTH_TP*]
Specify *A128*

[itmDISTRIBUTION_6 : BEDITN_DATA.DISTR_6]
Bednet distributed [A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_6 : BEDITN_DATA.REPLM_6]
Replacement period [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

BEDNET DETAILS: ACTUAL ITN [sctBEDNETDETAILS_AITN]

2.* ✔ Actual implementation
Target population
[Actual Target population]

[itmTARGETPOPULATION_AITN : BEDITN_DATA.TAR_POP]
[A:1] [cmpADIST_REPLACE_INFANTS]
Infants < 1 year [itmDISTRIBUTION_7 : BEDITN_DATA.DISTR_1]
Bednet distributed [A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_7 : BEDITN_DATA.REPLM_1]
Replacement period [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months
[A:2] [cmpADIST_REPLACE_CHD1T5YR]
Children >= 1 and < 5 years [itmDISTRIBUTION_8 : BEDITN_DATA.DISTR_2]
Bednet distributed [A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_8 : BEDITN_DATA.REPLM_2]
Replacement period [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months
[A:3] [cmpADIST_REPLACE_CHD5YR]
Children >= 5 years [itmDISTRIBUTION_9 : BEDITN_DATA.DISTR_3]
Bednet distributed [A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_9 : BEDITN_DATA.REPLM_3]
Replacement period [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months
[A:4] [cmpADIST_REPLACE_PRG]
Pregnant women [itmDISTRIBUTION_10 : BEDITN_DATA.DISTR_4]
Bednet distributed [A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_10 : BEDITN_DATA.REPLM_4]
Replacement period [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months
[A:5] [cmpADIST_REPLACE_ADU]
All adults(Except pregnant women) [itmDISTRIBUTION_11 : BEDITN_DATA.DISTR_5]
Bednet distributed [A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_11 : BEDITN_DATA.REPLM_5]

Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:6] [cmpADIST_REPLACE_OTH]
Others [itmSPECIFY_NET : BEDITN_DATA.OTH_TP]
Specify A128

[itmDISTRIBUTION_12 : BEDITN_DATA.DISTR_6]
Bednet distributed
[A:0] for free
[A:1] with charge

[itmREPLACEMENTPERIOD_12 : BEDITN_DATA.REPLM_6]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

3. ✔ Is there any difference between the Policy requirement and the Actual implementation ?
[Is there any difference between the Policy requirement and the Actual implementation ?]

[itmADIST_REPLACE_UPD : BEDITN_DATA.DIFFER]
[A:N] No
[A:Y] [itmADIST_REPLACE_UPD_COM : BEDITN_DATA.DIFF_COM]
Yes --> Please specify A250

BEDNET DETAILS: LLIN [sctBEDNETDETAILS_LLTN]

4.* ✔ Policy requirement
Target population
[Policy requirementTarget population]

[itmTARGETPOPULATION_LLTN : BEDLLTN_DATA.TAR_POP]
[A:1] [cmpDIST_REPLACE_INFANTS]
Infants < 1 year [itmDISTRIBUTION : BEDLLTN_DATA.DISTR_1]
Bednet distributed
[A:0] for free
[A:1] with charge

[itmREPLACEMENTPERIOD_1 : BEDLLTN_DATA.REPLM_1]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:2] [cmpDIST_REPLACE_CHD1T5YR]
Children >= 1 and < 5 years [itmDISTRIBUTION_2 : BEDLLTN_DATA.DISTR_2]
Bednet distributed
[A:0] for free
[A:1] with charge

[itmREPLACEMENTPERIOD_2 : BEDLLTN_DATA.REPLM_2]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:3] [cmpDIST_REPLACE_CHD5YR]
Children >= 5 years [itmDISTRIBUTION_3 : BEDLLTN_DATA.DISTR_3]
Bednet distributed
[A:0] for free
[A:1] with charge

[itmREPLACEMENTPERIOD_3 : BEDLLTN_DATA.REPLM_3]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months

[A:4] 18-23 months
[A:5] > =24 months

[A:4] [cmpDIST_REPLACE_PRG]
Pregnant women [itmDISTRIBUTION_4 : BEDLLTN_DATA.DISTR_4]
Bednet distributed
[A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_4 : BEDLLTN_DATA.REPLM_4]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:5] [cmpDIST_REPLACE_ADU]
All adults (Except pregnant women) [itmDISTRIBUTION_5 : BEDLLTN_DATA.DISTR_5]
Bednet distributed
[A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_5 : BEDLLTN_DATA.REPLM_5]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:6] [cmpDIST_REPLACE_OTH]
Others [itmSPECIFY_NET : BEDLLTN_DATA.OTH_TP]
Specify A128
[itmDISTRIBUTION_6 : BEDLLTN_DATA.DISTR_6]
Bednet distributed
[A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_6 : BEDLLTN_DATA.REPLM_6]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

BEDNET DETAILS:ACTUAL LLIN [sctBEDNETDETAILS_ALLTN]

5.* ✔ Actual implementation
Target population
[Actual iarget population]

[itmTARGETPOPULATION_ALLTN : BEDLLTN_DATA.TAR_POP]
[A:1] [cmpADIST_REPLACE_INFANTS]
Infants < 1 year [itmDISTRIBUTION_7 : BEDLLTN_DATA.DISTR_1]
Bednet distributed
[A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_7 : BEDLLTN_DATA.REPLM_1]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:2] [cmpADIST_REPLACE_CHD1T5YR]
Children >= 1 and < 5 years [itmDISTRIBUTION_8 : BEDLLTN_DATA.DISTR_2]
Bednet distributed
[A:0] for free
[A:1] with charge
[itmREPLACEMENTPERIOD_8 : BEDLLTN_DATA.REPLM_2]
Replacement period
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

		[A:3] ☐ [cmpADIST_REPLACE_CHD5YR] Children >= 5 years [itmDISTRIBUTION_9 : BEDLLTN_DATA.DISTR_3] Bednet distributed [A:0] ☐ for free [A:1] ☐ with charge [itmREPLACEMENTPERIOD_9 : BEDLLTN_DATA.REPLM_3] Replacement period [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:4] ☐ [cmpADIST_REPLACE_PRG] Pregnant women [itmDISTRIBUTION_10 : BEDLLTN_DATA.DISTR_4] Bednet distributed [A:0] ☐ for free [A:1] ☐ with charge [itmREPLACEMENTPERIOD_10 : BEDLLTN_DATA.REPLM_4] Replacement period [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:5] ☐ [cmpADIST_REPLACE_ADU] All adults(Except pregnant women) [itmDISTRIBUTION_11 : BEDLLTN_DATA.DISTR_5] Bednet distributed [A:0] ☐ for free [A:1] ☐ with charge [itmREPLACEMENTPERIOD_11 : BEDLLTN_DATA.REPLM_5] Replacement period [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:6] ☐ [cmpADIST_REPLACE_OTH] Others [itmSPECIFY_NET : BEDLLTN_DATA.OTH_TP] Specify A128 [itmDISTRIBUTION_12 : BEDLLTN_DATA.DISTR_6] Bednet distributed [A:0] ☐ for free [A:1] ☐ with charge [itmREPLACEMENTPERIOD_12 : BEDLLTN_DATA.REPLM_6] Replacement period [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months
6. ✔	Is there any difference between the Policy requirement and the Actual implementation ? [Is there any difference between the Policy requirement and the Actual implementation ?]	[itmADIST_REPLACE_UPD2 : BEDLLTN_DATA.DIFFER] [A:N] ☐ No [A:Y] ☐ [itmADIST_REPLACE_UPD2_COM : BEDLLTN_DATA.DIFF_COM] Yes --> Please specify A250
BEDNET DETAILS: OTHERS [sctBEDNETDETAILS_OTH]		
7.* ✔	Please specify other type of bednet [Please specify other type of bednet]	[itmOtherType : BEDOTH_DATA.OTH_TYP] A128

8.* ✔ Policy requirement
Target population
[Policy requirement Target population]

[itmTARGETPOPULATION_OTH : BEDOTH_DATA.TAR_POP]

[A:1] ☐ [cmpDIST_REPLACE_INFANTS]
Infants < 1 year [itmDISTRIBUTION : BEDOTH_DATA.DISTR_1]
Bednet distributed
[A:0] ☐ for free
[A:1] ☐ with charge
[itmREPLACEMENTPERIOD_1 : BEDOTH_DATA.REPLM_1]
Replacement period
[A:0] ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:2] ☐ [cmpDIST_REPLACE_CHD1T5YR]
Children >= 1 and < 5 years [itmDISTRIBUTION_2 : BEDOTH_DATA.DISTR_2]
Bednet distributed
[A:0] ☐ for free
[A:1] ☐ with charge
[itmREPLACEMENTPERIOD_2 : BEDOTH_DATA.REPLM_2]
Replacement period
[A:0] ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:3] ☐ [cmpDIST_REPLACE_CHD5YR]
Children >= 5 years [itmDISTRIBUTION_3 : BEDOTH_DATA.DISTR_3]
Bednet distributed
[A:0] ☐ for free
[A:1] ☐ with charge
[itmREPLACEMENTPERIOD_3 : BEDOTH_DATA.REPLM_3]
Replacement period
[A:0] ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:4] ☐ [cmpDIST_REPLACE_PRG]
Pregnant women [itmDISTRIBUTION_4 : BEDOTH_DATA.DISTR_4]
Bednet distributed
[A:0] ☐ for free
[A:1] ☐ with charge
[itmREPLACEMENTPERIOD_4 : BEDOTH_DATA.REPLM_4]
Replacement period
[A:0] ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:5] ☐ [cmpDIST_REPLACE_ADU]
All adults (Except pregnant women) [itmDISTRIBUTION_5 : BEDOTH_DATA.DISTR_5]
Bednet distributed
[A:0] ☐ for free
[A:1] ☐ with charge
[itmREPLACEMENTPERIOD_5 : BEDOTH_DATA.REPLM_5]
Replacement period
[A:0] ☐ Not specified
[A:1] ☐ < 6 months
[A:2] ☐ 6-11 months
[A:3] ☐ 12-17 months
[A:4] ☐ 18-23 months
[A:5] ☐ > =24 months

[A:6] ☐ [cmpDIST_REPLACE_OTH]
Others [itmSPECIFY_NET : BEDOTH_DATA.OTH_TP]
Specify A128
[itmDISTRIBUTION_6 : BEDOTH_DATA.DISTR_6]
Bednet distributed
[A:0] ☐ for free
[A:1] ☐ with charge

		[itmREPLACEMENTPERIOD_6 : BEDOTH_DATA.REPLM_6] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months
BEDNET DETAILS: ACTUAL OTHER [sctBEDNETDETAILS_AOTH]		
9.* ✔	Please specify actual other type of bednet [Please specify actual other type of bednet]	[itmOtherType_1 : BEDOTH_DATA.OTH_TYP] A128
10.* ✔	Actual implementation Target population [Actual Target population]	[itmTARGETPOPULATION_AOTH : BEDOTH_DATA.TAR_POP] [A:1] [cmpADIST_REPLACE_INFANTS] Infants < 1 year [itmDISTRIBUTION_7 : BEDOTH_DATA.DISTR_1] Bednet distributed [A:0] for free [A:1] with charge [itmREPLACEMENTPERIOD_7 : BEDOTH_DATA.REPLM_1] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months [A:2] [cmpADIST_REPLACE_CHD1T5YR] Children >= 1 and < 5 years [itmDISTRIBUTION_8 : BEDOTH_DATA.DISTR_2] Bednet distributed [A:0] for free [A:1] with charge [itmREPLACEMENTPERIOD_8 : BEDOTH_DATA.REPLM_2] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months [A:3] [cmpADIST_REPLACE_CHD5YR] Children >= 5 years [itmDISTRIBUTION_9 : BEDOTH_DATA.DISTR_3] Bednet distributed [A:0] for free [A:1] with charge [itmREPLACEMENTPERIOD_9 : BEDOTH_DATA.REPLM_3] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months [A:4] [cmpADIST_REPLACE_PRG] Pregnant women [itmDISTRIBUTION_10 : BEDOTH_DATA.DISTR_4] Bednet distributed [A:0] for free [A:1] with charge [itmREPLACEMENTPERIOD_10 : BEDOTH_DATA.REPLM_4] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months [A:5] [cmpADIST_REPLACE_ADU] All adults(Except pregnant women) [itmDISTRIBUTION_11 : BEDOTH_DATA.DISTR_5] Bednet distributed [A:0] for free [A:1] with charge

		[itmREPLACEMENTPERIOD_11 : BEDOTH_DATA.REPLM_5] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months [A:6] [cmpADIST_REPLACE_OTH] Others [itmSPECIFY_NET : BEDOTH_DATA.OTH_TP] Specify A128 [itmDISTRIBUTION_12 : BEDOTH_DATA.DISTR_6] Bednet distributed [A:0] for free [A:1] with charge [itmREPLACEMENTPERIOD_12 : BEDOTH_DATA.REPLM_6] Replacement period [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months
11. ✔	Is there any difference between the Policy requirement and the Actual implementation ? [Is there any difference between the Policy requirement and the Actual implementation ?]	[itmADIST_REPLACE_UPD3 : BEDOTH_DATA.DIFFER] [A:N] No [A:Y] [itmADIST_REPLACE_UPD3_COM : BEDOTH_DATA.DIFF_COM] Yes --> Please specify A250

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: QUESTIONNAIRE PART 3 (Ques Pg 3) [frmQUESTIONNAIREPART3]

[sctBEDNETCAMPAIGN]

1.* ✔	Was the distribution of the bed nets deployed through a campaign during the past year (12 months)? [Was the distribution of the bed nets deployed through a campaign during the past year (12 months)?]	[itmBEDNETCAMPAIGN : BEDDET_DATA.BDNTCAMP] [A:N] No [A:Y] Yes, Please add details below

	Type of the net	Area provided	Population provided	Age provided
2. ✔				

BEDNET: CAMPAIGN DETAILS Entry [sctBEDNETCAMPAIGNDEATILS]

2.1* ✔	Type of the net [Type of the net]	[itmBEDNETTYPE : BEDDET_DATA.BDNTTYP] [A:ITN] ITN [A:LLTN] LLIN [A:OTH] [itmOTH_SP_21 : BEDDET_DATA.OTH_TYP] Others, Please Specify A128
2.2* ✔	Area provided in square kilometers [Area provided]	[itmAREAPROVIDED_NET : BEDDET_DATA.ARPRVD] [A:01] Entire DSS area [A:02] Area smaller than DSS area [A:03] Area bigger than DSS area
2.3* ✔	Population provided [Population provided]	[itmPOPULATIONPROVIDED_NET : BEDDET_DATA.POPLN] [A:01] < 5 000 [A:02] 5 000 - <10 000 [A:03] 10 000 - <15 000 [A:04] >=15 000
2.4* ✔	Age provided [Age provided]	[itmAGEPROVIDED_NET : BEDDET_DATA.AGPRVD] [A:1] Infants < 1 year [A:2] Children >= 1 and < 5 years [A:3] Children >= 5 years [A:4] Pregnant women [A:5] All adults (Except pregnant women) [A:6] [itmOTH_SP_2 : BEDDET_DATA.OTH_AGE] Others, -->Please Specify A128

BEDNET: MONITORING SYSTEM [sctBEDNETMONITORINGSYSTEM]

3.* ✔	Is there any monitoring system to evaluate the use and impact of the distributed bed net in the study area? [Is there any monitoring system to evaluate the use and impact of the distributed bed net in the study area?]	[itmMONITORINGSYS : BEDDET_DATA.MN_FLG] [A:N] No [A:Y] [itmTYPEOFMONITORING : BEDDET_DATA.TYPMNTR] Yes--> Please specify Type of monitoring system [A:01] [itmDISPENSARIES : BEDDET_DATA.DISMAL] Dispensaries malaria surveillance --> Data Available [A:N] No [A:Y] Yes [A:02] [itmHOSPITALIZATION : BEDDET_DATA.HSPTLMAL] Hospitalization malaria surveillance--> Data Available [A:N] No [A:Y] Yes [A:03] [itmMALARIAINDICATION : BEDDET_DATA.MALSUR] Malaria Indicator surveys --> Data Available [A:N] No [A:Y] Yes

Key: [*] = Item is required [✔] = Source verification required
Note: Source verification critical settings made in InForm will override any settings made in Central Designer.

p116682: QUESTIONNAIRE PART 4 (Ques Pg 4) [frmQUESTIONNAIREPART4]

IRS (INTERIOR RESIDUAL SPRAYING) [sctIRSINTERIORRESIDUALSPRAYING]

1.* ✔	Is IRS used as a prevention measure in the study area? [Is IRS used as a prevention measure in the study area?]	[itmIRSPREVENTION : IRS_DATA.PREVTN] [A:N] ☐ No [A:Y] ☐ [itmIRSPREVENTION_DT : IRS_DATA.INTRO_DT] (MM/DD/YYYY) Yes,--> please specify since when introduced (day/month/year): ☐ Req/Unk ☐ / ☐ Req/Unk ☐ / ☐ Req/Unk ☐ (2003-2025)

IRS DETAILS [sctIRSDETAILS]

Please specify the policy requirement for distribution of IRS.

2. ✔	Policy requirement Target population (households with)	[itmTARGETPOPULATION_IRS : IRSDET_DATA.TAR_POP] [A:1] ☐ [cmpPERFORMED_INFANTS] Infants < 1 year [itmPERFORMED : IRSDET_DATA.PRFRM_1] Performed [A:0] ☐ for free [A:1] ☐ with charge [itmFEQUENCY_1_1 : IRSDET_DATA.FRQCY_1] Frequency in months [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:2] ☐ [cmpPERFORMED_CHD1T5YR] Children >= 1 and < 5 years [itmPERFORMED_2 : IRSDET_DATA.PRFRM_2] Performed [A:0] ☐ for free [A:1] ☐ with charge [itmFEQUENCY_2 : IRSDET_DATA.FRQCY_2] Frequency in months [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:3] ☐ [cmpPERFORMED_CHD5YR] Children >= 5 years [itmPERFORMED_3 : IRSDET_DATA.PRFRM_3] Performed [A:0] ☐ for free [A:1] ☐ with charge [itmFEQUENCY_3 : IRSDET_DATA.FRQCY_3] Frequency in months [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:4] ☐ [cmpPERFORMED_PRG] Pregnant women [itmPERFORMED_4 : IRSDET_DATA.PRFRM_4] Performed [A:0] ☐ for free [A:1] ☐ with charge [itmFEQUENCY_4 : IRSDET_DATA.FRQCY_4] Frequency in months [A:0] ☐ Not specified [A:1] ☐ < 6 months [A:2] ☐ 6-11 months [A:3] ☐ 12-17 months [A:4] ☐ 18-23 months [A:5] ☐ > =24 months [A:5] ☐ [cmpPERFORMED_ADU] All Adults (Except pregnant women) [itmPERFORMED_5 : IRSDET_DATA.PRFRM_5] Performed [A:0] ☐ for free [A:1] ☐ with charge [itmFEQUENCY_5 : IRSDET_DATA.FRQCY_5]

Frequency in months [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:6] [cmpPERFORMED_OTH]
Others, Please specify [itmOTHSPECIFY_IRS : IRSDET_DATA.OTH_TP]
A30

[itmPERFORMED_6 : IRSDET_DATA.PRFRM_6]
Performed [A:0] for free [A:1] with charge

[itmFEQUENCY_6 : IRSDET_DATA.FRQCY_6]
Frequency in months [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

ACTUAL IRS DETAILS [sctAIRSDETAILS]

Please specify actual implementation for distribution of IRS.

3. ✔ Actual implementation
Target population
(households with)

[itmATARGETPOPULATION_IRS : IRSDET_DATA.TAR_POP]
[A:1] [cmpAPERFORMED_INFANTS]
Infants < 1 year [itmPERFORMED_7 : IRSDET_DATA.PRFRM_1]
Performed [A:0] for free
[A:1] with charge

[itmFEQUENCY_7 : IRSDET_DATA.FRQCY_1]
Frequency in months [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:2] [cmpAPERFORMED_CHD1T5YR]
Children >= 1 and < 5 years [itmPERFORMED_8 : IRSDET_DATA.PRFRM_2]
Performed [A:0] for free
[A:1] with charge

[itmFEQUENCY_8 : IRSDET_DATA.FRQCY_2]
Frequency in months [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:3] [cmpAPERFORMED_CHD5YR]
Children >= 5 years [itmPERFORMED_9 : IRSDET_DATA.PRFRM_3]
Performed [A:0] for free
[A:1] with charge

[itmFEQUENCY_9 : IRSDET_DATA.FRQCY_3]
Frequency in months [A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:4] [cmpAPERFORMED_PRG]
Pregnant women [itmPERFORMED_10 : IRSDET_DATA.PRFRM_4]
Performed [A:0] for free
[A:1] with charge

[itmFEQUENCY_10 : IRSDET_DATA.FRQCY_4]
Frequency in months [A:0] Not specified

[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:5] [cmpAPERFORMED_ADU]
All Adults (Except pregnant women) [itmPERFORMED_11 : IRSDET_DATA.PRFRM_5]
Performed
[A:0] for free
[A:1] with charge
[itmFEQUENCY_11 : IRSDET_DATA.FRQCY_5]
Frequency in months
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

[A:6] [cmpAPERFORMED_OTH]
Others [itmOTHSPECIFY_IRS : IRSDET_DATA.OTH_TP]
A30

[itmPERFORMED_12 : IRSDET_DATA.PRFRM_6]
Performed
[A:0] for free
[A:1] with charge
[itmFEQUENCY_12 : IRSDET_DATA.FRQCY_6]
Frequency in months
[A:0] Not specified
[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

4. ✔ Is there any difference between the Policy requirement and the Actual implementation ?
[Is there any difference between the Policy requirement and the Actual implementation ?]

[itmAPERF_UPD : IRSDET_DATA.DIFFER]
[A:N] No
[A:Y] [itmAPERF_UPD_COM : IRSDET_DATA.DIFF_COM]
Yes --> Please specify
A250

IRS :CAMPAIGN DETAILS [sctIRSCAMPAIGNDEATILS]

5. ✔ Was the distribution of the IRS deployed through a campaign during the past year (12 months)?
[Was the distribution of the IRS deployed through a campaign during the past year (12 months)?]

[itmIRSCAMPAIGN : IRS_DATA.CAMPING]
[A:N] No
[A:Y] [cmpCAMPAIGNDETAILS_IRS]
Yes--> please specify

[itmAREAPROVIDED : IRS_DATA.ARPRVD]
Area provided in square kilometers
[A:01] Entire DSS area
[A:02] Area smaller than DSS area
[A:03] Area bigger than DSS area

[itmPOPULATIONPROVIDED : IRS_DATA.POPLN]
Population provided
[A:01] < 5 000
[A:02] 5 000 - <10 000
[A:03] 10 000 - <15 000
[A:04] >=15 000

[itmAGEPROVIDED_IRS : IRS_DATA.AGEPRVD]
Sprayed households with
[A:1] Infants < 1 year
[A:2] Children >= 1 and < 5 years
[A:3] Children >= 5 years
[A:4] Pregnant women
[A:5] All adults
[A:6] [cmpOTHERSPECIFY]
Others, [itmOTH_SP_2 : IRS_DATA.SPECIFY]
Please Specify
A128

IRS:MONITORING SYSTEM [sctIRSMONITORINGSYSTEM]		
6. ✔	Is there any monitoring system to evaluate the impact of the IRS in the study area? [Is there any monitoring system to evaluate the impact of the IRS in the study area?]	[itmIRSMONITORINGSYS : IRS_DATA.MN_FLG] [A:N] ☐ No [A:Y] ☐ [itmTYPEOFMONITORING : IRS_DATA.TPMONSYS] Yes--> Please Specify Type of monitoring system [A:01] ☐ [itmDISPENSARIES : IRS_DATA.DISMAL] Dispensaries malaria surveillance --> Data Available [A:N] ☐ No [A:Y] ☐ Yes [A:02] ☐ [itmHOSPITALIZATION : IRS_DATA.HSPTLMAL] Hospitalization malaria surveillance--> Data Available [A:N] ☐ No [A:Y] ☐ Yes [A:03] ☐ [itmMALARIAINDICATION : IRS_DATA.MALSUR] Malaria Indicator surveys --> Data Available [A:N] ☐ No [A:Y] ☐ Yes

Key: [*] = Item is required [✔] = Source verification required
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p116682: QUESTIONNAIRE PART 5 (Ques Pg 5) [frmQUESTIONNAIREPART5]

ACT (ARTEMISININ-BASED COMBINATION THERAPY) [sctACT]

1.* ✔ Are ACTs used in the study area?
[Are ACTs used in the study area?]

[*itmACTPREVENTION* : *ACT_DATA.PREVTN*]
[A:N] ☐ No
[A:Y] ☐ [*itmACTPREVENTION_DT* : *ACT_DATA.INTRO_DT*] **(MM/DD/YYYY)**
Yes ->please specify since when introduced (day/month/year): ☐ Req/Unk ☐ / ☐ Req/Unk ☐ / ☐ Req/Unk ☐ (1995-2025)

ACT DETAILS [sctACTDETAILS]

2. ✔ Policy requirement
Target population

[*itmTARGETPOPULATION* : *ACTDET_DATA.TAR_POP*]

[A:1] ☐ [cmpPRESCRIBED_INFANTS]
Infants < 1 year
[*itmPRESCRIBED_1* : *ACTDET_DATA.PRESCB_1*]
Prescribed
[A:0] ☐ for free
[A:1] ☐ with charge
[*itmINDICATION_1* : *ACTDET_DATA.INDICN_1*]
Indication
[A:0] ☐ Not specified
[A:1] ☐ Malaria symptoms
[A:2] ☐ RDT positive
[A:3] ☐ Malaria symptoms & RDT
[A:9] ☐ [*itmSPECIFY1* : *ACTDET_DATA.OTHIRS_1*]
Other --> Please specify: A30

[A:2] ☐ [cmpPRESCRIBED_CHD1T5YR]
Children >= 1 and < 5 years
[*itmPRESCRIBED_2* : *ACTDET_DATA.PRESCB_2*]
Prescribed
[A:0] ☐ for free
[A:1] ☐ with charge
[*itmINDICATION_2* : *ACTDET_DATA.INDICN_2*]
Indication
[A:0] ☐ Not specified
[A:1] ☐ Malaria symptoms
[A:2] ☐ RDT positive
[A:3] ☐ Malaria symptoms & RDT
[A:9] ☐ [*itmSPECIFY2* : *ACTDET_DATA.OTHIRS_2*]
Other --> Please specify: A30

[A:3] ☐ [cmpPRESCRIBED_CHD5YR]
Children >= 5 years
[*itmPRESCRIBED_3* : *ACTDET_DATA.PRESCB_3*]
Prescribed
[A:0] ☐ for free
[A:1] ☐ with charge
[*itmINDICATION_3* : *ACTDET_DATA.INDICN_3*]
Indication
[A:0] ☐ Not specified
[A:1] ☐ Malaria symptoms
[A:2] ☐ RDT positive
[A:3] ☐ Malaria symptoms & RDT
[A:9] ☐ [*itmSPECIFY3* : *ACTDET_DATA.OTHRIS_3*]
Other --> Please specify: A30

[A:4] ☐ [cmpPRESCRIBED_PRG]
Pregnant women
[*itmPRESCRIBED_4* : *ACTDET_DATA.PRESCB_4*]
Prescribed
[A:0] ☐ for free
[A:1] ☐ with charge
[*itmINDICATION_4* : *ACTDET_DATA.INDICN_4*]
Indication
[A:0] ☐ Not specified
[A:1] ☐ Malaria symptoms
[A:2] ☐ RDT positive
[A:3] ☐ Malaria symptoms & RDT
[A:9] ☐ [*itmSPECIFY4* : *ACTDET_DATA.OTHIRS_4*]
Other --> Please: A30

specify

[A:5] [cmpPRESCRIBED_ADU]
All Adults (Except pregnant women)
[itmPRESCRIBED_5 : ACTDET_DATA.PRESCB_5]
Prescribed
[A:0] for free
[A:1] with charge
[itmINDICATION_5 : ACTDET_DATA.INDICN_5]
Indication
[A:0] Not specified
[A:1] Malaria symptoms
[A:2] RDT positive
[A:3] Malaria symptoms & RDT
[A:9] [itmSPECIFY5 : ACTDET_DATA.OTHRIS_5]
Other --> Please specify
A30

[A:6] [cmpPRESCRIBED_OTH]
Others
[itmOTHSPECIFY_IRS : ACTDET_DATA.OTH_ACT]
A30
[itmPRESCRIBED_6 : ACTDET_DATA.PRESCB_6]
Prescribed
[A:0] for free
[A:1] with charge
[itmINDICATION_6 : ACTDET_DATA.INDICN_6]
Indication
[A:0] Not specified
[A:1] Malaria symptoms
[A:2] RDT positive
[A:3] Malaria symptoms & RDT
[A:9] [itmSPECIFY6 : ACTDET_DATA.OTHIRS_6]
Others --> Please Specify
A30

ACTUAL ACT DETAILS [sctAACTDETAILS]

3. ✔ Actual implementation Target population

[itmATARGETPOPULATION : ACTDET_DATA.TAR_POP]
[A:1] [cmpAPRESCRIBED_INFANTS]
Infants < 1 year
[itmPRESCRIBED_7 : ACTDET_DATA.PRESCB_1]
Prescribed
[A:0] for free
[A:1] with charge
[itmINDICATION_7 : ACTDET_DATA.INDICN_1]
Indication
[A:0] Not specified
[A:1] Malaria symptoms
[A:2] RDT positive
[A:3] Malaria symptoms & RDT
[A:9] [itmSPECIFY7 : ACTDET_DATA.OTHIRS_1]
Others --> Please Specify
A30

[A:2] [cmpAPRESCRIBED_CHD1T5YR]
Children >= 1 and < 5 years
[itmPRESCRIBED_8 : ACTDET_DATA.PRESCB_2]
Prescribed
[A:0] for free
[A:1] with charge
[itmINDICATION_8 : ACTDET_DATA.INDICN_2]
Indication
[A:0] Not specified
[A:1] Malaria symptoms
[A:2] RDT positive
[A:3] Malaria symptoms & RDT
[A:9] [itmSPECIFY8 : ACTDET_DATA.OTHIRS_2]
Others --> Please Specify
A30

[A:3] [cmpAPRESCRIBED_CHD5YR]
Children >= 5 years
[itmPRESCRIBED_9 : ACTDET_DATA.PRESCB_3]
Prescribed
[A:0] for free
[A:1] with charge
[itmINDICATION_9 : ACTDET_DATA.INDICN_3]
Indication
[A:0] Not specified
[A:1] Malaria symptoms

		[A:2] RDT positive [A:3] Malaria symptoms & RDT [A:9] [itmSPECIFY9 : ACTDET_DATA.OTHRIS_3] Others --> Please Specify A30 [A:4] [cmpAPRESCRIBED_PRG] Pregnant women [itmPRESCRIBED_10 : ACTDET_DATA.PRESCB_4] Prescribed [A:0] for free [A:1] with charge [itmINDICATION_10 : ACTDET_DATA.INDICN_4] Indication [A:0] Not specified [A:1] Malaria symptoms [A:2] RDT positive [A:3] Malaria symptoms & RDT [A:9] [itmSPECIFY10 : ACTDET_DATA.OTHIRS_4] Others --> Please Specify A30 [A:5] [cmpAPRESCRIBED_ADU] All Adults (Except pregnant women) [itmPRESCRIBED_11 : ACTDET_DATA.PRESCB_5] Prescribed [A:0] for free [A:1] with charge [itmINDICATION_11 : ACTDET_DATA.INDICN_5] Indication [A:0] Not specified [A:1] Malaria symptoms [A:2] RDT positive [A:3] Malaria symptoms & RDT [A:9] [itmSPECIFY11 : ACTDET_DATA.OTHRIS_5] Others --> Please Specify A30 [A:6] [cmpAPRESCRIBED_OTH] Others [itmOTHSPECIFY_IRS : ACTDET_DATA.OTH_ACT] A30 [itmPRESCRIBED_12 : ACTDET_DATA.PRESCB_6] Prescribed [A:0] for free [A:1] with charge [itmINDICATION_12 : ACTDET_DATA.INDICN_6] Indication [A:0] Not specified [A:1] Malaria symptoms [A:2] RDT positive [A:3] Malaria symptoms & RDT [A:9] [itmSPECIFY12 : ACTDET_DATA.OTHIRS_6] Others --> Please Specify A30
4. ✔	Is there any difference between the Policy requirement and the Actual implementation ? [Is there any difference between the Policy requirement and the Actual implementation ?]	[itmAPRESC_UPD : ACTDET_DATA.DIFFER] [A:N] No [A:Y] [itmAPRESC_UPD_COM : ACTDET_DATA.DIFF_COM] Yes --> Please specify A250
ACT: CAMPAIGN DETAILS [sctACTCAMPAIGNDEATILS]		
5. ✔	Was the distribution of the ACT deployed through a campaign during the past year (12 months)? [Was the distribution of the ACT deployed through a campaign during the past year (12 months)?]	[itmACTCAMPAIGN : ACT_DATA.CAMPING] [A:N] No [A:Y] [cmpCAMPAIGNDETAILS_ACT] Yes--> please specify [itmAREAPROVIDED : ACT_DATA.ARPRVD] Area provided in square kilometers [A:01] Entire DSS area [A:02] Area smaller than DSS area [A:03] Area bigger than DSS area [itmPOPULATIONPROVIDED : ACT_DATA.POPLN] Population provided [A:01] < 5 000

		[A:02] 5 000 - <10 000 [A:03] 10 000 - <15 000 [A:04] >=15 000 [itmAGEPROVIDED_A : ACT_DATA.AGPRVD] Age provided [A:1] Infants < 1 year [A:2] Children >= 1 and < 5 years [A:3] Children >= 5 years [A:4] Pregnant women [A:5] All Adults (Except pregnant women) [A:6] [cmpOTHERSPECIFY] Others, [itmOTH_SP_2 : ACT_DATA.OTH_AGE] Please Specify A128
ACT: MONITORING SYSTEM [sctACTMONITORINGSYSTEM]		
6. ✔	Is there any monitoring system to evaluate the impact of ACT prescription in the study area? [Is there any monitoring system to evaluate the impact of ACT prescription in the study area?]	[itmACTMONITORINGSYS : ACT_DATA.MN_FLG] [A:N] No [A:Y] [itmTYPEOFMONITORING : ACT_DATA.TYPMNSYS] Yes, Type of monitoring system [A:01] [itmDISPENSARIES : ACT_DATA.DISMAL] Dispensaries malaria surveillance --> Data Available [A:N] No [A:Y] Yes [A:02] [itmHOSPITALIZATION : ACT_DATA.HSPTLMAL] Hospitalization malaria surveillance --> Data Available [A:N] No [A:Y] Yes [A:03] [itmMALARIAINDICATION : ACT_DATA.MALSUR] Malaria Indicator surveys --> Data Available [A:N] No [A:Y] Yes

Key: [*] = Item is required [✔] = Source verification required
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p116682: QUESTIONNAIRE PART 6 (Ques Pg 6) [frmQUESTIONNAIREPART6]

IPT (Intermitent Preventive Therapy) [sctIPT]

1.* ✔ Is there IPT infant or SMC used as a prevention measure in the study area? [Is there IPT infant or SMC used as a prevention measure in the study area?]

[itmIPTPREVENTION : IPT_DATA.PREVN]
[A:N] No
[A:Y] [itmIPTPREVENTIONTYPE : IPT_DATA.IPTPRNTP]
Yes, - >please specify the type and since when introduced (day/month/year)

[A:91] [itmIPTPREVENTION_INFANT_DT : IPT_DATA.IPT_DT] **(MM/DD/YYYY)**
IPT infant --> Req/Unk / Req/Unk / Req/Unk (2003-2025)
[itmIPTMEDICATION_INFANT : IPT_DATA.MED_IFNT]
--> specify medication used [A:14] sulfadoxine/pyrimethamine [A:15] Artesunate [A:13] Amodiaquine [A:99] [itmSPECIFYMED_INF : IPT_DATA.SP_INF]
Others --->Specify A128

[A:3] [itmIPTPREVENTION_SMC_DT : IPT_DATA.SMC_DT] **(MM/DD/YYYY)**
SMC --> Req/Unk / Req/Unk / Req/Unk (2003-2025)
[itmIPTMEDICATION_SMC : IPT_DATA.MED_SMC]
-> specify medication used [A:14] sulfadoxine/pyrimethamine [A:15] Artesunate [A:13] Amodiaquine [A:99] [itmSPECIFYMED_SMC : IPT_DATA.SP_SMC]
Others, ---> Specify A128

[A:99] [itmSPECIFY_IPT : IPT_DATA.SP_IPT]
Others --> Specify A128

IPT DETAILS [sctIPTDETAILS]

Please specify the policy requirement for distribution of IPT

2. ✔ Policy requirement Target population

[itmTARGETPOPULATION_IPT : IPTDET_DATA.TAR_POP]
[A:91] [cmpPERFORMED_INFANTS_IPT]
IPT Infants [itmPERFORMED : IPTDET_DATA.PERFRM_1]
Performed [A:0] for free [A:1] with charge
[itmNB_DOSES_1 : IPTDET_DATA.NB_DOS]
Number of doses : N2
[itmAGEIPT_MIN_1 : IPTDET_DATA.IPTAGEMN]
Minimum AGE (in months) N3
[itmAGEIPT_MAX_1 : IPTDET_DATA.IPTAGEMX]
Maximum AGE (in months) N3

[A:8] [cmpPERFORMED_SMC_IPT]
SMC [itmPERFORMED_2 : IPTDET_DATA.PERFRM_2]
Performed [A:0] for free [A:1] with charge
[itmAGESMC_MIN_1 : IPTDET_DATA.SMCAGEMN]
Minimum AGE N3
[itmAGESMC_MAX_1 : IPTDET_DATA.SMCAGEMX]
Maximum AGE N3

[itmWHORECOMMED : IPTDET_DATA.WHORECMD]
Is it the same schedule as the WHO recommended one ? (Complete treatment course given at monthly intervals,
beginning at the start of the transmission season, to a maximum of four doses during the malaria season)

[A:N] [itmWHO_SPECIFY : IPTDET_DATA.OTH_SHED]
No,-->If No Please Specify A128

[A:Y] Yes

[A:6] [cmpPERFORMED_OTH]
Others [itmOTHSPECIFY_IRS : IPTDET_DATA.OTH_TP]
Please specify A30

[itmPERFORMED_6 : IPTDET_DATA.PERFRM_3]
Performed [A:0] for free [A:1] with charge
[itmFEQUENCY_6 : IPTDET_DATA.FRQNCY]
Frequency in months [A:0] Not specified

[A:1] < 6 months
[A:2] 6-11 months
[A:3] 12-17 months
[A:4] 18-23 months
[A:5] > =24 months

ACTUAL IPT DETAILS [sctAIPTDETAILS]

Please specify actual implementation for distribution of IPT

3. ✔	Actual implementation Target population	[itmAPTARGETPOPULATION_IPT : IPTDET_DATA.TAR_POP] [A:91] [cmpAPERFORMED_INFANTS_IPT] IPT Infants [itmPERFORMED : IPTDET_DATA.PERFRM_1] Performed [A:0] for free [A:1] with charge [itmAPNB_DOSES_2 : IPTDET_DATA.NB_DOS] Number of doses : N2 [itmAPAGEIPT_MIN_2 : IPTDET_DATA.IPTAGEMN] Minimum AGE N3 [itmAPAGEIPT_MAX_2 : IPTDET_DATA.IPTAGEMX] Maximum AGE N3 [A:8] [cmpAPERFORMED_SMC_IPT] SMC [itmPERFORMED_2 : IPTDET_DATA.PERFRM_2] Performed [A:0] for free [A:1] with charge [itmAGESMC_MIN_2 : IPTDET_DATA.SMCAGEMN] Minimum AGE N3 [itmAGESMC_MAX_2 : IPTDET_DATA.SMCAGEMX] Maximum AGE N3 [itmWHORECOMMED_AP : IPTDET_DATA.WHORECMD] Is it the same schedule as the WHO recommended one ? (Complete treatment course given at monthly intervals, beginning at the start of the transmission season, to a maximum of four doses during the malaria season) [A:N] [itmWHO_SPECIFY_AP : IPTDET_DATA.OTH_SHED] If No Please Specify A128 [A:Y] Yes [A:6] [cmpAPERFORMED_OTH] Others [itmOTHSPECIFY_IRS : IPTDET_DATA.OTH_TP] Please specify A30 [itmPERFORMED_12 : IPTDET_DATA.PERFRM_3] Performed [A:0] for free [A:1] with charge [itmFEQUENCY_12 : IPTDET_DATA.FRQNCY] Frequency in months [A:0] Not specified [A:1] < 6 months [A:2] 6-11 months [A:3] 12-17 months [A:4] 18-23 months [A:5] > =24 months
4. ✔	Is there any difference between the Policy requirement and the Actual implementation ? [Is there any difference between the Policy requirement and the Actual implementation	[itmAPERF_UPD_IPT : IPTDET_DATA.DIFFER] [A:N] No [A:Y] [itmAPERF_UPD_IPT_COM : IPTDET_DATA.DIFF_COM] Yes --> Please specify A250

?]

IPT: CAMPAIGN DETAILS [sctIPTCAMPAIGNDEATILS]

5. ✔ Was the distribution of the IPT deployed through a campaign or study during the past year (12 months)? [Was the distribution of the ITP deployed through a campaign or study during the past year (12 months)?]

[*itmIPTCAMPAIGN* : *IPT_DATA.IPTDIPLY*]
[A:N] No
[A:Y] [cmpCAMPAIGNDETAILS_IPT]
Yes--> please specify [*itmAREAPROVIDED* : *IPT_DATA.ARPRVD*]
Area provided in square kilometers
[A:01] Entire DSS area
[A:02] Area smaller than DSS area
[A:03] Area bigger than DSS area

[*itmPOPULATIONPROVIDED* : *IPT_DATA.POPLN*]
Population provided
[A:01] < 5 000
[A:02] 5 000 - <10 000
[A:03] 10 000 - <15 000
[A:04] >=15 000

[*itmAGEPROVIDED_IPT* : *IPT_DATA.AGPRVD*]
Age provided
[A:1] Infants < 1 year
[A:2] Children >= 1 and < 5 years
[A:3] Children >= 5 years
[A:4] Pregnant women
[A:5] All adults
[A:6] [cmpOTHERSPECIFY]
Others, [*itmOTH_SP_2* : *IPT_DATA.OTH_AGE*]
Please Specify A128

IPT: MONITORING SYSTEM [sctIPTMONITORINGSYSTEM]

6. ✔ Is there any monitoring system to evaluate the impact of the IPT distribution in the study area? [Is there any monitoring system to evaluate the impact of the ITP distribution in the study area?]

[*itmIPTMONITORINGSYS* : *IPT_DATA.MN_FLG*]
[A:N] No
[A:Y] [*itmTYPEOFMONITORING* : *IPT_DATA.TPMONSYS*]
Yes, -- > Type of monitoring system
[A:01] [*itmDISPENSARIES* : *IPT_DATA.DISMAL*]
Dispensaries malaria surveillance --> Data Available
[A:N] No
[A:Y] Yes
[A:02] [*itmHOSPITALIZATION* : *IPT_DATA.HSPTLMAL*]
Hospitalization malaria surveillance--> Data Available
[A:N] No
[A:Y] Yes
[A:03] [*itmMALARIAINDICATION* : *IPT_DATA.MALSUR*]
Malaria Indicator surveys --> Data Available
[A:N] No
[A:Y] Yes

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p116682: QUESTIONNAIRE PART 7 (Ques Pg 7) [frmQUESTIONNAIREPART7]

RDT (RAPID DIAGNOSTIC TEST) [sctRDT]

1.* ✔ Are RDTs used in the study area?
[Are RDTs used in the study area?]

[itmRDTPREVENTION : RDT_DATA.PREVTN]
[A:N] No
[A:Y] [itmRDTPREVENTION_DT : RDT_DATA.INTRO_DT] (MM/DD/YYYY)
Yes-->please specify since when introduced (day/month/year): Req/Unk / Req/Unk / Req/Unk (2003-2025)

RDT DETAILS [sctRDTDETAILS]

2. ✔ Policy requirement
Target population

[itmTARGETPOPULATION : RDTDET_DATA.TAR_POP]

[A:1] [cmpPRESCRIBED_INFANTS_RDT]
Infants < 1 year
[itmPERFORMED : RDTDET_DATA.PRFRMD_1]
Performed
[A:0] for free
[A:1] with charge
[itmINDICATION_RDT : RDTDET_DATA.INDICN_1]
Indication
[A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPISp1 : RDTDET_DATA.OTHRDT_1]
Other --> Please Specify A30

[A:2] [cmpPRESCRIBED_CHD1T5YR_RDT]
Children >= 1 and < 5 years
[itmPERFORMED_2 : RDTDET_DATA.PRFRMD_2]
Performed
[A:0] for free
[A:1] with charge
[itmINDICATION_RDT_2 : RDTDET_DATA.INDICN_2]
Indication
[A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPISp2 : RDTDET_DATA.OTHRDT_2]
Other --> Please Specify A30

[A:3] [cmpPRESCRIBED_CHD5YR_RDT]
Children >= 5 years
[itmPERFORMED_3 : RDTDET_DATA.PRFRMD_3]
Performed
[A:0] for free
[A:1] with charge
[itmINDICATION_RDT_3 : RDTDET_DATA.INDICN_3]
Indication
[A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPISp3 : RDTDET_DATA.OTHRDT_3]
Other --> Please Specify A30

[A:4] [cmpPRESCRIBED_PRG_RDT]
Pregnant women
[itmPERFORMED_4 : RDTDET_DATA.PRFRMD_4]
Performed
[A:0] for free
[A:1] with charge
[itmINDICATION_RDT_4 : RDTDET_DATA.INDICN_4]
Indication
[A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPISp4 : RDTDET_DATA.OTHRDT_4]
Other --> Please Specify A30

[A:5] [cmpPRESCRIBED_ADU_RDT]
All Adults (Except pregnant women)
[itmPERFORMED_5 : RDTDET_DATA.PRFRMD_5]
Performed
[A:0] for free
[A:1] with charge
[itmINDICATION_RDT_5 : RDTDET_DATA.INDICN_5]

Indication [A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPlSp5 : RDTDET_DATA.OTHRDT_5]
Other --> Please Specify: A30

[A:6] [cmpPRESCRIBED_OTH_RDT]
Others [itmOTHSPECIFY_IRS : RDTDET_DATA.OTH_RDT]
Please specify: A30

[itmPERFORMED_6 : RDTDET_DATA.PRFRMD_6]
Performed [A:0] for free
[A:1] with charge

[itmINDICATION_RDT_6 : RDTDET_DATA.INDICN_6]
Indication [A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPlSp6 : RDTDET_DATA.OTHRDT_6]
Other --> Please Specify: A30

ACTUAL RDT DETAILS [sctARDTDETAILS]

3. ✔ Actual implementation Target population

[itmATARGETPOPULATION : RDTDET_DATA.TAR_POP]
[A:1] [cmpAPRESCRIBED_INFANTS_RDT]
Infants < 1 year
[itmPERFORMED_7 : RDTDET_DATA.PRFRMD_1]
Performed [A:0] for free
[A:1] with charge
[itmINDICATION_RDT_7 : RDTDET_DATA.INDICN_1]
Indication [A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPlSp1 : RDTDET_DATA.OTHRDT_1]
Other --> Please Specify: A30

[A:2] [cmpAPRESCRIBED_CHD1T5YR_RDT]
Children >= 1 and < 5 years
[itmPERFORMED_8 : RDTDET_DATA.PRFRMD_2]
Performed [A:0] for free
[A:1] with charge
[itmINDICATION_RDT_8 : RDTDET_DATA.INDICN_2]
Indication [A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPlSp2 : RDTDET_DATA.OTHRDT_2]
Other --> Please Specify: A30

[A:3] [cmpAPRESCRIBED_CHD5YR_RDT]
Children >= 5 years
[itmPERFORMED_9 : RDTDET_DATA.PRFRMD_3]
Performed [A:0] for free
[A:1] with charge
[itmINDICATION_RDT_9 : RDTDET_DATA.INDICN_3]
Indication [A:1] Malaria symptoms
[A:4] Any outpatient visit
[A:5] Any hospitalization
[A:9] [itmPlSp3 : RDTDET_DATA.OTHRDT_3]
Other --> Please Specify: A30

[A:4] [cmpAPRESCRIBED_PRG_RDT]
Pregnant women
[itmPERFORMED_10 : RDTDET_DATA.PRFRMD_4]
Performed [A:0] for free

		[A:1] with charge [itmINDICATION_RDT_10 : RDTDET_DATA.INDICN_4] Indication [A:1] Malaria symptoms [A:4] Any outpatient visit [A:5] Any hospitalization [A:9] [itmPlSp4 : RDTDET_DATA.OTHRDT_4] Other --> Please Specify A30 [A:5] [cmpAPRESCRIBED_ADU_RDT] All Adults (Except pregnant women) [itmPERFORMED_11 : RDTDET_DATA.PRFRMD_5] Performed [A:0] for free [A:1] with charge [itmINDICATION_RDT_11 : RDTDET_DATA.INDICN_5] Indication [A:1] Malaria symptoms [A:4] Any outpatient visit [A:5] Any hospitalization [A:9] [itmPlSp5 : RDTDET_DATA.OTHRDT_5] Other --> Please Specify A30 [A:6] [cmpAPRESCRIBED_OTH_RDT] Others [itmOTHSPECIFY_IRS : RDTDET_DATA.OTH_RDT] Please specify A30 [itmPERFORMED_12 : RDTDET_DATA.PRFRMD_6] Performed [A:0] for free [A:1] with charge [itmINDICATION_RDT_12 : RDTDET_DATA.INDICN_6] Indication [A:1] Malaria symptoms [A:4] Any outpatient visit [A:5] Any hospitalization [A:9] [itmPlSp6 : RDTDET_DATA.OTHRDT_6] Other --> Please Specify A30
4. ✔	Is there any difference between the Policy requirement and the Actual implementation ? [Is there any difference between the Policy requirement and the Actual implementation ?]	[itmAPRESC_UPD_RDT : RDTDET_DATA.DIFFER] [A:N] No [A:Y] [itmAPRESC_UPD_RDT_COM : RDTDET_DATA.DIFF_COM] Yes --> Please specify A250
RDT: CAMPAIGN DETAILS [sctRDTCAMPAIGNDEATILS]		
5. ✔	Was RDT deployed through a campaign during the past year (12 months)? [Was RDT deployed through a campaign during the past year (12 months)?]	[itmRDTCAMPAIGN : RDT_DATA.CAMPING] [A:N] No [A:Y] [cmpCAMPAIGNDETAILS_ACT] Yes--> please specify [itmAREAPROVIDED : RDT_DATA.ARPRVD] Area provided in square kilometers [A:01] Entire DSS area [A:02] Area smaller than DSS area [A:03] Area bigger than DSS area [itmPOPULATIONPROVIDED : RDT_DATA.POPLN] Population provided [A:01] < 5 000 [A:02] 5 000 - <10 000 [A:03] 10 000 - <15 000 [A:04] >=15 000 [itmAGEPROVIDED_A : RDT_DATA.AGPRVD] Age provided [A:1] Infants < 1 year [A:2] Children >= 1 and < 5 years [A:3] Children >= 5 years [A:4] Pregnant women

		[A:5] All adults [A:6] [cmpOTHERSPECIFY] Others, [itmOTH_SP_2 : RDT_DATA.OTH_AGE] Please Specify A128
RDT: MONITORING SYSTEM [sctRDTMONITORINGSYSTEM]		
6. ✔	Is there any monitoring system to evaluate the impact of the RDT use in the study area? [Is there any monitoring system to evaluate the impact of the RDT use in the study area?]	[itmRDTMONITORINGSYS : RDT_DATA.MN_FLG] [A:N] No [A:Y] [itmTYPEOFMONITORING : RDT_DATA.TYP_MON] Yes-->Type of monitoring system [A:01] [itmDISPENSARIES : RDT_DATA.DISMAL] Dispensaries malaria surveillance --> Data Available [A:N] No [A:Y] Yes [A:02] [itmHOSPITALIZATION : RDT_DATA.HSPTLMAL] Hospitalization malaria surveillance--> Data Available [A:N] No [A:Y] Yes [A:03] [itmMALARIAINDICATION : RDT_DATA.MALSUR] Malaria Indicator surveys --> Data Available [A:N] No [A:Y] Yes

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