WHO Guidelines for malaria

Systematic reviews, background papers and other unpublished evidence considered in the development of recommendations

Prevention/Vaccine

Section

4.3 Vaccine. In *WHO Guidelines for malaria, originally published on 18 February 2022*.

Title

Health Utilisation Study (HUS) Round 2 - cross-country report on findings from the Primary Child Caregiver cohort sample

Authors

The study is being conducted by a consortium of research partners led by the:

a. University of Health and Allied Sciences (UHAS) in Ghana
b. Liverpool School of Tropical Medicine (LSTM) in consortium with the Kenya Medical Research Institute (KEMRI) and the US Centers for Disease Control and Prevention (CDC & KEMRI/CDC) in Kenya
c. Malawi-Liverpool Wellcome Trust (an affiliate of the College of Medicine) in Malawi

PATH is leading the overall study.

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(Originally reviewed as annex 5 of the "Full evidence report on the RTS,S/AS01 malaria vaccine" prepared by the RTS,S/AS01 SAGE/MPAG Working Group in September 2021).

This report was reviewed by the Strategic Advisory Group of Experts on Immunization (SAGE) and the Malaria Policy Advisory Group (MPAG) in October 2021 and was used to support the development of the recommendation included in the *WHO Guidelines for malaria*. It is being made publicly available for transparency purposes and information, in accordance with the *WHO handbook for guideline development, 2nd edition* (2014).

Healthcare Utilization Study (HUS) R2 Report: Cross-Country Findings from the Primary Child Caregiver Cohort Sample

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About This Report

HUS Background and Research Partners

This document is part of a collection of interim reports on selected findings from the Healthcare Utilization Study (HUS) for the Malaria Vaccine Implementation Programme (MVIP). The HUS is a multi-country, qualitative study designed to provide explanatory insight on the delivery and uptake of the world's first malaria vaccine, RTS,S/AS01 (RTS,S). Following more than 30 years of clinical development and study[a], two World Health Organization (WHO) advisory groups—the Strategic Advisory Group of Experts (SAGE) on Immunization and the Malaria Policy Advisory Group (MPAG)—jointly called for pilot implementation of the vaccine in three to five settings in sub-Saharan Africa to further evaluate the vaccine before recommending it for wider use[b]. The MVIP was subsequently created to introduce RTS,S in selected sites in Ghana, Kenya, and Malawi through routine immunization programmes led by ministries of health (MOHs). This phased introduction of RTS,S is accompanied by independent evaluations that focus on the feasibility of administering the recommended 4 doses of the vaccine in children, the vaccine's potential role in reducing childhood deaths, and its safety in the context of routine use. The MVIP is being coordinated by the WHO, in collaboration with PATH, GSK, and the ministries of health from Ghana, Kenya, and Malawi.

The HUS is among MVIP evaluations focused on understanding the feasibility of providing the 4-dose schedule—a schedule that requires new vaccination visits, including for the fourth dose at 24 months of age. Annex 1 shows the RTS,S delivery schedule and eligibility guidance for each country.

Applying a qualitative panel design, the HUS is collecting data from primary child caregivers, health sector personnel, and other community members at three critical points in the vaccine's 24-month delivery cycle. The study is being conducted by a consortium of research partners led by the University of Health and Allied Sciences (UHAS) in Ghana, the Liverpool School of Tropical Medicine (LSTM) in Kenya, and the Malawi-Liverpool Wellcome Trust in Malawi. PATH is leading the overall study.

Steps were taken to ensure that participants answered interview questions freely and truthfully. Prior to obtaining informed consent, interviewers presented themselves to prospective participants following recruitment scripts, specifying their affiliation with a research institution (see script in Annex 2). In the course of the interview, participants were also encouraged to speak openly and truthfully and reminded, as needed, of our commitment to confidentiality and privacy. Additionally, recognizing that repeated interviews with caregivers in the cohort could influence their attitudes and replies, the final round of data collection will include conducting similar interviews in a different, cross-sectional sample of child caregivers.

[a] Kaslow, D. et al. (2018). Vaccine candidates for poor nations are going to waste. *Nature, 564*(7736), 337-339. doi:http://dx.doi.org/10.1038/d41586-018-07758-3

[b] World Health Organization. (2016). Malaria vaccine: WHO position paper. *Weekly Epidemiological Record, 4*(91), 33-52.

Round 2 Reports

As of this report date, two data collection rounds for the HUS have been completed and the final round is underway. A report of preliminary findings from round 1 (R1) was completed in June 2020.[c] The complete packet of R2 reports includes this document (#2 below) along with a background document summarizing HUS methods and study status (#1 below), and three country-specific reports (#3-5 below).

1. Methods and Study Status: Background for HUS R2 Reports
2. Cross-Country Findings from the Primary Child Caregiver Cohort Sample
3. Key findings through Round 2: Ghana
4. Key findings through Round 2: Kenya
5. Key findings through Round 2: Malawi

Country-specific reports provide contextual details pertinent to the RTS,S introductions and uptake and present findings from interviews with health workers and other health personnel. This report presents high-level cross-country findings from R2 interviews with primary child caregivers (PCGs), whose children should have received RTS,S dose 3 at the time of R2 interviews. Primary focuses are:

1. The uptake of RTS,S through dose 3, including factors that facilitate or threaten receipt of all three doses.
2. The impact of RTS,S uptake on malaria treatment seeking and other prevention behaviors.
3. PCG perceptions about RTS,S, sources of RTS,S information, and new/or persistent questions and concerns about RTS,S.

Changes in themes and patterns compared to R1 findings are highlighted throughout.

Ethical Approvals

The HUS has been approved by PATH's Research Ethics Committee (REC), the Ghana Health Service's (GHS) Ethics Review Committee, the University of Malawi College of Medicine's Research and Ethics Committee, the Liverpool School of Tropical Medicine (LSTM) Research Ethics Committee, the Kenya Medical Research Institute's (KEMRI) Scientific and Ethics Unit, the London School of Hygiene & Tropical Medicine's (LSHTM) Observational/Interventions Research Ethics Committee, and the US Centers for Disease Control and Prevention's Center for Global Health (CDC). Written informed consent is sought from every study participant.

[c] Malaria Vaccine Implementation Programme Healthcare Utilization Study: Preliminary Findings From Round 1 Data Collection, 21 June 2020

Key Takeaways from R2 Findings from PCG Interviews

RTS,S uptake

- Uptake of the RTS,S vaccine through the third dose is generally strong.
    - Instances of children who have not received any RTS,S doses are typically due to early barriers, including PCG concerns about the vaccine's safety or confusion about eligibility which caused the PCGs to refuse or delay initial doses until they were no longer eligible.
    - Instances of children who have received fewer than the expected three doses of RTS,S are typically due to service access barriers or to the PCGs' personal circumstances.
- Most caregivers expressed their intent to take their children to receive dose 4, many enthusiastically.

Attitudes and fears about RTS,S

- Positive attitudes and trust in RTS,S among PCGs have increased substantially since R1 interviews, driven mainly by PCGs perceiving health benefits of the vaccine in their own children and in the broader community.
- Early concerns about safety have been replaced by widespread perception that adverse events following RTS,S immunization (AEFI) are "normal" and similar to other vaccines.
- Fewer threats to RTS,S uptake – e.g., rumors, fears about safety – are evident in R2 compared to R1 data; programmatic barriers (e.g., service access) are more frequently reported in R2.

Malaria treatment seeking and other prevention in the context of RTS,S

- Many of the RTS,S-eligible children have had malaria since receiving RTS,S doses, but this has generally not diminished the PCGs' enthusiasm for RTS,S. PCGs perceive malaria to be less frequent or severe because of the vaccine.
- RTS,S uptake does not seem to interfere with or change existing malaria treatment or prevention behaviors at the time of R2.

RTS,S information and unanswered questions about RTS,S

- While caregivers have greater knowledge of RTS,S and understanding of the 4-dose schedule, confusion and questions persist around the level and duration of protection conferred by the vaccine.

Primary Child Caregiver (PCG) Interviews

Timing of PCG interviews within the RTS,S delivery schedule

Data from multiple study groups are being collected for the HUS, including from primary child caregivers (PCGs), health providers who administer vaccines, sub-national and national health managers and leaders, and various community members (e.g., male household heads, female elders, community leaders). Three data collection rounds were planned to occur at three critical times in the 24-month delivery cycle (Table 1). Interviews in cohort samples of PCGs and health providers planned for each of three rounds of data collection.

Table 1. HUS fieldwork timing linked to RTS,S introduction.

Round 1		Round 2	Round 3
Lead up to initial RTS,S delivery	**Soon after dose 1 (5-6 months old)**	**In-between doses 3 & 4 (≈17 months old)**	**Soon after dose 4 (22-24 months old)**
Ethnographic immersion and data collection in all study groups		Data collection focused on PCGs and health providers Ethnographic immersion	Data collection in all study groups Ethnographic immersion

In order to capture initial reactions to RTS,S introduction and uptake of dose 1 in 5-6 month old children, R1 interviews were conducted soon after the initial launch of RTS,S in April 2019 in Ghana and Malawi and in September 2019 in Kenya. To assess experiences and changes in attitudes mid-way through the vaccine's two-year schedule, R2 interviews were planned to be completed by all individuals in the cohort after dose 3 was administered to RTS,S-eligible children, but before the child was eligible to receive dose 4. The COVID-19 pandemic required a suspension of research activities delaying R2 start-up by six months, which was initially planned to begin in April 2021. R2 interviews commences in September 2020 and were completed in all three countries by December 2020. Although most of the RTS,S-eligible children were still not eligible for dose 4, due to COVID-19 delays five of the PCGs interviewed in R2 had children old enough to receive dose 4. RTS,S uptake analyses presented below focus on PCG adherence through dose 3.

R2 PCG Sample

As described in the background documents to this report,[d] nine community sites per country (27 total) were selected for inclusion the study, with a minimum target sample of five PCGs per community completing all three interviews (R1-R3). To accommodate loss to follow-up (LTFU) and drop-outs, we initially sampled seven individuals per site, for a total of 63 PCGs per country. Twenty-five PCGs (13%) from R1 were LTFU in R2. The PCG sample sizes for R1 and R2 are summarized in Table 2.

[d] HUS Methods and Study Status: Background for HUS R2 Reports

Table 2. PCG cohort sample in R2 by country.

Country	R1 Sample	R2 Sample			
		LTFU	Continued	Replaced	Total
Ghana	62	9	53	0	53
Kenya	63	10	53	10	63
Malawi	63	6	57	0	57
Total	**188**	**25**	**163**	**10**	**173**

Note: LTFU = lost to follow-up; Continued = interviewed in R1 and R2; Replaced = newly recruited in R2.

The most common reason for LTFU was migration out of the study community, though at least one PCG (in Ghana) declined to continue with the study. Research teams in Ghana and Malawi – where LTFUs were generally evenly distributed across community sites – opted to not recruit replacement PCGs for the LTFUs. In Kenya, where LTFUs were concentrated in specific communities, the team opted to replace the lost individuals with newly recruited PCGs to ensure the sample in each community was adequate in round 3. With the exception for one community in Ghana (C3), where only four PCGs were interviewed in R2, all the other community sites retained the minimum target sample of five PCGs in each HUS community.

R2 Interview Focus

Table 3 shows that R2 interviews explored the same topics as in R1, adapting questions to reflect their follow-on nature and building specifically on what the PCGs recounted in R1. The questions and probing specifically explored changes in PCG sentiments and behaviors since the R1 interviews or since her child received initial RTS,S doses.

Table 3. PCG interview topics in R1 and R2.

Round 1 Topics	Round 2 Topics
• PCG sociodemographic and background information • Vaccination history of the RTS,S-eligible child based on review of the child health card • Malaria perceptions • Treatment seeking for malaria in the RTS,S-eligible child • Exposure to RTS,S messages in popular and professional sectors, probing for influences of messages on RTS,S uptake • Questions and concerns about RTS,S • Experiences at the last vaccination visit	• Verification and updates (original cohort); PCG sociodemographic and background information (replacements) • Updates on vaccinations received based on review of the child health card. • Malaria perceptions in the context of RTS,S • Treatment seeking for malaria in the RTS,S-eligible child in the context of RTS,S provision • Exposure to RTS,S messages in popular and professional sectors, probing for changes in PCG understanding and acceptance of RTS,S • Questions and concerns about RTS,S • Experiences at the last vaccination visit • COVID-19 perceptions and impact on service utilization

In R2 we also added questions regarding COVID-19, focused specifically on understanding if and how the pandemic affected the PCGs access to and utilization of child health services and taking their child for scheduled vaccines.

Findings

PCG characteristics and gender of the RTS,S-eligible child

All but two PCGs were female, and most were between 19-34 years old, married or cohabitating, had completed primary school or more, and had more than one child (Table 4). All but six individuals were the mothers of the RTS,S-eligible children. Within and across countries, the proportion of males and females among RTS,S-eligible children was nearly equal (Table 5).

Table 4. Description of primary child caregiver cohort characteristics that remain in the cohort (including replacements).

Characteristic		N (%)		
		Ghana	Kenya	Malawi
Sex	Female	53 (100.0)	62 (98.4)	56 (98.3)
	Missing	-	1 (1.6)	1 (1.8)
Age (years)	15–18	3 (5.7)	3 (4.8)	4 (7.0)
	19–24	14 (26.4)	13 (20.6)	26 (45.6)
	25–29	14 (26.4)	16 (25.4)	6 (10.5)
	30–34	14 (26.4)	17 (27.0)	11 (19.3)
	35–40	4 (7.6)	9 (14.3)	8 (14.0)
	40+	4 (7.6)	5 (7.9)	1 (1.8)
	Missing		-	1 (1.8)
Marital status	Married or cohabiting	42 (79.3)	58 (92.1)	46 (80.7)
	Divorced, widowed, or unmarried	11 (20.8)	5 (7.9)	11 (19.3)
Education	None	5 (9.4)	-	3 (5.3)
	Primary	12 (22.6)	43 (68.2)	42 (73.7)
	Secondary	26 (49.1)	16 (25.4)	8 (14.0)
	Post-secondary	10 (18.9)	4 (6.4)	-
	Missing	-	-	4 (7.0)
Number of children	1	9 (20.8)	10 (15.9)	20 (35.1)
	2	16 (30.2)	8 (12.7)	14 (24.6)
	3+	26 (49.1)	45 (71.4)	23 (40.4)
		2 (3.8)	-	-
Relation to child	Mother	52 (98.1)	59 (93.7)	56 (98.3)
	Grandparent or other	1 (1.9)	4 (6.4)	1 (1.8)

Table 5. Gender of RTS,S-eligible children that remain in the cohort (including replacements).

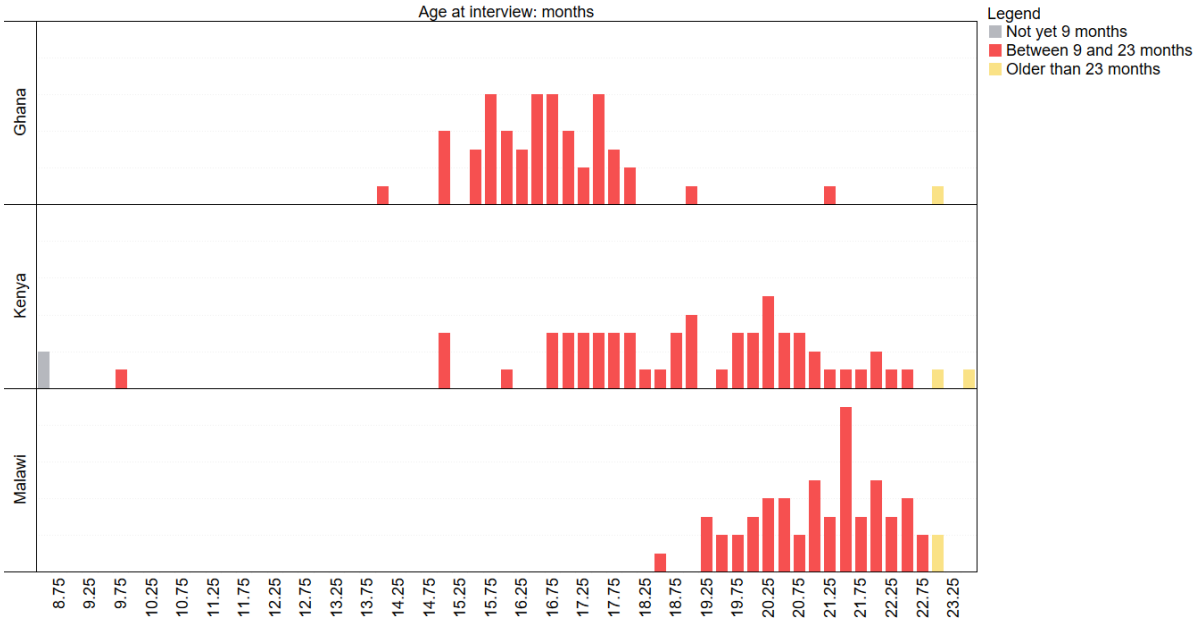
	N (%)		
	Ghana	Kenya	Malawi
Female	24 (45.3)	31 (49.2)	30 (52.6)
Male	29 (54.7)	32 (50.8)	27 (47.4)
Total	**53**	**63**	**57**

Age of RTS,S-eligible child at time of R2 interview

As we were anticipating a range of child ages between the third and fourth RTS,S doses (≈10-23 months) represented in R2 data, it was specified that the mid-point age was ≈17 months as the target. Despite delays in R2 data collection due to COVID-19, in addition to the long period between doses 3 and 4, many children were still between 9 and 23 months old at the time of R2 interviews, indicated by the red bars in Figure 1. Five children were just

over the 23-month mark, indicated by yellow bars in Figure 1. Only two children (whose mothers were newly recruited in R2) were not yet eligible for the third dose of RTS,S at the time of R2 interviews, indicated by the grey bar in Figure 1.

Figure 1. Ages of RTS,S-eligible children at the time of R2 interviews (n=173).



Note: Children indicated in grey are below the nine-month mark and potentially "not [officially] eligible" for RTS,S dose 3; children shown in yellow just exceeded the exact 23-month mark by one or two weeks at time of interview and thus may be fourth-dose eligible; those in red are between the nine-month and 23-month eligibility markers.

The distinct differences in interview timing may be explained, in part, by the fact that the Ghana research team was the first and Malawi's team the last to resume R2 fieldwork. The wide range of ages of children in Kenya in R2, including replacement PCGs, reflect a similarly large age spread from R1.

RTS,S doses received at time of R2 interview

Uptake Patterns

To understand RTS,S-eligible children's vaccination history and RTS,S uptake specifically through dose 3, data were abstracted from the children's vaccination cards. When vaccination cards were not available, PCGs were asked to recall vaccines their children had received. Data were collected on:

1. **Vaccinations/doses other than RTS,S**, including: their Bacille Calmette-Guérin (BCG) vaccine, which is scheduled at birth; the first dose of pentavalent vaccine[e] (Penta-1) scheduled at six weeks; the second dose of pentavalent vaccine scheduled at 10 weeks (Penta-2); and the third dose of pentavalent vaccine scheduled at 14 weeks (Penta-3). Data were also captured for the measles 9-month dose (not shown in the graph).

[e] Vaccine used to immunize against diphtheria, pertussis, tetanus, hepatitis B, and Haemophilus influenzae type b

2. **RTS,S doses**, including:
    a. Dose 1 which children are eligible to receive beginning at 5 months in Malawi and 6 months in Kenya and Ghana.
    b. Dose 2 which children are eligible to receive a month after the receipt of dose 1 in all three countries.
    c. Dose 3 which children are eligible to receive beginning at 7 months in Malawi and 9 months in Kenya and Ghana (in Malawi a child is eligible a month after the receipt of dose 2; in Kenya and Ghana, two months after the receipt of dose 2).
    d. If child is late, maintain 4 weeks apart between doses 2 and 3.

For the three countries combined, Figure 2 shows the children's receipt of RTS,S dose 1, dose 2, and dose 3, as well as other vaccines in the immunization schedule. The figure includes data collected from all PCGs, including returning, LTFU, and replacement PCGs. For LTFU cases, vaccination status of the child is shown through R1 (e.g., through RTS,S dose 1) and then marked in blue as LTFU for RTS,S doses 2 and 3. One participant did not have a vaccination card available in either R1 or R2; this cases is treated as missing and marked in yellow in the Figure 2.

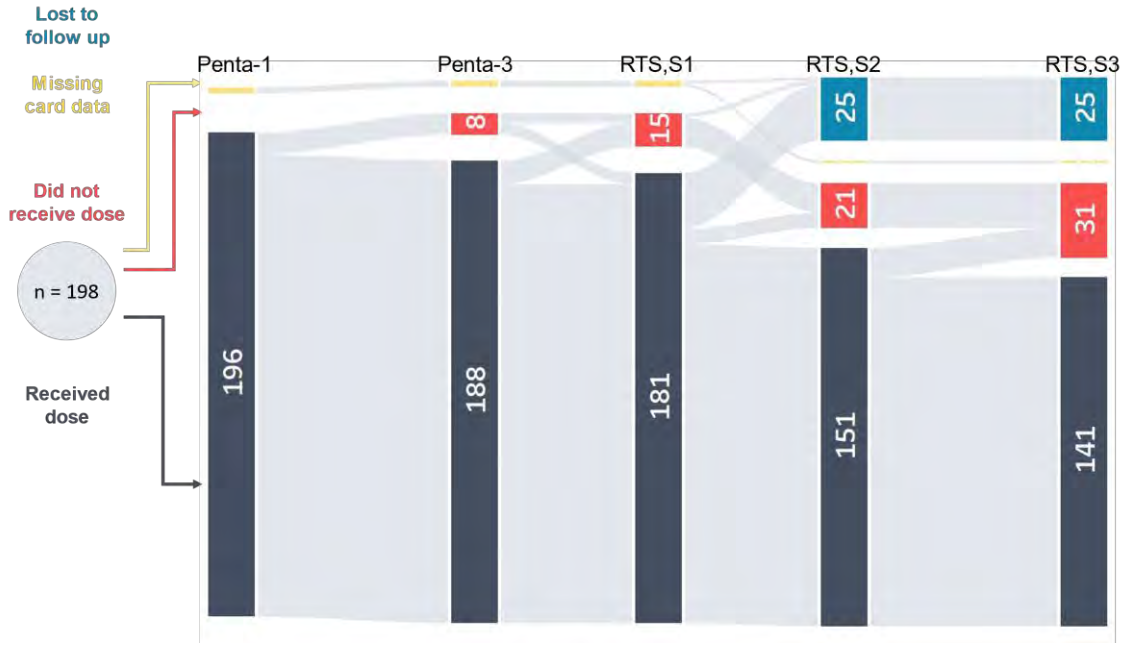
Among the remaining 172 participants, uptake of RTS,S doses is generally high with 141 children having received all three doses recommended at the time of interview. Of these 141 children, four had additionally completed the entire vaccination series and received all four RTS,S doses. Thirty-one children had not yet received at least three doses at the time of the R2 interview, of whom 10 had received doses 1 and 2, eight had received only dose 1, and 13 had yet to receive any RTS,S doses. Crucially, eight participants were missing a vaccine card in R2. Information provided from their vaccine cards in R1 was used to record their children's vaccine receipt. As a result, some of these children may have since received further doses of RTS,S that are not documented here.

Three RTS,S adherence categories as of R2 interviews were derived from the children's vaccination history data:

1. Fully adherent: children who have received three or more doses of RTS,S at the time of interview, as expected based upon eligibility.
2. Partially adherent: children who have received one or two doses of RTS,S but have yet to receive a third dose at time of interview. These children may have yet to receive dose 3 or the PCG has defaulted or delayed.
3. Non-adherent: children who have yet to receive any doses of RTS,S at the time of interview.

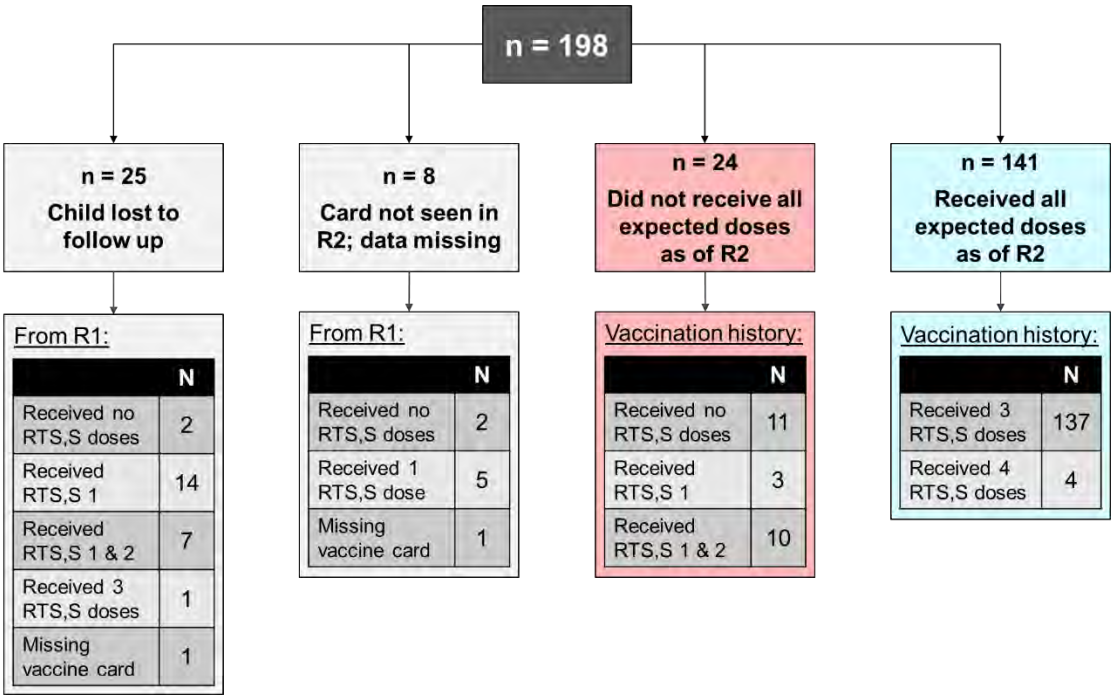
These three adherence categories are explored in further depth in Figure 3. Twenty-four non-adherent (n=11) or partially adherent (n=13) cases were observed in R2. Data were missing on eight cases due to missing vaccination cards; among these eight cases, two were categorized as non-adherent and five as partially adherent based on vaccination history data collected in R1. As noted above, data on one individual was missing in both R1 and R2.

Figure 2. Receipt of preceding vaccines and RTS,S dose 1 to dose 3 in primary child caregiver cohort.



Note: Each bar represents the frequency with which children either received (dark grey) or did not receive (red) a given antigen. Individuals missing a vaccination card are shown in yellow and LTFU in R2 are shown in blue. The light grey curves between the bars represent the path of individuals through the vaccination process. Receipt of doses is only included in the graphic if data were abstracted from vaccination card; data from PCG recall are not included.

Figure 3. Receipt of RTS,S doses in primary caregiver cohort, by uptake category.



Note: Receipt of doses is only included in this graphic if it is recorded on the vaccination card (no recall). Among the PCGs who were not LTFU, 8 did not have a vaccination card available for view in R2; the existing data from R1 is used to record any available information on their vaccination histories. Recall of any additional doses is explored in further detail below.

It is important to note that, as in R1, children in R2 who had not yet received dose 3 may have received it after the interview was conducted. More accurate uptake findings will be available from the final, R3 interviews.

Reasons for non- or partial adherence

PCGs categorized as non- or partially adherent were asked why their child had not received the expected RTS,S doses. Tables 6 - 8 group PCG responses by primary issues identified and summarize variable explanations given by the PCGs. Table 6 presents findings on the non-adherent cases, Table 7 the partially adherent cases, and Table 8 captures responses from eight individuals missing vaccination cards.

Table 6. Reasons given by PCGs for their children not receiving any RTS,S doses.

Primary Issue	Variable Explanations Given
Information gap (n = 3)	Three PCGs exhibited significant gaps in information about RTS,S and weak connections to the health system. Despite their children not receiving any doses, all three expressed trusts in vaccines generally, were enthusiastic about a malaria vaccine, and open to their children receiving the vaccine. One PCG, for instance, believed that her child had received three malaria vaccinations (R1) and as a concluding thought to the R2 interview asked: *"How many [malaria] vaccines does he have left"?* (C25_047). Another, who took her child to a private clinic for vaccinations, had very little information about RTS,S in both R1 and R2 interviews, asking as her final question: *"Given that the book says she hasn't received the malaria vaccine, where can I go to get it?"* (C18_004).
Injection-related adverse events following infection (AEFI) experience (n = 3)	Three of the caregivers described initially hesitating to accept RTS,S due to fears of the injection, recounting their own or a close relative's bad experience with an injection. For instance, one individual explains that her sister's child died soon after being vaccinated, causing her fears and her husband to forbid taking the child for vaccination (C5_006). All three of these caregivers ended up overcoming their initial hesitations and wanting their children to receive RTS,S, but were no longer eligible to receive the vaccination by that point. For example, one PCG decided to not allow the child to receive RTS,S when it was introduced because of prior AEFIs, but had a change of heart after hearing many positive messages and testimonials about it from others who took it (C11_004).
Early concerns, early rumors (n = 2)	Two PCGs delayed taking RTS,S due to early concerns and rumors about RTS,S. In one instance, the PCG was confused about "*this new vaccine*", wondering *"what disease is it for?*" (C2_006). She also was confused about the phased introduction of RTS,S and further discouraged by her husband's skepticism of the value of vaccines. Similarly, another of these individuals describes early skepticism in R1 induced by rumors about RTS,S being experimental on African children. In the R2 interview, both caregivers explained that they have changed their mind and now sees that the malaria vaccine is beneficial. Similar to other mothers who initially rejected the vaccine and are whose children are now ineligible, they are open to their children receiving the vaccine and hope that eligibility criteria will be broadened to include older children (C2_007).
Access to care (n = 2)	Two PCGs describe barriers to care as the main reasons for their children not receiving RTS,S. Though under-informed about RTS,S, one of these caregivers expresses significant trust in vaccines and a keen interested in her child receiving RTS.S. She has tried multiple times to have her child vaccinated without success due to health worker strikes and coming at the wrong time. As a closing thought to the R2 interview she says she wants to know: "when is it [malaria vaccine] coming?" (C11_005).
Perceived as received (n = 1)	In one case, the mother perceived that the child had received RTS,S doses, even though the child health card does not have any record of RTS,S. It was not clear whether the issue is a documentation error or, if not, why the vaccine was not received.

Overall, PCGs in the non-adherent category were accepting of RTS,S, but delays in receiving dose 1 – due to initial hesitancy or had limited awareness / access to RTS,S – led to their children becoming ineligible (too old) to start the schedule.

Table 7 summarizes issues related to initial hesitancy or low demand for the vaccine were less prevalent among the PCGs partially adherent category. Instead issues of access or supply-side barriers took precedence, such as facility stock outs, health worker strikes, or having been turned away. When personal circumstances interfered with the PCGs' ability to take their children for later doses, challenges were often framed as competing household responsibilities or personal circumstance (illness, work) rather than as doubts or fears about RTS,S. In this sense, drop-out for the later doses of RTS,S appears to be similar to what has been observed for other antigens.

Table 7. Reasons given for by PCGs for their children receiving only one or two doses.

Primary Issue	Variable Explanations Given
Access to care (n = 4)	Five mothers cited access reasons for not receiving subsequent doses of the vaccine. This included issues such as "*the nurses were not there*" (C12_006), "*there are times when I come here, I find vaccines are not available*" (C12_009_R), or "*when you go there […] they send us back and promise us that they will visit us*" (C19_004).
Personal situations, barriers (n = 3)	Several caregivers had personal or household challenges that prevented them from taking their child to the under-five clinics. For two of these mothers, this was personal sickness that prevented them from being able to make the journey to the clinic: "*I have been sick and at home and as such I never had a chance to bring him back for his vaccination visits*" (C18_006). For one mother she migrated out of the household for three months for work purposes, and this kept her away from the area where the under-five clinics were held.
Information gap (n = 2)	Two mothers said they had not been informed by the health worker of subsequent doses – or the timing for subsequent doses – and thus had failed to take the child back for the additional doses: *"They did not clarify to me that I need to take him back. I was only told about the one that he got that day before I took him."* (C16_006)
Perceived as received (n = 2)	Two mothers indicated their belief that their child has received all of the intended vaccines. One of these caregivers had an improperly documented vaccine card (no malaria vaccine stickers). This may be a case where the child was indeed taken for the subsequent doses, but this is not able to be verified through the child health card.
Complacency (n = 1)	One mother indicated that she had not yet taken the child for follow-up doses, because "*I can say I have just been lazy [chuckles]"* (C17_003). She did have other secondary possible threats (prior experiences of stock outs, having heard rumors), but this was the primary reason she cited for missing the later doses of the vaccine.
Anticipated at next appointment (n = 1)	One mother indicated that she anticipates her child receiving the vaccine at the next appointment, but the infant is not yet due for the third dose.

The majority of PCGs who were unable to present a vaccination card in R2 believed their children had received all recommended RTS,S doses to date. This perception may be a genuine reflection of children who have received all three doses but are missing a vaccine card to document receipt, or it may represent cases where the child has missed doses, but the PCG is not aware of it due to the lack of a child health card.

Table 8. Reasons given by PCGs missing vaccination cards for their children missing one or more RTS,S doses.

Primary Issue	Variable Explanations Given
Perceived as received (n = 5)	Many mothers without vaccine cards indicated their belief that their child has received all of the intended vaccines. This archetype may reflect mothers who genuinely have taken their child for the subsequent doses – but it is not able to be verified through the child health card – or mothers whose children have missed the latest doses but are not aware of it due to the lack of a child health card.
Access to care (n = 1)	One mother cited access reasons for not receiving subsequent doses of the vaccine. She specifically related this to the COVID-19 pandemic, saying that they *"we were pushed back… because of corona"* (C24_041).
Personal barriers (n = 1)	One caregiver had personal or household challenges that prevented them from taking their child to the under-five clinics, noting that "*I thought it wise to just be staying at home because I wasn't psychologically well*" (C27_063).
Unknown (n = 1)	One individual was missing a vaccine card in both Round 1 and Round 2. It is not clear why they did not receive the vaccine.

While we have grouped reasons non-adherence and partial adherence by main issue, it is important to emphasize that a confluence of factors is often at play and the tables above only document the most proximal factor. For example, one mother who said that she skipped the later RTS,S dose was because the facility is too far. But she also explains that her child had diarrhea since the last vaccine, which she perceived to be a side effect of RTS,S that seemed to confirm for her early negative rumors she heard about the vaccine. Thus, while the proximate barrier appears to be one of access, more distal barriers – exposure to rumors followed by perceived AEFI – may have influenced her decision to not seek the later doses. These varieties of factors – and the cumulative effect of several barriers or threats – may amplify caregiver vulnerability to under- or non-vaccination.

Factors promoting / threatening adherence to the RTS,S schedule through dose 3

To further understand issues affecting variable adherence to the RTS,S schedule through dose 3, we utilized our analytic framework applied to R1 data to identify factors that would likely promote or threaten RTS,S adherence. *Promotive* factors and *threats* shown in Table 9 represent a broad, deductive coding scheme used on R2 data, built from the existing R1 coding scheme. Additional themes were identified through inductive coding.

Table 9: Factors promoting (Promotive) or threatening (Threats) RTS,S uptake and adherence.

PROMOTIVE	THREATS

• Expressed confidence in:
  o vaccines/RTS,S safety and effectiveness
  o provider and health system competence
  o intentions of key actors (government, industry, research community)
• Historical reference to positive impact of vaccines on the population's health
• Positive experiences with child health/vaccination services
• Positive social support to receive vaccines/RTS,S (e.g. family member reminds PCG to take child for vaccination)
	• Exposure to rumors and misinformation about vaccines/RTS,S safety and effectiveness
	• Confusion and concerns about targeted (phased) RTS,S introduction
	• Fear of too many vaccines
	• Complacency or previous delays in vaccine uptake or refusal to receive vaccines/RTS,S
	• Negative clinical encounters and distrust in providers
	• Negative social support to receive vaccines/RTS,S (e.g., personal network member urges PCG to refuse vaccination)

PROMOTIVE	THREATS
	Added themes in R2: • Barriers to accessing services at the facility (e.g. stock outs, facility closures, or health worker strikes). • Personal or household challenges (e.g. ill family member or household responsibilities).

To visualize patterns of promotive and threat factors in the whole sample, coded text was subsequently reduced to binary present/absent variables and the results used to create spectrum displays shown in Figures 4 and 5. Each segment in the displays represents one individual. Bolded lines around blocks of individuals represents community sites. Position of individuals in the side-by-side promotive/threat displays are not necessarily the same.

We caution against over-interpretation of these initial data displays as systematic verification and internal validation of codes applied has yet to be done. Additionally, the absence of color, indicating no coded text, could be due to inconsistent probing or to participant reticence. With these precautions in mind, we find the patterns discovered "good to think with" and useful for directing future analytic focus.

Promotive Factors

Figure 4 (page 17) compares promotive factors found in data from R1 to R2. A majority of the PCGs in both rounds expressed one or more factors that were conducive to the acceptance of vaccines, however, the specific nature of promotive factors has evolved between the two rounds.

In R1, promotive factors were predominantly centered on trust in vaccines generally (indicated in dark green in the spectrum displays) and in the in the health system (indicated in light green in the spectrum displays). As a newly introduced vaccine, there was limited confidence in RTS,S, with participants instead citing their broad trust in the system and vaccines as a basis for having confidence in RTS,S:

> *If the government has approved something, I will go for it. I don't sit back and question it. The government has good reasons for launching any vaccine.* (C18_002, R1)

While similarly broad trust in the system and vaccines was evident in R2 replies, a strong majority of PCGs in R2 now also indicated specific confidence in RTS,S specifically (indicated in the spectrum displays in light purple), exemplified by the quote below:

> *Every year, a lot of children get malaria and some even die from it. Therefore, the vaccine was brought as a solution to this problem. So, it can also be beneficial to us, the parents. For me, I understand that this malaria vaccine is good.* (C5_007, R2)

Specific trust in RTS,S represents a shift in the overall pattern of promotive factors from R1 to R2. Most PCGs tied their confidence in RTS,S directly to firsthand observations or experience in their child: "[she's] not getting sick as often," "malaria does not attack him," and "now the malaria episodes have reduced." This observed change was directly attributed to the introduction of the RTS,S vaccine:

The fact is the child who has received the vaccine has been protected. A child may suffer from other diseases when we go to the hospital for a test they found out that it's not malaria. Also, when the child is sick the body temperature doesn't get so high, which means vaccine is really protecting. (C22_023)

Some PCGs directly compared the health of their vaccinated children their unvaccinated older children or others in the community as confirmation of the benefits of RTS,S:

Since I got my child vaccinated with the malaria vaccine I see that she is healthy. There's a mother in this household who doesn't vaccinate her child. I can see the difference between my child and hers. (C1_002)

Increasing trust in RTS,S was also associated with PCG observations that "nothing bad happened" after the vaccine was administered. Parents felt that AEFIs were generally not a problem and placed them in the category of "not severe," "normal," and thus manageable. The lack of scary side effects bolstered trust in RTS,S specifically.

Threats and Barriers

Figure 5 (page 18) compares threats to confidence in and uptake of RTS,S in R1 and R2. While similar threats are present in both rounds, R2 findings indicate a dramatic overall decline in threatening factors compared to R1. This is evidenced in Figure 5 by the increasing amounts of white space in the spectrum display. As with promotive factors, the nature of threats in R2 has shifted compared to R1.

Rumors (indicated in salmon red in the spectrum display) and negative clinical encounters (indicated in light pink in the spectrum display) persist as threats in R2. However, while several PCGs recounted having heard rumors about RTS,S or had seen someone refuse her child to receive the vaccine, most individuals now also display resilience to these rumors and doubts, saying they are "not true," "untrustworthy," "I found out they were lies". Lived experience and firsthand observation of RTS,S delivery in their communities – e.g., "personally, I've not seen that" – since launch of the vaccine contribute to observed declines in threats from R1 to R2, illustrated well by this PCG:

When I initially came for it, there was word going around that our children will be crippled, and many people avoided it. Since the implementation began, we have not heard any problem with it, not even a crippled child or even a bad swelling after an injection. The children are just okay. (C17_006)

Instead, the PCGs tend to recount their firsthand experiences of the health benefits of RTS,S, which outweighs the rumors:

At that time I heard that this vaccine is harming other kids as they are developing some itching things. But for me, when I accepted it because I saw that it was important and that my child won't be suffering from malaria. (C24_037)

In line with this decline in the potency of rumors, rumors and negative clinical encounters are no longer cited as key reasons for missing RTS,S doses.

R2 findings also show a decline in threats linked to the new vaccine introductions. In R1, many PCGs expressed concerns about the number of injections children are receiving (indicated in light blue in the R1 spectrum display). Confusion and specific fears about the phased introduction of RTS,S were also prevalent in R1 (indicated in navy blue in the R1 spectrum display). Both threats have almost disappeared from the dialogue in R2 data collection, so much so that they did not merit visualization in the spectrum displays in R2.

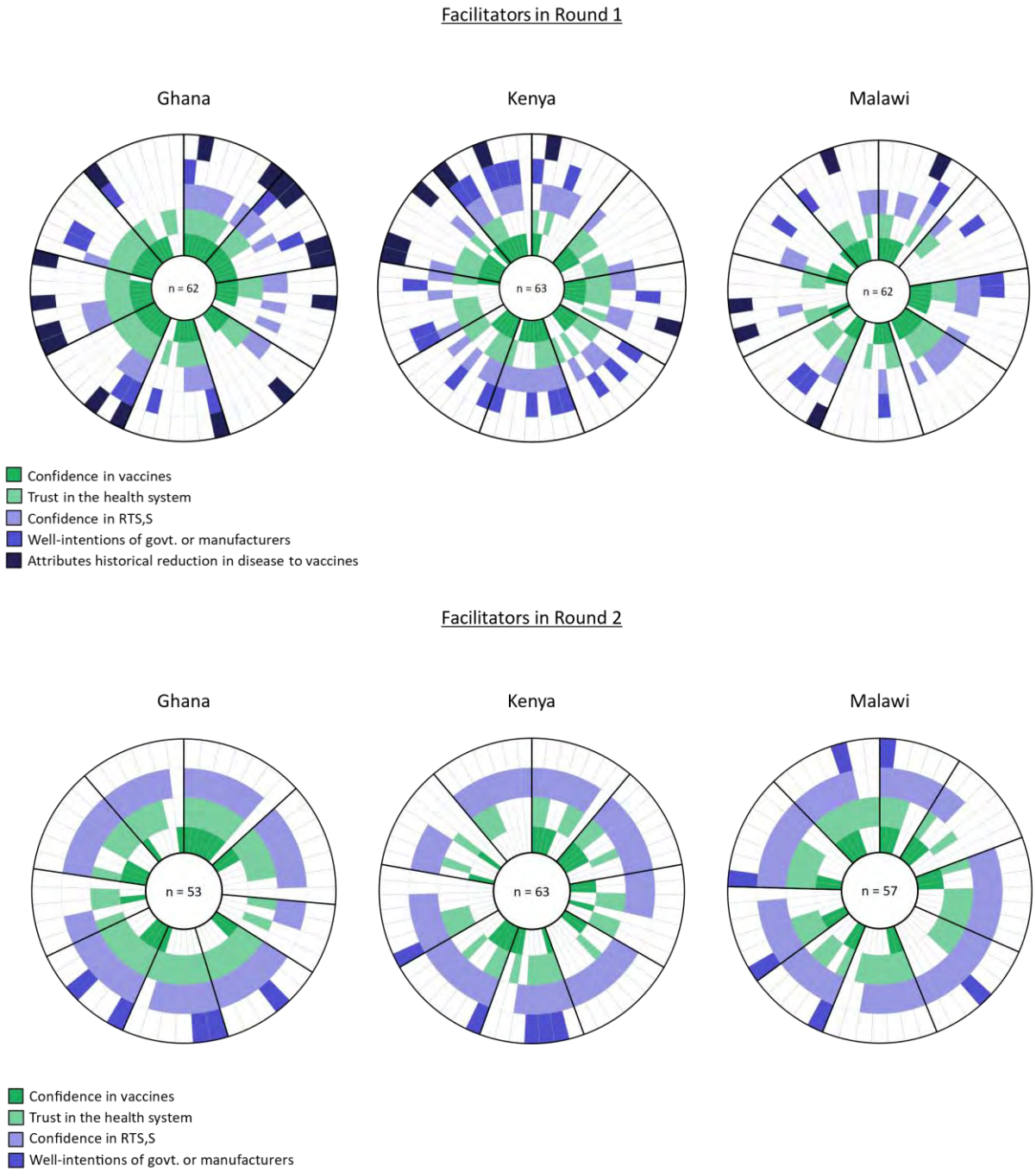
In the absence of these early threats around perception of the vaccine, access barriers have emerged as a slightly more predominant issue (indicated light blue in the R2 spectrum display). The threats that have emerged instead include health worker strikes (in Kenya), stock outs, or difficulty in accessing services (too far, too crowded, unable to access due to COVID-19 restrictions, or the health workers put preconditions to receive vaccination).

> *There are times when I come here to find vaccines aren't available. I go home and wait a while, then come back and to be told that the vaccines have still not been brought or the doctors are on strike then I would go back again.* (C12_009_R)

> *What I would like to let you know is that the way this RTS,S is timed, between six months, seven months, etc., when mothers go for it but are told that they are out of stock, it really discourages most of them. Let the ministry ensure that RTS,S is in all year round in the facilities.* (C14_001)

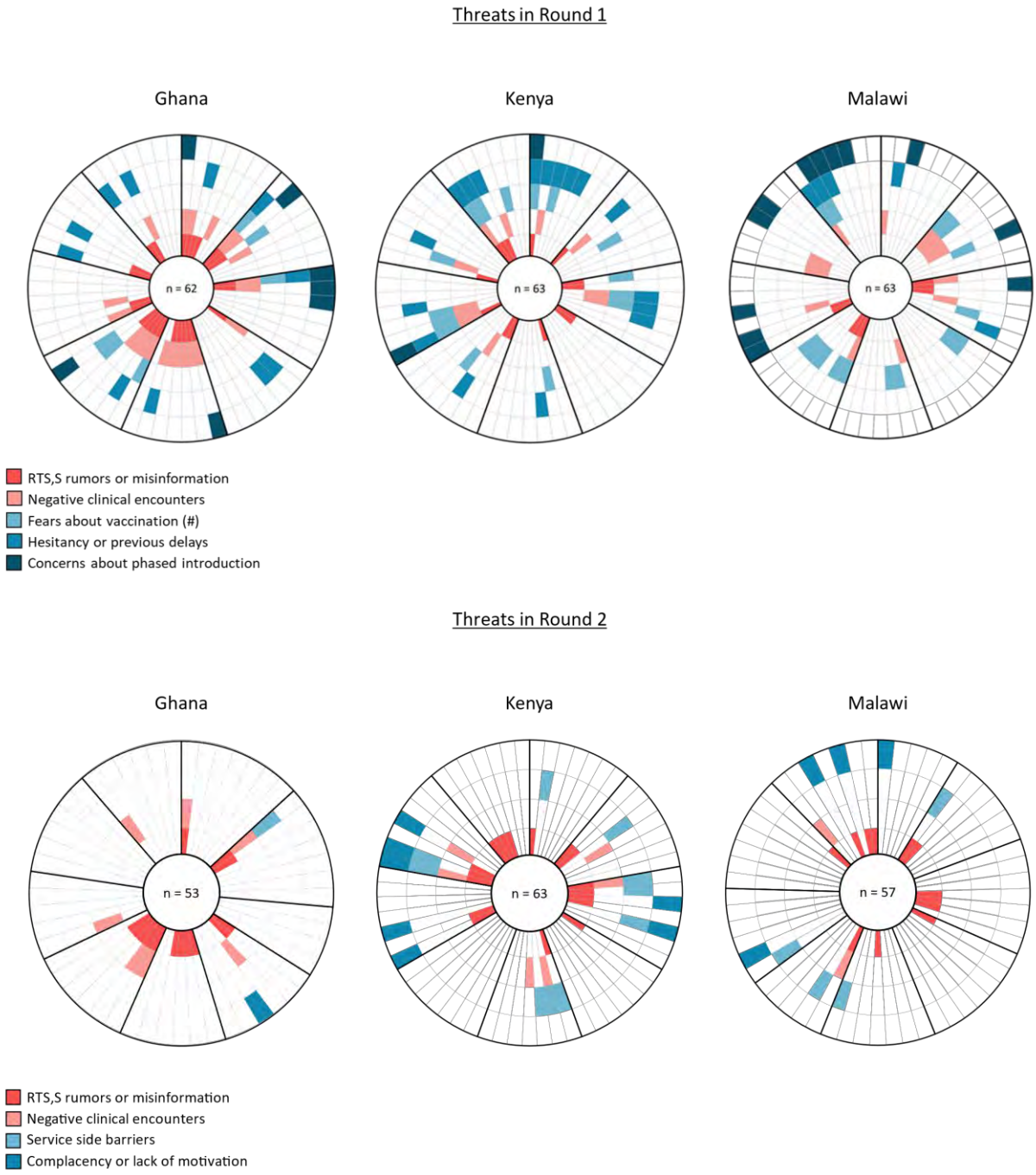
This pattern of access barriers becoming more important in R2 compared to R1 is consistent with the responses given by PCGs as to why their children have not received all recommended doses of RTS,S (see previous section).

Figure 4: Factors promoting RTS,S uptake and adherence reported in R1 compared to R2.



Note: Coded text was reduced to binary present/absent variables to visualize patterns of trust theme categories in the sample. Each color in the spectrum represents a trust category. Categories are not mutually exclusive, and individuals may have codes in zero, one, or multiple categories. Segments without any color indicate that the individual had zero trust themes coded to her. Segments with one of more colored ring(s) indicate that the individual had one or more trust themes coded to her. In short, more color indicates more trust. Different colors indicate different kinds of trust. Bolded lines are shown around blocks of individuals from the same community. Due to the very small numbers of reference to historical reduction in disease as a promotive factor for vaccines in R2, the category was omitted in the R2 spectrum. Individuals' side-by-side position in the promotive/threat displays are not necessarily the same.

Figure 5: Threats RTS,S uptake and adherence reported in R1 compared to R2.



Note: Coded text was reduced to binary present/absent variables to visualize patterns of threat categories in the sample. Each color in the spectrum represents a threat category. Categories are not mutually exclusive, and individuals may have codes in zero, one, or multiple categories. Segments without any color indicate that the individual had zero threat themes coded to her. Segments with one of more colored ring(s) indicate that the individual had one or more threat themes coded to her. In short, more color indicates more threats. Different colors indicate different kinds of threats. Bolded lines are shown around blocks of individuals from the same community. Due to the very small numbers of reference to fears about vaccines (injection and numbers) and to concerns about the phased introduction of RTS,S in R2, these categories were omitted in the R2 spectrum. Individuals' side-by-side position in the promotive/threat displays are not necessarily the same.

Malaria perceptions and behaviors in the context of RTS,S

In addition to lending further support for the key findings described above – that confusion and concerns about RTS,S are diminishing while enthusiasm is increasing – R2 data focused on malaria treatment and prevention behaviors add insight on other important questions for the MVIP evaluations, namely:

- How does the introduction of RTS,S affect other prevention behaviors? A related concern, is caregiver understanding and acceptance of partial protection of RTS,S?
- Similarly, how does the introduction of RTS,S affect treatment seeking behavior in the event of fever and other common malaria symptoms?
- More broadly, will child caregivers accept a partially protective malaria vaccine, and, if so, why, and if not, why not?

We review R2 findings focused on malaria treatment and prevention around these three questions below.

Impact of RTS,S uptake on other preventions

Of the 173 PCGs interviewed in R2, 145 (84%) reported that their RTS,S-eligible child slept under a bed net the previous night. Often accompanied by an explanation of partial protection from the malaria vaccine, most of the caregivers said that their prevention behaviors have not changed since their child started receiving RTS,S doses. Replies to the fixed-choice question, *How often does [RTS,S-eligible child] sleep under a bed net?*, are consistent with these qualitative findings (Table 10).

Table 10. How often does [RTS,S-eligible child] sleep under a bed net?

	Child Slept Under Bed Net Last Night		
	Yes	**No**	**Total**
Every time s/he is in bed	130	2	132
Most of the time s/he is in bed	3	4	7
Sometimes when s/he is in bed	12	5	17
Rarely	0	13	13
Total	**145**	**24**	**169**
Missing data	*1*	*3*	*4*

Equally small numbers of caregivers described either increasing or decreasing bed net use with the child since the introduction of RTS,S. Explanations for increasing bed net use tended to reflect more consistency in putting the net down every time the child was in bed, sometimes connected to messages emphasized by health workers. We found only eight cases where caregivers explicitly said that bed net use had declined since their child received RTS,S, two linking the decline to uptake of RTS,S.

Bed net use increased:

It has changed. At first, I could stay outside for long in the evening [but I did not] release the bed net unless I am also going to sleep. They [nurses] made me understand that I should put him in the net as soon as he is bed. (C5_001)

Bed net use decreased:

I wanted to see whether it [the vaccine] was good or not. That's why I stopped using it after 3 months. I used the coil too for sometimes and I also stopped it. After I stopped the coil and the bed net, till now, they have not had malaria. (C6_002)

Main Barriers to Bed Net Use

- Heat, suggesting net use may vary across the seasons
- Skin rashes, attributed to the insecticide and sometimes leading to washing the net prior to use
- Torn or damaged nets
- Not enough nets in the household

Findings from R2 suggest that uptake of RTS,S does not generally lead to reductions in bed net use. It is possible, in fact, that intensified messaging about malaria and malaria prevention with the introduction of RTS,S may help to maintain or increase bed net use. Data from R3 may shed more light on this possibility, but more definitive understanding of this dynamic will need to be confirmed in studies with representative samples.

Impact of RTS,S uptake on treatment seeking for malaria symptoms

Sixty-four of the PCGs reported that the RTS,S eligible child had one or more episodes of malaria since the R1 interview, Table 11).

Table 11. Bed net use and RTS,S uptake by recent malaria episode in the RTS,S-eligible child.

Reported Bed Net Use and Documented RTS,S Uptake		Malaria Episode Perceived in RTS,S-Eligible Child Since R1 Interview			
		≥1 reported (n = 64)		None (n = 108)	
Bed Net Use Last Night	Yes	52	81%	92	85%
	No	11	17%	16	15%
	Missing data	1	2%	0	0
RTS,S Doses Received	0 doses	8	13%	5	5%
	1-2 doses	10	16%	8	7%
	3 doses	45	70%	95	88%
	Missing data	1	2%	0	0

* 1 case missing data

Regardless of the number of RTS,S doses received, almost all of these 64 caregivers whose child experienced a malaria episode said they promptly sought help at a health facility or from a community health worker, 59 of whom said that malaria was diagnosed by finger prick or a lab. Over-the-counter fever medication was often also given to child initially and, less frequently, home remedies. But neither of these home-based treatment actions seemed to delay care seeking. Like R1 findings, the main triggering symptoms were fever, lethargy, child not eating, and other various symptoms.

Acceptance of partial protection in a malaria vaccine

A strong majority of caregivers expressed favorable impressions of how RTS,S is affecting child health in their own households and in the broader community. Among the 173 PCGs interviewed in R2, at least 130 perceived malaria in their household and in their community to occur less frequently (n≈117), to be less severe when it did occur (n≈26), and/or to be generally beneficial to child health (n≈13). These positive impressions were expressed with equal frequency by 45 caregivers whose children had recently experienced malaria despite having received three doses of RTS,S. All three quotes below, which exemplify caregivers' positive sentiments, are from this sub-set of 45 individuals:

Malaria is less frequent

I think the malaria vaccine has helped. I left the community and returned last Thursday but since I came, I have not seen anything like malaria. I can also say that it is good because, if it wasn't for her getting sick in XXX, she hasn't fallen sick the whole year. So, I will say that it is good for me. (C2_003)

Malaria is less severe

I would say that the attack was not severe [this time], but in the past when my twins got malaria, they would even have seizures. I have not seen this with this vaccine. Sometimes when you are at the market, you receive a call that the child is having seizures and when he is taken to the hospital, the report is that he had a high fever plus malaria. I have seen some beneficial changes with this vaccine. (C18_002)

The vaccine is beneficial to child health

It [the vaccine] is good and I can see it is helping her. This child had been sickly, but since she started receiving that vaccine, she does not have problems nowadays. Since she was vaccinated, she has only fallen sick once. (C11_007)

We coded eight instances where caregivers felt that the vaccine was not making any difference ("I don't think it's helping"; "even with the vaccine he still gets malaria") and one case where the caregiver perceived risk associated with the vaccine:

At first, I thought it [the vaccine] would protect her, but it has rather caused hardship on me. No one told me anything but if I look at the way she has been having diarrhea I thought maybe it could be from the vaccine. (C4_002; child had received fewer than 3 doses at time of interview)

Despite the prevailing perception among caregivers that RTS,S is having a positive impact on malaria in their communities and families, among the most frequently cited remaining questions about RTS,S had to do with the duration and level of protection the vaccine offers.

Experiences and information received at the last vaccination visit

Visit triggers, barriers, and overall satisfaction

> *When they told us when to take our kids for malaria vaccination, I kept the dates in my heart.* (C24_037)

A large majority of the caregivers described one or more ways they remembered vaccination visit dates. The most common way they remembered, cited by more than half of the participants, was to consult the child's health card. Whether the caregiver tried to "keep the date in my head" or to "write it down and put it in a special place," checking the child health book was an important reminder to not miss the vaccination visit date. Reminders from health staff, particularly on weighing day, but also community health worker announcements and outreach, were also important and frequently cited reminders: "*We are told by community health workers. On our own we can't remember*." (C26_056) Reminders from personal network members – husbands, neighbors, other

mothers – were another prominent trigger to take their child for vaccination, while radio or TV announcements, cell phone alerts, and prompts from and other health visits were other, but less frequently, cited reminders.

A wide variety of challenges to remember or make the vaccination visit were described by almost 50 caregivers. Various personal circumstances (e.g., cannot read, lack of time, extenuating circumstances, travel/migration, illness, etc.) were the most prominent reasons cited, followed by anticipated or known vaccine stockouts, health worker strikes, or off-putting health worker attitudes (n≈20), and various other issues (distance to facility, lack of documentation/lost card, information gap/confusion about dates, and conditions to receive care).

Interviewers did not consistently ask PCGs to describe their overall satisfaction with the last visit. Paralleling overall positive views about the health system, generally, when asked about the last vaccination visit, PCG responses were most often positive (e.g., “all that they do I like”, n=79) or neutral (e.g., “there were no problems”, n=33) in nature. Very few replies reflected a negative experience, and these tended to be based on specific complaints (painful for the child, stockout, not enough information was given, etc.)

Information received and perceived AEFIs

Close to two-thirds of caregivers recalled receiving one or more messages about RTS,S during their last vaccination visit, while the others replied that they “forgot what was said,” that they could not hear the health talk “because we were many,” “I got there late,” or that the providers “didn’t tell us anything.”

Among the caregivers who could recall hearing an RTS,S message at the last visit, reminders to bring the child for the fourth dose were cited most frequently (n=51). In giving fourth dose messages, providers often emphasized greater protection from receiving all four doses and/or reminded the caregivers to bring the child at 22 months or around two years of age:

> *The providers told me that even though she had received 3 doses, I should not stop there because for her to get full protection she must receive all the doses.* (C10_003)

Given that messaging from health talks was inconsistently heard or recalled, mothers at times recounted one-on-one encounters with the provider which, however brief, served as important vehicles for messaging:

> *I woke up very early that day and walked all the way to facility X. Many clients were already there, so we had to queue. The provider collected all our mother-child books and started calling our names in the order in which we had come in. She called the babies’ names one at a time, and as she gave the malaria vaccine, she urged us to complete all the four doses. She jabbed my son and told me that it was the third one and that he still had one more to go when he turns two.* (C14_002)

These encounters suggest that RTS,S messaging may be strengthened in the course of service provision through simple personalization or one-on-one exchanges with the provider. While the mother quoted above appears to be, on her own, motivated to accept the vaccine,

that the reminder was personalized to her child and delivered in a one-on-one exchange with the provider may have helped make the mother aware of key information about the timing of dose 4, instead of being potentially lost in a difficult-to-hear group education session.

Caregivers frequently recalled advice about managing mild adverse events following immunization (AEFIs) and information about when to seek professional help for an AEFI. Distinct from messages about AEFIs, eight caregivers alluded to providers emphasizing that the vaccine was safe:

> *Every day that we go for CWC, they tell us that we should not be afraid and that all those rumors that it will sterilize or paralyze the child are not true.* (C2_001)

Six of these eight individuals were from Ghana, likely reflecting the MOH's aggressive response to early rumors there about RTS,S.

The need to continue bed net use was infrequently recalled; messages about the need to seek care promptly in the event of fever was not cited by any of the participants. Combined with findings on persistent questions, the rare recall of malaria prevention and treatment messages from the last vaccination visit underscores the programmatic challenge to communicate effectively about partial protection.

Plans for receiving dose four

A strong majority of caregivers indicated that they intend on bringing their child to receive the fourth RTS,S dose. While some individuals replied simply that they will do as instructed and go when it is time, most of the caregivers expressed a rather strong commitment to ensuring their children received the last dose:

> *I have put it in mind that, when she turns two years, no matter what, she will receive the malaria vaccine. So, I'm planning toward it. No matter where am or what I'm doing, I will stop and take her to receive the vaccine when she's two.* (C1_001)

> *If I had second thoughts about it, I wouldn't have taken her to the clinic today.* (C16_009_R)

> *I am trying to keep track of the date to bring him back at twenty-four months. I won't get tired. It's just a regular clinic visit that you must keep bringing him to until the last clinic appointment. I'll make sure he gets all the vaccine doses.* (C17_001)

> *She already started receiving the vaccine, so I can't stop on the way. I need my child to complete it in December to make it better.* (C21_019)

Relatively few caregivers indicated that they had no clear plans to take their children for the last dose or were unaware of dose four details and timing.

Persistent questions and concerns

At three points in the R2 interview, participants were invited to share any questions, concerns, or thoughts they have about RTS,S. Specifically we asked:

- What questions did you have during the last vaccination visit?
- What concerns or worries to you have about the malaria vaccine?
- Do you have any final thoughts or questions about RTS,S or other topics we talked about today?

Additionally, PCGs sometimes volunteered their questions or concerns while responding to interviewer probes. This section summarizes findings on data from these open questions and probes. All told, we coded 122 questions/concerns cited by 98 caregivers. Questions/concerns were inductively coded and grouped into the following four broad categories: Protection, Eligibility/Schedule, AEFIs, and Other.

As described in Table 12, the most frequent questions/concerns related to the level, duration, and type of protection offered by RTS,S, often revealing persistent information needs about partial protection. Although understanding of these issues was much stronger in R2 compared to R1, many of the caregivers continued to have questions about the timing and number of doses their child should receive as well as about age-based eligibility. As relates to AEFI and safety concerns, far fewer caregivers expressed concerns about adverse events generally and injection-related AEFIs specifically. Most AEFI concerns focused on the seeing their child suffer from and managing "normal" AEFI, with only a few individuals having questions about the vaccine's safety.

Table 12. Persistent Questions and Concerns.

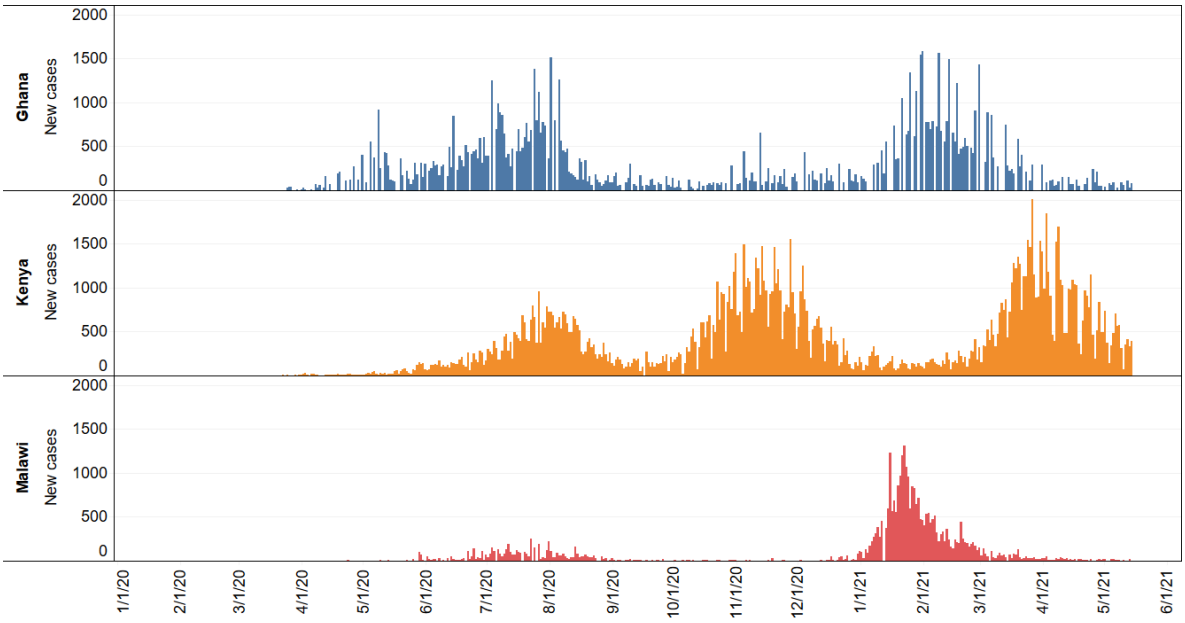
Category	Description and Examples
Protection (n = 54)	Questions about type, level, and duration of RTS,S protection, variably focused on: **Partial protection:** *I just wanted to know why the child gets sick despite being vaccinated.* (C19_006) **Duration of protection:** *I would only like to ask about how long this vaccine stays in the child's system because that is what I don't know.* (C11_005) **Protection after the 4th dose:** *I want to know if the baby will experience malaria after two years since the last dose would be taken at two years.* (C6_007) **Need for the 4th dose:** *But I wish to know… what would happen if the child does not receive the last dose?* (C9_007) **Severity of illness after receiving the vaccine:** *Should assume malaria when the child has a fever and . . . should take her to the hospital or just ignore.* (C16_002) **Protection against other diseases:** *I asked if it will protect my child from all sickness.* (C4_007) **General questions about reason RTS,S was introduced:** *Why did the government decide that children must get the malaria vaccine?* (C16_008_R)
Eligibility / Schedule (n = 33)	Issues focused on the timing and number of doses, as well as age of eligibility to receive RTS,S. Recurrent themes included: **Specific questions about the number of doses or the schedule:** *What I want to know is the number of times my child is supposed to take the vaccine*. (C3_007) *I asked her the reason for taking the third vaccine*. (C8_006) **What happens after dose 4:** *When she gets to 2 years, she wouldn't be injected again till she grows, or will she receive additional doses at a certain age?* (C1_007) **Eligibility age:**

Category	Description and Examples
	Why do you guys just dwell on the young children? Why can't those ones who are like five years or so be given a vaccine too? (C14_002) **Other issues:** *[If she misses a 6-month dose], can she take it maybe one month later?* (C1_001) *Why is the schedule so long, What happened to lengthen the months and days like that?* (C25_043)
AEFI and Safety (n = 19)	The majority of questions and concerns about adverse events related to mild or normal AEFIs and only a few reflecting greater concerns about safety and the rumors they had heard. Issues raised were included: **General questions about AEFIs:** *What I want to know is that, when my sister's child received the vaccine she had an adverse effect but when my child received hers nothing happened to her so I wanted to know.* (C8_002) *I would like to know why the baby develops fever after receiving this vaccine.* (C14_006) **Worries about managing normal AEFIs:** *What worries me is only fever whenever I take her, then I must deal with fever.* (C10_003). **Questions and lingering concerns stemming from rumors:** *What I want to ask is about those who are saying the malaria vaccine is not good. Is it true that that it is not good?* (C2_003) *Because of the rumors, sometimes I worry and ask myself, 'He is young and is taking this vaccine. Do I burden him if the rumors turn out to be true and as a result he ends up infertile?'. Then again, I tell myself that if the vaccine was not good, they wouldn't have injected him with it.* (C5_001)
Category	**Description and Examples**
Other issues (n = 15)	Various other issues include questions and concerns about: **Phased introduction and, closely related, how the vaccine came about:** *I would like to know where that vaccine came from and how it started because other children aren't getting it. Why can't these others [with same-age children] told that they were not eligible?* (C13_003) *I just ask myself that how did this vaccine came about?* (C27_063) *Who has brought it?* (C22_022) **Service access:** *Because most people are receiving it but, in this area, it is not yet there.* (C11_005) *I wanted to ask what happens when something [adverse event] happens at night and we come to knock the nurse's door, will they be willing to help us?* (C8_002)

COVID-19 Context

Ghana, Kenya, and Malawi had all recorded their first COVID-19 cases by early April 2020, with subsequent surges of new cases over the following year (see Figure 6). Governments in all three countries reacted swiftly with containment measures placing restrictions on public gatherings as cases emerged. Ghana and Kenya also introduced restrictions on public transit. Recommendations to stay at home were announced in all three countries several weeks after the first cases, though Kenya's were the most stringent of the three.[6]

Figure 6. Number of new COVID-19 cases, by date (month/day/year), in Ghana, Kenya, and Malawi[7].



Health facilities in all three countries were directed to remain open to continue providing essential health services, including immunization. Service delivery was adapted to mitigate spread of COVID-19. To understand the potential impact of COVID-19 on use of child health services, including adherence to RTS,S doses, in R2 interviews PCGs were asked about their experience of vaccination services during the COVID-19 pandemic, and whether they had noted any changes at their health facility.

While a few PCGs reported delays or interruptions to vaccination visits, by and large the caregivers reported that vaccination was ongoing and that they continued to access services as before. The main changes noted by the PCGs were:

a. Implementation of physical distancing and other risk reduction procedures, such as masks.
b. Attending the facility in smaller groups.
c. Increased wait times for services.
d. Increased concerns in the community about going to the facility due to fear of COVID-19.

[6] https://covidtracker.bsg.ox.ac.uk/

[7] Data from the COVID-19 Data Repository by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University. Accessed May 15, 2021 from https://github.com/CSSEGISandData/COVID-19.

e. Suspension of health education talks or weighing (rarely).

Implementation of physical distancing and risk reduction procedures

The most frequently described effect of COVID-19 on vaccination services was the implementation of physical distancing and other risk reduction measures (hand washing, mask wearing, etc.) at the health facility. Some reported that if you did not come equipped with a mask, you would be turned away from the facility:

> *Anyone without a mask is not allowed to receive treatment. All of us women put them on when going there as we were given enough of them.* (C24_036)

Attending the facility in smaller groups

Several caregivers noted that facilities tried to limit crowding by having fewer clients attend child health clinics at the same time. Individuals described being able to attend clinic on a wider number of days, being given appointments for when to attend, or being broken up into smaller groups. Using these measures, facilities staggered the patient flow:

> *Before we used to sit and wait for others to join us before the welfare service starts and we were many. But now it is not like that. They provide services in batches. Even when you get there, there will be only two or three other mothers.* (C5_003)

Some PCGs noted that this has removed the collegial atmosphere where mothers were able to interact and socialize with one another at the clinic.

Increased concerns in the community about going to the facility due to fear of COVID-19

A small number of PCGs also noted that there was increased fear in the community about going to health facilities, particularly hospitals, due to the presence of COVID-19. Concerns ranged from exposing their child to sickness, being perceived as having COVID-19, or being caught up in containment policies (such as curfews). Caregivers who mentioned concerns about COVID-19 did not generally say that these fears had dissuaded them, instead expressing a preference for more localized care:

> *Yes, I was concerned about that. I knew that if I take her to the facility then there would be mingling with other people who may have already contracted the disease (COVID-19) which could make my baby sick too. I therefore preferred taking her to the CHV.* (C14_007)

Increased wait times for services

An equally small number of PCGs also noted that wait times at the clinic had increased, due to the adaptations in service delivery (such as physical distancing and staggering of clients). As a result, they described vaccination taking significantly more time than it had prior to COVID-19:

> *I remember it took me over 4 hours during my last visit. I was very annoyed and frustrated. I hadn't spent 1 hour and 30minutes at vaccination before [COVID], so it was very frustrating experiencing that.* (C1_006)

Suspension of services

Finally, a small number of mothers noted that clinics had initially reduced certain services due to the constraints of COVID-19. Some mothers reported hearing that they should not

attend the child health clinics or weighing sessions unless they were due for an injection (vaccination):

> *We're informed by the providers that if we have a scheduled vaccine, we can come, but other than that we should stay at home because there will be no weighing of the children.* (C6_007)

A small number of mothers also noted that health education sessions had also decreased at the outset:

> *When COVID started they stopped giving us health talks, like what they did every morning when we go for weighing. Now they have started giving health talk again.* (C4_002)

There were elements of community clustering observed in the responses around service suspension, suggesting that suspension of certain services or health education talks was discretionarily done only in certain facilities. Most participants also noted that services had since resumed as normal, suggesting that disruptions to services, if any, were temporary.

CONCLUDING REMARKS

As in R1, this report presents preliminary PCG findings, which have yet to be triangulated with other HUS, MVIP, or program data. Findings reported here are likely to change with deeper analysis and as new data from the final round are considered. Lastly, cross-country findings on PCG data require country-specific contextualization to better call out and understand consistencies and variations across the three countries, some of which is provided in country-specific reports as part of the packet of HUS R2 reports.

With these limitations in mind, there are a few emergent patterns worthy of highlighting. Despite some initial challenges in the introduction of RTS,S/AS01, it seems that many of the "growing pains" have been resolved. Most notably, acceptance of RTS,S is generally high while rumors and concerns about the vaccine have markedly declined. The PCGs in R2 display more positive sentiments about RTS,S, perceiving firsthand benefits of the vaccine for their children while also observing an absence of negative effects or unusual AEFIs. In this sense, uptake of RTS,S seems to be normalizing as PCGs become used to the vaccine being part of their children's vaccination schedule.

Additionally, in our qualitative sample RTS,S uptake did not interfere with malaria treatment seeking or prevention behaviors. Regardless of the number of RTS,S doses received, caregivers promptly sought professional help in instances of fever or suspected malaria in the child, several caregivers perceiving the episode to be less severe due to child's RTS,S vaccination status. Similarly, bed net use in our sample was neither negatively nor positively affected by RTS,S uptake. Although specific mention of bed net use messages received during the most recent vaccination visit was low, overall the caregivers understood and accepted the need for the child to continue sleeping under a net along with RTS,S vaccination. These findings suggest that malaria education was reinforced at additional vaccination visits, this has the potential to increase proper bed net use and prompt care-seeking. While our data do not shed light on the possible effect of RTS,S uptake on other vaccine uptake, they do indicate that child caregivers prioritize child health visits that include vaccination.

While RTS,S is now widely perceived as safe and beneficial to children, there are still barriers to access and unresolved questions for some individuals in our sample. Stockouts and health worker strikes hindered the ability of some participants to receive the vaccine, and many others still have questions about the duration and nature of protection offered by RTS,S. Data from the final round will allow us to investigate if and how these issues influence receipt of the fourth dose of RTS,S and what operational challenges still require resolution.

Notably, PCG findings through R2 shed light on unique programmatic challenges created by the sub-national ("phased") introduction of RTS,S, which to date has not been typical for new vaccines that target widespread diseases such as malaria. Although, from our purposive PCG sample, it is impossible to characterize the degree of impact on RTS,S uptake, our findings suggest that the sub-national introductions likely confounded initial acceptance of RTS,S and receipt of subsequent doses. An important early confounder in Ghana were

social media posts portraying RTS,S introduction as unethical research. In Malawi, a “silent introduction” of RTS,S was used to avoid creating demand that could not be met in non-MVIP areas. This silent introduction strategy led to substantial confusion among PCGs early on, with many conceptualizing RTS,S introduction as research to “know if the vaccine works,” possibly conflating the introduction with an ongoing RTS,S clinical trial in the country. While RTS,S introduction in Kenya was neither ‘silent’ nor affected by early rumors, several PCGs from Kenya expressed questions and concerns similar in nature. In all three countries, a small but important number of PCGs questioned why a malaria vaccine would be introduced sub-nationally when it could benefit all children.

The confusion and sometimes suspicion linked to the phased introduction of RTS,S may have resulted in lower uptake results than would otherwise be the case. While far less prevalent an issue in R2 data compared to R1, as the findings reviewed above show, it remains a source of confusion for a few PCGs and, in at least one case, may have contributed to dose 1 uptake delays resulting in the child becoming ineligible once the PCG was ready to adopt the vaccine. To ascertain if and the extent to which the sub-national introduction of RTS,S accounts for RTS,S refusals or delays, it may be useful to include in MVIP end-line surveys in representative samples, if feasible. The RTS,S phased introduction experience and findings from the PCG cohort also have relevance beyond MVIP. As WHO considers a recommendation on the broader use of RTS,S, including potentially sub-national introductions in some countries, insights from our PCG data may help vaccination programs to anticipate and preempt potential negative effects from questions and concerns people may have about why a vaccine is being provided in select communities or sub-populations.

In all three countries, the R2 findings from PCGs underscore substantial trust and confidence in child health programs generally and vaccines specifically. At the same time, the data reveal issues and events that may undermine this trust, namely: disinformation (e.g., early rumors in Ghana), inadequate information (e.g., the silent launch in Malawi), and service access barriers (e.g., health worker strikes and stockouts in Kenya). There is much to be learned from each of these situations and how they were identified, monitored, and dealt with by EPI programs.

The final round of data collection in PCGs will cover the main topics addressed in R1 and R2 but will focus on uptake of dose 4.

ANNEX 1: RTS,S SCHEDULES AND ELIGIBILITY GUIDANCE BY COUNTRY

GHANA

Dose schedule: 6 months, 7 months, 9 months, and 24 months

Health worker guidance:

- Give dose 1 to any child who is 6 months or older, the first dose can be given through 11 months of age.
- Give the first 3 doses of malaria vaccine with a minimum of 1 month between the doses.
- Give the 4th dose of malaria vaccine as close as possible to the child's 2nd birthday. The fourth dose can be given up to 3 years of age.

KENYA

Dose schedule: 6 months, 7 months, 9 months, and 24 months

Health worker guidance:

- Give Dose 1 as soon as possible after a child turns 6 months. All eligible children can receive the first dose from 6 months through 11 months of age and before they celebrate their first birthday.
- Although the 3rd dose can be given 4 weeks after the 2nd dose, the MoH recommends giving the third dose with the measles-rubella vaccine at 9 months of age to reduce the number of vaccination visits a child requires.
- Give the 4th dose at 24 months (2nd birthday). The 4th dose can be given up to 36 months of age (3rd birthday).
- if child is late, maintain 4 weeks between doses 2 and 3.

MALAWI

Dose schedule: 5 month, 6 months, 7 months, and 22 months

Health worker guidance:

- Children ages 5 months through 12 months are eligible for the first dose of the malaria vaccine.
- A minimum of 4 weeks should be maintained between the subsequent doses.
- Give the 4th dose of malaria vaccine from 22 months or soon after. The fourth dose can be given up to 3 years of age.

ANNEX 2: PCG RECRUITMENT SCRIPT, R1-R3 (EXAMPLE FROM GHANA)

Hello, my name is _____. I am from the University of Health and Allied Sciences.

We are doing research to learn about how people in your community view the new malaria vaccine, called [RTS,S].

You have been selected to participate in this study because you have a young child who can get vaccinations.

We would like you to take part in three interviews. The first interview will be today or another day that is convenient to you. A second interview will be after 6 months, and the third one, in about 18 months from today. Each interview will last for about one hour.

During the interview, we will ask you questions about malaria in your household and how you try to prevent it. We will also ask you about your experience taking your children for health care. We will ask you about your use of vaccination services and about what you think of the services. We will also ask you to tell us what you have learned about the RTS,S vaccine and if your child has received the vaccine.

No research activity will be conducted until you have had an opportunity to understand what the study is about, ask any questions you may have, and agree to the conditions of participating in the study.

Let me know if you would like me to tell you more about the study.