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Factors associated with vaccine default in Southern Ghana based on data from the RTSS malaria vaccine trial in Cape Coast

Vincent Bio Bediako[1]✉, Josephine Akua Ackah[2], Theophilus Junior Yankey[3], Joshua Okyere[4,5], Emmanuella Acheampong[6], Bernard Afriyie Owusu[6], Wonder Agbemavi[6,7], Adanna Uloaku Nwameme[8], Edward Mberu Kamau[9] & Emmanuel Asampong[8]

Malaria has been a severe global and public health concern for the last couple of decades. Ghana, like many other countries in sub–Saharan Africa, is most affected by the disease, with children facing dire consequences. The recent introduction of the RTS, S malaria vaccine holds great potential in reducing malaria fatalities in children. However, RTS, S implementation have inherent challenges that raise the stakes of vaccine defaults in piloted areas in Ghana. In this study, we examine the predictors of RTS, S vaccine defaults using a cross-sectional research design that covers a sample of 765 caregivers in Southern Ghana. Classification models (Binary logistic regression and Random Forest) were performed to identify critical socio-demographic, health and RTS, S related predictors. The findings show that more than a third (38.43%) of children defaulted at least one dose of the malaria vaccine. Key predictors of defaults included sub-metro of residence, cost of traveling to health facilities, experience of adverse events, knowledge about the vaccine doses, caregiver's employment status, and religion. Our findings emphasize the need for targeted interventions to reduce defaults, mainly focusing on caregiver education on vaccines, reducing financial barriers to healthcare access, and addressing concerns about adverse events.

Keywords RTS, S vaccine, Malaria, Vaccine default, Public health

Malaria is a significant public health challenge, especially in poor-resourced areas and has dire consequences for individuals, especially children and pregnant women, in endemic countries. In 2021, of the 619,000 malaria case fatalities that occurred globally, 77% involved children aged below five years[1]. In Ghana, malaria is an endemic disease and puts the entire population at risk[2]. It remains a leading cause of morbidity and mortality in children, accounting for more than a quarter of all visits to Ghanaian hospitals and more than half of all outpatient visits in the country[3,4]. Consequently, malaria remains a significant public health concern despite the availability of effective treatments and prevention strategies[5].

Several malaria control initiatives have been implemented in sub-Saharan Africa (SSA). In Ghana, interventions such as targeted indoor residual spraying (IRS), long-lasting treated Nets (LLINs), intermittent preventive treatment for pregnant women (IPTp), malaria monitoring, and malaria chemotherapy have been explored[6]. Vaccines are among the most effective and cost-effective treatments for reducing childhood mortality across low- and middle-income countries, including those caused by malaria[7]. The RTS, S/AS01 (Mosquirix) vaccine, primarily targeting children in SSA, was endorsed by the World Health Organisation (WHO) in 2021 after Phase III clinical trials demonstrated its efficacy in reducing malaria in children[8]. This vaccine has been a

[1]The Graduate Group in Demography, University of Pennsylvania, Philadelphia, USA. [2]Department of Population Health, London School of Hygiene and Tropical Medicine, London, UK. [3]Department of Health Sciences and Social Work, Western Illinois University, Macomb, IL, United States of America. [4]Department of Nursing, College of Health Sciences, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. [5] School of Human and Health Sciences, University of Huddersfield, Queensgate, Huddersfield, England, UK. [6]Department of Population and Health, University of Cape Coast, Cape Coast, Ghana. [7]School of Demography, Australian National University, Canberra, Australia. [8]School of Public Health, University of Ghana, Accra, Ghana. [9]The Special Programme for Research and Training in Tropical Diseases (TDR), World Health Organisation, Geneva, Switzerland. ✉email: vbediako@sas.upenn.edu

significant milestone in the fight against malaria, with trials beginning in 2009[9]. To ensure the efficacy and safety of RTS, S malaria vaccines, several clinical trials have been conducted by the WHO and other agencies[10–12].

The Malaria Vaccine Implementation Programme (MVIP) in Ghana was first introduced through the Ministry of Health and the Ghana Health Service in some districts in the Brong Ahafo Region (now the Bono, Bono East and Ahafo Regions), Central, Volta (now Oti and Volta) and Upper East Regions[13]. The MVIP recommends administering four doses of the RTS, S/AS01E vaccine to children between the ages of 6 and 24 months old[14]. To successfully ensure the enrolment and uptake of the malaria vaccine, the Ministry of Health and Ghana Health Service linked the implementation of the RTS, S vaccine to the Expanded Programme on Immunisation (EPI), which has been enacted since 1976. When it comes to the EPI, Ghana has a solid record[15], but the country faces significant difficulties with continuity. Especially after the first year, the risk of default increases. According to Mekuria, Hailu, Bedimo and Tefera[16], vaccination default is a situation whereby a child skips a minimum of one dose from a recommended vaccination schedule. A high default rate could jeopardise the expansion of the MVIP and to create efficient implementation strategies, it is crucial to comprehend the dynamics and causes of such defaults.

While achieving high vaccine coverage is pivotal for disease prevention and control, such as with malaria, understanding the determinants of vaccine coverage is essential for crafting effective public health strategies. Previous research[17–21] have highlighted factors like education, occupation, parental perceptions, and vaccine-related febrile reactions as pivotal in influencing the uptake of the RTS, S vaccine. Similarly, Yeboah, Owusu-Marfo, and Agyeman[22] underscored the importance of health education and trust in vaccine efficacy. However, a gap remains in the literature regarding the predictive power of different classification models for vaccine defaulting. Our study aims to fill this void by employing and evaluating three classification models—binary logistic regression, decision tree, and random forest—to ascertain which most accurately predicts vaccine defaulting and its influencing factors. This methodological comparison, focused squarely on the prediction of vaccine defaulting, aims to build upon the foundational work of previous studies by offering a novel analytical perspective on the factors affecting RTS, S vaccine uptake. By doing so, we not only address the limitations identified in prior research but also expand the discussion to include an evaluation of predictive models, thus enriching the understanding of vaccine coverage dynamics.

The analytical approach adopted by this study not only addresses urgent issues in a timely manner but also helps to pinpoint more critical factors in comparison to others. Furthermore, considering that the RTS, S vaccine is integrated within the EPI schedule, we postulate that the factors that lead to defaulting for the RTS, S vaccine may parallel those of other multiple-dose vaccines within the same schedule, thus enhancing the applicability of our findings across various immunisation programs.

Methods

Study area

The study was conducted in the Cape Coast Metropolis, Central Region, Southern Ghana (Fig. 1). The Cape Coast Metropolis is one of the 22 administrative districts in the Central Region of Ghana. It lies within latitudes 50.07' to 50.20' north of the Equator and between longitudes $1^0$11' to 1^0.41' west of the Greenwich Meridian. It covers a total land area of approximately 122 sq. km. (12,200 ha.) and is majorly urban. The primary rainy season lasts between May and July when malaria incidence is at its highest. Within this period, the relative humidity ranges between 85 and 99%[23]. In the Central region, an average estimate of 38.2% of clinically confirmed falciparum malaria has been reported, with children having higher odds of having malaria[24]. Among school children in Cape Coast, the prevalence of malaria (asymptomatic and clinical) ranged between 24 and 35%[25]. Thus, on average, about one-third of children in Cape Coast could be having malaria.

Among the 33 districts implementing the RTS, S vaccine, the Cape Coast Metro had the highest fallback of the fourth dose of the malaria vaccine. Out of the 38 336 children who were given RTS, S 3 in Cape Coast Metro, only 22 423 were administered the RTS, S 4[23]. This makes the Cape Coast Metropolis ideal for exploring vaccine default. The metropolis has five sub-metros, as shown in Table 1. Each of the sub-metros has health facilities (vaccination outreach points) to serve the health needs of surrounding communities.

Study sample

The target population were primary caregivers of children aged between 24 and 59 months who had initiated the Malaria RTS, S vaccination schedule. At the commencement of the study's fieldwork, the fourth dose of the RTS, S was administered at 24 months. As a result, setting a lower age limit of 24 months was to ensure that our study population comprised primary caregivers of children who have been exposed to all four RTS, S dose timelines. An upper age limit of 59 months was set to emphasise our research interest in children under five, among whom the consequence of malaria is severe. The 2021 Population and Housing Census estimates that about 8,997 children aged 2–4 years live in the Cape Coast metropolis[26]. Table 1 shows the distribution of these children by sub-metro.

The study's sample size was estimated using Yamane's formula, which is calculated as follows:

$$n = \frac{N}{1 + N\,(e)^2}$$

Where n = sample size, N is the population size, and e is the level of precision. The precision level was set at 4% to capture the inherent representativeness and generalisation of the study. The study opted for a 4% precision level instead of the traditional 5% to enhance the accuracy of the study findings by reducing the margin of error, thereby providing more reliable and precise results. This adjustment is scientifically justified when the research aims for higher precision in estimates, especially in studies where outcomes have significant implications or

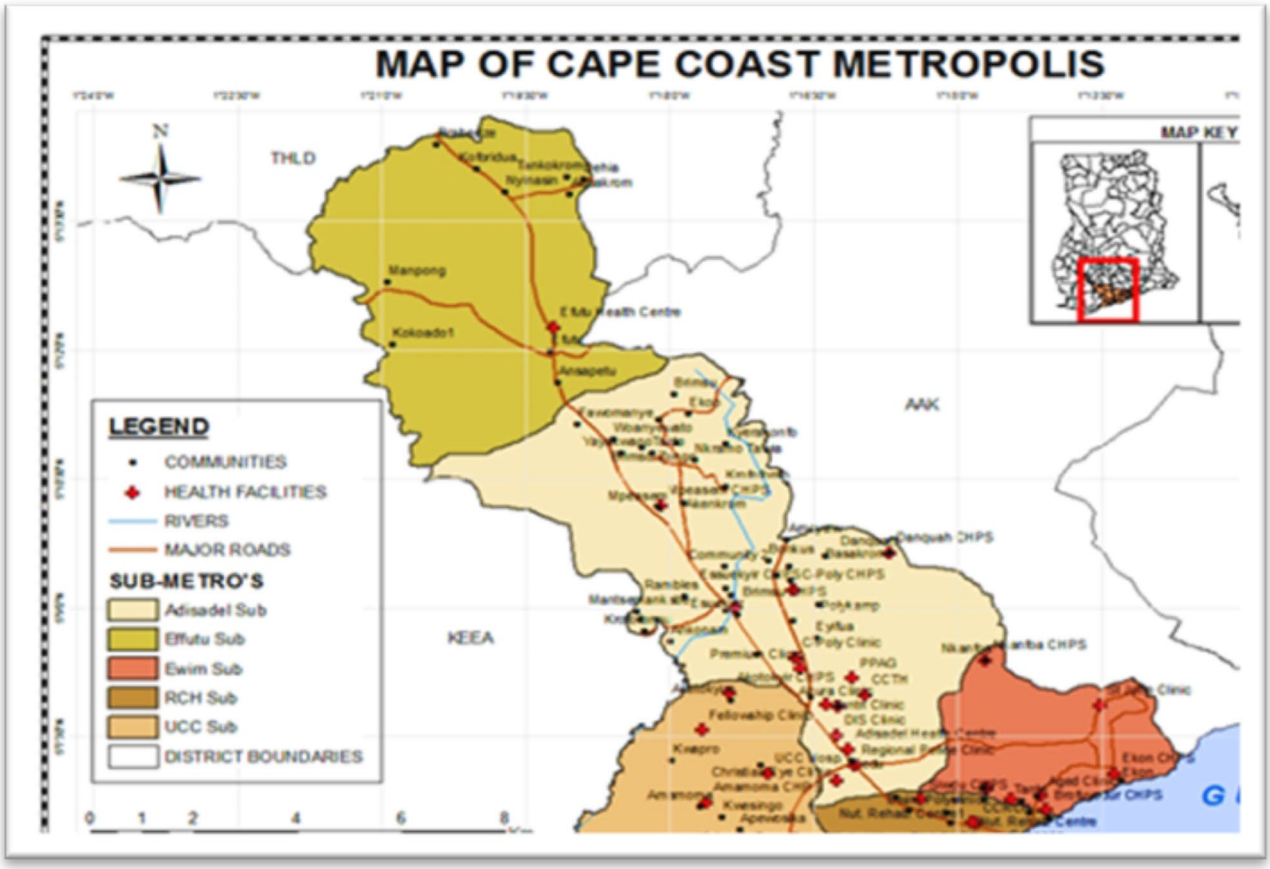

Fig. 1. A map of Cape Coast metropolis. Source: Cape Coast Metropolis Health Directorate (2022), Cape Coast.

Sub metro	Estimated population	Proportion
Cape Coast Central (CCC)	2069	23%
Adisadel	2518	28%
Ewim	1979	22%
University of Cape Coast (UCC)	1619	18%
Efutu	812	9%
Total	8997	100%

Table 1. Study population across the five sub-metros in the Cape Coast metropolis. Source: Ghana Statistical Service (2021).

when the population variance is expected to be low. Adam[27] in "Sample Size Determination in Survey Research" proposed an adjustment to the margin of error in Yamane's formula to make it applicable for determining optimum sample size for both continuous and categorical variables at all levels of confidence, implying that a lower precision level can enhance the accuracy and reliability of survey research outcomes. Also, Ciccarelli, Semeraro, Leinoudi, Trani, Ciampana, and Ciccarelli[28] in "Sample size planning and the statistical significance of official controls by sampling", discuss how sample size determination is crucial in setting up accepted levels of non-compliance and error, highlighting the importance of precision in statistical sampling for food safety. The study's sample based on this formula is provided below.

$$n = \frac{8997}{1 + 8997(0.04)^2}$$

$$n = 584.40$$

We accounted for a non-response of 10%. Non-response rates could occur as a result of refusals, unreturned questionnaires, and incomplete responses[29].

$$n = 584.40 + (0.1*584.40)$$

$$n = 584.40 + 58.44$$

$$n = 642.84$$

A proposed sample size of 643 primary caregivers from the Cape Coast Metropolis was defined. However, within this period, based on population size, a stratified sampling method was used to select participants from the five sub-metros. Because each sub-metropolis had unique characteristics, stratified sampling was the best way to ensure that the entire metro area was represented and to allow for comparison. The study estimated the proportionate sample size for each sub-metro using the formula below.

$$A = \frac{y}{z}$$

Where A is the sampling fraction, 'y' is the sample size = 643, and 'z' is the 2021 monthly target coverage for vaccines in Cape Coast Metropolis[30]. In each of the sub-metros, the health directorate assigns monthly vaccination targets. The sampling fraction was applied to each sub-metro monthly target to determine the sample size for each sub-metro, as shown in Table 2.

Table 2 shows the estimated sample size selected from each of the five sub-metros in the Cape Coast Metropolis. The proposed sample size before data collection was 643; however, we were able to retrieve data from 765 caregivers, given the substantial interest from caregivers in the new malaria vaccine. The current sample used for this paper is substantive enough to ensure more precision in estimates than the sample which was initially anticipated.

Sampling of individual respondents

Respondents were selected using a systematic sampling method. Samples were drawn from each participating health facility's Child Welfare Clinic (CWC) registers. All eligible children in the catchment area of the health facilities have been listed in the frame alongside their vaccination status. All the registers were combined and checked for duplicity. After a complete sampling frame was achieved, a random sampling approach using the lottery method was used to select respective sub-metro samples. Primary caregivers of selected children in the sample were called for interviews.

Data collection

This study received ethical clearance from the Ghana Health Service (GHS-ERC:006/09/22). Informed consent was obtained from each mother to ensure voluntary participation in the study. The data was collected in December 2022. The study used 16 field officers across the five sub-metros in the Cape Coast Metropolis for the data collection. Each field officer interviewed approximately 50 primary caregivers using a computer-assisted questionnaire; CWC cards were observed. The questions captured information on vital socio-demographic characteristics, health facility accessibility (location and cost), attitude of health workers and RTS, S vaccination experience. Information on the number of RTS, S doses the child has received was retrieved from CWC health cards. Caregivers were contacted at CWCs or their homes, depending on where they were most likely available to respond to the questionnaires. The CWC card observation and questionnaire administration took about 45 min.

Variables

Outcome variable

The outcome variable is RTS, S vaccine defaults. If a child missed either the second, third, or fourth dose, he/she was considered to have defaulted. Children who received all four RTS, S vaccine doses were coded as 0 and otherwise as 1.

Explanatory variables

The explanatory variables for this study are grouped into three thematic areas - sociodemographic characteristics, healthcare-related factors and RTS, S-related factors, following evidence from existing studies. The variables and their categories can be found in Table 3 below.

Sub-metropolis	Monthly targets (x)	Sample fraction* (x)	Sample size
Adisadel	210	$Adisadel = \frac{643}{751} * 210$	179.80
Ewim	165	$Ewim = \frac{643}{751} * 165$	141.27
Cape Coast Central	173	$CCC = \frac{643}{751} * 173$	148.12
Efutu	68	$Efutu = \frac{643}{751} * 68$	58.22
UCC	135	$UCC = \frac{643}{751} * 135$	115.59
Total	751		643

Table 2. Sample size determination by sub-metro (proportionate to size).

Variables	Categories
Socio-demographic characteristics	
Sub-metro	Adisadel
	CCC
	Ewim
	UCC
	Effutu
Sex of child	Male
	Female
Primary caregiver's age	<25
	25–29
	30–34
	35–39
	40+
Primary caregiver's education	No formal education
	Primary
	Secondary
	Tertiary
Primary caregiver's occupation	Employed
	Unemployed
Primary caregiver's religion	Christian
	Islam
Health-related factors	
Place of child's delivery	Health facility
	Home
Minutes to a health facility	Less than 30 min
	30–60 min
	1–2 h
Cost to go to a health facility	No cost
	< GHC 5
	GHC 5–10
	> GHC 10
Attitude of health workers	Positive
	Neutral
	Negative
RTS, S-related	
Ever heard of the malaria vaccine	Yes
	No
Stating the number of times the vaccine is taken	Correct number stated
	Incorrect number stated
	Don't know
Age (months) at which the vaccine is taken	Correct ages stated
	Incorrect ages stated
	Don't know
Heard negative report/issue	No
	Yes
Feel vaccines are too many	No
	Yes
Adverse events	None
	Fever
	Diarrhoea
	Abscess

Table 3. Explanatory variables and their categories.

Data analysis

Data analysis for this research was performed in phases. First, a descriptive analysis was conducted to determine the univariate and bivariate distribution of the outcome and explanatory variables. This was followed by an evaluation of three classification models - binary logistic regression, decision tree, and random forest to determine the model that best classifies RTS, S vaccine defaults. Classification models were examined because the outcome variable is binary. The sample was divided into training and testing data in a 70:30 ratio and dummy variables were created for each of the explanatory variables. Five classification metrics - precision, recall, F1-score, accuracy, and area under the curve (ROC AUC) – were used to evaluate the performance of the models. The metrics are shown in Table 4 below.

The best classification model is binary logistic regression, as it scores highest in all evaluation metrics. This was followed by random forest. Based on the results, logistic regression was used as the primary classification model and random forest as a supplementary model to identify significant predictors of RTS, S vaccine defaults in southern Ghana. The Variable Inflation Factor (VIF) was computed to determine highly correlated variables (supplementary file 1). *The ages at which vaccines are taken were excluded from the multivariate logistic regression model as they strongly correlate* with the *number of times vaccines are taken.* We, however, provide descriptive results for this excluded variable. The binary logistic regression analysis was performed on four models. Model 1 accounted for only sociodemographic characteristics, while Model 2 and 3 included only health and RTS, S-related factors, respectively. Model 4 combined all socio-demographic, health and RTS, S-related factors ($p < 0.05$). An array of model statistics, including the R-squared, Akaike Information Criterion, and Bayesian Information Criterion, were reported. We also run random forest models to determine the most essential features. The random forest helps identify critical factors of a target outcome but is limited in proving a statistically significant relationship between the predictor and the outcome variables. Binary logistic regression allows for statistical relationships to be tested but does not necessarily classify predictors by importance. Therefore, we combined the strengths of these models to examine the essential and statistically significant factors that are associated with RTS, S vaccine defaults in southern Ghana. The analysis was performed using Python 3.

Results

Participants' background characteristics

About 28% of caregivers resided in the CCC Sub-Metro and an estimated 30% were aged between 30 and 34 years (Table 5). Most children were males and less than 10% were delivered at home. A high proportion of caregivers had primary education (45.0%), were employed (83.1%), and Christian (88.4%). It took most caregivers less than 30 min to go to the nearest health facility, and it was mostly free of charge. About 44% reported that health workers showed positive attitudes towards them. Most caregivers had ever heard of the malaria vaccine; however, a high proportion did not know the total number of vaccines that needed to be taken or the ages at which they were supposed to be taken (42.2%). There are four RTS, S doses and at the time of the study, they were taken at 6 months, 7 months, 9 months, and 24 months after the child was born. Adjustments have been made and the last dose is currently taken at 18 months. Only a handful of caregivers reported that they have heard some negative news about the vaccine and almost a third felt the vaccines were too many. A substantial number of mothers reported that their children had a fever (25.1%), diarrhoea (15.4%) or abscess (12.5%) after taking the RTS, S vaccine.

Prevalence of RTS, S defaults in Southern Ghana

As shown in Fig. 2, more than a third of children who initially started the RTS, S vaccine dose administration defaulted at some point. This might have been after the first, second or third dose(s) (Fig. 2A). The bivariate results in Table 5 show how the proportion of those who defaulted differs by background characteristics. A higher proportion of children in the Adisadel Sub-Metro (61.1%) and female (40.9%) defaulted. There was no unique pattern in RTS, S vaccine defaults by age of the primary caregiver. For children whose primary caregivers had tertiary education, there was a lower RTS, S default prevalence of 24% compared to those with no education (48.1%). About half of all children whose caregivers were unemployed or Islamic defaulted. Pearson's chi-square revealed that the differences observed for religion ($p = 0.272$), caregiver's age ($p = 0.801$), and sex of the child (0.760) were only a product of chance.

In terms of health-related factors, only the *cost of going to the health facility* ($p = 0.000$) and the *attitude of the health workers* ($p = 0.039$) had a significant bivariate association with the default of RTS, S vaccine. RTS, S vaccine defaults were low at 27.1% if caregivers incurred no cost going to a health facility, but this increased to more than 40% if money was spent. The proportion of defaults among children whose caregivers felt the attitudes of health providers were positive was lower at 32.4% compared to when they were neutral (38.9%) or negative (48.6%). If primary caregivers have ever heard of the RTS, S malaria vaccine, knew the correct number of times and ages at which the vaccine is supposed to be taken, heard no negative report/issue about the vaccine,

Classification model	Precision (%)	Recall (%)	F1-score (%)	Accuracy (%)	AUC (%)
Logistic regression	70	70	69	70	75
Decision tree	58	57	58	57	56
Random forest	66	67	65	67	74

Table 4. Evaluation metrics for three classification models.

	Univariate	RTSS vaccine defaults			
	% (n)	No	Yes	X^2	*P*-value
Socio-demographic characteristics					
Sub metro				55.045	0.000
Adisadel	20.5(157)	38.9(61)	61.1(96)		
CCC	27.7(212)	71.2(151)	28.8(61)		
Ewim	26.8(205)	67.8(139)	32.2(66)		
UCC	12.7(97)	73.2(71)	26.8(26)		
Efutu	12.3(94)	52.1(49)	47.9(45)		
Sex of child				1.868	0.760
Male	51.8(396)	63.9(253)	36.1(143)		
Female	48.2(369)	59.1(218)	40.9(151)		
Primary caregiver's age				6.165	0.801
<25	18.7 (143)	60.1(86)	39.9(57)		
25–29	22.6 (173)	54.9(95)	45.1(78)		
30–34	29.4 (225)	65.3(147)	34.7(78)		
35–39	21.0 (161)	65.8(106)	34.2(55)		
40+	8.2 (63)	58.7(37)	41.3(26)		
Primary caregiver's education				15.967	0.043
No formal education	10.6(81)	51.9(42)	48.1(39)		
Primary	45.0(344)	58.4(201)	41.6(143)		
Secondary	27.6(211)	61.6(130)	38.4(81)		
Tertiary	16.8(129)	76.0(98)	24.0(31)		
Primary caregiver's occupation				10.629	0.031
Employed	83.1(636)	64.1(408)	35.8(228)		
Unemployed	16.9(129)	48.8(63)	51.2(66)		
Primary caregiver's religion				5.156	0.272
Christian	88.4(676)	63.0(426)	37.0(250)		
Islam	11.6(89)	50.6(45)	49.4(44)		
Health-related factors					
Place of child's delivery				0.080	0.999
Health facility	90.8(695)	61.7(429)	38.3(266)		
Home	9.2(70)	60.0(42)	40.0(28)		
Minutes to a health facility				10.227	0.115
Less than 30 min	55.2(422)	64.9(274)	35.1(148)		
30–60 min	22.3(171)	63.7(109)	36.3(62)		
1–2 h	22.5(172)	51.2(88)	48.8(84)		
Cost to go to a health facility				41.467	0.000
No cost	49.3(377)	72.9(275)	27.1(102)		
< GHC 5	12.2 (93)	53.8(50)	46.2(43)		
GHC 5–10	21.7(166)	48.2(80)	51.8(86)		
> GHC 10	16.8(129)	51.2(66)	48.8(63)		
Attitude of health workers				13.285	0.039
Positive	43.9(336)	67.6(227)	32.4(109)		
Neutral	31.9(244)	61.1(149)	38.9(95)		
Negative	24.2(185)	51.4(95)	48.6(90)		
RTSS-related					
Ever heard of the malaria vaccine				8.391	0.078
Yes	81.0(620)	64.0(397)	36.0(223)		
No	19.0(145)	51.0(74)	49.0(71)		
Stating the number of times the vaccine is taken				63.767	0.000
Correct number stated	26.9(206)	79.6(164)	20.4(42)		
Incorrect number stated	30.9(236)	66.9(158)	33.1(78)		
Don't know	42.2(323)	46.1(149)	53.9(174)		
Age (months) at which the vaccine is taken				65.108	0.000
Continued					

	Univariate	RTSS vaccine defaults			
	% (n)	No	Yes	X^2	*P*-value
Correct ages stated	26.5(203)	80.3(163)	19.7(40)		
Incorrect ages stated	31.2(239)	66.5(159)	33.5(80)		
Don't know	42.2(323)	46.1(149)	53.9(174)		
Heard negative report/issue				4.127	0.389
No	94.9(726)	62.4(453)	37.6(273)		
Yes	5.1(39)	46.2(18)	53.8(21)		
Feel vaccines are too many				8.695	0.069
No	72.7(556)	64.7(360)	35.3(196)		
Yes	27.3(209)	53.1(111)	46.9(98)		
Adverse events				12.014	0.151
None	46.9(359)	68.0(244)	32.0(115)		
Fever	25.1(192)	57.3(110)	42.7(82)		
Diarrhoea	15.4(118)	55.1(65)	44.9(53)		
Abscess	12.5(96)	54.2(52)	45.8(44)		
Total	100 (765)	61.57 (471)	38.43 (294)		

Table 5. Univariate and bivariate frequency distribution of RTSS vaccine defaults and background characteristics.

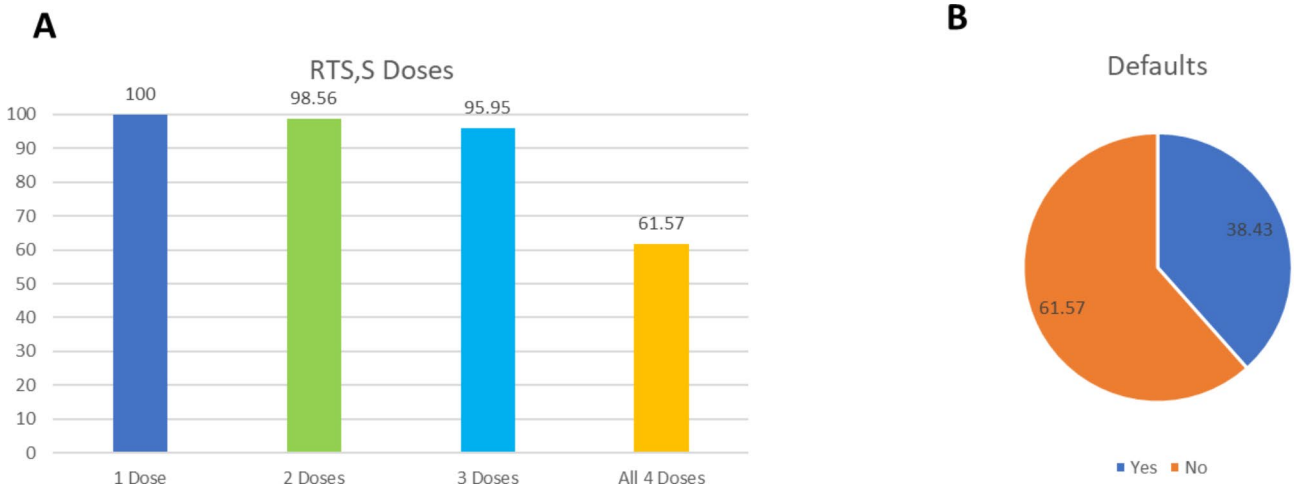

Fig. 2. RTS, S dose distribution (**A**) and the proportion who defaulted (**B**) in Southern Ghana.

felt the vaccines were not too many and did not have any adverse events, the proportion of defaults was usually lower (Table 5).

Predictors of RTS, S defaults in Cape Coast

Socio-demographic determinants of RTS, S defaults

The key socio-demographic predictors of RTS, S vaccine defaults, as shown in Model 1, were sub-metro of residence, caregiver's education, and occupation (Table 6). Residence at CCC, Ewim, UCC and Efutu yielded lower odds of 0.26[0.16,0.41], 0.31[0.20,0.48], 0.30[0.16,0.54], and 0.58[0.34,0.98] of RTS, S vaccine default, respectively, compared to residents at Adisadel. Children of caregivers who had primary, secondary and tertiary education had significantly lower odds of 0.69[0.41,1.15], 0.65[0.37,1.13], and 0.49[0.26,0.94] of defaulting, respectively, compared to those whose caregivers had no education. If a caregiver was employed, the odds of default were significantly lower at 0.61[0.39,0.94] compared to being unemployed. In Model 4, when health and RTS, S-related factors were accounted for, the associative effect of education became weak. Figure 3 shows a rank of essential features of RTS, S defaults based on the Random Forest model. The top two predictors were religion and sub-metro of residence. Even though religion was not significantly ($p=0.088$) associated with RTS, S defaults, it was a critical classification feature. Muslim children had higher odds of vaccine defaults. This highlights inherent socio-religious influences that could be contributing indirectly and subtly to RTS, S vaccine multi-dose completion in Cape Coast Metro, Ghana.

Variables	Model 1 Odds [95% CI]	p-value	Model 2 Odds [95% CI]	p-value	Model 3 Odds [95% CI]	p-value	Model 4 Odds [95% CI]	p-value
Socio-demographic characteristics								
Sub_Metro								
Adisadel	1.00						1.00	
CCC	0.26[0.16,0.41]	0.000					0.28[0.16,0.48]	0.000
Ewim	0.31[0.20,0.48]	0.000					0.28[0.16,0.47]	0.000
UCC	0.30[0.16,0.54]	0.000					0.21[0.10,0.42]	0.000
Effutu	0.58[0.34,0.98]	0.041					0.67[0.36,1.27]	0.219
Sex of child								
Male	1.00						1.00	
Female	1.25[0.92,1.71]	0.156					1.26[0.90,1.78]	0.182
Primary caregiver's age								
<25	1.00						1.00	
25–29	1.32[0.80,2.16]	0.274					1.42[0.83,2.44]	0.202
30–34	0.86[0.58,1.57]	0.859					1.07[0.63,1.82]	0.802
35–39	0.93[0.54,1.59]	0.790					0.99[0.56,1.78]	0.909
40+	1.21[0.62,2.36]	0.569					1.37[0.66,2.82]	0.398
Primary caregiver's education								
No formal education	1.00						1.00	
Primary	0.69[0.41,1.15]	0.156					0.63[0.36,1.11]	0.112
Secondary	0.65[0.37,1.13]	0.125					0.66[0.36,1.23]	0.191
Tertiary	0.49[0.26,0.94]	0.033					0.52[0.25,1.08]	0.082
Primary caregiver's occupation								
Unemployed	1.00						1.00	
Employed	0.61[0.39,0.94]	0.027					0.57[0.36,0.93]	0.026
Primary caregiver's religion								
Christian	1.00						1.00	
Islam	1.51[0.94,2.42]	0.088					1.64[0.97,2.78]	0.063
Health-related factors								
Place of child's delivery								
Health facility			1.00				1.00	
Home			1.25[0.74,2.12]	0.409			0.97[0.51,1.82]	0.917
Minutes to a health facility								
Less than 30 min			1.00				1.00	
30–60 min			0.96[0.66,1.42]	0.855			1.03[0.66,1.59]	0.902
1–2 h			1.46[0.99,2.15]	0.052			1.12[0.72,1.74]	0.605
Cost to go to a health facility								
No cost			1.00				1.00	
<GHC 5			2.25[1.40,3.60]	0.001			2.10[1.23,3.61]	0.007
GHC 5–10			2.73[1.86,4.03]	0.000			2.89[1.87,4.47]	0.000
> GHC 10			2.24[1.46,3.44]	0.000			2.21[1.36,3.63]	0.001
Attitude of health workers								
Positive			1.00				1.00	
Negative			1.73[1.18,2.55]	0.005			1.17[0.73,1.86]	0.513
Neutral			1.24[0.86,1.77]	0.244			0.96[0.63,1.45]	0.835
RTSS-related								
Ever heard of the malaria vaccine								
Yes					1.00		1.00	
No					0.96[0.63,1.45]	0.847	1.05[0.67,1.67]	0.814
Number of times vaccine is taken								
Correct number stated					1.00		1.00	
Incorrect number stated					2.01[1.28,3.14]	0.002	2.16[1.29,3.62]	0.004
Don't know					5.06[3.24,7.90]	0.000	3.76[2.21,6.38]	0.000
Heard negative report/issue								
No					1.00		1.00	
Yes					2.54[1.26,5.13]	0.009	4.08[1.85,8.97]	0.000

Continued

Variables	Model 1 Odds [95% CI]	p-value	Model 2 Odds [95% CI]	p-value	Model 3 Odds [95% CI]	p-value	Model 4 Odds [95% CI]	p-value
Feel vaccines are too many								
No					1.00		1.00	
Yes					1.45[1.02,2.05]	0.034	1.38[0.92,2.08]	0.119
Adverse events								
None					1.00		1.00	
Fever					1.64[1.12,2.42]	0.011	2.32[1.49,3.65]	0.000
Diarrhoea					1.69[1.08,2.65]	0.021	1.32[0.79,2.18]	0.287
Abscess					1.68[1.03,2.74]	0.038	1.88[1.09,3.25]	0.023
Pseudo R-squared (%)	7.6		5.5		8.9		18.6	
AIC	972.2		981.5		946.4		892.1	
BIC	1041.8		1023.2		988.2		1035.9	

Table 6. Logistic regression models showing the odds of RTS, S default by socio-demographic, health and RTS, S-related factors.

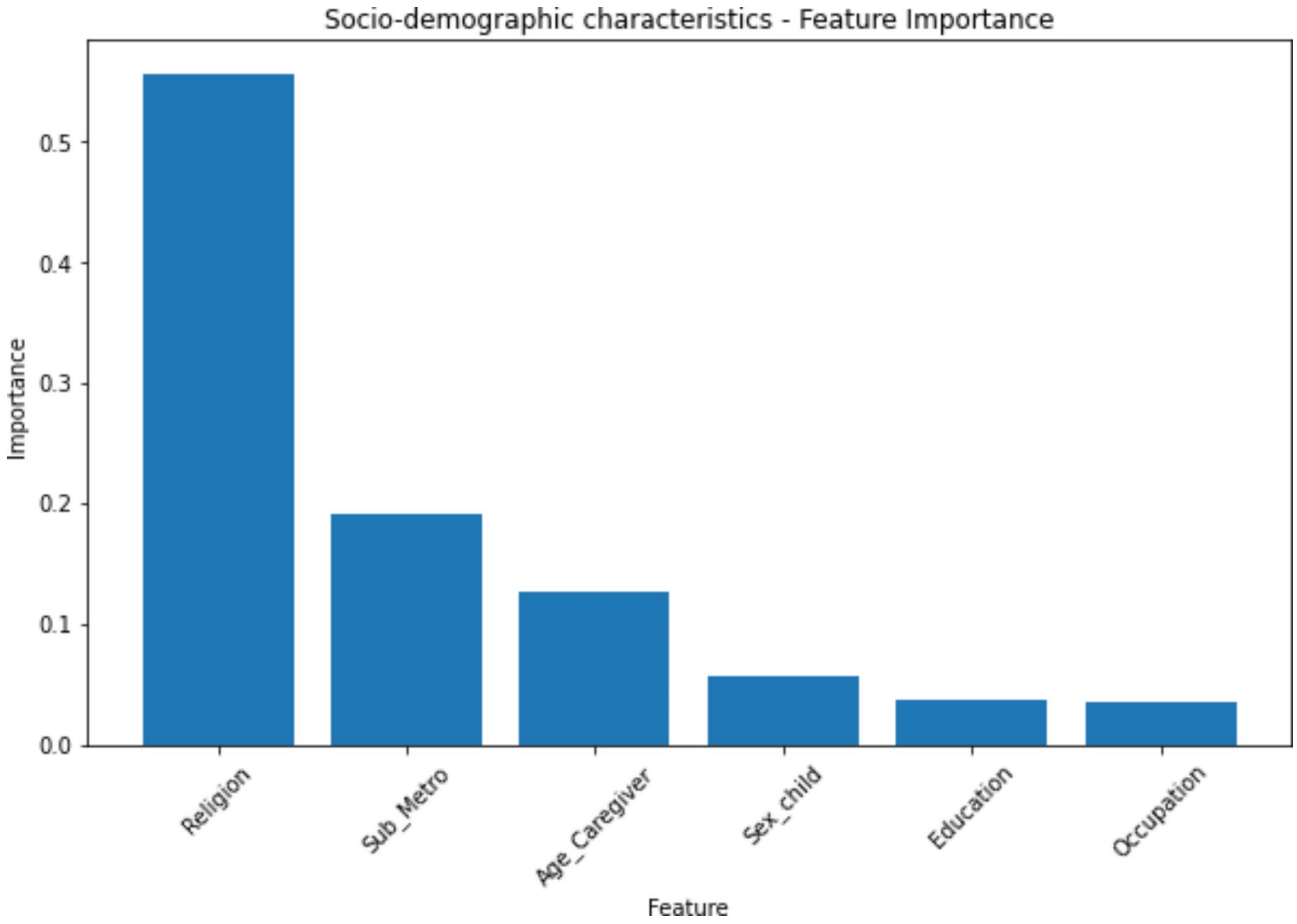

Fig. 3. A rank of socio-demographic predictors of RTS, S defaults using random forest.

Health-related determinants of RTS, S defaults

The study explored four health-related determinants of RTS, S defaults and only *cost to visit health facilities* and the *attitude of health workers* were significant (Table 6). These also comprised the top two features of the Random Forest model as shown in Fig. 4. As shown in Model 2, for children whose caregivers incurred some amount of cost to travel to the nearest health facility, the odds of defaulting were twice that of those whose mothers incurred no cost. If the attitudes of health workers were negative, children had higher odds of 1.73[1.18,2.55] of not completing their vaccination compared to being positive. When socio-demographic and RTS, S-related factors were accounted for in Model 4, the associative effect of the *attitude of health workers* became weak.

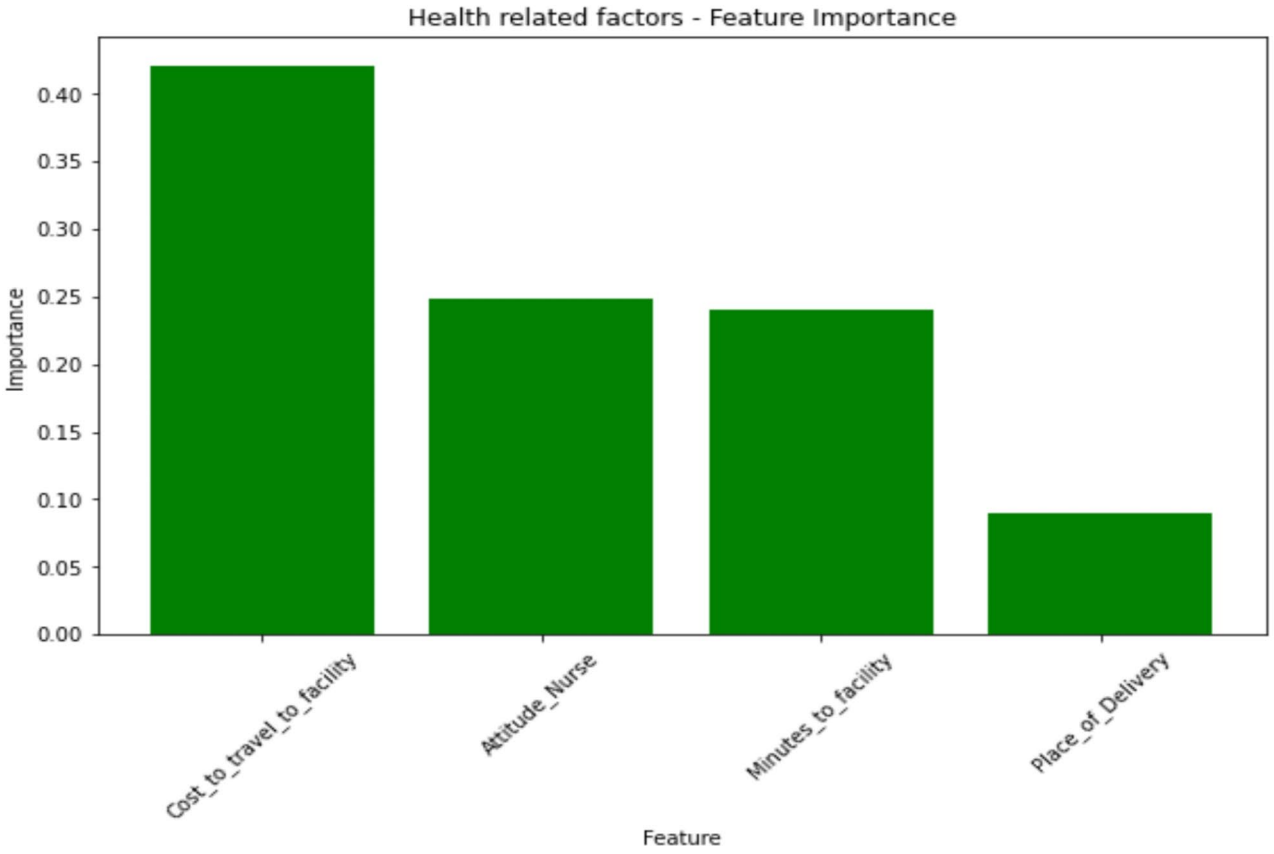

Fig. 4. A rank of health-related predictors of RTS, S defaults using random forest.

RTS, S-related factors

As shown in Model 3, all RTS, S-related factors were strongly associated with vaccine default except for *ever heard of the malaria vaccine* (Table 6). Compared to children of caregivers who knew the correct number of doses to be taken, the odds of default were two times and five times higher for those whose caregivers stated the incorrect number and did not know, respectively. The odds of default if the caregiver had heard of a negative report, ranged between 1.26 and 5.13 compared to those who did not hear any negative report. In addition, those who felt the vaccines were too many were more likely to discontinue. The odds of default ranged between 1.02 and 2.05. The experience of adverse events such as fever, diarrhoea, and abscess increased the odds of default compared to not having these events. The odds were 1.64[1.12,2.42] for fever, 1.69[1.08,2.65] for diarrhoea and 1.68[1.03,2.74] for abscess. When socio-demographic and health-related factors were accounted for, *the feeling that vaccines are too many* became insignificant ($p = 0.119$). Figure 5 shows a rank of RTS and S-related factors, and the top two constitute the number of times vaccines are *taken* and *adverse events*.

Top five crucial predictors of RTS, S defaults in Cape Coast Metro Ghana

Figure 6 shows a rank of statistically significant predictors of RTS, S defaults in Ghana. The predictors were selected based on Model 4 and ranked using Random Forest. As shown, the top five significant predictors of RTS, S defaults in Southern Ghana, in order of importance, are *sub-metro of residence*, *cost of travel to healthcare facilities*, *experience of adverse events*, *knowledge on the correct number of vaccine doses* and *caregiver's occupation*. The relevance of ranking these predictors lies in its potential advantage in guiding resource allocation to areas of dire need.

Table 6 Cont'd: Logistic regression models showing the odds of RTSS default by socio-demographic, health and RTS, S-related factors.

Discussion

In this study, we examined the factors that predict RTS, S/AS01E vaccine defaults in Ghana. Among our participants, more than a third defaulted in the uptake of the RTS, S/AS01E vaccine (38.43%). Given that Ghana's rollout of the RTS, S/AS01E vaccine was on a pilot basis and could potentially increase during a national scale-up, the 38% default is disturbing. Our findings suggest that the observed defaults were primarily due to sub-metro of residence, cost to travel to health facility, experience of adverse events, knowledge of the correct number of vaccine doses and caregiver's employment status.

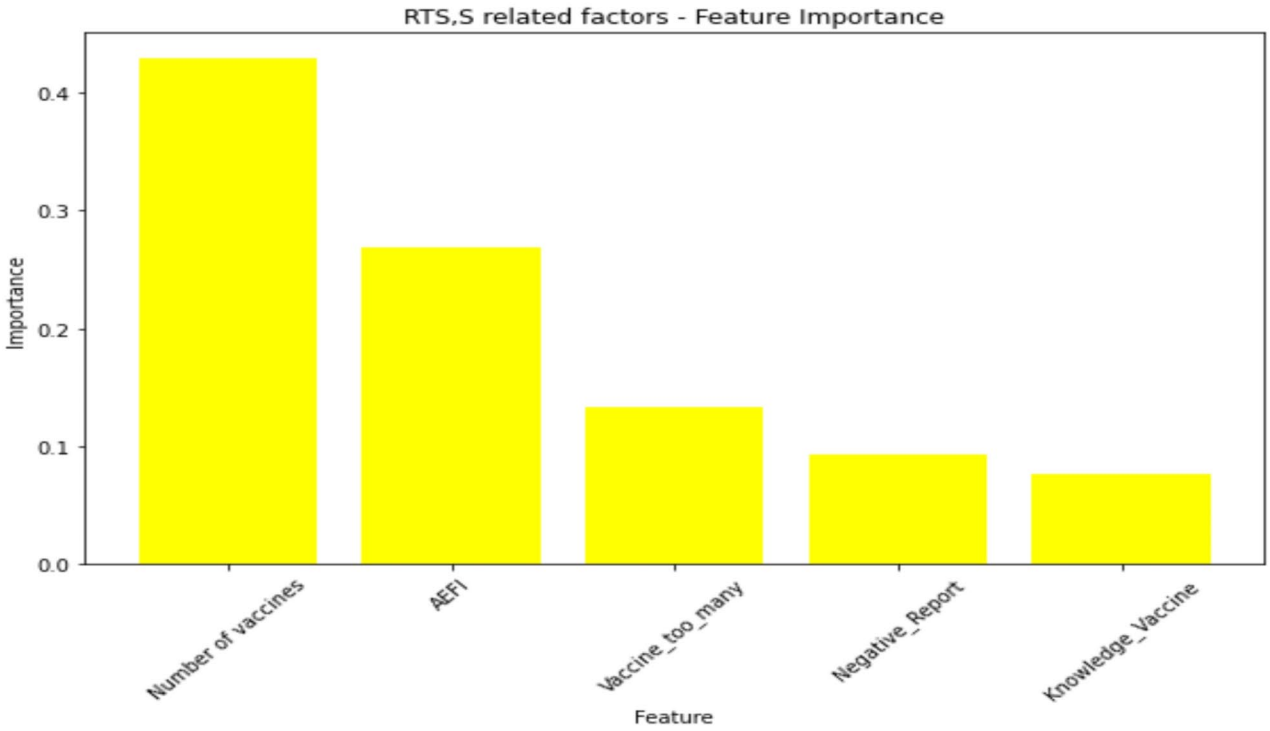

Fig. 5. A rank of RTS, S-related predictors of RTS, S defaults using random forest.

Sub-metro of residence emerged as the principal factor that predicted vaccine defaults. Compared to caregivers in Adisadel, all other sub-metros were less likely to default. It is unclear what the reasons might be, necessitating the need for additional research. Our research highlights a concerning correlation between financial barriers and the likelihood of defaulting malaria vaccines among caregivers. This is consistent with Adjei et al.[13], who found the cost incurred to reach healthcare facilities to be one of the significant factors that influenced the uptake of the malaria vaccine in Ghana. A similar pattern of association has been found for other childhood vaccines. For instance, studies from Uganda[31] and Sub-Saharan Africa[32] have shown that the cost incurred in travelling to healthcare facilities was a significant barrier that exacerbated incomplete vaccine uptake, drop-outs and defaults. Thus, it highlights the need for targeted interventions that address economic barriers, such as subsidizing transportation costs or implementing community-based vaccination programs, to ensure equitable access to malaria vaccines and mitigate the risk of defaults among caregivers from poor households.

We observed that defaulting on the RTS, S/AS01E vaccine was significantly high among caregivers whose children had experienced some adverse health effects. The result is corroborated by a qualitative study conducted in Ghana[25], which showed that concerns about potential negative side effects (e.g., abscess) and the discomforts influenced caregivers' decision to miss subsequent doses of the RTS, S/AS01E vaccine. It is, therefore, not surprising that our findings also revealed that caregivers who had heard adverse reports and experience adverse effects following immunization about the vaccine were four times more likely to default. Theoretically, the observed association can be explained by the health belief model's cues to action. Cues to action are pivotal factors influencing individuals' decisions regarding vaccination, as information and communication exert a profound impact on public perceptions[33,34]. The dissemination of information about vaccine side effects, whether conveyed through word of mouth, media, or other sources, acts as a significant cue to action. Consequently, negative information regarding potential adverse reactions can serve as a powerful deterrent, heightening concerns and exacerbating defaulter intentions. Abscess formation following vaccination is particularly of concern, showing possible poor injection techniques or conditions among nurses. Regular training of health workers on safe injection practices is recommended.

The study also shows a strong association between knowledge of the correct vaccine dose and the likelihood of defaulting. Specifically, caregivers who demonstrated poor understanding of the number of vaccine doses were two times more likely to default than their counterparts who knew the correct number of vaccine doses. This finding aligns with previous research, such as Adjei et al.'s study[13], which identified a lack of information on the malaria vaccine and its schedule as crucial barriers to vaccine uptake among caregivers. Tadesse et al.[35] also reported findings that support the opinion that poor knowledge about vaccine doses and schedules exacerbates the risk of defaulting. A plausible explanation could be that inadequate awareness about vaccination schedules may contribute to confusion and uncertainty among caregivers, potentially leading to missed doses. Additionally, the lack of accurate information might engender misconceptions or fears regarding the safety and necessity of the vaccine, further deterring individuals from adhering to the recommended immunisation regimen.

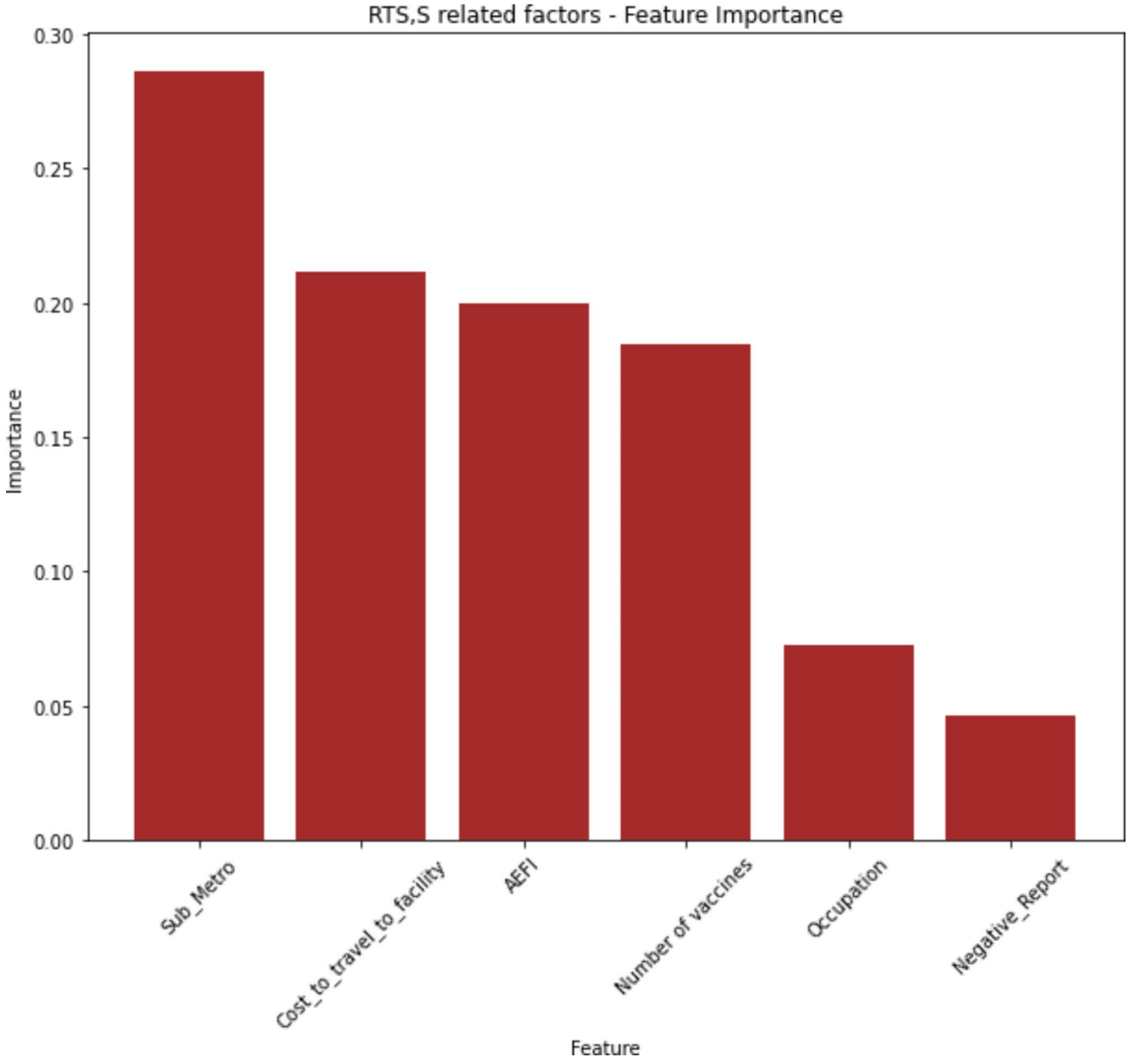

Fig. 6. A rank of significant predictors of RTS, S defaults using random forest.

Compared to caregivers who were not employed, those currently employed at the time of the study had significantly lower odds of defaulting. Our finding agrees with Banjari et al.[36], who reported that unemployed caregivers are four times more likely than those employed to delay and miss vaccination for their children. The observed association is also corroborated by Anokye et al.[37], whose study revealed that being employed was significantly associated with a higher likelihood of the child being fully immunised – thus reflecting a lower risk of defaults. Employed caregivers may have better access to information about vaccination schedules, possibly due to workplace health programs or better access to healthcare resources, thereby reducing the risk of missed appointments and doses. Additionally, employed individuals may have more structured routines, making it easier for them to plan and adhere to vaccination appointments. We also postulate that economic stability associated with employment might also reduce barriers related to transportation costs and time constraints, contributing to higher compliance and reduced likelihood of defaults.

Implications of findings

The findings of this study carry significant implications for both policy and practice in the realm of childhood vaccination in Ghana. Firstly, the identified sub-metro disparities emphasise the need for targeted interventions at the regional level, with a particular focus on areas exhibiting higher default rates. It is, therefore, imperative for the Central Regional Directorate of the Ghana Health Service to evaluate the Adisadel area and consider tailoring vaccination programs to address the specific challenges faced by caregivers in this sub-metro, possibly through community engagement initiatives and accessible healthcare services. In the intended national rollout

of the vaccine, community-based or home-based modules should be considered to reduce the financial burden of transport to healthcare facilities. Additionally, the Central Regional Directorate of the Ghana Health Service could strengthen strategies to dispel misconceptions and address caregiver concerns about potential side effects. This may involve leveraging various communication channels, including healthcare providers, community leaders, and media, to disseminate accurate information and build trust in the vaccination process.

Strengths and limitations

The sample size used for the study allows for the findings from the study to be generalised to the study area. Moreover, the sampling method used in the study minimises the possibility of selection bias with positive implications for the study findings. In terms of limitations, due to the cross-sectional nature of the study, causality cannot be established. While our findings are generalisable to Cape Coast, they may not necessarily reflect the situation in other piloting districts.

Conclusion

More than a quarter of caregivers had defaulted in completing the malaria vaccine uptake. To mitigate the risk of defaults, targeted interventions should focus on addressing sub-metro disparities, alleviating financial barriers, enhancing awareness, and tailoring communication strategies. This study urges collaborative efforts among policymakers, healthcare professionals, and community stakeholders to strengthen vaccination program effectiveness and achieve optimal public health outcomes.

Data availability

Data for this study is available upon reasonable request from the lead author, Vincent Bio Bediako. Interested parties should direct their requests to him.

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Author contributions
All authors meet the criteria for authorship as stated in the International Committee of Medical Journal Editors (ICMJE) authorship guidelines. VBB and JA conceived and designed the study. VBB secured the grant funding. JA analysed the data. WA designed the online application for the data collection. VBB and JA provided methodological insights. VBB, JA and WA oversaw data curation. VBB, JO and WA collected the data. JO, BAO, EA, TJY and WA drafted the initial manuscript. AUN, EMK, and EA supervised the research. All authors reviewed and commented on the manuscript and approved the final draft for publication.

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Declarations

Competing interests
The authors declare no competing interests.

Ethical approval and consent to participate
All procedures adhered to pertinent guidelines, and ethical approval for this study (GHS-ERC:006/09/22) was obtained from the Ghana Health Service. Further permissions were secured from relevant health facilities. The methodologies were in accordance with the Helsinki and Belmont principles. Prior to their participation, explicit written and oral consent was acquired from all participants. Comprehensive information encompassing the study's objectives, duration, procedures, potential discomforts, and benefits was provided to participants through an information sheet. Emphasis was placed on their rights to confidentiality, privacy, and anonymity throughout the research process.

Additional information

Correspondence and requests for materials should be addressed to V.B.B.