# RESEARCH

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# Receipt of antimalarials among children aged 6–59 months in Nigeria from 2010 to 2021

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# Abstract

**Background** Nigeria has the highest malaria burden globally, and anti-malarials have been commonly used to treat malaria without parasitological confirmation. In 2012, Nigeria implemented rapid diagnostic tests (RDTs) to reduce the use of anti-malarials for those without malaria and to increase the use of artemisinin-based combination therapy (ACT) for malaria treatment. This study examined changes in anti-malarial receipt among children aged 6–59 months during a 12-year period of increasing RDT availability.

**Methods** A cross-sectional analysis was conducted using the Nigeria Malaria Indicator Survey (NMIS) data from 2010 (before RDT implementation in 2012), 2015, and 2021. The analysis assessed trends in prevalence of malaria by survey RDT result, and fever and anti-malarial/ACT receipt in the 2 weeks prior to the survey. A multivariable logistic regression was used to account for the complex survey design and to examine factors associated with anti-malarial receipt, stratified by survey RDT result, a proxy for recent/current malaria infection.

**Results** In a nationally-representative, weighted sample of 22,802 children aged 6–59 months, fever prevalence remained stable over time, while confirmed malaria prevalence decreased from 51.2% in 2010 to 44.3% in 2015 and 38.5% in 2021 (trend test p < 0.0001). Anti-malarial use among these children decreased from 19% in 2010 to 10% in 2021 (trend test p < 0.0001), accompanied by an increase in ACT use (2% in 2010 to 8% in 2021; trend test p < 0.0001). Overall, among children who had experienced fever, 30.6% of survey RDT-positive and 36.1% of survey RDT-negative children had received anti-malarials. The proportion of anti-malarials obtained from the private sector increased from 61.8% in 2010 to 80.1% in 2021 for RDT-positive children; most of the anti-malarials received in 2021 were artemisinin-based combinations. Factors associated with anti-malarial receipt for both RDT-positive and RDT-negative children included geographic region, greater household wealth, higher maternal education, and older children.

**Conclusion** From 2010 to 2021 in Nigeria, both malaria prevalence and anti-malarial treatments among children aged 6–59 months decreased, as RDT availability increased. Among children who had fever in the prior 2 weeks, anti-malarial receipt was similar between children with either positive or negative survey RDT results, indicative of persistent challenges in reducing inappropriate anti-malarials uptake.

Keywords Malaria, Rapid diagnostic tests, RDT, Fever, Anti-malarial, Artemisinin-based combination therapy, ACT

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# Background

Nigeria, with a population of over 200 million, had the highest global burden of malaria in 2022, accounting for 27% of global malaria cases, 31% of global malaria deaths, and 38% of global malaria deaths among children under 5 years of age [1]. The malaria parasite Plasmodium fal*ciparum* infects at least 50% of the Nigerian population annually and contributes to over 45% of total outpatient visits, 25% of infant mortality, and 30% of childhood mortality [2, 3]. Diagnosing and managing malaria has presented significant challenges in malaria-endemic countries, such as Nigeria, due to limited access to diagnostic tests and effective, quality-assured anti-malarials. Fevers are often presumed to be malaria-related by patients/caregivers and healthcare providers and are, therefore, treated empirically, even though the differential diagnosis for fever among children in Nigeria is broad [4–8]. Consequently, the overuse of anti-malarials without confirming the presence of malaria parasites remains a concern. This can contribute to inappropriate diagnoses, ineffective treatment of febrile illnesses, and may foster the emergence of anti-malarial drug resistance.

In 2010, the World Health Organization (WHO) recommended universal parasitological confirmation of malaria before treatment using either microscopy or rapid diagnostic tests [9, 10]. Nigeria, along with many other countries, revised its national malaria treatment guidelines in 2011 [11] and introduced malaria rapid diagnostic tests (RDTs) in primary healthcare facilities in 2012 [12]. RDTs, which utilize lateral flow immunochromatography to identify malaria parasite antigens in under 30 min [13], have revolutionized malaria diagnosis, treatment, and surveillance [14], enabling accurate diagnosis at point of care and differentiation of malaria from other febrile illnesses. Many studies carried out in malaria-endemic countries have found that the increasing availability of RDTs improved the prescription of the recommended first-line artemisinin-based combination therapy (ACT) for people with malaria and reduced the rate of empiric treatment [15–17].

However, despite the widespread availability and accessibility of RDTs, inappropriate use of anti-malarials persists especially at the community level [23]. Some febrile children who don't have malaria still get anti-malarials, while other children with malaria are either not treated or do not promptly receive ACT [18–20]. Studies have reported varying rates of anti-malarial treatment among people without malaria, ranging from 0.1% to 81% [21–23]. Key drivers for this include a lack of confidence in RDTs, preference for presumptive treatment, lack of access to RDTs in both the formal and informal private sectors where many people access anti-malarials, and limited access to diagnostic tests for non-malarial fevers

[20, 22, 23]. Although population-based surveys routinely report malaria care cascades among children with fever, fewer data are available on the extent of anti-malarial receipt among RDT-negative children and which children are most likely to receive anti-malarials when they do not have malaria.

This secondary analysis leveraged the nationally representative cross sectional Nigeria Malaria Indicator Survey (NMIS) data from 2010 (prior to RDT implementation in 2012), 2015, and 2021. As part of all three of these surveys, children aged 6-59 months in sampled households were tested with RDTs detecting histidine-rich protein 2 (HRP II), a protein specific to *P. falciparum*, which causes about 95% of malaria infections in Nigeria [4]. HRP2based RDTs remain positive for several weeks after successful treatment, due to the slow clearance of the HRP2 antigen from the blood [24, 25]. Thus, RDT results at the time of the NMIS surveys provide a unique opportunity to assess self-reported anti-malarial use among children who have a negative survey RDT result and likely did not have malaria, compared to those with positive RDT results (evidence of current or recent infection). The goal of the study was to examine trends in anti-malarial use from 2010-2021 to understand how increasing availability of RDTs has affected anti-malarial use at the community level. Also, the study aimed to examine factors associated with the receipt of anti-malarial treatment in the prior 2 weeks among both RDT-positive and RDTnegative children.

#### Methods

# Study setting and data

Nigeria is a West African country bordered by Cameroon, Niger, Chad, Benin, and the Atlantic Ocean. Children under 5 years of age make up 17.1% of Nigeria's population [26]. Urban areas are inhabited by one-third of the population, while the remaining two-thirds reside in rural areas. Malaria is prevalent across Nigeria, spanning diverse ecological zones that transition from south to north. The country is divided into six geopolitical zones-North-East, North-Central, North-West, South-East, South-South, and South-West-which collectively encompass 36 states. Nigeria has distinct climate zones with varying rainfall patterns. In the southern regions, heavy rainfall occurs from March to October, while the central and coastal areas have well-defined rainy seasons. In the north, rainfall mainly occurs from June to September. The dominant species of Anopheles mosquitoes include Anopheles funestus, Anopheles gambiae complex, and Anopheles arabiensis.

The NMIS is a cross-sectional household survey conducted approximately every 5 years to provide nationally representative data on malaria epidemiology and control, including insecticide-treated net ownership, fever prevalence and treatment in young children, and malaria prevalence rates [26-28]. In a 2-stage sampling process, clusters (census enumeration areas from the Nigeria Population and Housing Census sampling frames) were selected with probability proportional to population size, and a household listing was conducted in selected clusters to form the sampling frame for random selection of approximately 25 households per cluster. The 2021 NMIS had a larger sample size, covering 568 clusters compared to the 240 and 333 clusters in the 2010 and 2015 surveys, respectively, including urban and rural areas. The surveys were conducted from October to December during the peak malaria transmission season. All three surveys tested children under 5 years with RDTs for each year, even though RDTs had not yet been routinely implemented in Nigeria as of 2010, and individual-level data collected from all three surveys was used for this analysis. This analysis was determined to be not Human Subjects Research by the UAB Institutional Review Board (IRB-300010792). The 2010, 2015 and 2021 NMIS protocol were reviewed and approved by the National Health Research and Ethics Committee of Nigeria and the ICF Institutional Review Board for Demographic and Health Surveys.

#### **Study population**

The study population consisted of children aged 6–59 months who were tested with RDTs at the time of all three NMIS surveys and their mothers/caregivers. The population included both individuals who tested positive for malaria (RDT-positive) and those who tested negative for malaria (RDT-negative) at the time of the survey.

## Variables

The primary outcome of the analysis was the receipt of any anti-malarial (categorized into artemisinin-based combinations and non-artemisinin-based combinations) among children who had fever in the 2 weeks before the survey, as reported by the mother/caregiver of the child at the time of the survey. Other variables were the result of the survey RDT, and data reported by the mother/ caregiver of children tested, including the child's age and sex, mother/caregiver's age, education, religion, wealth quintile, residential area, region of residence, and whether the child slept under a bed net the night prior to the survey. Mothers/caregivers were also asked if their child had fever in 2 weeks prior to the survey, and for all febrile children, variables captured in the care cascade included seeking care from any source, being tested for malaria, being told they had malaria (regardless of test status), receiving an anti-malarial, and receiving an ACT. The sources of anti-malarials were classified into two

categories: public health facilities (e.g., community health workers, government health facilities, government hospitals) and private health facilities (e.g., private hospitals, pharmacies, private medicine vendors).

## Data management and analysis

The prevalence of malaria by RDT result at the time of the 2010, 2015, and 2021 NMIS survey overall, at each survey and by sociodemographic characteristics of the children tested and their mothers/caregivers. The analysis examined characteristics of RDT-positive and RDTnegative children by survey year, presenting proportions for categorical variables and median/ interguartile range (IQR) for continuous variables. Also, trends in the proportions of children with fever, testing positive for malaria by RDT, and receiving anti-malarials and ACT in the two weeks preceding the survey were assessed using logistic regression with survey year as a continuous independent variable (with 2010 as the referent). To examine socio-demographic factors associated with the receipt of anti-malarial treatment in the prior 2 weeks, a multivariable logistic regression including all variables listed above using the SAS survey procedures to account for the sampling design, clustering, and weights was conducted. In addition, the proportions of children with fever in the prior 2 weeks for each step of the care-seeking cascade were examined, stratified by the RDT result at the time of the survey. The proportions of the RDT-positive and RDT-negative children receiving either artemisininbased combinations and non-artemisinin-based combinations by year of survey and source of treatment are also presented. Data were analysed using SAS V 9.4 (SAS Institute, NC) and all significant tests were performed at an alpha level of 0.05.

# Results

## Malaria prevalence and trends

The 2010, 2015, and 2021 NMIS included a total sample size of 22,802 children aged 6-59 months who were tested for malaria by RDT at the time of the survey (Table 1 and Supplemental Table 1). The proportion of children testing positive for malaria by RDT decreased from 51.2% (95% CI 46.7–55.6%) in 2010 to 44.3% (95% CI 41.1-47.5%) in 2015 and 38.5% (95% CI 36.0-41.1%) in 2021 (p for trend < 0.0001). For all survey years, the proportion of children with a positive RDT increased with increasing age. Across survey years, malaria prevalence was consistently highest among children within the age group of 48–59 months of life (decreasing from 57.4% [95% CI 52.2-62.5%] in 2010 to 46.2% [95% CI 43.0-49.5%] in 2021) compared to children within the age group of 6-11 months (decreasing from 42.8% [95% CI 34.6-51.1%] in 2010 to 20.9% [95% CI 17.5-24.3%] in

	2010 N = 5543 % RDT Positive (95% Cl)	2015 N = 6174 % RDT Positive (95% Cl)	2021 N = 11,085 % RDT Positive (95% Cl)	
Overall	51.2 (46.7, 55.6)	44.3 (41.1, 47.5)	38.5 (36.0, 41.1)	
Child's age in months				
Median (IQR)	34.6 (18.8, 47.3)	36.2 (21.4, 48.3)	37.2 (24.1, 49.1)	
6–11	42.8 (34.6, 51.1)	31.3 (25.6, 36.8)	20.9 (17.5, 24.3)	
12–23	47.6 (42.2, 53.1)	37.8 (33.4, 42.2)	32.2 (29.0, 35.5)	
24–35	50.0 (44.6, 55.4)	44.3 (39.9, 48.6)	39.6 (35.9, 43.3)	
36–47	53.5 (47.8, 59.2)	48.6 (44.5, 52.6)	42.7 (39.4, 46.0)	
48–59	57.4 (52.2, 62.5)	52.4 (48.2, 56.6)	46.2 (43.0, 49.5)	
Child's sex				
Male	52.3 (47.2, 57.3)	44.4 (40.6, 48.1)	39.6 (36.7, 42.6)	
Female	50.0 (45.5, 54.6)	44.3 (40.8, 47.8)	37.4 (34.8, 40.1)	
Mother/caregiver's age in years				
Median (IQR)	27.8 (22.8, 34.2)	25.2 (21.0, 31.2)	27.2 (21.3, 33.3)	
Residence				
Rural	55.2 (50.4, 60.1)	55.5 (51.6, 59.5)	44.2 (41.2, 47.3)	
Urban	37.7 (27.5, 47.8)	22.8 (18.2, 27.3)	23.6 (20.4, 26.8)	
Mother's education				
No education	58.7 (53.1, 64.1)	59.9 (55.6, 64.2)	52.4 (48.8, 56.0)	
Primary education	53.6 (47.3, 59.9)	43.6 (38.5, 48.7)	42.2 (38.3, 46.2)	
Secondary education	38.5 (33.1, 43.9)	30.2 (26.4, 33.9)	25.1 (22.7, 27.5)	
More than secondary education	33.8 (25.4, 42.3)	12.6 (7.9, 17.1)	13.4 (10.4, 16.3)	
Religion				
Catholic	47.4 (42.3, 52.6)	36.6 (32.4, 40.8)	28.1 (21.2, 35.0)	
Islam	53.0 (47.0, 59.0)	49.6 (45.1, 54.2)	44.7 (41.4, 48.1)	
Other religion	76.5 (66.3, 86.8)	78.8 (58.3, 99.3)	27.2 (24.1, 30.4)	
Wealth quintile				
Lowest	57.5 (50.1, 64.8)	64.7 (58.9, 70.5)	54.9 (49.6, 60.2)	
Second	64.4 (58.6, 70.2)	62.0 (56.6, 67.4)	53.4 (49.7, 57.2)	
Middle	55.6 (49.1, 62.1)	48.4 (43.1, 53.6)	37.8 (34.5, 41.2)	
Fourth	43.5 (37.0, 50.0)	29.3 (25.1, 33.4)	27.3 (24.3, 30.4)	
Highest	30.6 (24.1, 37.2)	12.1 (9.3, 14.7)	12.3 (10.0, 14.7)	
Region				
North-Central	44.1 (36.4, 51.7)	49.9 (42.8, 57.0)	27.4 (21.8, 32.9)	
North-East	47.5 (35.5, 59.4)	42.7 (33.9, 51.4)	38.6 (33.1, 44.1)	
North-West	56.2 (47.9, 64.5)	58.1 (51.6, 64.7)	22.6 (18.4, 26.7)	
South-East	35.6 (28.4, 42.7)	29.9 (23.1, 36.6)	37.0 (31.7, 42.3)	
South-South	52.3 (42.3, 62.2)	26.8 (20.8, 32.7)	51.9 (46.5, 57.3)	
South-West	59.8 (45.8, 73.8)	30.1 (23.7, 36.5)	35.7 (29.3, 42.2)	
Child slept under mosquito bed net the p ous night		( , , )	()	
Yes	50.9 (44.8, 57.0)	48.1 (43.8, 52.3)	42.6 (39.3, 45.9)	
No	51.3 (46.3, 56.4)	41.0 (37.3, 44.6)	35.1 (32.3, 37.9)	

# Table 1 RDT positivity among children aged 6 to 59 months at the time of survey, by survey year

2021). Malaria prevalence was also higher among children residing in rural areas (decreasing from 55.2% [95% CI 50.4–60.1%] in 2010 to 44.2% [95% CI 41.2–47.3%] in 2021) compared to children residing in urban areas

(decreasing from 37.7% [95% CI 27.5-47.8%] in 2010 to 23.6% [95% CI 20.4-26.8\%] in 2021), and among children whose mothers or caregivers had no formal education (decreasing from 58.7% [95% CI 53.1-64.1%] in

2010 to 52.4% [95% CI 48.8–56.0%] in 2021) compared to children whose mothers had more than secondary education (decreasing from 33.8% [95% CI 25.4–42.3%] in 2010 to 13.4% [95% CI 10.4–16.3%] in 2021). The highest malaria prevalences were observed in the two poorest wealth quintiles, with the second (poorer) wealth quintile having the highest prevalence in 2010 (Table 1). Additionally, there were variations in malaria prevalence across regions, with the South-Western region having the highest prevalence in 2010 (59.8% [95% CI 45.8–73.8%]), the North-Western region in 2015 (58.1% [95% CI 51.6–64.7%]), and the South-Southern region in 2021 (51.9% [95% CI 46.5–57.3%]).

Although malaria prevalence by RDT among children aged 6–59 months decreased from 2010 to 2021, the prevalence of fever in the 2 weeks prior to the survey remained generally stable (39.2% in 2010, 42.1% 2015, and 38.2% in 2021) (Fig. 1). During this time, receipt of any anti-malarials among this population decreased from 19.6% in 2010 to 17.3% in 2015 and 10.3% in 2021 (trend test p < 0.0001), while receipt of ACT increased from 2.6% in 2010 to 6.4% in 2015 and 8.2% in 2021 (trend test p < 0.0001).

#### Care-seeking cascade for fever

Analyses of the care-seeking cascade for children who had experienced fever in the prior 2 weeks by survey year are reported in Fig. 2A and B for children with positive and negative survey RDT results. The proportion of children with a positive survey RDT and fever in the prior 2 weeks who sought care or treatment from any provider decreased from 81.0% (95% CI 74.0-88.0%) in 2010 to 61.7% (95% CI 53.2-70.4%) in 2021. Malaria testing among children with positive survey RDT and fever in the prior 2 weeks rose from 4.0% (95% CI 2.0– 5.0%) in 2010 to 24.7% (95% CI 17.2-31.1%) in 2021, while the proportion who were told they had malaria regardless of whether they reported being tested increased from 13.4% (95% CI 9.4-18.2%) in 2010 to 46.1% (95% CI 39.3-52.0%) in 2021. Receipt of any antimalarial among children with a positive survey RDT who reported fever in the prior 2 weeks declined from 46.3% (95% CI 38.1-51.6%) in 2010 to 15.4% (95% CI 9.3-22.7%) in 2021, while ACT receipt increased, from 6.2% (95% CI 3.3-10.1%) in 2010 to 12.7% (95% CI 7.3-18.3%) in 2021. The care-seeking cascade among children with negative survey RDT results with fever in the prior 2 weeks was similar to the cascade among RDTpositive children. Receipt of any anti-malarials among children with negative survey RDT results declined from 53.9% (95% CI 45.6-62.9%) in 2010 to 24.9% (95% CI 17.6-32.6%) in 2021, but across survey years, reported anti-malarial receipt in the prior 2 weeks was similar between children with negative survey RDT

results and those with positive survey RDT results.

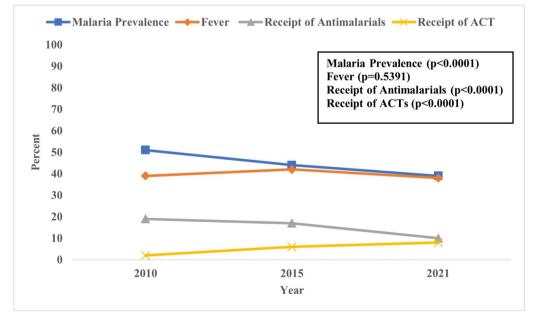


Fig. 1 Trends in malaria prevalence by RDT at the time of the survey, report of fever, receipt of anti-malarials, and receipt of ACT in the 2 weeks prior to the survey among children aged 6 to 59 months. Anti-malarials include both artemisinin-based combinations and non-artemisinin-based combinations received by the children in 2010, 2015 and 2021. The p-values reported are for tests of trend

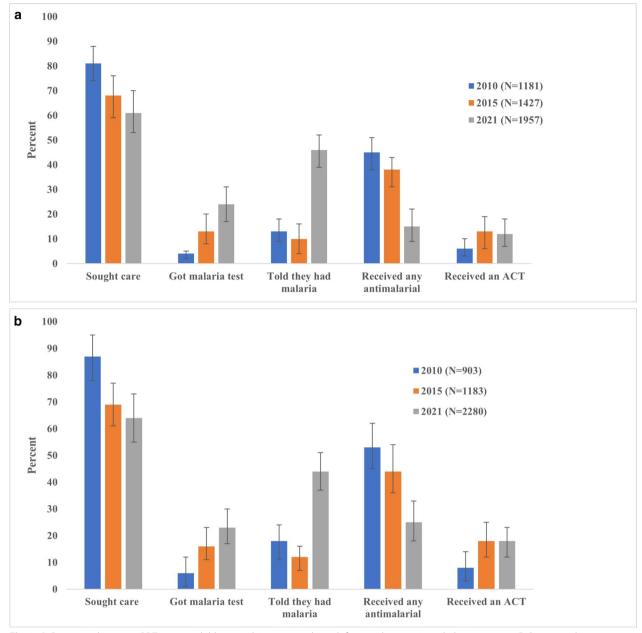


Fig. 2 A Care cascade among RDT-positive children aged 6 to 59 months with fever in the prior 2 weeks by survey year. B Care cascade among RDT-negative children aged 6 to 59 months with fever in the prior 2 weeks by survey year

# Factors associated with anti-malarial receipt among children with positive and negative survey RDTs

In all 3 survey years combined, 30.6% of children with a positive survey RDT who had experienced fever in the prior 2 weeks had received any anti-malarial. Factors associated with receipt of any anti-malarial in the prior 2 weeks are presented in Table 2. Children from house-holds in urban areas had 1.34 times higher odds of receiving any anti-malarial treatment than children from rural

areas (aOR 1.34 [95% CI 1.03–1.78]). Household wealth quintile was also significantly associated with anti-malarial receipt, with children from the fourth and fifth (least poor) wealth quintiles having 1.89 and 2.01 times higher odds of receiving any anti-malarial treatment, respectively, compared to children from the first (lowest) wealth quintile (aOR 1.89 [95% CI 1.29–2.78], aOR 2.01 [95% CI 1.18–3.43]). While children from the South-East and South-South regions had lower odds of receiving any **Table 2**Factors associated with antimalarial receipt for those with fever in the prior 2 weeks, among children aged 6 to 59 monthswith an RDT-positive result at survey, 2010- 2021

Variables	Antimalarial Receipt % (95% CI)	Unadjusted Odds Ratios (95% CI)	Adjusted Odds Ratios (95% CI)	
Child's age in months				
6–11	31.3 (24.1, 38.5)	1.00	1.00	
12–23	29.5 (25.0, 34.1)	0.92 (0.64–1.33)	1.01 (0.69–1.49)	
24–35	31.1 (26.7, 35.5)	1.02 (0.70-1.44)	1.20 (0.82-1.75)	
36–47	30.2 (25.9, 34.5)	0.95 (0.67-1.36)	1.15 (0.79–1.68)	
48–59	30.4 (26.6, 34.1)	0.97 (0.68–1.38)	1.19 (0.82–1.73)	
Child's sex				
Male	29.9 (26.8, 33.1)	1.00	1.00	
Female	30.9 (27.1, 34.7)	1.04 (0.86–1.26)	1.08 (0.89–1.31)	
Mother/caregiver's age in years				
15–20	28.6 (23.7, 33.5)	1.00	1.00	
21–29	30.2 (26.6, 33.9)	1.09 (0.85–1.39)	1.01 (0.80-1.29)	
30–39	31.2 (27.3, 35.1)	1.14 (0.87–1.48)	1.07 (0.80–1.44)	
≥40	32.1 (25.7, 38.4)	1.20 (0.86–1.67)	1.16 (0.81–1.67)	
Residence				
Rural	28.5 (25.6, 31.6)	1.00	1.00	
Urban	39.5 (32.2, 46.7)	1.62 (1.16–2.27)	1.34 (1.03–1.78)	
Mother's education				
No Education	27.7 (24.0, 31.4)	1.00	1.00	
Primary Education	29.8 (25.3, 34.3)	1.11 (0.85–1.43)	1.08 (0.80-1.44)	
Secondary Education	37.0 (32.8, 41.2)	1.52 (1.20–1.94)	1.30 (0.95–1.77)	
More than Secondary Education	48.3 (36.2, 60.4)	2.42 (1.44–4.05)	1.71 (0.93–3.17)	
Religion				
Catholic	42.0 (37.5, 46.5)	1.91 (1.48–2.46)	1.89 (1.32–2.69)	
Islam	27.5 (23.9, 31.1)	1.00	1.00	
Other Religion	27.2 (20.6, 33.9)	0.98 (0.67–1.43)	1.38 (0.89–2.13)	
Wealth quintile			, , , , , , , , , , , , , , , , , , ,	
Lowest	24.6 (20.0, 29.1)	1.00	1.00	
Second	29.2 (24.9, 33.6)	1.27 (0.97–1.66)	1.32 (0.97–1.79)	
Middle	29.8 (25.3, 34.3)	1.30 (0.94––1.80)	1.16 (0.83–1.63)	
Fourth	40.6 (34.9, 46.3)	2.10 (1.50–2.94)	1.89 (1.29–2.78)	
Highest	47.7 (39.3, 56.1)	2.79 (1.84–4.22)	2.01 (1.18–3.43)	
Geopolitical zone			( , , , , , , , , , , , , , , , , , , ,	
North-Central	33. 9 (27.2, 40.6)	1.00	1.00	
North-East	37.2 (29.6, 44.8)	1.16 (0.75–1.78)	1.78 (1.14–2.78)	
North-West	43.2 (37.8, 48.7)	1.50 (1.04–2.17)	2.01 (1.30–3.10)	
South-East	16.8 (12.6, 21.1)	0.40 (0.27–0.60)	0.50 (0.32–0.79)	
South-South	17.5 (13.2, 21.8)	0.41 (0.27–0.63)	0.57 (0.36–0.92)	
South-West	27.8 (21.1, 34.5)	0.75 (0.48–1.18)	0.73 (0.44–1.22)	
Child slept under mosquito bed net the proous night				
Yes	28.5 (25.2, 31.9)	1.00	1.00	
No	32.2 (28.3, 36.0)	1.18 (0.96–1.47)	0.89 (0.73–1.08)	
Year of survey				
2010	45.6 (39.3, 51.8)	1.00	1.00	
2015	38.3 (34.4, 42.2)	0.73 (0.54–0.99)	0.72 (0.530.97)	
2021	15.5 (12.6, 18.3)	0.22 (0.16–0.30)	0.37 (0.26–0.53)	

anti-malarial treatment (aOR 0.50 [95% CI 0.32–0.79] and aOR 0.57 [95% CI 0.36–0.92], respectively), children from the North-East and North-West regions had higher odds of receiving any anti-malarial treatment (aOR 1.78 [95% CI 1.14–2.78] and aOR 2.01 [95% CI 1.30–3.10], respectively) compared to children from the North-Central zone. Moreover, RDT-positive children in 2015 and 2021 had 0.72 [95% CI 0.53–0.97] and 0.37 [95% CI 0.26–0.53] times lower odds of receiving any anti-malarial treatment in the prior 2 weeks compared to children who tested positive in 2010. In the analyses stratified by year (Supplemental Tables 2A, 3A, and 4A), the association between wealth quintile and geopolitical zone with anti-malarial receipt was also observed across the different survey years.

Of the children with a negative survey RDT who had experienced fever in the prior 2 weeks in all three survey years combined, 36.1% had received an antimalarial. The RDT-negative children had similar factors associated with anti-malarial receipt in the prior 2 weeks as the RDT-positive children; however, for this group, the child's age and the mother's/caregiver's education level were also significantly associated with antimalarial receipt (Table 3). Children aged 24–35 months and 48-59 months had 1.44 [95% CI 1.06-1.95] and 1.51 [95% CI 1.10-2.08] times higher odds of receiving any anti-malarial treatment in the prior 2 weeks compared to younger children aged 6-11 months. Children whose mothers/caregivers had either a secondary or a higher educational qualification had 1.48 [95% CI 1.09-2.01] and 1.62 [95% CI 1.08-2.42] times higher odds of receiving any anti-malarial treatment than children whose mothers/caregivers had no educational qualification. Similar associations between child's age, wealth quintile, and geopolitical zones with anti-malarial receipt were observed across survey years (Supplemental Tables 2B, 3B, and 4B).

#### Source and type of anti-malarial medication

Among children with fever in the prior 2 weeks (with either positive or negative survey RDTs), the proportions who received any anti-malarial from public health facilities (incl. government hospitals and health centres, mobile clinics, community health workers) decreased over time, while the proportions that received any antimalarial from private health facilities (incl. private hospitals and clinics, pharmacy shops, NGO hospitals and clinics, chemist shops, itinerant drug sellers) increased. In 2010, 38.2% (95% CI 33.7–42.8%) of the children with fever in the prior 2 weeks and a positive survey RDT received anti-malarials from public health facilities, but this proportion had decreased to 19.9% (95% CI 14.2– 25.6%) in 2021. Similarly, 42.7% (95% CI 35.2–50.3%) of the children with fever in the prior 2 weeks and a negative survey RDT received anti-malarials from public health facilities in 2010, decreasing to 28.0% (95% CI 23.8–32.2%) in 2021. The proportion of children with fever in the prior 2 weeks with both positive and negative survey RDT results who received ACT from either public or private sectors increased across the years, corresponding to a decrease in the receipt of non-artemisinin-based combination anti-malarials. Nonetheless, in 2021, over 40% of children receiving non-artemisinin-based combination anti-malarials in the private sector were still prescribed chloroquine (43.2% of RDT-positive and 44.5% of RDT-negative children who received non-artemisininbased combination anti-malarials) (Tables 4 and 5).

# Discussion

This study observed a significant decline in malaria prevalence among children aged 6-59 months in Nigeria, spanning a period from 2010 before the routine availability of RDTs in 2012 to the increasing implementation of RDTs in 2015 and 2021. Consistent with other studies, the prevalence of malaria was higher among older children than infants, among children living in households in the poorest wealth quintiles, among children whose mothers or caregivers had no formal education, and among those residing in rural areas [28-30]. The study found a declining trend in receipt of any anti-malarial treatment for children with a recent history of fever, regardless of their survey RDT result. Similar proportions of children with negative survey RDTs and children with positive RDTs had received an anti-malarial for fever in the prior 2 weeks across the survey years, raising concerns about indiscriminate use of anti-malarials [31]. While previous studies have highlighted that some children testing positive for malaria do not receive appropriate treatment [16–18], this study identified similar factors associated with recent anti-malarial receipt for children with either positive or negative survey RDT results. The findings of the study also highlight an increase in the uptake of artemisinin-based combinations and a reduction in the receipt of other less effective anti-malarials.

Although this study overall suggests a significant decrease in empiric treatment for malaria in Nigeria from 2010 to 2021, the proportions of children with fever who had received anti-malarial treatment in the prior 2 weeks was similar between those with negative survey RDT results and those with positive survey RDT results across the survey years. Multiple studies in other sub-Saharan African countries have reported the use of anti-malarials among children in the absence of a positive parasitological malaria diagnosis [19, 21, 32]. The similar proportions receiving anti-malarial treatment between RDT-positive and RDT-negative

**Table 3** Factors associated with antimalarial receipt for those with fever in the prior 2 weeks, among children aged 6 to 59 monthswith an RDT-negative result at survey, 2010- 2021

Variables	Antimalarial Receipt % (95% CI)	Unadjusted Odds Ratios (95% CI)	Adjusted Odds Ratios (95% CI)	
Child's age in months				
6–11	28.8 (24.1, 33.6)	1.00	1.00	
12–23	35.2 (31.0, 39.4)	1.36 (1.01–1.81)	1.21 (0.87–1.68)	
24–35	38.1 (33.7, 42.5)	1.53 (1.16–2.01)	1.44 (1.06–1.95)	
36–47	37.5 (32.9, 42.1)	1.48 (1.10–1.98)	1.35 (0.97-1.86)	
48–59	38.9 (34.2, 43.5)	1.56 (1.18–2.09)	1.51 (1.10-2.08)	
Child's sex				
Male	36.5 (33.3, 39.7)	1.00	1.00	
Female	35.8 (32.6, 39.1)	0.98 (0.81-1.15)	0.93 (0.77-1.11)	
Mother/caregiver's age in years				
15–20	32.9 (28.6, 37.3)	1.00	1.00	
21–29	37.1 (33.7, 40.4)	1.20 (0.97–1.49)	0.99 (0.78-1.26)	
30–39	37.1 (33.6, 40.6)	1.20 (0.96–1.51)	0.99 (0.76-1.29)	
≥40	36.7 (30.1, 43.2)	1.19 (0.87–1.62)	0.99 (0.70–1.38)	
Residence				
Rural	32.7 (29.7, 35.6)	1.00	1.00	
Urban	43.6 (38.8, 48.4)	1.60 (1.25-2.02)	1.16 (0.90–1.51)	
Mother's education				
No Education	28.0 (24.3, 31.7)	1.00	1.00	
Primary Education	35.9 (30.9, 40.8)	1.44 (1.11–1.85)	1.32 (0.96–1.83)	
Secondary Education	41.5 (37.9, 45.1)	1.81 (1.44–2.26)	1.48 (1.09–2.01)	
More than Secondary Education	49.7 (42.8, 56.6)	2.51 (1.81–3.49)	1.62 (1.08–2.42)	
Religion				
Catholic	48.8 (44.4, 53.3)	2.08 (1.64–2.62)	1.41 (1.05–1.88)	
Islam	31.3 (27.9, 34.7)	1.00	1.00	
Other Religion	36.8 (31.6, 42.0)	1.27 (0.96–1.67)	1.30 (0.91–1.85)	
Wealth quintile				
Lowest	22.6 (17.6, 27.5)	1.00	1.00	
Second	30.1 (25.6, 34.6)	1.46 (1.04–2.04)	1.65 (1.17–2.34)	
Middle	30.1 (25.2, 35.0)	1.45 (1.01–2.11)	1.36 (0.93–1.98)	
Fourth	41.1 (36.1, 46.1)	2.37 (1.67–3.36)	2.10 (1.41–3.14)	
Highest	51.7 (46.6, 56.8)	3.60 (2.55–5.10)	2.87 (1.84–4.47)	
Geopolitical zone		5.00 (2.55 5.10)	2.07 (1.01 1.17)	
North-Central	41.7 (35.1, 48.3)	1.00	1.00	
North-East	39.2 (33.6, 44.8)	0.91 (0.64–1.30)	1.19 (0.82–1.73)	
North-West	48.5 (42.8, 54.1)	1.33 (0.93–1.89)	1.45 (1.02–2.11)	
South-East	20.4 (15.9, 25.0)	0.36 (0.24–0.53)	0.38 (0.25–0.56)	
South-South	27.1 (21.6, 32.6)	0.52 (0.35–0.77)	0.55 (0.36–0.84)	
South-West	40.9 (33.9, 47.9)	0.98 (0.66–1.45)	0.91 (0.61–1.36)	
Child slept under mosquito bed net the pr ous night		0.90 (0.00 1.+5)	0.91 (0.01 1.50)	
Yes	32.7 (29.3, 36.1)	1.00	1.00	
No	39.2 (36.0, 42.4)	1.32 (1.10–1.60)	0.92 (0.75–1.12)	
Year of survey				
2010	55.3 (49.7, 60.9)	1.00	1.00	
2015	44.1 (39.4, 48.6)	0.62 (0.46-0.83)	0.57 (0.43–0.77)	
2021	24.9 (21.9, 27.8)	0.26 (0.20-0.34)	0.26 (0.19–0.37)	

Antimalarials	Year of Survey					
	2010 N=547 % (95% Cl)		2015 N = 546 % (95% Cl)		2021 N=302 % (95% CI)	
	Public Sector 38.2 (33.7, 42.8)	Private Sector 61.8 (56.6, 67.1)	Public Sector 27.7 (24.8, 30.6)	Private Sector 72.3 (68.6, 76.1)	Public Sector 19.9 (14.2, 25.6)	Private Sector 80.1 (76.6, 83.6)
Any ACT	8.6 (5.4, 11.9)	11.2 (6.9, 15.5)	28.5 (23.4, 33.6)	36.5 (31.2, 41.8)	81.7 (76.8, 86.6)	63.6 (58.5, 68.8)
Non-ACT antimalarial	91.4 (87.3, 95.5)	88.8 (84.9, 92.7)	71.5 (66.8, 76.3)	63.5 (59.2, 67.9)	18.3 (13.7, 23.0)	36.4 (31.6, 41.2)
Of which:						
SP/Fansidar	28.3 (21.6, 35.0)	21.7 (16.4, 27.0)	17.6 (13.9, 21.3)	24.3 (19.4, 29.2)	27.3 (24.9, 29.8)	13.6 (9.4, 17.8)
Chloroquine	37.7 (32.5, 42.9)	42.0 (39.4, 44.6)	29.6 (25.8, 33.5)	38.2 (33.1, 43.3)	27.3 (23.5, 31.1)	43.2 (39.4, 47.1)
Amodiaquine	8.4 (4.6, 12.2)	10.0 (5.3, 14.7)	9.3 (4.7, 14.1)	4.4 (0.5, 8.4)	18.2 (14.3, 22.2)	6.8 (3.7, 9.9)
Quinine pills/injection/IV	6.3 (3.8, 8.8)	6.3 (3.1, 9.5)	2.8 ( 0.7, 5.0)	6.8 (2.7, 10.9)	-	2.3 (0.9, 3.8)
Artesunate rectal/injection/IV	2.6 (0.9, 4.3)	4.3 (0.9, 7.7)	25.0 (21.2, 28.8)	10.4 (5.2, 15.6)	18.2 (13.9, 22.6)	5.7 (3.2, 8.2)
Other antimalarial	16.7 (12.8, 20.7)	15.7 (11.3, 20.2)	15.7 (10.4, 21.1)	15.9 (11.5, 20.4)	9.0 (4.8, 13.2)	28.4 (23.3, 33.5)

Table 4 Reported antimalarial medication received in the prior 2 weeks among RDT-positive children, by survey year and source of treatment

Table 5 Reported antimalarial medication received in the prior 2 weeks among RDT-negative children, by survey year and source of treatment

Antimalarials	Year of Survey					
	2010 N=487 % (95% Cl)		2015 N = 521 % (95% Cl)		2021 N=567 % (95% Cl)	
	Public 42.7 (35.2, 50.3)	Private 57.3 (50.6, 64.0)	Public 31.5 (26.7, 36.4)	Private 68.5 (65.2, 71.8)	Public 28.0 (23.8, 32.2)	Private 72.0 (68.2, 75.9)
Any ACT	13.9 (7.1, 20.7)	15.4 (8.8, 22.0)	51.8 (47.5, 56.2)	35.6 (32.2, 39.0)	74.2 (69.7, 78.7)	70.8 (66.6, 75.1)
Non-ACT antimalarial	86.1 (79.3, 92.9)	84.6 (78.8, 90.4)	48.2 (43.8, 52.6)	64.4 (60.5, 68.4)	25.8 (21.7, 29.9)	29.2 (25.7, 32.7)
Of which:						
SP/Fansidar	23.5 (19.3, 27.8)	23.7 (18.9, 28.6)	20.2 (16.3, 24.1)	24.8 (21.6, 28.0)	17.1 (13.4, 20.9)	26.1 (22.8, 29.5)
Chloroquine	36.3 (32.5, 40.1)	36.9 (32.7, 41.1)	32.9 (28.2, 37.6)	36.1 (31.9, 40.4)	29.3 (25.1, 33.5)	44.5 (40.2, 48.8)
Amodiaquine	6.7 (2.4, 11.0)	10.6 (5.7, 15.5)	8.9 (5.2, 12.7)	4.8 (1.5, 8.1)	9.8 (6.1, 13.5)	5.0 (2.3, 7.8)
Quinine pills/injection/IV	9.5 (5.7, 13.4)	6.8 (2.9, 10.8)	3.8 (0.2, 7.4)	7.4 (3.9, 10.9)	7.3 (3.6, 11.0)	1.7 (– 1.6, 5.1)
Artesunate rectal/injection/IV	5.6 (1.9, 9.3)	4.6 (0.3, 8.9)	19.0 (14.6, 23.5)	9.6 (5.7, 13.5)	14.6 (10.4, 18.8)	5.9 (2.8, 9.1)
Other antimalarial	18.4 (13.8, 23.0)	17.4 (12.8, 22.0)	15.2 (11.5, 18.9)	17.3 (13.9, 20.7)	21.9 (18.1, 25.8)	16.8 (12.6, 21.1)

The public sector included: government hospital, government health center, government health post, mobile clinic, community health worker/fieldworker and other public sectors. The private sector included: private hospital, private clinic, pharmacy, private doctor, other private medical sector, NGO hospitals and clinics, chemist, traditional practitioner, market, itinerant drug seller and community-oriented resource person

Of the RDT-positive children who received an antimalarial in the private sector, 56% went to an informal provider (chemist, traditional practitioner, market, itinerant drug seller and community-oriented resource person) in 2010, 47% in 2015 and 59% in 2021

Of the RDT-negative children who received in the public sector, 52% went to an informal provider (chemist, traditional practitioner, market, itinerant drug seller and community-oriented resource person) in 2010, 46% in 2015 and 57% in 2021

children highlights a potential gap in adherence to WHO guidelines, which recommend that anti-malarial drugs should only be administered to patients with confirmed malaria infections [21, 32]. Indiscriminate anti-malarial use can contribute to the development of drug resistance, wastes scarce health resources, and may overlook the actual cause of fever in these children, delaying appropriate treatment for non-malaria febrile illnesses [21].

Interestingly, among the RDT-positive children who had experienced fever in the 2 weeks prior to the survey, only about 30% received an anti-malarial, predominantly those from wealthier households residing in urban areas, which are generally considered at lower risk for malaria. The observed association of anti-malarial receipt among RDT-positive children with urban residence and higher socioeconomic status indicates underlying disparities in access to anti-malarial treatment and care. Moreover, children with a positive survey RDT had lower odds of receiving any anti-malarial in the years 2015 and 2021 compared to 2010 (see Table 2). These findings may reflect broader issues such as reduced healthcare engagement or challenges in accessing diagnostics and treatments, like RDTs or ACT, and points to the need for focused efforts to ensure that all children have equal access to the necessary malaria care.

The study found that the child's age, mother's education, and belonging to a wealthier household were significant factors associated with anti-malarial receipt among RDT-negative children, as well as RDT-positive children. This is consistent with findings of a previous study conducted in Uganda [31], which showed that certain sociodemographic factors including the caregiver's age, educational status, and the child's age were independently associated with anti-malarial use among children with febrile illnesses. For example, mothers with higher education may be eager to seek medical care for their children, and their children may be more likely to receive anti-malarial treatment, regardless of whether malaria diagnosis is confirmed or not. Wealthier households may have greater access to healthcare services, increasing the probability of seeking treatment for febrile illnesses and receiving anti-malarial drugs, regardless of a definitive malaria diagnosis [31, 33].

The study also observed a shift in the source of antimalarial treatment for children under the age of 5 from public toward private health care. In a study in South Africa, Govender et al. [34] found that the increased preference for private health facilities can be attributed to their higher accessibility and convenience, particularly in urban areas, where they offer shorter waiting times and more flexible operating hours. Caregivers may also choose private facilities due to the perceived higher quality of care, personalized attention, and patient-centred approach they offer, which may be particularly appealing for the treatment of young children. Additionally, the availability of a broader range of anti-malarial treatment options and specific medications in private facilities may further influence caregivers' decisions on where to seek care for their children [34]. However, this shift may be cause for concern, as studies have shown relatively low utilization of RDTs and persistent availability of antimalarial monotherapies in the private sector in Nigeria [33, 35, 36]. In the private sector, patients may be reluctant to bear the costs of both diagnostic testing and treatment, potentially hindering the utilization of both RDTs and ACT, as found in a study conducted in Kenya [37].

In addition to the observed shift towards private healthcare facilities as the preferred source of treatment for children, a greater proportion of RDT-positive and RDT-negative children who got an anti-malarial received ACT in 2021 compared to prior years. This trend underscores the expanding use of ACT, aligning with global malaria treatment guidelines, despite Nigeria facing challenges such as accessibility, awareness, and supply chain issues. However, the utilization of ACT, while on the rise, remains suboptimal, suggesting the need for ongoing efforts to ensure that effective malaria treatments are accessible to all affected children [14, 33]. This study also found some persistent cases of chloroquine prescription in the private sector in 2021, highlighting the importance of continuous monitoring and education to promote the use of first line anti-malarials [33]. Sustaining and enhancing the effectiveness of the current recommended malaria case management in Nigeria will depend on continued collaboration among stakeholders such as government health departments, healthcare providers, NGOs, private health facilities, community leaders and traditional healers, patent medicine vendors, and community members.

# **Strengths and limitations**

The strengths of this study include its large nationally representative sample size, allowing for generalizability of the findings to the Nigerian population. Data from 3 NMIS surveys conducted over the span of more than a decade allowed us to identify trends and assess changes over time in malaria prevalence and anti-malarial receipt. Comparison of children with positive and negative survey RDT results provided valuable insight into factors contributing to appropriate or inappropriate anti-malarial receipt.

However, this study had several limitations. Prior studies have indicated that surveys such as the NMIS can have low specificity for positive test recall and low sensitivity for caregivers' recall of ACT given to their children [38]. This study relied on self-reported data from the children's caregivers, which may be affected by social desirability biases. Furthermore, misclassification of survey RDT results is possible. The ability of RDTs to detect malaria antigen at lower concentrations can vary substantially [39], potentially underestimating malaria prevalence in NMIS data. This study assumed that children with negative RDT results at survey had not had malaria in the prior 2 weeks, since HRP2-based RDTs used in the survey are usually positive for several weeks due to the slow clearance of the HRP2 antigen from the blood [24, 25]. However, it is possible that a small proportion of RDT-negative children who had fever in the prior 2 weeks had malaria but experienced rapid HRP2

clearance. This study analyzed data from three separate nationally representative surveys conducted in 2010, 2015, and 2021. As malaria diagnosis and treatment policies evolved, survey respondents may have become more knowledgeable about specific antimalarial drugs and the routine practice of diagnostic confirmation before treatment at health facilities. However, it is unlikely that these changes influenced the relationship between reported antimalarial drug use and the results of the malaria diagnostic tests conducted during the survey visits. Finally, this study did not assess potential barriers to RDT utilization such as regional stockouts of RDTs and artemisininbased combination anti-malarials or inadequate provider training and supervision.

# Conclusion

Despite declining transmission and prevalence, malaria continues to have a major impact on young children aged 6 to 59 months in Nigeria. From 2010, when availability of malaria diagnostic testing and artemisinin-based combinations were limited, to their increasing implementation in 2015 and 2021, the proportion of febrile children getting tested for malaria and receiving appropriate treatment increased, albeit insufficiently. This study found that similar proportions of children with negative and positive RDTs at the time of the survey had received an anti-malarial for fever in the prior 2 weeks across the survey years, indicating both gaps in malaria care and persistent challenges with indiscriminate anti-malarial use. Additional efforts are needed, both in the public and private sectors, to educate and motivate providers to adhere to testing and treatment recommendations.

#### Supplementary Information

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Supplementary Material 1

#### Author contributions

JT conceived the idea. SCO, JT, SPK, and KB conceptualized and designed the analysis. SCO conducted the analysis and wrote the first draft of the manuscript. JAD and RI provided critical feedback on the type of analysis. All authors reviewed and approved the final draft of the manuscript.

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#### Availability of data and materials

NMIS datasets are available on request from the DHS Program website (https://www.dhsprogram.com/data/available-datasets.cfm).

#### Declarations

#### Ethics approval and consent to participate

The Demographic and Health Survey anonymized all data before making it publicly accessible. The ICF IRB reviewed and approved the Nigeria Malaria

Indicator Surveys for 2010, 2015, and 2021. The ICF IRBs adhered to the United States Department of Health and Human Services regulations for the protection of human research subjects (45 CFR 46). Informed verbal consent was obtained from all participants, and for minors, consent was provided by their parents or guardians. The analysis was also determined to be not Human Subjects Research by the UAB Institutional Review Board (IRB-300010792).

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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