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Malaria epidemics and its drivers in Uganda in 2022

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Abstract

Background In Uganda, malaria is a year-round health threat, with transmission intensity varying across regions. Despite ongoing intensified interventions, an unprecedented malaria resurgence in early 2022 affected several districts, prompting a swift response from the National Malaria Control Division (NMCD). This study aims to assess the scale and underlying causes of the epidemics, quantify the excess cases and deaths, and propose targeted prevention and response strategies.

Methods District Health Information System (DHIS2) data from 2017 to 2022 were analysed. A 75th percentile threshold from 2017 to 2021 was used to define true malaria epidemics and compare them to the suspected 2022 epidemic. Excess cases, admissions, and deaths were quantified using area under the curve (AUC) calculations. The level of epidemics was compared across districts with Indoor Residual Spraying (IRS) and Integrated Community Case Management (iCCM) interventions. Precipitation data from multiple sources were used to evaluate rainfall patterns and their impact on malaria epidemics.

Results Malaria cases were lowest in 2018 but rose by 31% in 2022 compared to the 2017–2021 3rd quartile. Sixty-four of 146 districts experienced epidemics, with 4 facing persistent epidemics year-round. The 2022 epidemic accounted for 3,379,309 (95% CI 1,553,714, 5,339,709) total excess outpatient malaria cases (confirmed and presumed), 3,018,920 (95% CI 1,321,951, 4,661,201) excess confirmed cases, 149,789 (95% CI 66,029, 235,743) excess inpatient cases. Paradoxically, more epidemics occurred in IRS and iCCM districts. Precipitation patterns were consistent across years and were insignificantly correlated with the 2022 epidemic. Provinces with bimodal rainfall patterns were more prone to epidemics, while unimodal regions had fewer epidemics but higher incidence rates. Rainfall lagged by two months (Lag 2) significantly increased malaria incidence ($p < 0.01$), with each millimetre of rainfall two months prior associated with 13.4 additional malaria cases.

Conclusion The 2022 malaria epidemic affected 64 districts, with over 3.3 million excess cases and nearly 150,000 excess admissions. Gaps in IRS, iCCM, and intervention coverage, along with minimal rainfall correlation and high vulnerability in bimodal regions, highlight the need for better surveillance, sustainable funding, and tailored responses. While climate was not the main driver, programmatic deficiencies, vector composition shift, reduced efficacy of insecticides, coverage and effectiveness of the interventions likely fueled the epidemic. Strengthening epidemic preparedness, response, and investment will be crucial to preventing future outbreaks and achieving long-term malaria control in Uganda.

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Background

Uganda consists of 146 administrative districts with an approximate population of 48.6 million in 2022 [1]. Malaria transmission occurs year-round and varies in intensity and parasite prevalence among regions characterized by bimodal and unimodal rainy seasons. Over a period of continuous investment and intervention efforts, the prevalence of parasites in the country has significantly decreased. The national average parasite prevalence dropped from 42% in 2009 [2] to 19% in 2014 [3], and further down to 9% in 2019 [4]. However, variations exist across different regions. The Karamoja region has the highest prevalence at 34.3%, followed by West Nile at 21.8%, and Busoga at 21.1%. Conversely, Kampala exhibits the lowest prevalence at just 0.2% [5].

The main malaria vectors in Uganda are *Anopheles gambiae* sensu stricto (s.s.), *Anopheles funestus*, and *Anopheles arabiensis*. The majority of reported infections confirmed with Rapid Diagnostic Tests (RDT) and microscopy are caused by *Plasmodium falciparum* (98%), while a small portion involves mixed infections with *Plasmodium ovale* and *Plasmodium malariae*. Molecular studies showed increased non-falciparum and mixed malaria infections, especially in those over 5 years of age [6]. The Uganda Malaria Reduction and Strategic Plans (UMRSP) 2014–2020 and 2021–2025, outline a mix of interventions for maximum impact across various epidemiological settings.

Main vector control interventions included the distribution of Long-Lasting Insecticidal Nets (LLINs) and Indoor Residual Spraying (IRS). The government and its partners distributed 28.4 million LLINs from November 2020 to March 2021, achieving a 90% administrative coverage. No recent household surveys have been available since 2019 to inform latest community-level LLIN ownership. Campaigns targeted both urban and rural areas and were supplemented by continuous distribution through Antenatal care (ANC), Expanded Programme for Immunization (EPI), and schools. A post-campaign study found that 93.4% of households owned at least one LLIN, with 56.8% of households had one LLIN for two persons, and 71% of the residents sleeping under LLIN the previous night [7].

In Uganda's malaria reduction strategic plan, IRS complements LLINs by targeting high-burden districts. Initially introduced in high-transmission areas, IRS from targeted districts is gradually phased out as malaria prevalence decreases, while LLINs continue to provide protection. Because of funding issues, the number of IRS/districts fluctuated between 10 and 16 districts during 2009–2022. IRS was initiated in 10 districts in the North, funded by the President's Malaria Initiative (PMI), from 2009 to 2014 but was interrupted by the end of 2014. During 2015–2016, IRS was shifted to a new set of 16 districts in the central east. However, this was later scaled down to 14 districts in 2020. Throughout 2015–2022, IRS was consistently implemented in only 10 districts (Pallisa, Kibuku, Butebo, Budaka, Butaleja, Tororo, Bugiri, Namutumba, Serere and Lira), funded by PMI (Fig. 1). In all districts where IRS was interrupted, as well as in the rest of the country, LLINs remained the primary vector control intervention.

IRS implementation was guided by routine insecticide monitoring in sentinel sites. Studies from 2009 revealed high pyrethroid resistance [8], leading to insecticide changes. Initially, carbamates like Bendiocarb replaced pyrethroids, followed by organophosphates like Actellic in 2017, and later neonicotinoids like Sumishield and Fludora Fusion (from March 2020 to the end of 2022). Studies reveal a significant shift in vector species composition and biting behavior over time, notably from *An. gambiae s.s.* to *An. arabiensis*, with regional variations [9, 10].

On case management, Rapid Diagnostic Test (RDT) is the main diagnostic tool (> 90%) while microscopy is mainly used in the major hospitals. Artemether-lumefantrine (AL) is the primary treatment for uncomplicated malaria, while dihydroartemisinin-piperaquine (DHPQ) serves as the second-line option. Severe malaria is treated with injectable artesunate, with quinine i.v. as an alternative when artesunate is unavailable. Free Artemisinin-based Combination Therapy (ACT) is accessible to public and private not-for-profit health facilities via the government's Central Medical Stores. Integrated Community Case Management (iCCM), which started in 2013 and was later scaled up, is now deployed in 72 districts with partner support to provide malaria treatment at the community level for children under five years (Fig. 1). Additionally, iCCM is offers treatment for diarrhoea and pneumonia. However, sustaining the full iCCM package has been financially challenging. As per the Malaria Indicator Survey (MIS 2019), 26% of children under 5 experienced fever in the two weeks before the survey. Among these children, 51% who underwent a diagnostic test accessed ACT on the same day, leaving around 43% of those with fever not seeking treatment on the same or following day [4], highlighting the necessity for enhanced awareness and prompt treatment-seeking behaviour for malaria in Uganda.

In early 2022, resurgence of malaria was reported in several Ugandan districts promoting the Ministry of Health National Malaria Control Division (NMCD) to respond. The objective of this study is to assess the extent and causes of the epidemics, quantify the additional

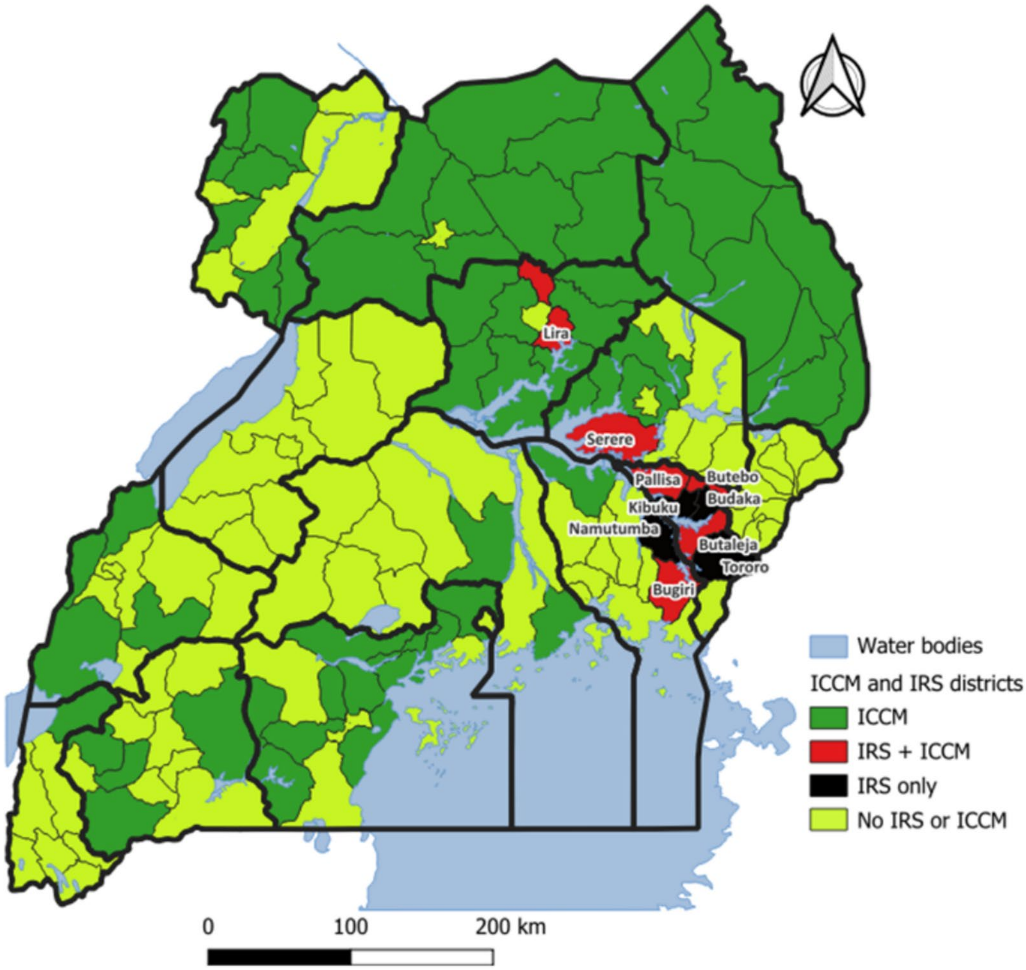

Fig. 1 Map of Uganda showing 2022 and former IRS and iCCM-districts

malaria cases and deaths linked to them, and propose impactful prevention and response strategies.

Methods

For the investigation of suspected epidemics, monthly district-level District Health Information System (DHIS2) data from January 2017 to December 2022 were employed as the epidemiological dataset. The health facility data in DHIS2 for the study years was cleaned, validated, and aggregated by district. In addition to routine data quality audits, data was validated using standard rules to identify and flag inconsistencies. Outliers were detected using the mean ± 5 standard deviations (SD) method, and corrections were made by cross-referencing source documents at health facility. The study presented monthly trends for key malaria indicators across districts from 2017 to 2022. These indicators included outpatient malaria cases (both confirmed and presumed), confirmed cases, test positivity rates for RDT and microscopy, inpatient (admitted) malaria cases, and malaria-related deaths. Malaria-related deaths are reported into DHIS2 by health facilities as deaths in patients with a confirmed severe malaria diagnosis (with RDT or microscopy) as the primary cause of admission. These deaths are verified weekly through calls by national officers from the Health Information Management System (HMIS) to the respective facilities. However, reported deaths may not reflect the true burden, as some facilities fail to report due to poor adherence to surveillance guidelines (e.g., families removing bodies or terminally ill patients before death for cultural or cost reasons, leading to missed registry entries).

The incidence of malaria cases and incidence of inpatient malaria cases for each district were calculated as follows:

- Incidence of malaria cases = total number of outpatient malaria cases (confirmed and presumed) divided by the district population.

- Incidence of inpatient malaria cases = total number of admitted malaria cases (inpatients) divided by the district population.

Additionally, trends in non-malaria cases and non-malaria deaths were examined to ensure that changes in malaria trends were not influenced by other health system factors affecting all diseases. The calculations were as follows:

- Non-malaria outpatient cases = total outpatient cases−malaria cases
- Non-malaria inpatient cases = total inpatient cases−inpatient malaria cases
- Non-malaria deaths = total deaths−malaria deaths

The Third Quartile (75th percentile) threshold method, applied to data from 2017 to 2021, was used to establish a cutoff line for defining true malaria epidemics in Uganda and to compare these with the suspected epidemic of 2022. A year with suspected epidemic with exceptionally higher number of malaria cases were removed from the threshold calculation. The third quartile was favored over other thresholds to classify districts as "epidemic" because it accommodates extreme values and normal seasonality without misclassifying them as an epidemic. Besides, using the 3rd quartile method for outbreak detection is recommended in Uganda [11, 12], where endemicity levels vary widely, very low to low, moderate, and high transmission, with significant heterogeneity across regions. An increase in both outpatient and inpatient malaria cases was identified as a reliable epidemic indicator due to improved diagnostic confirmation during the study period.

The analysis focused on three key criteria:

i) Intervention-based comparison: This included contrasting "IRS districts" (those that received IRS interventions between 2019 and 2022) with "non-IRS districts," as well as comparing "iCCM districts" with "non-iCCM districts."
ii) Age-group variations: Age groups were categorized as under 5 years and 5 years and above.
iii) Area under the curve (AUC): The AUC was calculated for the suspected epidemic months of 2022 and the 75th-percentile threshold (2017–2021) to estimate the excess cases, admissions, and deaths attributed to the epidemic. The difference between the cumulative AUC for 2022 and the cumulative AUC for the 3rd quartile threshold was used to quantify the excess cases and deaths during the epidemic year. This analysis assumes that, in the absence of an epidemic, cases would have remained below the 75th-percentile threshold. The data was analysed using R statistical software [13], and the 95% confidence interval for the annual AUC estimates of excess malaria cases and deaths due to the 2022 epidemic was determined using the bootstrap method [14, 15].

The percentage of relative change was determined by calculating the difference between the annual average of the baseline period (2017–2021) and the values in 2022, then dividing that difference by the average of the baseline period. Mathematically, for all indicators, the relative change was calculated as follows:

$$Relative\ Change = 100 \times \frac{B_{avg\ 17-21} - B_{22}}{B_{avg\ 17-21}}$$

where $B_{avg 17-21}$ denotes for (2017–2021). B_{22} denotes for (2022).

The Wilcoxon rank-sum exact statistical test [16] was used to assess whether there is a significant difference between the third quartile of the data from 2017 to 2021 and the year 2022. The test was performed on all malaria indicators, comparing IRS versus non-IRS districts, as well as ICCM versus non-ICCM districts.

WorldPop [17] were used to extract population data and calculate incidence Health boundary data from WHO Geographical Information Systems (GIS) Centre hub [18] were used for national, provincial and district-level boundaries in Uganda.

Meteorological data, with rainfall as the principal predictor for malaria transmission in the context of Uganda, was collected from multiple sources. On-site precipitation data was obtained from the Uganda National Meteorological Authority (UNMA) for eight regions. Additionally, precipitation datasets were sourced from the Climate Hazards Group InfraRed Precipitation Station (CHIRPS) monthly dataset [19], a globally recognized source that combines satellite imagery and ground station data for high-resolution rainfall estimates.

Meteorological data, primarily rainfall, was used as the main predictor for malaria transmission, sourced from various providers. On-site rainfall data was obtained from the Uganda National Meteorological Authority (UNMA) for eight regions, while the CHIRPS datasets, combining satellite and ground station data, were used for high-resolution rainfall estimates. Spatial–temporal rainfall data were extracted and aggregated at the regional and district levels using R packages [20]. Correlation analysis [21] between on-site precipitation data and CHIRPS data were conducted to verify the accuracy of the CHIRPS dataset.

Medium rainfall for each district was calculated, and Harmonic analysis [22] was used to identify seasonality patterns by decomposing the sinusoidal components. A cutoff of 1.0 was applied to distinguish between unimodal and bimodal seasonal patterns. A ratio of second harmonic amplitude to the first harmonic amplitude above 1.0 indicated a bimodal pattern, with two significant peaks, while a ratio of 1.0 or below indicated a unimodal pattern with a single peak within the annual cycle. This threshold provided a clear criterion for categorizing seasonal behaviors. QGIS [23] was used for mapping and geospatial analysis of rainfall's impact on malaria epidemics. Interrupted Time Series analysis was conducted to evaluate whether rainfall in 2022 influenced malaria incidence differently compared to 2017–2021, while accounting for seasonality.

Ethical considerations

Ethical approval was not required for this study, as it relies on secondary data obtained from the Uganda Ministry of Health's Health Information Data System. The data used in this analysis is part of ongoing malaria program activities that fall under the Ministry's purview. The Ministry of Health has provided explicit consent for the use and analysis of this data for research purposes, ensuring compliance with relevant regulations and ethical standards. This study is aligned with the Ministry's goals of enhancing public health understanding and improving evidence-based malaria control strategies in Uganda.

Results

National level trends of malaria cases and deaths

In 2022, Uganda reported a total of 15,646,203 outpatient malaria cases (confirmed and presumed), including 14,162,936 confirmed cases, reflecting an 90.5% confirmation rate. Additionally, there were 821,343 inpatient malaria cases, corresponding to a 5% admission rate among outpatient cases, and 3389 malaria-related deaths, resulting in a case fatality rate of 0.4% among admitted patients. Figure 2 shows that total and confirmed outpatient malaria cases were lowest in 2018 but increased by 31% in 2022 compared to the 2017–2021 average. The pattern of total malaria cases (confirmed and probable) and confirmed cases remained consistent, with a

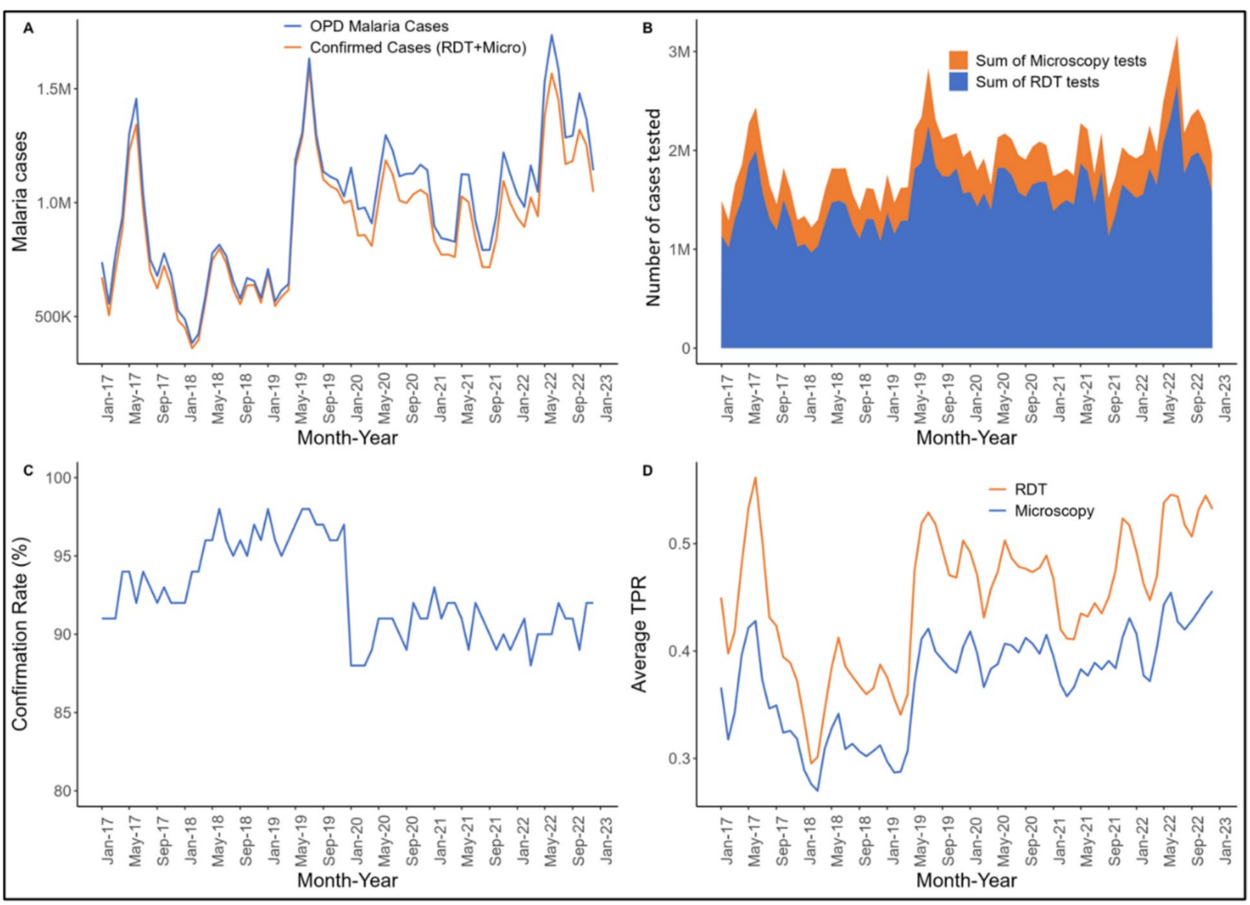

Fig. 2 Trends in outpatient Malaria Cases, Testing, and Positivity Rates Across All Ages, Uganda 2017–2022

high confirmation rate peaking in 2019. Monthly trends consistently showed seasonality from May to September each year.

In Fig. 1 and other relevant figures, the labelling for malaria indicators is described as:

OPD: Outpatient (department).

IPD: Inpatient(department).

OPD_Mal:Total outpatient malaria cases (confirmed and presumed),

All_Pos: Total confirmed cases in All Ages (with RDT or microscopy),

Sum_Mic_test: Total tested with microscopy,

Sum_RDT_test: Total tested with RDT,

Average_TPR: Average test positivity rate using microscopy or RDT.

OPD Non-malaria: Non malaria outpatient cases (all OPD cases except malaria).

IPD malaria: Inpatient malaria cases.

IPD Non-malaria: Inpatient non-malaria cases (all inpatients except malaria).

Non-Malaria: Non-malaria cases, deaths.

Non-IRS = Non-IRS district (districts with no IRS).

Non-iCCM = Non-iCCM (districts with no iCCM).

Figure 3 shows an increase in total malaria cases (both total and confirmed outpatient cases), while non-malaria cases, including inpatients, either remained constant or increased. The trends of total malaria cases (confirmed and probable) increased, while non-malaria outpatient consultations remained stable (Fig. 3a). Both confirmed outpatient malaria cases and non-malaria outpatient cases increased, when the probable cases were removed from the total malaria cases (Fig. 3b). Percentage of confirmed cases decreased to nearly 90% as of January 2020, following the emergence of Covid-19 and decline in parasitological testing. Inpatient malaria cases rose, while total non-malaria inpatient cases remained constant (Fig. 3c). The trend for malaria deaths fluctuated, while non-malaria deaths increased (Fig. 3d).

In Fig. 4, incidence of malaria cases (Fig. 4a) was higher in the northern and northeastern parts of Uganda. Similarly, the high incidence of inpatient cases (Fig. 4b) was higher in the northern and northeastern regions.

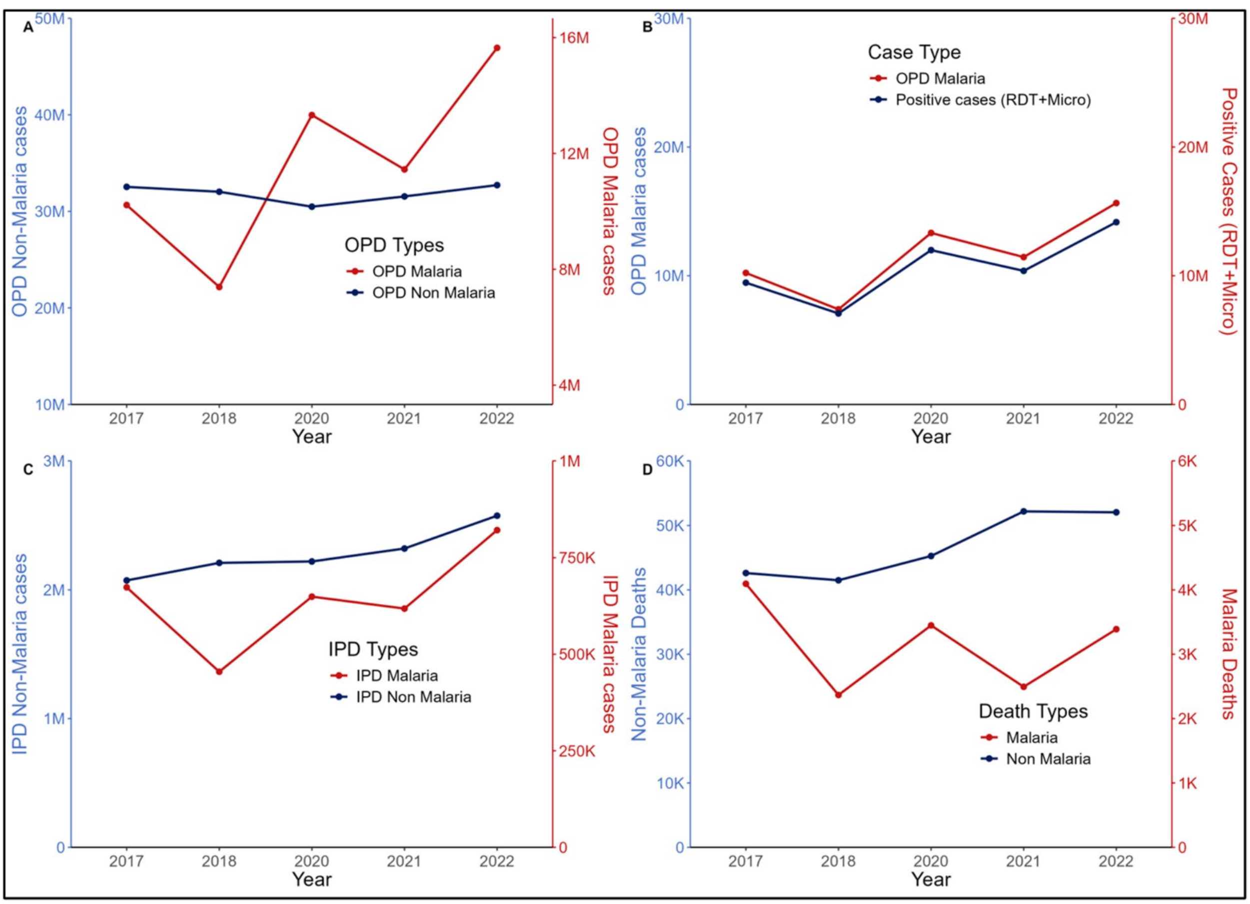

Fig. 3 Trends in Malaria Cases, Inpatients, and Deaths vs. Non-Malaria Metrics, Uganda 2017–2022

National trends against epidemic thresholds

Out of 146 districts, 64 experienced malaria epidemics in 2022, with confirmed cases exceeding the 3rd quartile for at least one month compared to 2017–2021 data. In contrast, 82 districts remained within the normal threshold. The average duration of epidemics in the 64 affected districts was 5.6 months (median = 5) (Table 1), with four districts experiencing epidemics throughout the entire year. Trends in outpatient and inpatient malaria cases consistently surpassed the 3rd quartile of 2017–2021, confirming significant national epidemics in 2022 across all age groups (Fig. 5a, b). Inpatient malaria cases were more prominent in those aged 5 and older than in children under 5 (Fig. 5b). Malaria-related deaths in 2022 remained within or below the threshold, although slightly higher in children under 5 during the first quarter (Fig. 5c). The average test positivity rate in all ages in 2022 increased to 50%, compared to the third quartile threshold of 45%, representing a net increase of 5% (Fig. 5d).

The incidence of outpatient malaria cases and inpatient or admissions per 1,000 population showed similar epidemic patterns. Among children under five years old, outpatient incidence was at least 10 cases per 1000 each month, consistently higher than in those over five years old. Similarly, the incidence of inpatient (admissions) was nearly three times higher in children under five compared to those over five years old (Fig. 5e).

Figure 6a shows the district-level relative difference (%) in the absolute number of confirmed malaria cases in 2022 compared to the 3rd quartile of 2017–2021. Districts marked in red experienced a significant percentage increase in cases due to the epidemic. Similarly, Fig. 6b highlights the district-level relative difference (%) in the incidence of confirmed malaria cases per 1000 population in 2022 compared to the 3rd quartile of 2017–2021. Districts in red clearly exhibited a higher incidence of cases in 2022 due to the epidemic (Fig. 6b) .

The excess cases and admissions due to the epidemic in 2022 are given in Table 2. Comparing 2022 to the 3rd quartile (2017–2021) using national area under the curve

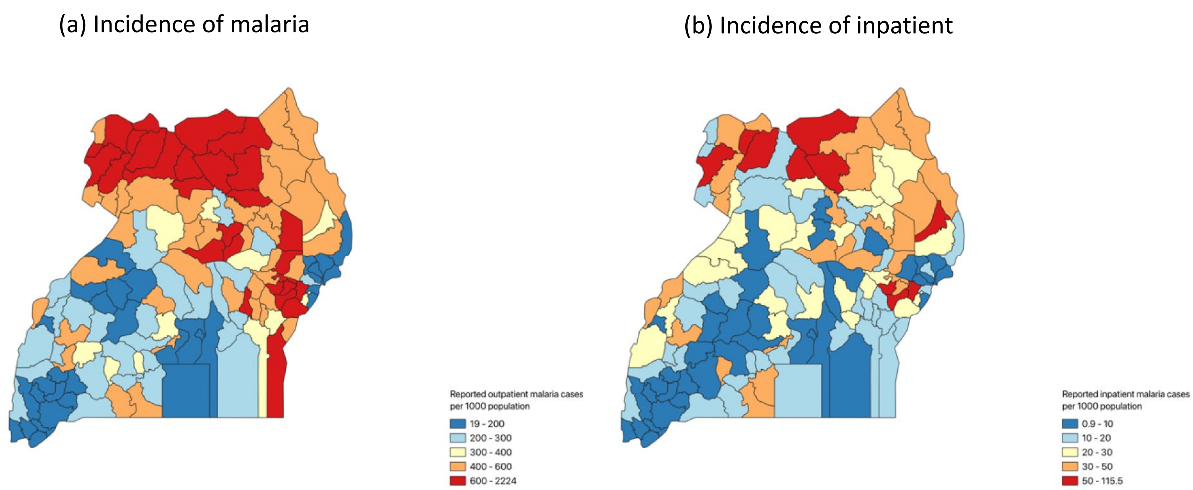

Fig. 4 Outpatient malaria cases per 1000 population and inpatient malaria cases per 1000 population, 2022

Table 1 Number of districts experiencing epidemics and corresponding number of epidemic months in 2022

Number of epidemic months	0	1	2	3	4	5	6	7	8	9	10	11	12	Total with epidemic	Total no of districts
Number of districts	82	7	8	7	6	8	4	4	4	3	6	3	4	64	146

(See figure on next page.)

Fig. 5 **a** Monthly outpatient malaria cases in 2022 vs. 2017–2021 3rd quartile thresholds* by age group, Uganda (*2019 values removed). **b** Monthly inpatient malaria cases in 2022 vs. 2017–2021 3rd quartile thresholds* by age group, Uganda (*2019 values removed). **c** Monthly malaria deaths in 2022 vs. 2017–2021 3rd quartile thresholds* by age group, Uganda (*2019 values removed). **d** Monthly Test Positivity Rate (TPR) in 2022 vs. 2017–2021 3rd quartile thresholds* by age group, Uganda (*2019 values removed). **e** Monthly outpatient malaria and inpatient incidence in 2022 vs. 2017–2021 3rd quartile thresholds by age group, Uganda

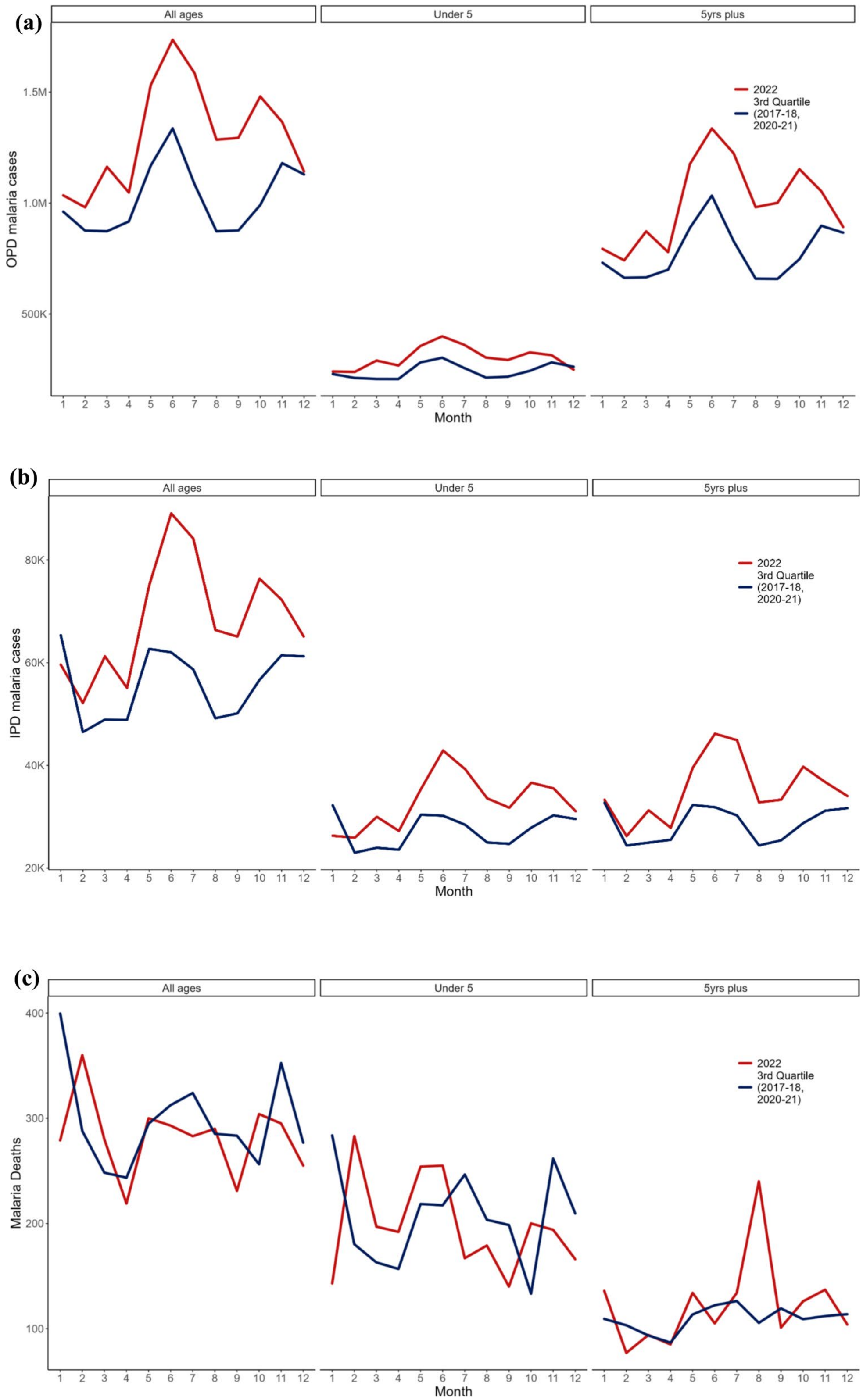

Fig. 5 (See legend on previous page.)

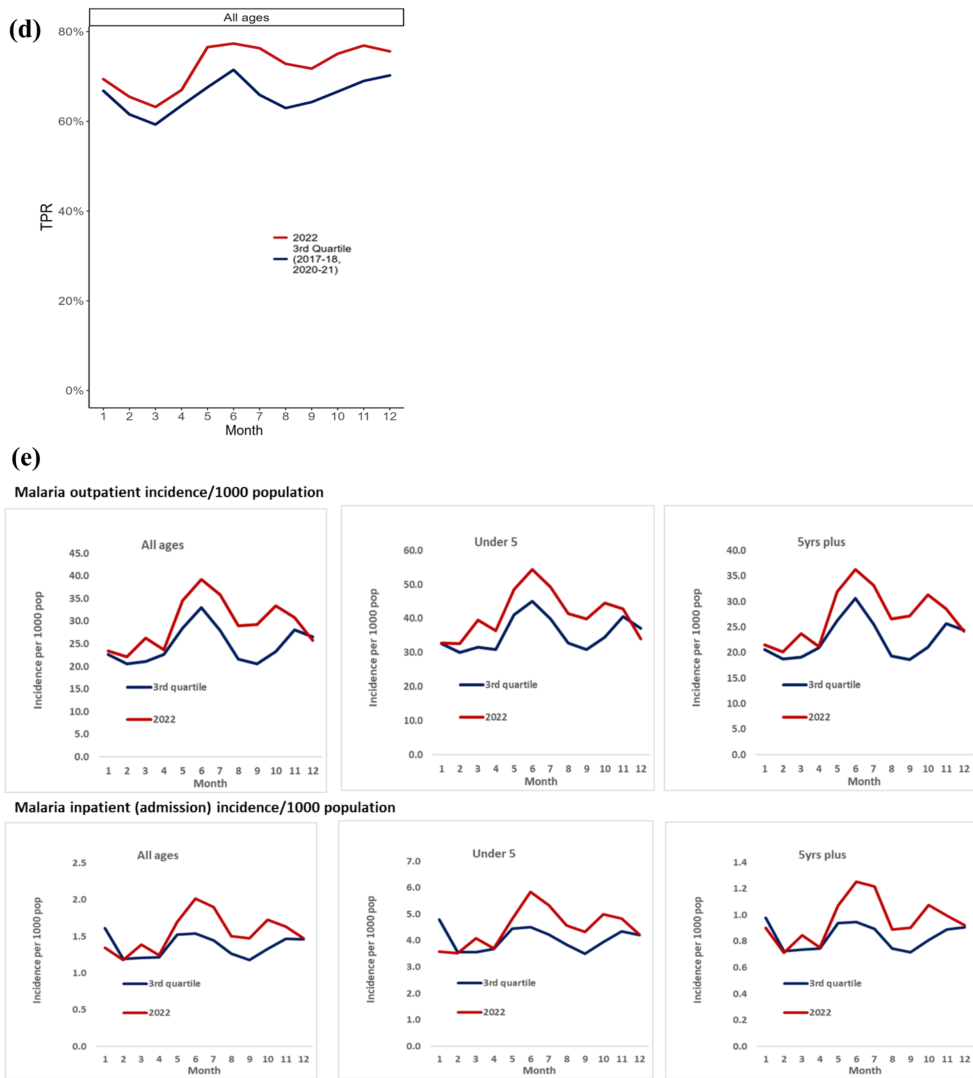

Fig. 5 continued

(AUC) analysis, there was an excess of 3,379,309 (95% CI 1,553,714, 5,339,709) total outpatient malaria cases (confirmed and presumed), and 3,018,920 (95% CI 1,321,951, 4,661,201) excess confirmed cases. Excess inpatient cases were 149,789 (95% CI 66,029, 235,743). Notably, malaria-related deaths in 2022 were reduced by 210 (95% CI − 578.45, 108.05) compared to the 3rd quartile baseline. June recorded the highest excess across all indicators (except for malaria deaths), followed by July.

Trends of malaria in IRS and non-IRS districts, and iCCM and non-iCCM

Figures 7, 8, 9, 10 visually depict the trends of malaria indicators in IRS vs. non-IRS and iCCM vs. non-iCCM districts. These visual observations are confirmed by the statistical significance results presented in Tables 3 and 4.

The test positivity rate (TPR) in 2022 consistently exceeded the threshold throughout the year. Paradoxically, TPR was higher in IRS and iCCM districts (Fig. 9), compared to the Non-IRS and Non-iCCM districts respectively, despite these interventions being implemented in the designated districts during the epidemic year.

Similar to the TPR, IRS districts paradoxically experienced a much higher increase in outpatient malaria cases in 2022—at least twice the threshold—compared to non-IRS districts. Likewise, iCCM districts recorded

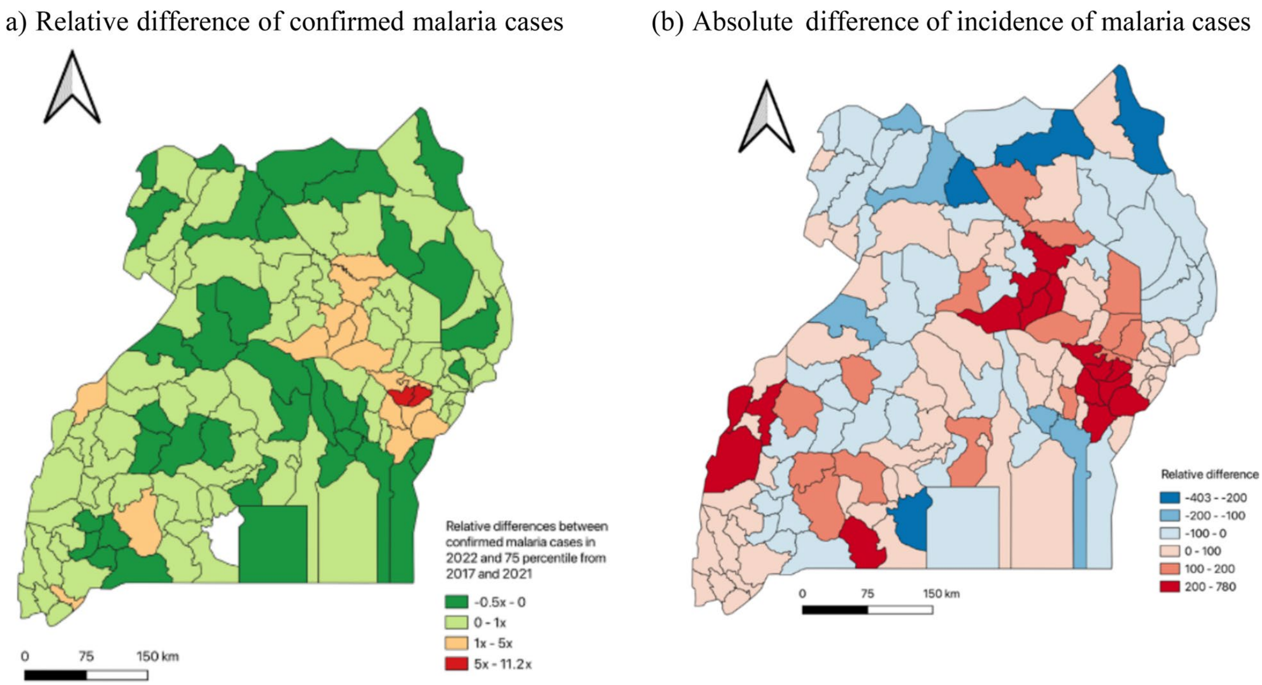

Fig. 6 District-level differences in malaria cases and incidence: 2022 vs. 2017–2021 3rd quartile thresholds. **a** Relative difference of confirmed malaria cases **b** Absolute difference of incidence of malaria cases

Table 2 Monthly and cumulative malaria indicator excess in 2022 attributed to epidemics compared to the 3rd quartile using AUC

Month	Outpatient		Confirmed cases		Inpatient		Deaths	
	Year 2022	3rd Quartile (2017–2021)	Year 2022	3rd Quartile (2017–2021)	Year 2022	3rd Quartile (2017–2021)	Year 2022	3rd Quartile (2017–2021)
1	1,034,815	961,260	934,173	876,199	59,583	65,340	320	400
2	981,107	875,683	893,852	792,066	52,154	46,488	320	288
3	1,163,182	873,092	1,023,479	794,085	61,232	48,913	250	248
4	1,047,346	917,119	940,008	829,005	55,071	48,852	260	244
5	1,531,759	1,169,054	1,381,510	1,077,382	74,978	62,679	297	295
6	1,735,611	1,336,424	1,567,098	1,224,983	89,052	62,003	288	313
7	1,585,215	1,084,731	1,451,242	1,008,437	84,151	58,672	287	324
8	1,285,450	872,978	1,168,992	790,443	66,355	49,167	261	285
9	1,294,108	876,324	1,183,020	787,047	65,072	50,128	268	284
10	1,480,166	991,277	1,320,045	891,139	76,353	56,646	268	256
11	1,365,372	1,179,974	1,252,337	1,065,919	72,248	61,448	268	353
12	1,142,072	1,128,980	1,047,180	1,007,313	65,094	61,219	268	277
Total	15,646,203	12,266,894	14,162,936	11,144,016	821,343	671,554	3355	3565
Difference (CI)	3,379,309 (1,553,714, 5,339,709)		3,018,920 (1,321,951, 4,661,201)		149,789 (66,029, 235,743)		− 210 − 578.45, 108.05)	

a higher number of outpatient cases than non-iCCM districts (Fig. 8).

The trends of inpatient malaria cases in both IRS and non-IRS districts were significantly more pronounced in 2022 compared to the thresholds. Paradoxically, iCCM districts exhibited a much higher increase in inpatient malaria cases than non-iCCM districts (Fig. 9).

Unlike outpatient and inpatient malaria cases, malaria-related deaths in 2022 exceeded the thresholds in non-IRS districts compared to IRS districts. Similarly, while malaria deaths in non-.

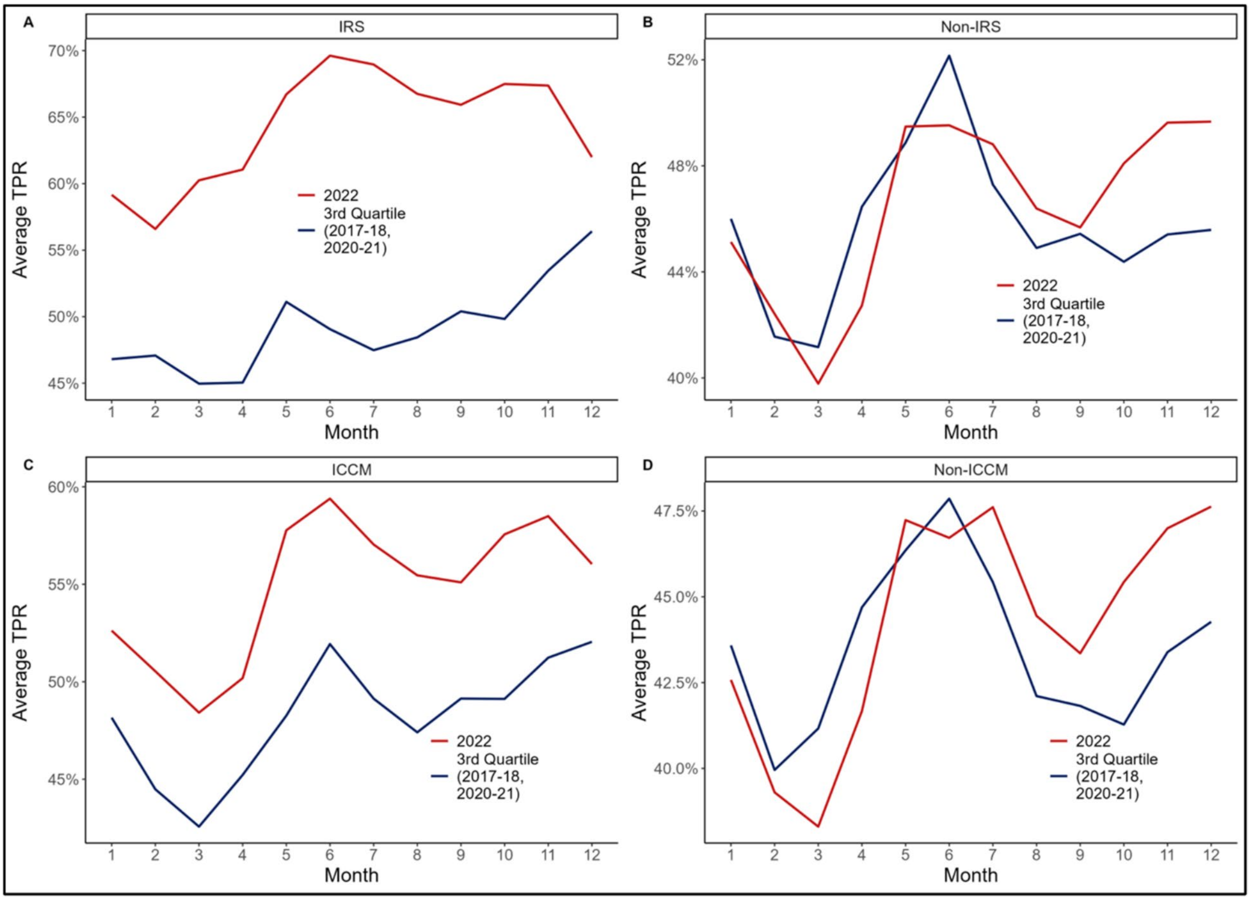

Fig. 7 National trends of test positivity rate (TPR) in 2022 compared to 2017–2021* thresholds in IRS and iCCM districts (*threshold doesn't include 2019 values)

iCCM districts were slightly above the threshold, the trend remained well below the threshold in iCCM districts (Fig. 10).

The Wilcoxon rank-sum test results for malaria indicators comparing IRS vs. non-IRS and iCCM vs. non-iCCM districts were consistent with the visual trends presented in Figs. 7, 8, 9, 10. In IRS districts, the increases in TPR, outpatient malaria cases, and inpatient malaria cases in 2022 compared to the 3rd quartile threshold were statistically significant ($p < 0.01$), while the increase in malaria deaths was not significant ($p > 0.05$). Conversely, in non-IRS districts, all indicators were statistically insignificant ($p > 0.05$), except for outpatient malaria cases ($p < 0.05$) as shown in Table 3 and reflected in Figs. 7, 8, 9, 10a and b.

In iCCM districts, the increases in TPR, outpatient malaria cases, and inpatient malaria cases in 2022 compared to the 3rd quartile threshold were strongly statistically significant ($p < 0.01$), and the decrease in malaria deaths was statistically significant ($p < 0.05$). In contrast, in non-iCCM districts, all indicators were statistically insignificant ($p > 0.05$), except for outpatient malaria cases ($p < 0.05$) as shown in Table 4 and reflected in Figs. 7, 8, 9, 10c and d.

Climatic factors

Based on the national meteorological precipitation data for 2017–2022, Uganda received typical rainfall, with the highest recorded in April 2018 (228mm), followed by 2019 (220mm), though these years did not align with the epidemic pattern seen in 2019 (Fig. 11). In Fig. 11 the indicators are described as Sum of mean RF = Monthly mean Rainfall, Sum of opd mal = total monthly outpatient cases.

Scatterplot analysis of the aggregated rainfall for 2022 versus 2017–2021 (Fig. 15b) indicated no statistically significant correlation between rainfall deviation and incidence deviation ($r = -0.06$ [-0.23–0.10], $p = 0.44$) confirming the visual observation of lack of association between rainfall and malaria cases in Fig. 11. The monthly rainfall data from the Uganda National Meteorological Authority (UNMA) for the period January 2017 to June

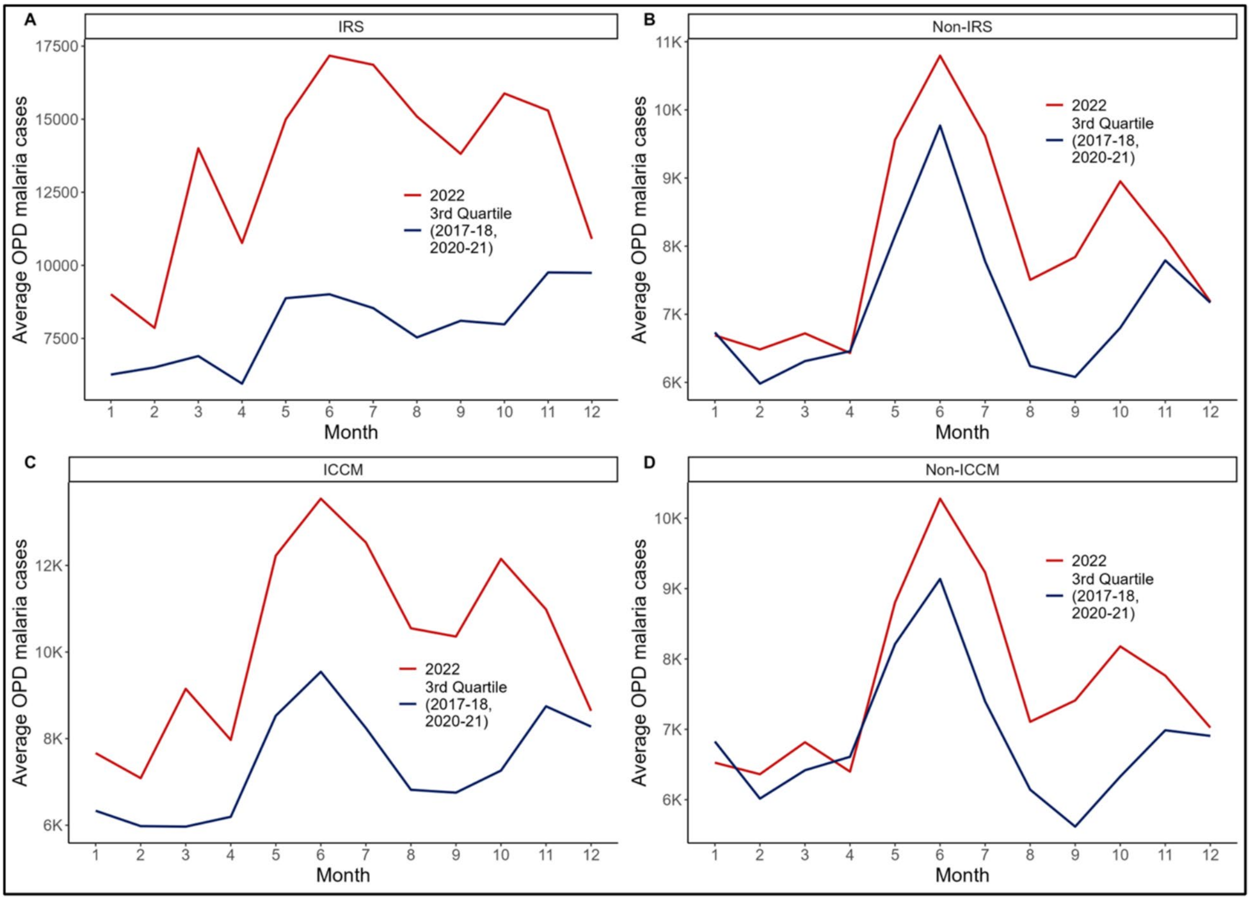

Fig. 8 National trends of outpatient malaria cases in 2022 compared to 2017–2021 thresholds in IRS and iCCM districts

2022, covering eight regions, showed a 73% correlation with the CHIRPS data for the same period (Fig. 12). Due to its comprehensive coverage and availability across all districts, CHIRPS climatic data was preferred for analysing the association between seasonal patterns of precipitation and malaria epidemics in Uganda (Additional file 1, Figs. 13–16).

Statistical analysis using Interrupted Time Series Analysis of monthly rainfall as a predictor for increased confirmed malaria cases at the national level, comparing data from 2022 to the years 2017–2021 is given below in Table 5.

Interpretation

Rainfall Lag 0: No immediate effect on malaria cases ($p > 0.05$).

Rainfall Lag 1: No significant impact from rainfall one month prior ($p > 0.05$).

Rainfall Lag 2: Significant effect ($p < 0.01$); each mm increase in rainfall two months prior predicts ~ 13.36 more malaria cases.

Model Summary: The model is significant (F-statistic $p < 0.001$) and explains 48.64% of malaria case variability. However, factors beyond rainfall (e.g., healthcare access, vector control, socioeconomic conditions) may also influence trends.

Programmatic response

In response to the malaria epidemics, the NMCP implemented measures such as regular meetings, a costed response plan, and collaboration with partners. However, domestic funding remained insufficient despite strong political commitment, and resource mobilization and a multi-sectoral approach were limited. Inadequate program data on stock management hindered the analysis of RDT and ACT stockouts during the epidemics.

At the regional and district levels, challenges persist, including staffing shortages, weak communication mechanisms, limited community-level social behavioral communication Social and Behavior Change Communication (SBCC), and procurement issues like stockouts.

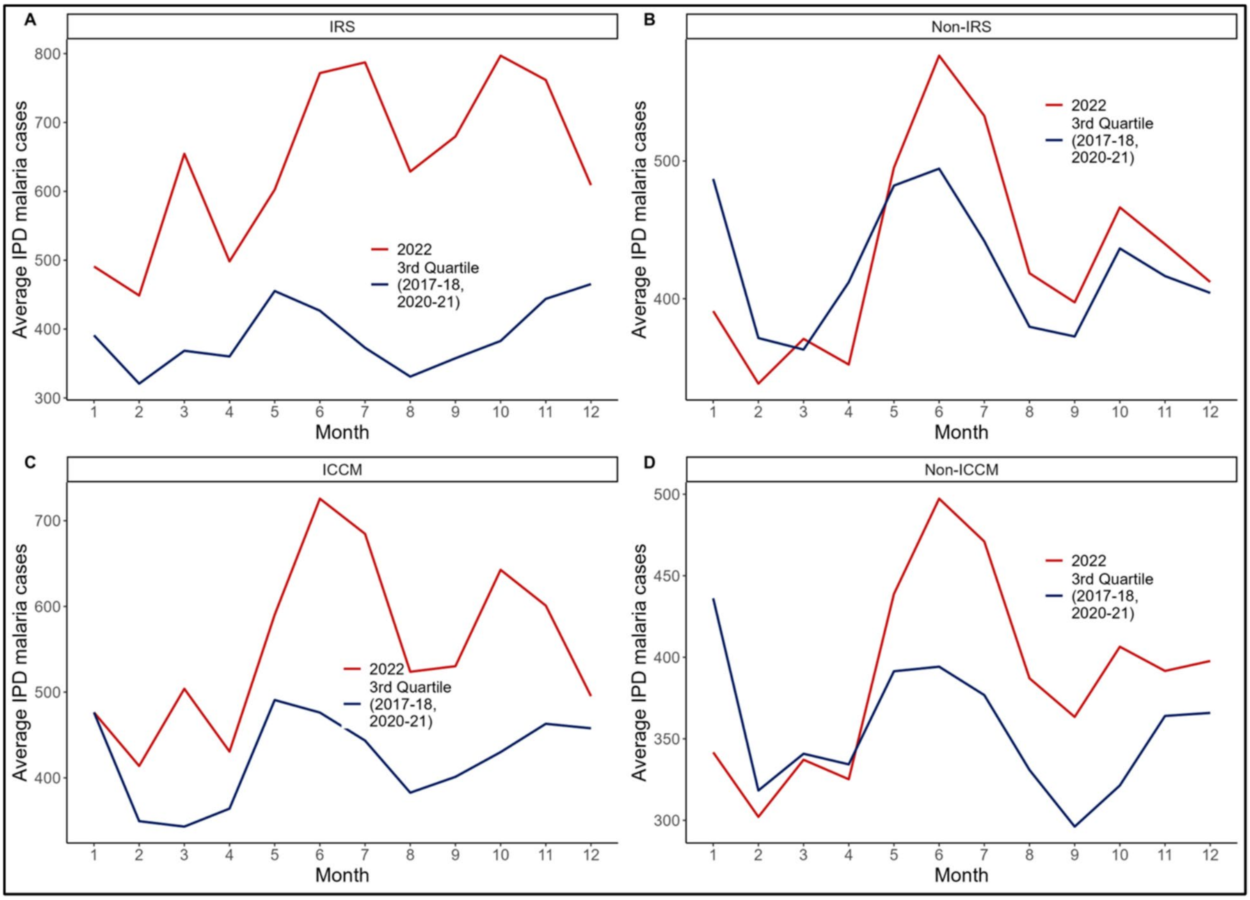

Fig. 9 National trends of malaria inpatients in 2022 compared to 2017–2021 thresholds in IRS and iCCM districts

Discussion

This study highlights a nationwide malaria epidemic in Uganda throughout 2022, evidenced by a substantial increase in outpatient cases, admissions, and test positivity rates across all age groups compared to the 2017–2021 third quartile threshold. The epidemics led to 3,379,309 excess outpatient malaria cases (confirmed and presumed), 3,018,920 excess confirmed cases and 149,789 excess inpatient cases were compared to the pre-2022 threshold. These findings align with previous studies indicating that climatic, environmental, and operational factors can precipitate widespread malaria transmission surges expressed in significant increase of cases and sever cases [24]. Despite this, malaria-related deaths decreased or remained stable, though facility-based death records likely underestimate the true burden of mortality. A mortality survey in Sierra Leone reported that most malaria deaths occur in rural areas or at home, highlighting the need for improved community-based surveillance [25]. In 2022, Uganda reported over 820,000 malaria admissions, presumed to represent severe cases. However, not all admissions may meet the clinical criteria for severe malaria, as practices can vary based on factors such as clinician judgment or patient characteristics, including comorbidities and age, which may lead to overestimation. Standardized criteria and improved diagnostics are necessary to accurately classify and manage severe malaria cases [26, 27]. Despite no recent nationwide household survey on LLIN ownership, a 2020–2021 cluster-randomized trial in 32 districts showed low ownership two years post-distribution (41.1% for pyrethroid-piperonyl butoxide (PBO) vs. 38.6% for pyrethroid-pyriproxyfen), with no difference in effectiveness between the two LLIN types [28].

IRS districts in Uganda paradoxically, experienced higher malaria epidemic levels than non-IRS districts, potentially due to factors related to type of chemical used, reduced insecticide efficacy, suboptimal IRS implementation, vector behaviours favouring outdoor resting, or low community compliance. Cone wall bioassays conducted under the PMI VectorLink Uganda Project [29] showed over 80% *An. gambiae* sens lato (s.l.) mortality for seven months, indicating retained insecticide efficacy. These findings highlight the need for further

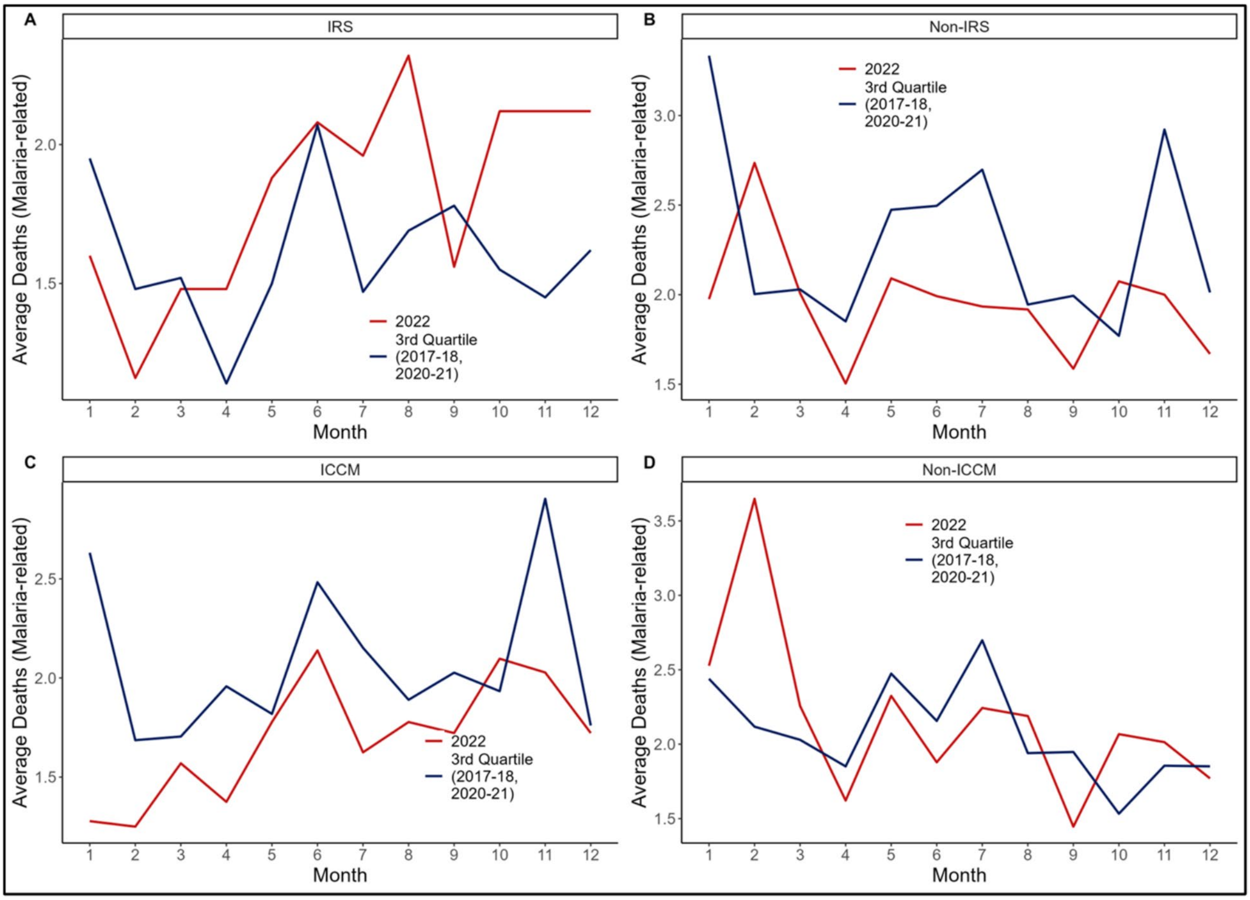

Fig. 10 National Malaria Death Trends in 2022 vs. 2017–2021 Thresholds in IRS and iCCM Districts

Table 3 Regression analysis of malaria epidemics in 2022 vs. 3rd quartile*: Comparing monthly TPR, Cases, and Deaths in IRS vs. Non-IRS Districts (*2019 values removed)

Malaria Indicator	IRS, N = 10			Non-IRS, N = 136		
	2022 N = 12[a]	3rdquartile (2017–18, 2020–21) N = 12[a]	p-value[b]	2022 N = 12[a]	3rdquartile (2017–18, 2020–21) N = 12[a]	p-value[c]
OPD	362,458 (270,896, 389,695)	201,080 (167,567, 223,563)	**< 0.001**	928,424 (811,311, 1,120,042)	798,202 (703,611, 901,520)	**0.028**
IPD	16,041 (13,759, 19,167)	9,445 (8,973, 10,882)	**< 0.001**	50,254 (46,089, 58,173)	46,926 (41,249, 50,727)	0.10
TPR	16.58 (15.16, 16.86)	12.19 (11.73, 12.69)	**< 0.001**	57.2 (53.2, 59.9)	53.7 (50.3, 55.9)	0.068
Death	48 (38, 53)	38 (37, 43)	0.078	240 (217, 247)	249 (227, 276)	0.2

[a] Median (Q1, Q3)

[b] Wilcoxon rank sum exact test; Wilcoxon rank sum test

[c] Wilcoxon rank sum exact test

Bold values indicate statistically significant at p 0.01 or p<0.05

investigation into vector bionomics, insecticide quality, IRS implementation, and community compliance to optimize IRS strategies [30, 31]. To prevent upsurges or epidemics in moderate-high transmission districts benefiting from IRS, decisions regarding the withdrawal of IRS, replacement of insecticides, or changes in interventions should be based on evidence and long-term epidemiological assessments [32].

Table 4 Regression analisis of malaria epidemics in 2022 vs 3rd quartile: Comparing TPR, Cases, and Deaths in iCCM vs. Non-iCCM districts (*2019 values removed)

Malaria Indicator	ICCM, N = 72			Non-ICCM, N = 74		
	2022 N = 12[a]	Q3 (2017–18, 2020–21) N = 12[a]	p-value[b]	2022 N = 12[a]	Q3 (2017–18, 2020–21) N = 12[a]	p-value[c]
OPD	752,600 (598,031, 877,587)	506,913 (444,746, 601,571)	**0.001**	537,179 (493,647, 628,376)	490,488 (444,283, 514,065)	**0.039**
IPD	37,945 (34,979, 44,772)	31,251 (26,686, 33,569)	**< 0.001**	28,812 (25,118, 31,276)	25,733 (22,896, 27,466)	0.068
TPR	40.1 (37.1, 41.5)	34.9 (33.1, 36.1)	**< 0.001**	33.25 (31.17, 34.87)	31.74 (29.26, 32.45)	0.089
Death	124 (106, 137)	138 (125, 164)	**0.046**	158 (135, 170)	140 (135, 161)	0.4

[a] Median (Q1, Q3)

[b] Wilcoxon rank sum exact test; Wilcoxon rank sum test

[c] Wilcoxon rank sum exact test

Bold values indicate statistically significant at p 0.01 or p<0.05

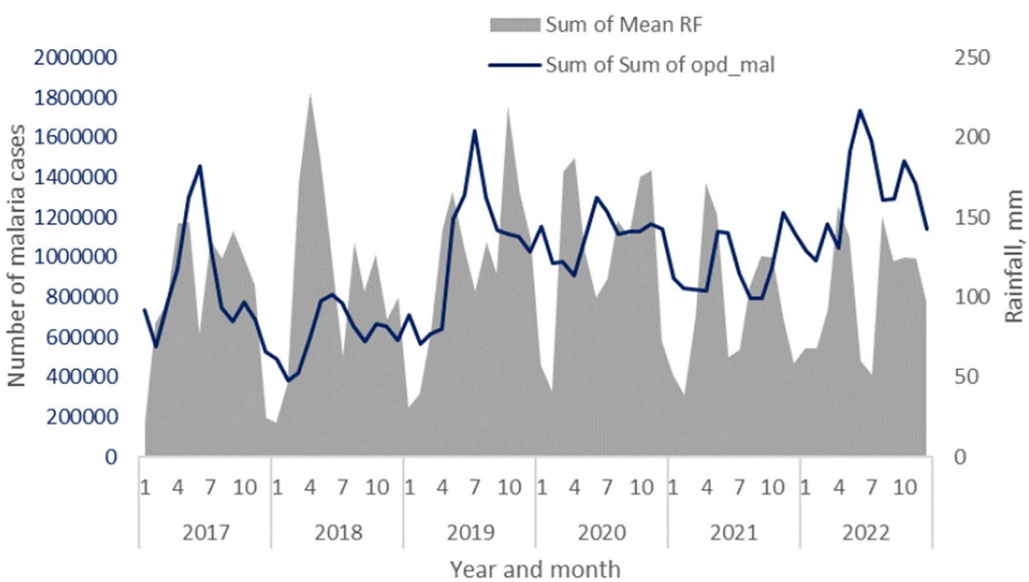

Fig. 11 National average monthly rainfall vs malaria cases (outpatient) 2017–2022

Malaria epidemics unexpectedly were more prominent in iCCM districts than non-iCCM districts, suggesting that iCCM implementation is not universal or fully effective in Uganda. Although accurate data on the percentage of iCCM districts experiencing stockouts of commodities was lacking for this study, programmatic summaries (unpublished) during the study period indicated that the median ACT stockout rate per village (villages with stockouts/villages reporting) in the iCCM districts was 51%, with an interquartile range (IQR) of 35.8–70%, highlighting the system's inefficiency. While a sub-Saharan Africa trial showed a 76% greater decline in child mortality (ages 2–59 months) in iCCM areas [33], and a 2015 study in Uganda demonstrated iCCM's effectiveness in reducing child deaths (106 lives saved in the iCCM intervention area versus 611 lives lost in the comparison areas), there is an urgent need to evaluate its current impact in Uganda [34]. Additionally, stockouts of RDTs and medicines and financial availability may affect iCCM's effectiveness.

The 2022 malaria epidemics in Uganda were likely driven by epidemiological, biological, structural, and climatic factors, along with healthcare challenges and limited intervention coverage and effectiveness discussed below.

Epidemiological factors

Malaria transmission in Uganda is influenced by receptivity, vector behavior, host immunity, and community practices. MIS surveys showed a decline in parasite

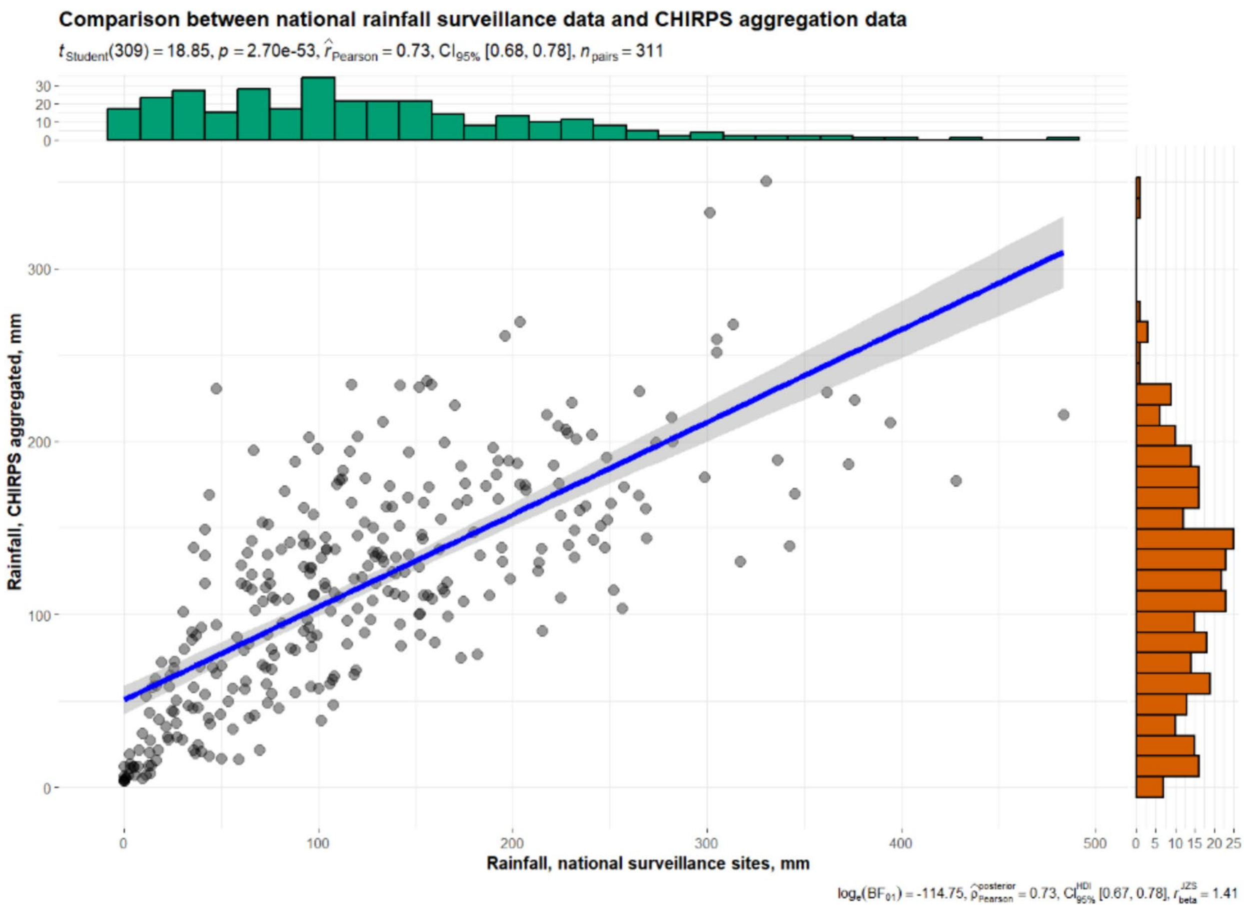

Fig. 12 Scatterplot of monthly rainfall from Uganda National Meteorological Authority (UNMA) vs. CHIRPS, 2017–2022

Table 5 Impact and statistical significance of rainfall on malaria cases (2022 vs. 2017–2021) using Interrupted Time Series Analysis (Lag 0, Lag 1, Lag 2)

Term	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	385,100	94,580	4.071	0.000129***
Time	3955	1579	2.505	0.014776*
Intervention	190,800	143,800	1.326	0.189397
Post-trend	4,544	17,834	0.255	0.799639
Rainfall lag0	1.933	4.545	0.425	0.672102
Rainfall_lag1	6.339	5.949	1.065	0.290601
Rainfall_lag2	13.36	5.418	2.466	0.016301*

Model Summary: Adjusted R-squared: 0.439, F-statistic: 10.26 (on 6 and 65 DF), Overall model p-value: 0.001

Significance Codes:*** p < 0.001, ** p < 0.01, * p < 0.05

prevalence from 42% in 2009 [2], to 19% in 2014 [3], and to 9% in 2019 [4], shifting from hyperendemic to heterogeneous settings [10]. Reduced malaria exposure may have lowered community immunity, increasing vulnerability, especially where vector control is inconsistent [35].

A study in Tororo, Uganda, examining impact of IRS from 2013 to 2017, found that 4–5 years post-IRS, compared to the 3 years prior, annual Entomological Inoculation Rate (EIR) dropped 500-fold (0.43 vs. 238), malaria incidence declined 50-fold (0.054 vs. 2.96 per child aged 0.5–10 years old), and infection prevalence decreased tenfold (6.8% vs. 67.5%). This likely led to a significant loss of partial immunity [36].

Biological factors

i) Vector Composition, Behaviour, and Invasive Species: In Uganda's Bukedi region, LLIN and IRS interventions increased outdoor-biting mosquitoes from 11.6% to 49.4%, with *An. arabiensis* dominating (99.5%) as *An. gambiae* s.s. declined. The invasive *Anopheles stephensi*, adaptable to urban areas, poses new challenges but likely played a minimal role in the 2022 epidemic [37].

ii) Insecticide resistance: a large-scale cluster randomized trial of conventional LLINs and piperonyl butoxide (PBO)-LLINs, conducted in 104 health sub-districts in Uganda from 2017 to 2019, documented very high (> 50%) knockdown resistance (*kdr*) in *An. gambiae* (s.s.) and high rates of transmission in all areas, despite widespread use of conventional LLINs [38]. A recent study in Uganda reports a significant increase in *Anopheles funestus* abundance and high resistance to clothianidin-based spraying, suggesting a vector shift and insecticide resistance as key drivers. Combined with low LLIN ownership, this likely worsened the 2022 malaria epidemics, underscoring the need for ongoing monitoring [39].

iii) Parasite Dynamics and Drug Resistance: Partial ACT resistance in northern Uganda (10–54% prevalence) is spreading to other regions, raising concerns. Its role in the 2022 epidemics and impact on morbidity and mortality remain unclear, requiring ongoing surveillance [40].

iv) Histidine-Rich Protein 2 (HRP2) HRP2 deletion: HRP2 gene deletion (12.3% prevalence) in Uganda causes false-negative RDTs, potentially affecting diagnosis. Its impact on malaria outcomes remains unclear, requiring further research [41, 42].

Climate factor

Harmonic and Interrupted Time Series analyses showed no significant year-to-year rainfall differences, including in 2022, suggesting rainfall was not the primary driver of the 2022 malaria epidemic. The analysis validates the CHIRPS dataset against national records, confirming its reliability for district-level use, especially in areas lacking local climate data. The geographical disparity may be due to Uganda's consistent unimodal and bimodal rainfall patterns, which influence malaria transmission. In bimodal regions, malaria cases peak twice—after the initial rains and again after the second rainy season—driven by post-rain increases in vector populations [43, 44]. Unimodal provinces with a single rainy season may experience sustained malaria transmission with fewer epidemics, while bimodal areas show periodic peaks. In both, the highest malaria peaks occurred two months (lag 2) after the rains, reflecting vector and parasite life cycles [45]. Localized assessments and province-specific strategies are, therefore, essential, as transmission dynamics vary. Comparing rainfall data against the 3rd quartile was more effective for identifying epidemic trends, especially in northern unimodal regions, where preemptive interventions before heavy rains could be crucial. In southeastern bimodal regions, sustained efforts and seasonally timed vector control measures, such as LLINs and IRS, are needed before each rainy season.

Programme aspects, healthcare systems and access to services:

The 2022 epidemic response was hindered by unclear guidance, insufficient training, and limited resources, despite the NMCD's EPR plan. Strengthening preparedness requires diversified resources, including increased domestic funding, timely supply procurement, and an emergency fund. Interventions like IRS and ITNs should be based on technical evidence, with clearly defined roles for partners and governments. Strengthening and sustaining functional iCCM in high-burden districts is critical to address the shortage and inequitable distribution of healthcare workers, which hinder early access to effective treatment [2]. Domestic financing for malaria control remains minimal at < 5% [46]. Sustainable, long-term funding mechanisms are essential to maintain and build on existing malaria control efforts.

This study faced some limitations: (i) lack of updated Malaria Indicator Survey (MIS) data limited the assessment of national malaria prevalence, service coverage, and social and behavior change communication (SBCC) indicators. Consequently, triangulation with health facility data was restricted, hindering a more comprehensive analysis of malaria trends; (ii) lacked data on the quality and programmatic coverage of key malaria interventions, such as LLINs and IRS; (iii) unavailability of data on stockouts of diagnostics and antimalarial medicines during the study period restricted the ability to evaluate the adequacy of malaria case management efforts and their impact on disease outcomes; (iv) differentiation of inpatient cases: although inpatient malaria cases were parasitologically confirmed and majority were presumed to represent severe malaria, there was no way of systematically identifying the proportion of uncomplicated malaria admitted due to other causes with malaria co-infections; (iv) under-reporting of malaria cases and deaths: given the higher percentage of children with fever not seeking despite care, the overall health facility reported number of cases and deaths are expected to be significantly underreported. Despite over 820,000 reported inpatient malaria cases, the reported malaria-related deaths at health facilities were disproportionately low. This under-reporting likely distorted mortality estimates, limiting the study's ability to determine the true burden of malaria-related fatalities; and (v) lack of representative national meteorological data for each of the provinces limits the analysis. Addressing these limitations in future research would improve the precision and applicability of findings, enabling more effective planning and implementation of malaria control strategies.

Conclusion

The 2022 malaria epidemic in Uganda affected 64 districts, resulting in over 3.3 million excess cases and 150,000 excess admissions. The unexpectedly higher epidemic rates in districts with IRS and iCCM interventions point to shortcomings in the implementation of these measures. The 2022 epidemic occurred despite mass LLIN campaign in 2020/2021 and very high administrative coverage, indicates the likely impact of vector composition shift, insecticide resistance and poor LLIN ownership. Recent biological changes, particularly HRP2 deletion and drug resistance require time to manifest in large scale epidemics. Limited correlation with rainfall highlights the role of other drivers, though regions with bimodal rainfall patterns exhibited greater vulnerability. Epidemic response efforts were hindered by challenges in funding, coordination, and supply chain management.

To prevent future epidemics and sustain malaria control progress, it is essential to strengthen targeted interventions in high-burden areas, develop costed and well-resourced epidemic preparedness and response plans, and ensure consistent availability of key supplies such as RDTs and ACT. Maintaining IRS in high receptive districts, with any withdrawal guided by epidemiological impact and accompanied by robust surveillance and alternative control measures, is critical. Functional iCCMs tailored to remote, high-incidence areas and strengthened SBCC efforts to improve net use and timely health-seeking behaviours are also vital. A holistic approach that reinforces healthcare systems, enhances vector control, improves access to services, and ensures sustainable funding will be key to reducing malaria outbreaks and achieving long-term control in Uganda.

Abbreviations

ACTs	Artemisinin-based Combination Therapy
AL	Artemether-lumefantrine
ANC	Antenatal care
AUC	Area under the curve
CHIRPS	Climate Hazards Group InfraRed Precipitation with Station
DHIS2	District Health Information System
DHPQ	Dihydroartemisinin-piperaquine
EPI	Expanded Programme for Immunization
iCCM	Integrated Community Case Management
IRS	Indoor Residual Spraying
LLIN	Long-Lasting Insecticidal Nets
MIS	Malaria Indicator Survey
NMCD	National Malaria Control Division
RDTs	Rapid Diagnostic Test
UMRSP	Uganda Malaria Reduction and Strategic Plans
UNMA	Uganda National Meteorological Authority
WHO	World Health Organization

Supplementary Information

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Additional file 1.

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Author contributions

MA, CM, RC, BA and JO, conceived and designed the study, MA, CZ, and SK developed the first draft and performed the data analysis and interpretation. MR, CK and BA, reviewed and provided critical inputs. MA led the entire study design, analysis and write-up. CZ collected and analyzed all climatic data. SK led all statistical methods. All authors contributed to the manuscript development, read and approved the final manuscript.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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