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From Children to Adults? Shifting Age Patterns of Malaria in Kenya, 2008 – 2023

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Abstract

Estimation of the impact of the doubled malaria funding over the past two decades targeting high-risk populations warrants use of age-attentive metrics. This study assessed temporal trends in malaria burden and parasite density across age groups in Kenya.

Between 2008 and 2023, malaria burden and parasite density among symptomatic individuals were estimated and analyzed using RStudio.

Up to 4,184 participants, comprising 2,737 (65.42%) Lake-endemic region, 1,278 (30.54%) highland endemic region, and 169 (4.04%) coast endemic zones were enrolled. Median age of participants was 5 years, (IQR 3–15, SD,11.68). Enrolment differed significantly across age groups: 0–5 (51.6%), 6–11 (18.8%), 12–17 (7.4%), 18–26 (13.1%), and 27–78 years (9.2%) (χ^2, $p < 0.001$). Median age increased significantly, from 4 to 13 years suggesting a shift in disease burden toward older age groups, χ^2 $p = 0.0001$. Median parasite density in parasites/μL declined significantly from 37,500/μL (n = 196, 2008) to 5,080/μL (n = 102, 2023) (Kruskal–Wallis, $p = 0.0001$).

The age of individuals presenting with malaria symptoms increased significantly alongside a reciprocal decrease in parasite density. These changes suggest need to reassess age-targeted malaria interventions to ensure adequate protection of those at the highest risk of malaria.

Introduction

As resistance to artemisinin-based combination therapies (ACTs) grow, malaria continues to pose a serious threat to public health with sub-Saharan Africa accounting for the highest burden of morbidity and mortality (1). The malaria burden is anticipated to worsen in the context of declining global malaria financing, particularly following recent funding reductions by the U.S. government, a key contributor to malaria control efforts (2, 3). These budgetary limitations run the risk of undermining efforts at prevention, diagnosis, treatment, and surveillance, which could undo hard-won progress in the control and eradication of malaria (2).

Mitigating the effects of these disjointed, yet harmful challenges in malaria calls for tailored approaches that align with reducing malaria related deaths in line with the WHO's drifting away from a one-size-fits-all approach toward targeted, data-driven strategies (*High Burden to High Impact: A Targeted Malaria Response*) (2, 4). The success of this strategy relies on recognizing the marked geographic heterogeneity in transmission, shaped by variations in host immunity, population movement, environmental suitability for vectors, and healthcare access (5). Population stratification based on demographic vulnerability, ecological context, and epidemiological risk presage successful implementation of malaria interventions. In this context, the World Health Organization (WHO) recommends that malaria burden stratification as a core principle of national malaria control and elimination strategies, emphasizing that intervention packages should be tailored according to transmission intensity and local epidemiology (6).

One of the most significant factors influencing the risk of malaria is age. Children under five years old are most affected in settings with moderate-to-high transmission due to their low immunity (7). This age group is the primary target of malaria control interventions, including universal access to long-lasting insecticidal nets (LLINs), prompt parasitological diagnosis using rapid diagnostic tests, and treatment with artemisinin-based combination therapies (ACTs) (6, 7). Similarly, pregnant women, who are at increased risk of malaria due to reduced immunity and its associated adverse outcomes, including maternal anemia, low birth weight, and neonatal mortality, are specifically targeted through these interventions in addition to intermittent preventive therapy in pregnancy (IPTp) with sulfadoxine–pyrimethamine (6).

The geographic heterogeneity of malaria requires context-specific, ecologically targeted interventions. Specifically for Kenya, high-transmission lake endemic zones differ from highland regions that are prone to epidemics due to low population immunity therefore needing indoor residual spraying (IRS) deployment and early warning systems for preparedness and timely response (6) .

Tracking the evolving age distribution of disease as transmission wanes is fundamental to estimating clinical disease burden (8). The World Health Organization includes age in burden estimation; however, it does not fully account for transmission-driven changes in the age profile of malaria, which may underestimate disease burden in older populations as transmission declines and immunity acquisition slows (9). Patterns of clinical malaria vary by age and transmission intensity (10), with children aged < 5 years bearing the greatest burden in highly endemic settings, whereas older children and adults are increasingly affected in areas of lower transmission due to delayed acquisition of naturally acquired immunity (10, 11). Although there has been a general decline in malaria in recent decades, driven by multifaceted malaria interventions, studies show specific periods of increased burden suggestive of shifts to older ages (9, 11, 12). In Kenya, malaria risk has generally declined but remains highly heterogeneous across regions, with these epidemiological shifts changing the age distribution of affected populations (13–15). After rising in the mid-1900s and peaking around 1999, severe cases began to significantly decline until 2009. The geographical distribution has shifted, with a rise in prevalence in certain areas, even as overall prevalence drops in malaria endemic regions influenced by several factors (12).

Estimation of malaria burden in Kenya is periodically conducted by the Ministry of Health to guide control efforts, in line with a key objective of the Kenya Malaria Strategy (KMS) to strengthen malaria surveillance and data use for informed decision-making and improved program performance (16). Despite these efforts, challenges remain, including inadequate malaria surveillance, monitoring, and evaluation, which compromise the quality of health information needed to support evidence-based malaria programming at county and sub-county levels. (16). Furthermore, the surveys are normally conducted during different seasons, with the 2015 survey conducted during the long rainy season and the 2020 survey during the short rainy season, thus the seasonal misalignment may bias findings. Implementing year-long rolling surveys would help address this challenge, but it remains infeasible due to high costs. In addition although modelling and geospatial analytics have been recently used for

malaria prediction and forecasting, reports suggests that, at a crude level, it does distinguish communities exposed to differing levels of malaria transmission intensity (9, 12) and that using modelling to categorically distinguish populations at differing intensities of malaria transmission in Kenya may under-represent those who are exposed to stable, endemic transmission and over-represent those at no risk (17).

Parasite changes resulting in antimalarial drug resistance (18, 19) alongside vaccination campaigns, may influence malaria transmission dynamics (20, 21). Seasonal malaria chemo prevention is currently recommended for children aged from 3 months to 5 years based on trial data from areas with high seasonal endemic transmission (22), but it may also be beneficial for older children in areas where transmission has been reduced, as has recently been shown in Mali and Senegal (15, 23). Other interventions, including access to free treatment, long-lasting insecticide-treated net distribution and the new RTS,S vaccine target children under 5 years of age (9, 24). The effect of prevailing interventions on the burden of malaria at age level remains unknown. Therefore, this data is important for informing stratification for the targeting of these interventions.

Results

Descriptive analysis

A total of 4,184 participants presenting symptoms of malaria at the outpatient department of respective healthcare facilities were enrolled into the study between 2008 and 2023. The lake endemic sites cumulatively had the highest number of participants, 2,737(65.42%) : Kisumu 1460/4184(34.89%), Kombewa 991/4184(23.69%), and Busia 286/4184(6.84%); followed by highland epidemic region 1,278(30.54%): Kisii 16/4184(17.11%), Kericho 364/4184(8.70%), and Marigat 198/4122(4.73%); and finally coast endemic region, 169(4.04%): Malindi 169/4184(4.04%) (Table 1). The number of females, 52.75% (2,207) were comparable to males 47.25% (1,977) p = 0.270.

Table 1
Participants' demographics and clinical summary statistics

Site (n)	Region[a]	Age in years*	Sex (% Female)	Temperature (degrees Celsius*)	Parasite density per ul
Busia (286)	Lake Endemic	16.81 [14.99–18.62]	64.34%	37.43[37.29–37.56]	35583.92 [28806.16-42361.67]
Kisumu (1460)	Lake Endemic	9.00 [8.45–9.56]	52.74%	37.93[37.86–38.01]	84115.26[76986.5-91244.01]
Kombewa (991)	Lake Endemic	8.52 [7.97–9.08]	51.36%	37.81[37.65–37.97]	62319.17[57102.45-67535.9]
Kisii (716)	Highland Epidemic	10.32 [9.41–11.23]	50.98%	38.59[38.46–38.73]	23422.78[17685.9-29159.67]
Kericho (364)	Highland Epidemic	14.51[13.17–15.85]	52.47%	38.41[38.04–38.78]	44386.37[24844.64-63928.09]
Marigat (198)	Highland Epidemic	14.81[13.12–16.51]	53.54%	38.11[37.96–38.27]	14959.08 [9680.96-20237.19]
Malindi (169)	Coast Endemic	13.59[11.20-15.98]	48.52%	38.22[38.04–38.40]	40806.5[33276.98-48336.02]
All (4184)	Overall	10.61 [10.25–10.97]	52.75%	38.04 [37.98–38.11]	58374.94[54832.88–61917]

*Mean [95% Confidence Interval]. Region [a] refers to the transmission zone based on Kenya's malaria burden map as per the Kenya National Malaria Indicator Survey 2020 (KIMS 2020).

Table 1: **Participants' demographics and clinical summary statistics**

*Mean [95% Confidence Interval]. Region [a] refers to the transmission zone based on Kenya's malaria burden map as per the Kenya National Malaria Indicator Survey 2020 (KIMS 2020).

Temporal trends of age

The overall median age of participants enrolled was 5yrs, (IQR 3-15yrs, range 1-78yrs) and assessment of the overall density by age of the participants revealed two peaks, first around the young children (0-5yrs) who had the highest number followed by young adults (**Supplementary Fig. 1**). Although, this was varied by region with highland epidemic and coast endemic having 7yrs highest and lake endemic having the lowest median age of 5yrs. The temporal median ages ranged from 4.5yrs in 2008 (n = 235) to 6yrs in 2009 (n = 186), 5yrs in 2010 (n = 269), 4yrs in 2011 (n = 249), 4.5yrs in 2012 (n = 358), 5yrs in 2013 (n = 519) and 2014 (n = 708), 4yrs in 2015 (n = 225) and 2018 (n = 149), 7yrs in 2019 (n = 314), 9.5yrs in 2020 (n = 132), 8yrs in 2021 (n = 378), 11yrs in 2022 (n = 358), and 13yrs in 2023 (n = 104) respectively, depicting a significantly upward trend p = 0.0001 (Fig. 1a**).** The temporal median age across the different

regions was significantly variable p = 0.0001, with that of the highland epidemic increasing from 5yrs in 2015 to 10yrs in 2018, while the coast endemic and lake endemic maintained an upward trend with peaks in 2020, 17yrs and 2019, 6 yrs respectively (Fig. 1b**).**

Based on age bands, participants comprised 0-5yrs 51.58% (2,158), 6-11yrs 18.79% (786), 12-17yrs 7.36% (308), 18-26yrs 13.05% (546) and above 27-78yrs 9.23% (388) (**Supplementary Table 1**). The age categories were significantly variable across the study period p = 0.000 (**Supplementary Table 1).**

Temporal change in age categories of participants between 2008 and 2023

When assessing the number of participants enrolled each year over time by age categories, it was noted that the frequencies were varying with a rising trend seen in the 18-26yrs age categories while a decline is seen in the 0-5yrs categories (Fig. 2**).** Between 2008 and 2018, the number of children aged 0-5yrs remained more than 5-fold higher than either of the other age bands. In 2018-19, the number of this age band dropped sharply to less than 2-fold. In reciprocity, there was a gradual increase in number of all other ages except the 27–78 years age band. The number of age bands 18 to 26 continued to rise gradually, alongside 27–78 age bands, till 2023 (Fig. 2**).** Assessment of age categories counts per enrollment year revealed changing patterns with the 0-5yrs having the greatest burden overall with the least being 12-17yrs **(Supplementary Fig. 2, Supplementary Table 2**).

Temporal trends of parasite density

Overall median parasite density was 16,800/µl (IQR 4,320 – 65,000/µl range 0–1,612,500/µl). Assessment of per-year parasite density revealed an incline from 37,500/µl in 2008 to 47,500/µl in 2009 this was then followed by a declining trend as follows 40,000µl in 2010, 37,500/µl in 2011, 25,120/µl in 2012, 22,470/µl in 2013, 25,000/µl in 2014, 34,360/µl in 2015, 4,840/µl in 2018, 6,800/µl in 2019, 8,720/µl in 2020, 8,540/µl in 2021, 8,000/µl in 2022, ending up to 5,080/µl in 2023, with minor peaks within the period p = 0.0001 (Fig. 3a**)**. The median parasite density for the ecological regions across the study periods revealed significant shifts p = 0.0001, with high peaks in the coast endemic 2019 (39,600/µl), highland epidemic 2015 (19,210/µl), and lake endemic 2008 (78,750/µl). The lake endemic region revealed a declining trend during the study period (Fig. 3b**)**.

Parasite density and age

Analyses of parasite carriage across varying ages of participants by Pearson correlation revealed higher parasite density among younger individuals and declining progressively with increasing age (Fig. 4). Correlation analysis demonstrated a weak but highly significant negative association between age and parasite density ($R = -0.19$, $p < 2.2 \times 10^{-16}$). Despite this trend, substantial variability was observed across all age groups, including occasional high parasite densities in older individuals (Fig. 4).

Additionally, a subset of individuals across ages exhibited very low or sub-detectable parasite densities. By age categories, children 0-5yrs (28,280/µl) and 6-11yrs (17,500/µl) had the highest median parasite density, respectively, while the other age ranges had lower median parasite densities: 12-17yrs (14,760/µl), 18-26yrs (8,280/µl), and 27-78yrs (7,500/µl) (**Supplementary Fig. 3**) which was statistically significant, p = 0.0001. Regionally, the parasite density varied widely with Kombewa, Kisumu, and Marigat having the 0-5yrs categories with high median parasite densities compared to the other age categories (**Supplementary Fig. 4**). Assessment of within age band temporal changes in median parasite density revealed dramatic decline in the parasite densities for age band 27-78yrs, from 6,360/µl in the year 2021 to 920/µl, in the year 2022, suggesting somewhat, increased susceptibility to symptoms of malaria (**Supplementary Fig. 5**). Across the study period (2008–2023), parasite density distributions demonstrated consistent age-dependent variation, with younger age groups (0–11 years) generally exhibiting higher and broader density distributions, indicative of higher parasite burdens. In contrast, older individuals (≥ 18 years) showed narrower distributions with lower peak parasite densities, suggesting reduced parasite loads (**Supplementary Fig. 5)**.

Temporal trends revealed notable shifts such that between 2008–2014, median parasite density distributions were relatively broad across all age groups, with overlapping peaks, indicating widespread transmission and less pronounced age differentiation. This was followed by a gradual rightward shift and tightening of distribution among younger age groups, suggesting improved control and possible reduction in high-density infections between 2015 and 2019. In a sharp, narrow peak in 2020 in the 18-26yrs age band showing transient concentration of parasite density in this age despite general reduction in density across all age groups (**Supplementary Fig. 5**).

Regression analysis

A multiple linear regression model was fitted to log-transformed parasite density as the outcome, adjusting for age, ecological region, and the enrolment year. The regression model was used to test if the age, ecological region, and enrolment period was significantly associated with parasite density. (**Supplementary Fig. 6**).

The overall regression was statistically significant (R2 = [0.174], F (16, 3,559) = [F-48.17], p = [< 0.000]). There was a statistically significant inverse association between age and parasite density, indicating that for each one-unit increase in age, the parasite density decreased by 0.03 units **(**Fig. 5**)** suggesting that age is a predictor of the parasite density (β = [-0.03], p = [< 0.000]), (OR 9.67, 95%CI 9.60–9.75) whereby as the age increases, the parasite density decreases by the coefficient's value, while all other variables in the model are held constant. In addition, ecological region also influenced the parasite density, with individuals from the highland epidemic region having nearly twofold higher odds (OR = 1.94, 95% CI: 1.22–3.09, p < 0.001) and those from the lake endemic region showing approximately fivefold higher odds (OR = 4.99, 95% CI: 3.18–7.85, p = 0.001) compared with the reference ecological zone (coast endemic). Further, year of enrollment was significantly positively associated with changes in parasite density with plateau between enrolment years 2012 [OR 1.29, 95% CI 0.79–2.13, p = < 0.298], 2013 [OR

1.22, 95% CI 0.73–1.93, p = 0.391] and 2015 [OR 1.50, 95% CI 0.88–2.55, p = 0.134] that did not significantly predict parasite density(Fig. 5).

Discussion

This study established temporal trends of *Plasmodium* parasite density among 4,184 participants of varying age from different ecological regions, presenting symptoms of malaria at the outpatient department of participating healthcare facilities between 2008 and 2023 in four transmissions zones of Kenya. High enrollment in lake endemic 2,737(65.42%) was observed due to continuous transmission and reported children as the majority. This study had four major findings. First, the number of adults presenting with symptoms at the outpatient department increased while that of children reduced during the study period despite consistency in inclusion criteria. Secondly, temporal trends of participants' parasite density declined significantly over the study period. Thirdly, assessment of within age band temporal changes in the parasite densities revealed dramatic decline in parasite density in the year 2022, especially for age band 27-78yrs suggesting increased susceptibility to symptoms of malaria. This sharp decline appears to suggest transient loss of acquired immunity, likely due to reduced malaria exposure in preceding years occasioned by intensified coverage of intervention (25), thereby increasing susceptibility to symptomatic malaria events at lower parasitemia. Similar findings have been reported in Kenya (14). Finally, multiple linear regression model revealed that age, ecological region, and enrolment period were significantly associated with parasite density.

Recent reports consistently shows a shift in malaria epidemiology characterized by declining malaria parasite burden in traditionally high-risk groups (especially young children) alongside an increasing burden in older age groups (26). Studies from East Africa, including Tanzania, report that while malaria parasite burden has decreased or stabilized among under-fives—likely due to targeted interventions such as bed nets and improved treatment—there is a relative increase in infections among school-aged children and adults, with prevalence in adults rising from ~ 13.9% to 22.5% (26). In Kenya, the risk of malaria is generally declining but highly varied by region, and this shift is changing which age groups are most affected.

The current study highlighted varying frequencies of the age categories with a rising trend seen in the 18-26yrs age categories while a decline is seen in the 0-5yrs categories. Between 2008 and 2018, the number of children aged 0-5yrs remained more than 5-fold higher than either of the other age bands. In 2018-19, the number of this age band dropped sharply to less than 2-fold. In reciprocity, there was a gradual increase in number of all other ages except the 27–78 years age band. Although the current study revealed children bear the greatest malaria burden similar to previous studies therefore serve as infectious reservoirs (27), there is an age shift in malaria cases to older populations with wide within-county variability in the age groups at the highest risk(27, 28). While these changes tend to imply ease of acquisition of infection by the less targeted age groups, which are less immune because they were effectively protected from malaria at a young age, or greater access to healthcare, there is a need to

reassess age-targeted control to ensure that those at the highest risk of developing clinical disease and its sequelae are sufficiently protected.

The age distribution of clinical cases is essential when targeting interventions (29). Case in point, seasonal malaria chemo prevention is currently recommended for children aged from 3 months to 5 years based on trial data from areas with high seasonal endemic transmission (22), but it may also be beneficial for older children in areas where transmission has been reduced, as has recently been shown in Mali and Senegal (15, 23). Moreover, other interventions, including access to free treatment, long-lasting insecticide-treated net distribution and the new RTS,S vaccine, target children under 5 years of age, although universal coverage of LLINs is now promoted (9, 24). Therefore, this data is important for informing stratification for the targeting of these interventions more effectively.

Participants' median parasite density in the ecological regions across the study periods revealed significant shifts, with high peaks in the coast endemic 2019 (39,600/µl), highland epidemic 2015 (19,210/µl), and lake endemic 2008 (78,750/µl). The lake endemic region revealed a declining trend during the study period. Declining parasite density seen from (2010–2012) and (2015–2018) may be attributed to targeted IRS for vector control which was deployed in 12 counties to reduce transmission then expanded to 16 epidemic prone and 4 endemic counties during 2010/2011 before being suspended after 2012 to address insecticide resistance issues (30). However, in 2017, IRS activities resumed in two counties, Migori and Homa Bay, located in the lake endemic zone (16). In addition, the Ministry of Health distributed ITNs to high malaria transmission zones targeting children aged under 5 years. Subsequent mass distribution of ITNs in 2011/2012, 2014/2015 and 2017/2018 targeted all individuals living in the malaria-prone zones with the objective of achieving universal coverage. However, the year 2013 to 2014 revealed a slight upsurge in parasite density and may be associated with reduced IRS activities since 2013 according to WHO guidance on insecticide resistance management following the detection of high resistance to pyrethroids. The major decline in 2018 may be attributed to improved capacity in coordination, leadership, governance, and resource mobilization at all levels for all stakeholders engaged in malaria control (16). In addition, Kenya Malaria Strategy reported an increase in testing rates of suspected malaria cases in public health facilities, from 24 percent (2010) to 64 percent (2017), with 89 percent of all confirmed malaria cases presenting to public health facilities being treated with ACT as well as increased adherence to national treatment guidelines in public health facilities, from 16 percent (2010) to 59 percent (2017). Furthermore, between 2014 and 2017, 7,350 community health volunteers (CHVs) in 10 counties were trained on community case management of malaria (16).

The rise in median parasite density in 2020 and slightly steady trend observed up to 2022 with a peak in 2023 may be attributed to COVID 19 pandemic. A significant increase in global malaria deaths in 2020 compared with 2019 (from 568,000 to 620,000) was observed because of the COVID-19 epidemic and the associated disruption of health services, which has led to a resurgence of malaria epidemics in parts of Africa (31, 32). In 2022, the global incidence of malaria reached approximately 249 million cases, resulting in 608,000 fatalities, which is a significant increase compared with previous years (33). In 2023, the estimated number of malaria cases rose to approximately 263 million across 83 countries where

malaria is endemic, reflecting an increase of 11 million from the previous year (2). Furthermore, malaria incidence slightly increased in 2023, increasing from 58.6 to 60.4 cases per 1,000 individuals at risk compared with 2022 (2).

Overall, age, ecological region, and several enrolment years were significantly associated with increased odds of the malaria parasite burden, with the strongest effects observed for increasing age, residence in the lake endemic region, and enrolment during 2020. The decline in malaria parasite burden observed in the lake endemic zone is promising. Therefore, there is need to continue to fully scale up malaria control interventions in the lake endemic region and to continue focused intervention efforts in the highland epidemic and coast endemic regions to stem the slight increase in malaria parasite burden observed. In some regions, malaria case reporting may be sufficient. However, because the population accessing the public sector is heterogeneous, and often only represents a minority of total cases (34) and treatment-seeking behavior may vary with age hence case reports may not give a reliable picture of the true age-burden of disease. The methodology and estimates presented here therefore add to the information that can be used at national level to aid such decision-making. The focus of some interventions towards young children may need to be reconsidered and should be informed by the current local transmission intensity (9).

The current study had its strengths; one, it had enough sample size which increased the power of the study; second, it included all age segments of the populations (from children up to the old age groups). However, this study was limited by data gaps in the coast endemic region and missing information for the 2016–2017 period. In addition, sampling of the study participants was done conveniently by recruiting individuals who volunteered to take part in the study with no prior selection of participants. This may have influenced participation in the study, leading to over-representation or under-representation of some groups, potentially affecting the generalizability of the findings. Lastly, the study was conducted in high and moderate malaria transmission regions and did not cover low and very low transmission regions. Data stratification technique was used to reduce variability and ensure that subsets are accurately represented. Future studies should be conducted to cover all regions and ensure balanced representation by employing a nationally representative, multicenter design that captures heterogeneity in malaria transmission as well as strengthen collaborations with regional hospitals and surveillance centers to ensure regular reporting.

Conclusion

Age-targeted policies may increasingly need to be refined between and even within regions. To underpin such decisions, country control programmes need estimates of the age distribution of cases to guide ongoing malaria control and elimination strategies. With the age shift in malaria cases, involving the entire community, not only children and pregnant women will have greater impact. Moreover, to sustain the gains, investment levels need to be maintained, especially in the high burden areas around Lake Victoria and in the coastal region. In other regions, investment in surveillance and preventive measures will be key to combat malaria transmission in those areas. The prevention plan for Kenya includes more

focused tailor-made targeted interventions in high-burden areas. Therefore, continuous epidemiological surveillance is essential to guide targeted interventions.

Methods

Study aim

This study sought to use long-term data to estimate changes in the temporal malaria burden and parasite density trends across varying age of individuals presenting with symptoms of malaria at healthcare facilities. This is essential for identifying age groups at highest risk within the context of existing malaria control strategies, providing critical evidence to guide targeted interventions and refine malaria elimination efforts aimed at reducing disease burden.

Study sites

Individuals were enrolled at seven Kenya Ministry of Health (MOH) sentinel hospitals located in three of the five malaria burden zones of Kenya, including Lake endemic (Kisumu- Kombewa Sub-County Hospital; Kisumu County Referral Hospital and Busia – Busia County Referral Hospital), Highland epidemic (Kisii - Kisii County Referral; Kericho- Kericho County Referral; and Baringo – Marigat Sub-County Hospital), Coast endemic (Malindi-Malindi Sub-County Hospital) regions. Informed consent was obtained from all subjects and/or their legal guardian(s) prior to enrollment. The study enrolled at least 6 months old and above, presenting at outpatient department with symptoms consistent with uncomplicated malaria. Demographics and clinical information were obtained using a structured questionnaire and subsequently two malaria blood smears were prepared for microscopy.

Parasite density estimation

Malaria blood smears were processed as previously described (25). This was followed by microscopic diagnosis of malaria, including parasite quantification (25, 26). Malaria diagnosis and parasite quantification were done in all positive smears. Specifically, Plasmodium infections was presented as the number of counted parasites within 2000 high power fields white blood cells (WBCs) for low density infections or red blood cells (RBCs) for high density infections and expressed as parasite density as previously described (25–27).

Data management and statistical analysis

Data was collected on standardized case report forms and subsequently secured on a dedicated database. To ensure data integrity, we implemented double data entry, performed regular quality checks, and conducted range and consistency validations. Any missing or outlier data was carefully reviewed and managed according to pre-established protocols. Exploratory data analysis technique was used to examine the temporal trends of malaria parasite density and participants' age over a period of 15 years in Kenya. This was used to identify the shift in malaria infections and corresponding age over time in selected regions. Trends of malaria infected participants across three of the five geographically distinct

malaria zones in Kenya based on parasite density and age distribution were also determined. Statistical analyses were performed using RStudio version 4.5.1. Shapiro-Wilk test for normality was used to determine the distribution of continuous variables including parasite density and participants' age. Parasite density per microliter was transformed to the natural log and expressed as log transformed parasite density. The participants' ages were also grouped into five categories. Descriptive statistics were employed to illustrate the burden of malaria parasites among the participants with positive infections. Non-parametric Kruskal-Walli's rank sum tests for non-normally distributed data were used to determine the distribution of parasite density and participants' age across enrollment year, age categories and ecological regions for comparisons. Proportions were compared using the $\chi 2$-test or Fisher's exact test, as appropriate.

Regression analysis was also conducted by fitting the multiple linear regression model to assess changing malaria risk. The regression coefficients describe the mathematical relationship between each independent variable (age, ecological region, enrolment year) and the dependent variable (parasite density). The p values for the coefficients indicate whether these relationships are statistically significant. After fitting the regression model, the residual plots were checked to confirm unbiased estimates and that the assumptions of the regression analysis are not robust to violation specifically for linearity, reliability of measurement, homoscedasticity, and normality. All the statistical analyses were performed at 5% significance level with the Confidence Interval (CI) set at 95%; the statistical significance was defined as $p < 0.05$, and the data presented in figures and tables.

Declarations

Ethics approval and consent to participate

The study was conducted under the approval of the Kenya Medical Research Institute (KEMRI), Scientific and Ethics Review Unit (SERU) and Walter Reed Army Institute of Research (WRAIR) institutional review boards, protocol numbers: WRAIR 2454, KEMRI 3628: "Epidemiology of malaria and drug sensitivity patterns in Kenya." Participants' informed consent in relation to study enrollment for adults and parents/legal guardians provided informed consent for minors (consent and assent) were obtained prior to subsequent enrollment into the study at seven Kenya Ministry of Health (MOH) sentinel hospitals located in three of the five malaria burden zones of Kenya. All procedures were conducted in accordance with relevant guidelines and regulations.

Consent for publication

A written informed consent was obtained from enrolled participants for publication. A copy of the written informed consent is available for review by the journal Editor.

Disclaimer

Material has been reviewed by the Walter Reed Army Institute of Research. There is no objection to its presentation and/or publication. The opinions or assertions contained herein are the private views of the author, and are not to be construed as official, or as reflecting true views of the Department of the Army or the Department of War. The investigators have adhered to the policies for protection of human subjects as prescribed in AR 70–25.

Competing interests statement

All the authors declare no competing interests.

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Author Contribution

G.C.; Study implementation, data curation, formal data analysis, preparation of the original draft, final manuscript review; B.O., A.C.C.; Study implementation, data analysis and draft manuscript writing, R.Y., R.M., M.M., J.J.; Study implementation and draft manuscript review, R.O., E.M., F.S., C.O.; Data analysis and draft manuscript write-up, D.N., M.O.; Study implementation, field coordination, M.O., C.E; Design of the study protocol, study implementation, and manuscript review, R.C.H., L.P.S.; Manuscript writing and final manuscript review, B.R.O.; Study oversight, manuscript review and scientific guidance, D.W.J.; Study implementation, data analysis, draft manuscript write up, final manuscript review, H.M.A.; Design of the study protocol, study implementation, manuscript write up, final manuscript review and submission. All authors reviewed the manuscript.

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Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

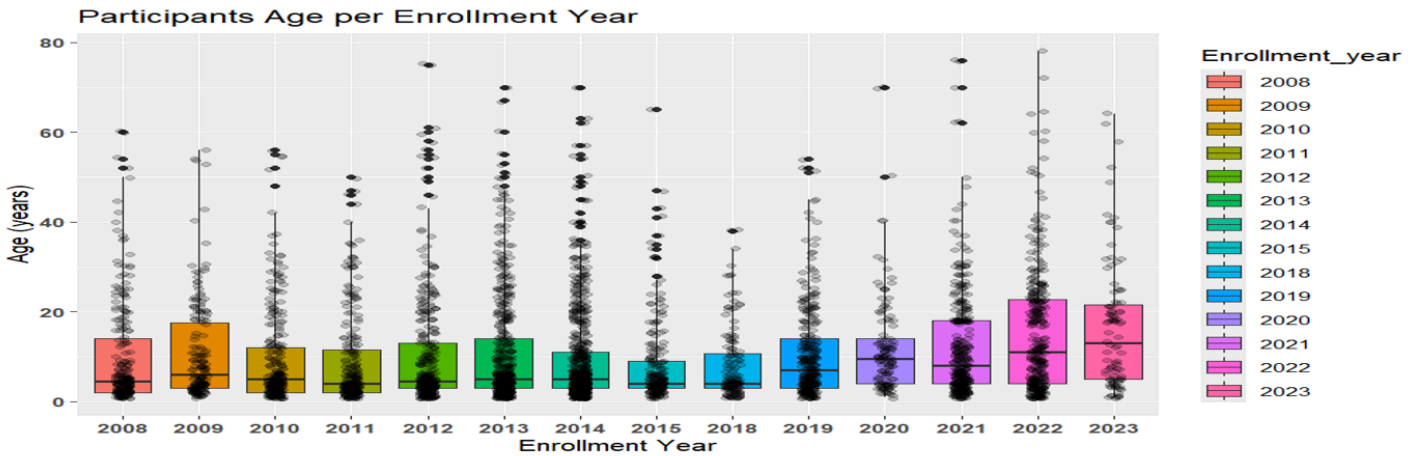


Figure 1a. Box plot with overlaid jittered points showing overall distribution of participants' age. Over the study period from 2008 to 2023, a significant shift in the median age can be seen with a rising trend despite missing data for 2016 and 2017 since it was during a transition period for the study.

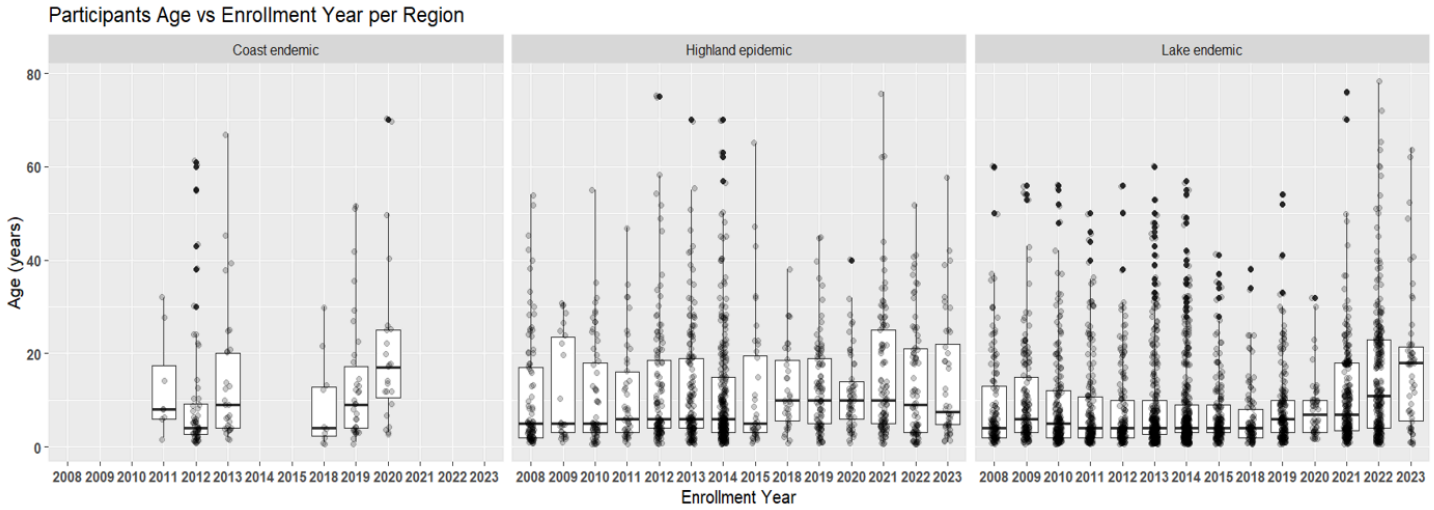


Figure 1b. Box plot with overlaid jittered points showing regional distribution of participants' age per study region. Assessment of participants median age across study period was significant for each region including Coast endemic, Highland epidemic and Lake endemic with shifting trends.

Figure 1

See image above for figure legend

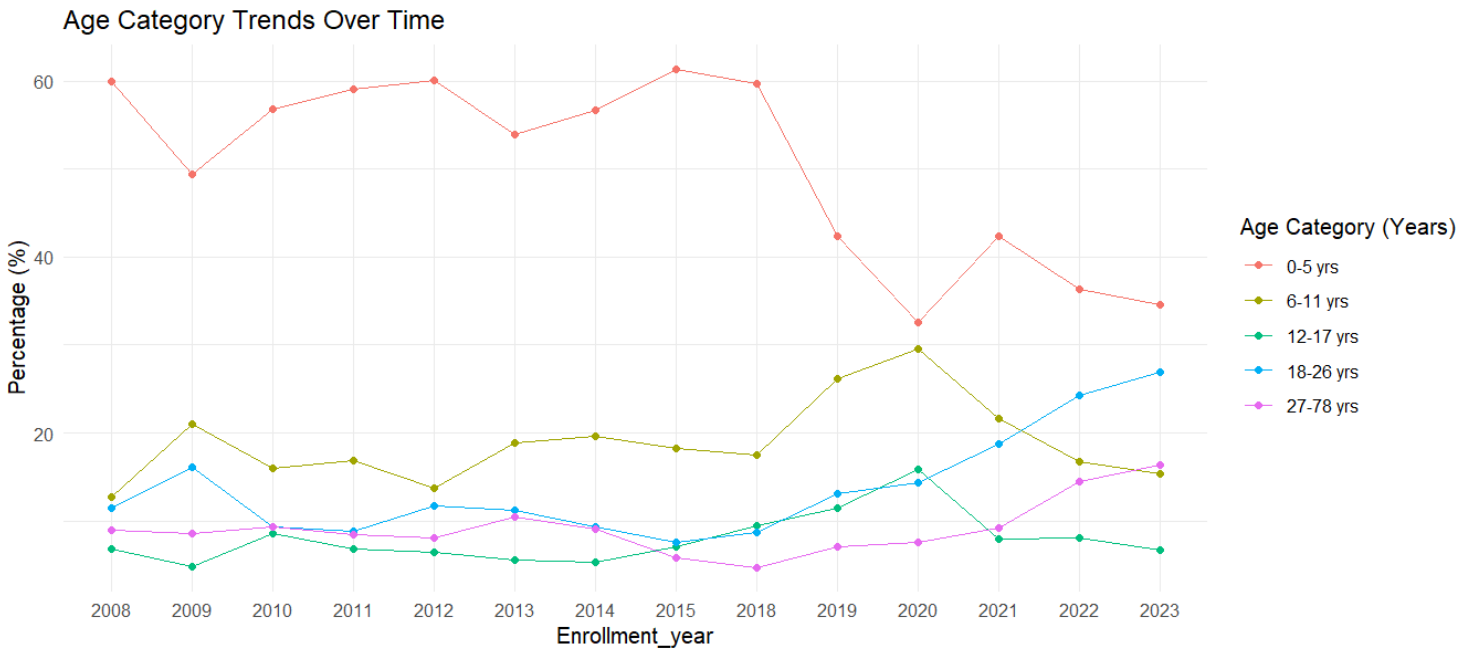


Figure 2

Line graph indicating frequency of temporal trends for the age categories. The frequencies vary with a rising trend seen in the 18-26yrs and 27-28yrs age categories while a decline is seen in the 0-5yrs categories.

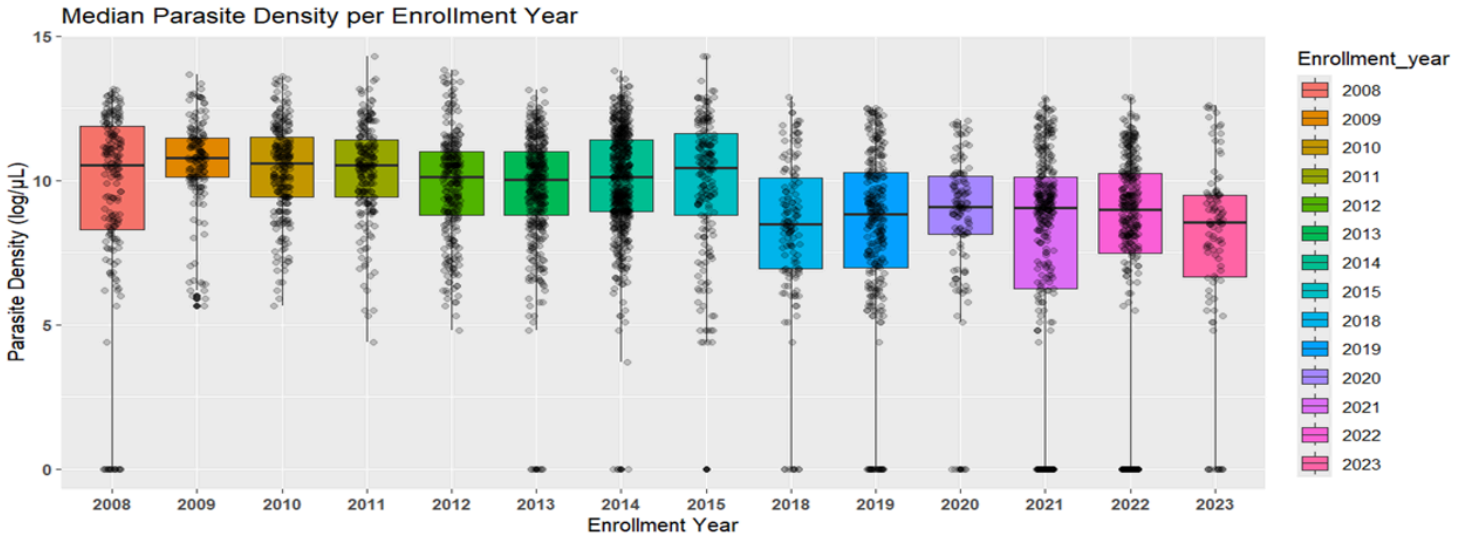


Figure 3a. Box plot with overlaid jittered points showing participants' parasite density temporal trends. Declining trends can be seen in the median parasite density from 2018 – 2023.

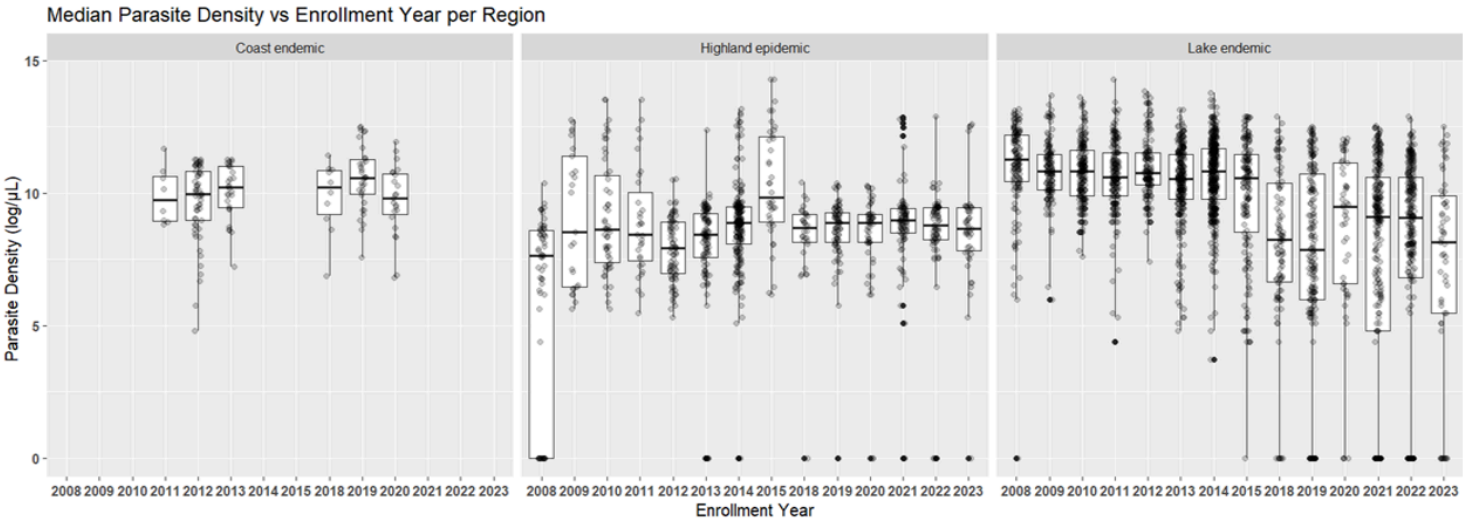


Figure 3b. Box plot with overlaid jittered points showing participants' parasite density for the ecological regions. The parasite density in Coast endemic, Highland epidemic and Lake endemic was significantly variable across the study periods. Significant declining trends were observed in the Lake endemic region while Highland epidemic had relatively steady trends.

Figure 3

See image above for figure legend

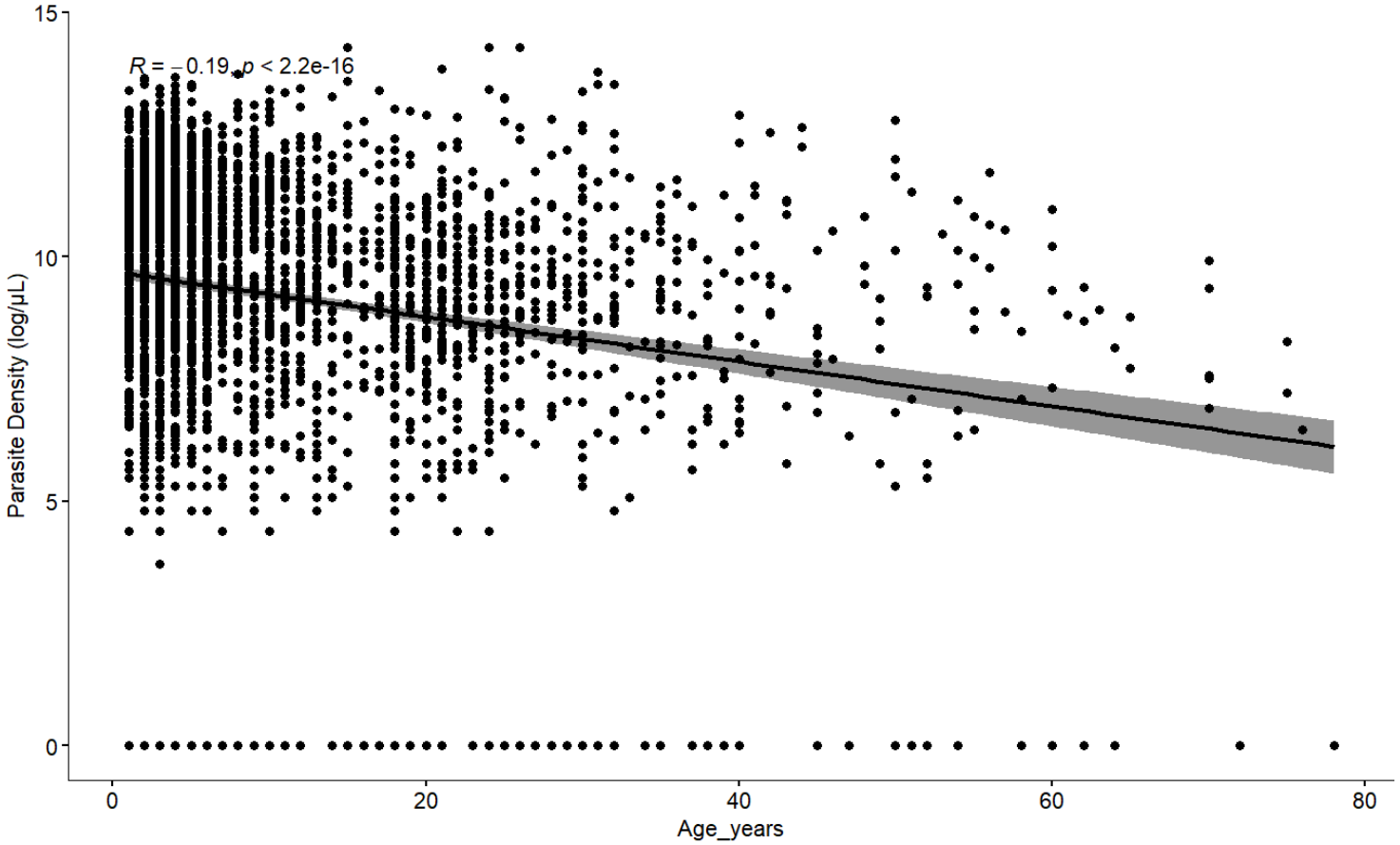


Figure 4

Scatter plot illustrates the relationship between age in years and parasite density. Each dot represents an individual observation. The solid line shows the fitted linear regression line, with shaded region indicating the 95% confidence interval. Weak but statistically significant inverse correlation was observed between age and parasite density ($R = -0.19$, $p < 2.2 \times 10^{-16}$).

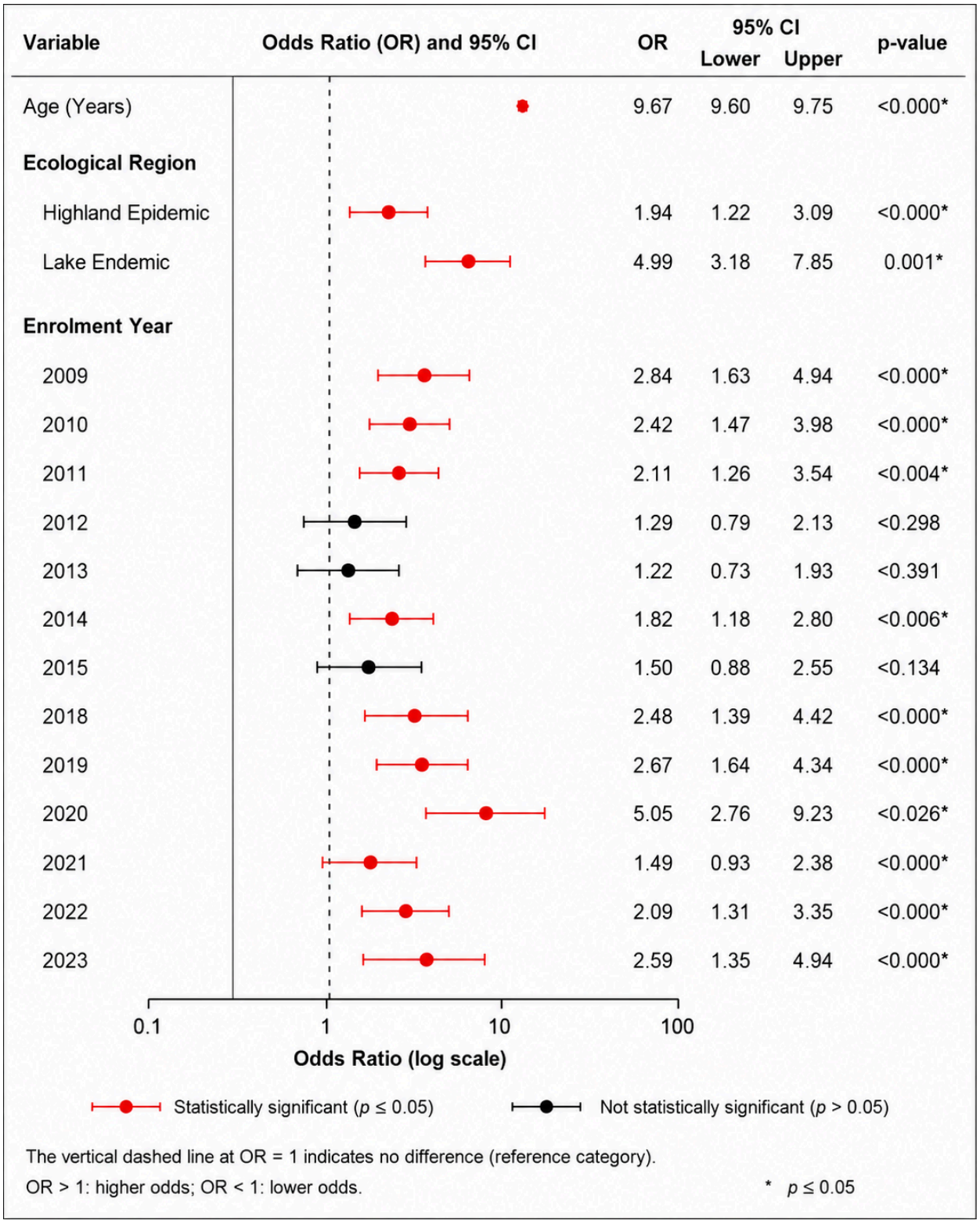


Figure 5

Forest plot indicating summary of the association between demographic and temporal factors and the odds of the outcome (parasite density) relative to their respective reference categories. The vertical dashed line at OR = 1 represents no association; estimates to the right indicate increased odds, while those crossing the line are not statistically significant. Red confidence interval (CI) lines represent statistically significant associations (p ≤ 0.05), whereas black lines indicate non-significant results.

Supplementary Files

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- SupplementaryInformation2026June17.pdf