

Examining the Malaria Burden: Estimates of Repeat Malaria Cases in Select Counties in the Lake Endemic Region, Kenya, June 2021-May 2022

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Abstract

Background

According to the 2020 malaria indicator survey, in Kenya, the prevalence of malaria in children aged 6 months to 14 years was 6%, with the highest prevalence in Busia at 38.5%, followed by Siaya at 28.8%, and Kisumu at 15.6%. Repeat malaria cases are infections confirmed by lab tests that occur after seven days of treatment. However, there is limited information on the prevalence of repeat cases. Thus, this study aims to examine the characteristics of repeat cases in select hospitals in Busia, Kisumu, and Siaya, with high incidence rates.

Methods

We conducted retrospective record reviews in several hospitals in Busia, Kisumu, and Siaya, which were selected based on their high incidence rates. We extracted patient data from outpatient, laboratory, and inpatient registers into MS Excel, including the date of visit, age, sex, residence, and malaria tests. We analyzed categorical data using frequencies and percentages and continuous variables using the median and interquartile range.

Results

In this study, there were 26,133 cases, out of which 3,136 (12%; 95% CI, 11.6–12.4) were repeat cases. Children under 15 years accounted for 64% (1,993) of the repeat cases, with females making up 58% (1,833), and Busia contributing 72% ($n = 2,249$). Urban and peri-urban facilities contributed 44% (1,333) and 42% (1,275) of repeat cases, respectively. Microscopy diagnosed 22% (687) of repeat cases in both the first and second episodes, while mRDT diagnosed 43% (1,335) in both episodes. Of those diagnosed with mRDT in both episodes, 80.8% (1,079) exceeded the 42-day interval between tests. The laboratory testing compliance with national malaria diagnosis, testing, and treatment guidelines was 88% for first repeat cases. Children under 5 years were 1.5 times more likely to undergo laboratory testing according to national guidelines than those aged 5–14 years. The use of microscopy versus rapid test in the first repeat episode was strongly associated with patients' age ($\chi^2 28.2$, $p = 0.004$). The median interval between the first and second malaria episodes was 146 days (IQR, 51–341).

Conclusion

Repeat malaria cases represented 12% of the total, depicting similar distribution in person and place. The majority of these cases were contributed by females and children below 15 years. However, the actual burden of these cases could be greater as lower-level healthcare facilities were not investigated.

To curb repeat malaria infections in children, the malaria lake-endemic counties should enhance laboratory surveillance and treatment

Background

Malaria infections are a significant global health concern with an estimated 24.7 million malaria cases in 2021, of which the WHO African Region contributed an estimated 23.4 million cases (95%). Kenya contributed 3% of the Sub-Saharan malaria burden with over 18% outpatient consultations related to malaria (1).

Research on repeat malaria infections has been conducted globally, particularly in therapeutic efficacy studies and cohort studies. These studies classify repeat infections as relapse, recrudescence, or new infections (2, 3). Relapses are specific to *Plasmodium vivax* and *Plasmodium Ovale* which has latent liver stage parasites that become activated into erythrocytic stages (4–6). Recrudescence is reappearance of infection with all malaria species that do not have hypnozoites. This occurs when the infection persists in the blood at undetectable levels after treatment and then becomes detectable again (7). On the other hand, re-infection takes place when a person is bitten by an infectious mosquito after treatment and recovery from a previous infection (8). In this study, repeat malaria was defined as more than one laboratory confirmed malaria episode during the study period.

In Kenya, malaria is diagnosed using both microscopy and rapid diagnostic tests. Microscopy is the preferred method in malaria endemic areas and involves identifying and quantifying the parasite on a thick blood slide, while species are differentiated on a thin smear using a light microscope under a power 100 oil immersion objective lens. Health centers, sub county and county health facilities with equipped laboratories, electricity connection and laboratory staffs implement diagnosis by microscopy. Rapid diagnostic tests are the mainstay in dispensaries and at the community level. They may also be used to complement microscopy in higher level facilities at the points of care. To differentiate *Plasmodium falciparum* from other plasmodium species, immunochromatographic malaria rapid diagnostic tests (mRDT) are used. These tests use parasite histidine-rich protein 2 (HRP2) antigens specific to *Plasmodium falciparum* and parasite lactate dehydrogenase (p LDH) or aldolase. They are used in dispensaries and complement microscopy in higher level facilities. Polymerase chain reaction (PCR) is used to detect parasite deoxyribonucleic acid (DNA) and differentiate species, although it is not used in routine clinical diagnosis. PCR is, however, the gold standard for therapeutic efficacy studies. (9–12).

The Kenya Malaria Indicator Survey (KMIS) conducted in 2020 revealed that 6% of children aged 6 months to 14 years tested positive for malaria parasites by microscopy, while 7% tested positive for *Plasmodium falciparum* antigens by Rapid Diagnostic Test (mRDT) (13). The survey found the overall malaria prevalence among children to be 6%, with significantly higher rates in certain counties, such as Busia (38.5%), Siaya (28.8%), and Kisumu (15.6%). In 2021, the malaria incidence per 1000 population in these counties was recorded as Siaya (520.5), Busia (432.4), and Kisumu (310.4).

The current prevalence and incidence data do not provide information on the burden of repeat malaria. This is a critical gap in achieving sustained reduction in the number of new cases as the nation strives towards malaria elimination (15–17). To address this gap, it is necessary to characterize the epidemiological profiles of repeat cases. Accurate data on the burden of repeat malaria infections can inform decision-making and targeted prevention efforts aimed at eliminating malaria (18). This investigation aimed at describing cases of repeat malaria in select health facilities in Busia, Siaya, and Kisumu in time, place and person.

Methods

Investigation site and population

Kisumu (0° 5' 30.1272" S, 34° 46' 4.6416 "E), Busia (0° 25' 59.99" N, 34° 08' 60.00" E) and Siaya (0° 3' 45.4644" N and 34° 17' 16.1052" E) are three counties located in the western part of Kenya. They border Lake Victoria with elevations of 1140–1400 meters above sea level. The region is characterized by stable malaria transmission all year round. Rainfall, temperature and humidity are the drivers of the perennial transmission of malaria. The female anopheles' mosquito is the primary vector for human malaria transmission. Vector abundance varies by species in these counties: Busia has predominantly *Anopheles gambiae*, while Kisumu and Siaya have *Anopheles arabiensis*, *funestus*, and *rivolorum*. In this region, the *Anopheles* mosquito life cycle lasts 7–14 days due to suitable climatic conditions, and vector breeding is facilitated by the presence of various water bodies, including streams, rivers, rice paddies, irrigation trenches, and Lake Victoria. The transmission of malaria is intense all year round, with annual entomological inoculation rates ranging from 30 to 100 (19).

To identify study sites, we selected three sub-county hospitals in each county with a malaria incidence exceeding 300 cases/1000 population. The facilities were geographically distributed to include an urban, rural and peri-urban area. The investigation sites included Nambale, Butula and Budalangi sub counties in Busia County, Kisumu West, Seme and Nyakach in Kisumu County, Bondo, Alego Usonga and Gem in Siaya County (Fig. 1). We worked with the county malaria control coordinators to identify the facilities.

We conducted a retrospective review of patient records who were diagnosed with suspected or confirmed malaria between June 2021 and May 2022.

Suspected malaria cases were defined as those with a record of fever along with at least one of the following symptoms: headache, backache, chills, sweating, myalgia, nausea, or vomiting. Confirmed malaria cases were those with a positive blood smear or positive malaria rapid diagnostic test (mRDT). Repeat malaria cases were defined as repeated entries of previously confirmed cases in the health facility records, with a repeat diagnosis of confirmed malaria through a positive blood smear or positive mRDT.

Data collection

We abstracted data from the health facilities' outpatient registers for patients under five years of age (MOH 204a) and over five years of age (MOH 204b), the laboratory register (MOH 240), and the inpatient registers (MOH 301). These registers contain patient information such as outpatient numbers, dates of visit, age, sex, residence, symptoms, clinical diagnosis, laboratory tests, results and treatment information. We obtained the registers from the records department or point of service and examined the columns for malaria diagnosis, laboratory result and treatment with Artemether Lumefantrine (AL) or artesunate. Using an Excel template, we extracted patients full names, age, sex, residence, date of diagnosis, laboratory test done and results. Out-patient records of confirmed or suspected malaria were cross checked against the laboratory register for confirmation of diagnosis. Cases were categorized as confirmed malaria only if positive microscopy or malaria rapid diagnostic test (mRDT) results were documented. Patients treated with AL without laboratory confirmation were assumed to have been treated presumptively and were not included in the final list.

Data Analysis

Data were cleaned by removing blanks, checking for spelling errors of patient names and residence. We sorted the names alphabetically, formatted the name column using conditional formatting to identify duplicates and manually scanned through all the duplicates. This was followed by checking for consistency in residence and age before categorizing duplicate records as repeat cases. Duplicated entries were further analyzed for consistency in residence and age before being categorized as repeat cases. Additional criteria used to identify repeat cases from the registers included matching of at least two names, age and residence, matching names and residence with difference of one or two years in subsequent age records, matching age and residence with different spelling of the name, matching name and age with a different residence but within the same geographical area. The additional criteria were applied to sets of ambiguous records and was decided by consensus of two or more data analysts.

We performed descriptive statistics including means and medians and their corresponding standard deviations or inter quartile range on continuous variables, frequencies and proportions and their confidence intervals for categorical variables. For summary statistics on repeat cases, the denominator was the total number of cases or stratum totals for diagnostic method, age, sex or residence. We presented place data using QGIS version 3.16.0 Hannover maps and summary of county specific distribution by top five villages in each sub county. We analyzed the time between repeat visits by difference in days and presented categorized time intervals in frequencies and percentages. This was achieved by listing dates of the first, second, third or fourth visit in columns then applying MS Excel function "DAYS" to obtain the difference in days, then stratifying the intervals into "less than 7 days, 7–14 and more than 14 days using "COUNTIFS" logical function. The laboratory diagnosis method on each visit was listed and expressed as a proportion. In addition, diagnostic method at repeat visits categorized as microscopy or rapid diagnostic test by age was assessed for independence. Second malaria episodes occurring within two weeks were specifically assessed for adherence to national diagnosis guideline recommending the use of microscopy for suspected treatment failure.

Ethical consideration

We sought permission from the County Directors of Health before data collection. During data abstraction, confidentiality was ensured by password protection of sheets with patient names. After completion of analysis, names were recoded and deleted. The findings were disseminated to the Counties and Division of National Malaria Program.

Results

A total of 26,133 records of confirmed malaria cases were abstracted from the three counties, with females accounting for 57% of the cases. Of the total, 12% (3,132) were repeat cases, with children under 15 accounting for 64% (1,993) and females 58% (1,833) of the cases (Table 1). Busia contributed 72% (n = 2249) while Kisumu contributed 12% (n = 373). Urban facilities contributed 44% (1333); peri-urban 42% (1275). Among repeat cases, 87% had two episodes, 13.2% (422) three, and 2% (54) had four. The median interval between the first and second malaria was 146 days (IQR, 51–341) overall, with Busia 208 days (IQR, 57–316), Kisumu 75 days (IQR, 35–154) and Siaya 83.5 days (IQR, 41–163). The duration between malaria infections exceeded 28 days in 86% (2748) of the second (Table 2), 67% of the third (n = 284) and 67% of the fourth (n = 36) episodes. Repeat malaria diagnoses made in less than seven days were 2% (72) in the second visit, 5% (23) in the third and 7% (4) in the fourth visit.

Table 1
Characteristics of cases and repeat cases, Kisumu, Siaya and Busia counties, June21 –May 22.

Variable	Total Cases (n, %)	Repeat cases (n, %)
Total	26133	3132
Age group (years)		
< 5	7268,28	844,27
7–14	8970,34	1149,37
15–24	5788,22	718,23
25–34	1770,7	193,6
35–59	1612,6	160,5
≥ 60	674,3	68,2
Sex		
Female	14924, 57	1833,58
Male	11209, 43	1303,42
Test status		
Microscopy positive	14174, 54	1823,51
mRDT positive	11959, 46	1730,49

Table 2
Time interval to second malaria episode, Kisumu, Siaya and Busia, June21 –May 22.

Time (days) to second episode	Results (n)	Proportion %
< 7	71	2
7–14	138	4
15–28	242	8
29–42	203	7
> 42	2458	79
Total	3112	

Of the 3132 repeat cases, 22% (687) were diagnosed by microscopy in both their first and second malaria episodes. Meanwhile, 35% (1096) tested positive by mRDT on their first visit and retested by microscopy, while 43% (1335) were retested by mRDT. The duration between two consecutive mRDT exceeded 42 days in 1079 (81%), while in 22 (1.6%) cases, it was less than 7 days (Table 3). For repeat

infections occurring within 14 days of the initial diagnosis, the laboratory diagnosis by microscopy was 54%, and by mRDT was 34%. Among those retested by mRDT, 22(3.2%) returned in less than seven days.

Table 3

Laboratory tests done in first visit, second visit, Kisumu, Siaya and Busia County, June21 –May 22.

First visit test, Repeat visit test						
Age(years)	BS, BS	BS, mRDT > 42 days	BS, mRDT < 42days	mRDT, mRDT > 42days	mRDT, mRDT < 42days	mRDT, BS
< 5	217	156	22	260	53	94
5–14	228	203	48	403	103	122
Total	445	359	70	663	156	216

BS, mRDT- Microscopy implies blood slide microscopy during first visit, mRDT during second visit.

The analysis revealed that children under 5 years were 1.5 times more likely (cOR 1.5, $p = 0.004$) to receive laboratory testing in line with national guidelines compared to those aged 5–14 years (Table 4). Test practices adherent to national guidelines including microscopy testing in both visits, microscopy testing in all repeat visits and use of mRDT 42 days after initial test was strongly associated with patients age ($\chi^2_{2} 8.2$, $p = 0.004$).

Table 4

Laboratory testing per guidelines by age group, Kisumu, Siaya and Busia County, June21 –May 22.

Age group (years)	Tests adherent to guidelines	Tests not Adherent	Total
< 5	727	75	802
5–14	956	151	1107
Total	1683	226	1909

The number of confirmed cases decreased between June and August 2021, rising steadily thereafter till December, dropped slightly then increased, peaking from March through May 2022 (Fig. 2).

Discussion

Our study found that the highest number of malaria cases, both initial and repeat, were reported in children under 15 years old. Budalangi Sub-County in Busia County had the highest number of cases. This could be because parents and guardians of young children are more likely to seek medical attention for febrile symptoms. Furthermore, children often exhibit febrile signs and symptoms due to their underdeveloped immunity. Conversely, older individuals tend to have greater clinical immunity against

malaria, which reduces their chances of repeat infections (20). Although asymptomatic adults may not seek care, they can still carry and spread malaria, leading to an underestimation of the reported repeat malaria burden (21, 22). The 2020 Kenya Malaria indicator survey reported the highest prevalence of malaria in Busia where ideal conditions for the proliferation of malaria vectors may lead to repeated exposure to mosquito bites and transmission of malaria parasites, contributing to the high number of repeat cases observed in Busia (23, 24).

Repeat malaria cases showed a similar distribution to initial cases, with the < 15 age group, females, and those living in urban and peri-urban areas being the most affected. However, the investigation sites were mainly peri-urban in Busia county, which may have distorted the findings. The national malaria treatment guidelines recommend microscopy as the gold standard for diagnosis in endemic areas, but staff shortages and power outages led to inconsistent use of this method. Overreliance on rapid diagnostic tests can lead to erroneous diagnoses of non-malarial febrile illnesses as repeat malaria reinfections especially when rapid diagnostic tests are used for detecting infections recurring earlier than six weeks (25, 26).

Our study revealed that patients experienced up to five malaria infections, with most having one reinfection within a year. These findings are consistent with a previous study in Thailand in 2019, which estimated one to three re-infections annually (6).

The majority of repeat malaria diagnoses occurred after 28 days, however, the possibility of progression from uncomplicated to severe malaria or new infections could not be ruled out for those returning in less than seven days. These populations have different levels of exposure to malaria due to environmental factors such as presence of stagnant water bodies and varying levels of vaccination against malaria. Analytic studies could control for potential effect modification and confounding; however, this was beyond the scope of this investigation. The median time between repeat visits could be used to inform the counties of the diagnostic and therapeutic commodities stocks required. This will aid forecasting and quantification which avoiding overstocking, expiries or understocking leading incomplete patient care. Malaria treatment guidelines recommend assessing treatment compliance before confirming repeat infection by microscopy for patients returning within seven days. Treatment compliance includes completing the prescribed dose at correct time. For the first line of treatment with AL, dosage is based on the patients' weight. The first dose should be taken under direct observation, followed by a second dose eight hours later, and subsequent doses every 12 hours until the three-day regimen is complete. It's important to also inquire about vomiting of medication within 30 minutes of intake during further assessment. In this investigation there was a significant dependence on mRDT for diagnosing repeat infections. Most of the cases underwent a second mRDT test after an initial one, which could potentially overestimate the burden of repeat infections due to the low specificity of mRDT within two weeks of infection (9). Testing practices that did not adhere to national guidelines call for reinforcement of three yearly mentorship on case management among healthcare workers and onboarding of new employees.

Limitations of the investigation

While this investigation provided valuable insights into the prevalence and epidemiology of repeat malaria cases in the Lake endemic region, it is important to recognize limitations posed by the study design. The investigation did not explore the factors associated with repeat malaria cases, such as treatment failure. Treatment data was not collected at either the facility or patient level, which made it challenging to assess adherence to treatment guidelines, and it is possible that asymptomatic cases or those who self-medicated were overlooked. Furthermore, low levels of parasitemia may have been missed on microscopy. The study did not assess the malaria vaccination status of children, which could have impacted their susceptibility to malaria infection. Patients residing in regions with several health facility options may also have sought care elsewhere, leading to potential underestimation of repeat cases in study facilities. In addition, public hospital are plagued by long queues and waiting times further discouraging repeat visits especially for non-severe illness(27).

Regardless, this investigation was able to estimate the prevalence of repeat malaria cases in three counties in the lake endemic region where data on differentiating total malaria cases from repeat cases was previously scarce. These findings can serve as a foundation for future studies that explore risk factors, molecular surveillance, and therapeutic efficacy.

Conclusion

According to the study, around 12% of malaria cases are repeat occurrences, with females and children under 15 being the most affected in urban and peri-urban areas. The investigation revealed shortcomings in adherence to national guidelines for malaria diagnosis and treatment, such as not using microscopy as the gold standard for diagnosis. The investigation also emphasized the need for regular mentorship and training for healthcare workers to ensure adherence to guidelines and proper testing procedures.

Despite the investigation's limitations, such as the failure to assess treatment adherence and asymptomatic cases, the study offers crucial information about the frequency and distribution of recurring malaria cases in the lake-endemic area. This data could aid in identifying risk factors and evaluating treatment efficacy, as well as facilitating the development of targeted interventions to alleviate the malaria burden in affected communities.

Recommendation

In order to promote adherence, it is necessary to address the shortage of staff in sub-county facilities, particularly on weekends. Additionally, providing three-yearly mentorship on case management for healthcare workers and training for new employees can improve testing practices.

To decrease malaria transmission, it is essential to intensify interventions such as the use of insecticide-treated bed nets and indoor residual spraying in high transmission areas like Busia County. Further

research is needed to identify risk factors for repeat malaria cases and evaluate the effectiveness of targeted prevention measures in reducing the burden of repeat cases.

In general, the results of this investigation emphasize the significance of enhancing malaria surveillance, case management, and prevention strategies in endemic areas, especially among vulnerable populations such as children under 15 and females. Standardizing the reporting of confirmed cases as initial or repeat cases is crucial for accurately estimating the malaria burden and tracking progress towards the goal of malaria elimination.

Abbreviations

AL	Artemether Lumefantrine
DNA	deoxyribonucleic acid
DNMP	Division of National Malaria Program
FELTP-K	Field Epidemiology and Laboratory Training Program Kenya
KMIS	Kenya Malaria Indicator Survey.
KMS	Kenya Malaria Strategy
mRDT	malaria rapid diagnostic tests
MOH	Ministry of Health
PCR	Polymerase chain reaction
pHRP2	Parasite histidine-rich protein 2
pLDH	Parasite lactate dehydrogenase
PMI	Presidential Malaria Initiative

Declarations

Ethics approval and consent to participate

The study was authorized by the Ministry of Health through the Field Epidemiology and Laboratory Training Program. Individual county Directors for Health permitted the investigation in the respective counties.

Consent for publication

Not applicable

Availability of data and materials

The data sets informing results of this investigation are available upon request from the corresponding author.

Conflict of interests

The authors declare that they have no conflict of interest

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Authors contribution

JK led the investigation in the design, data collection, analysis, interpretation as well as drafting the manuscript. FO, made substantial contribution in the investigation design, data collection, analysis and revision of the manuscript. FO,MO and EO supervised the protocol development, study execution and reviewed drafts of the manuscript.

CM, VK, CA, GG made contribution to data collection, analysis and report writing.

All authors read and approved the final manuscript.

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Figures

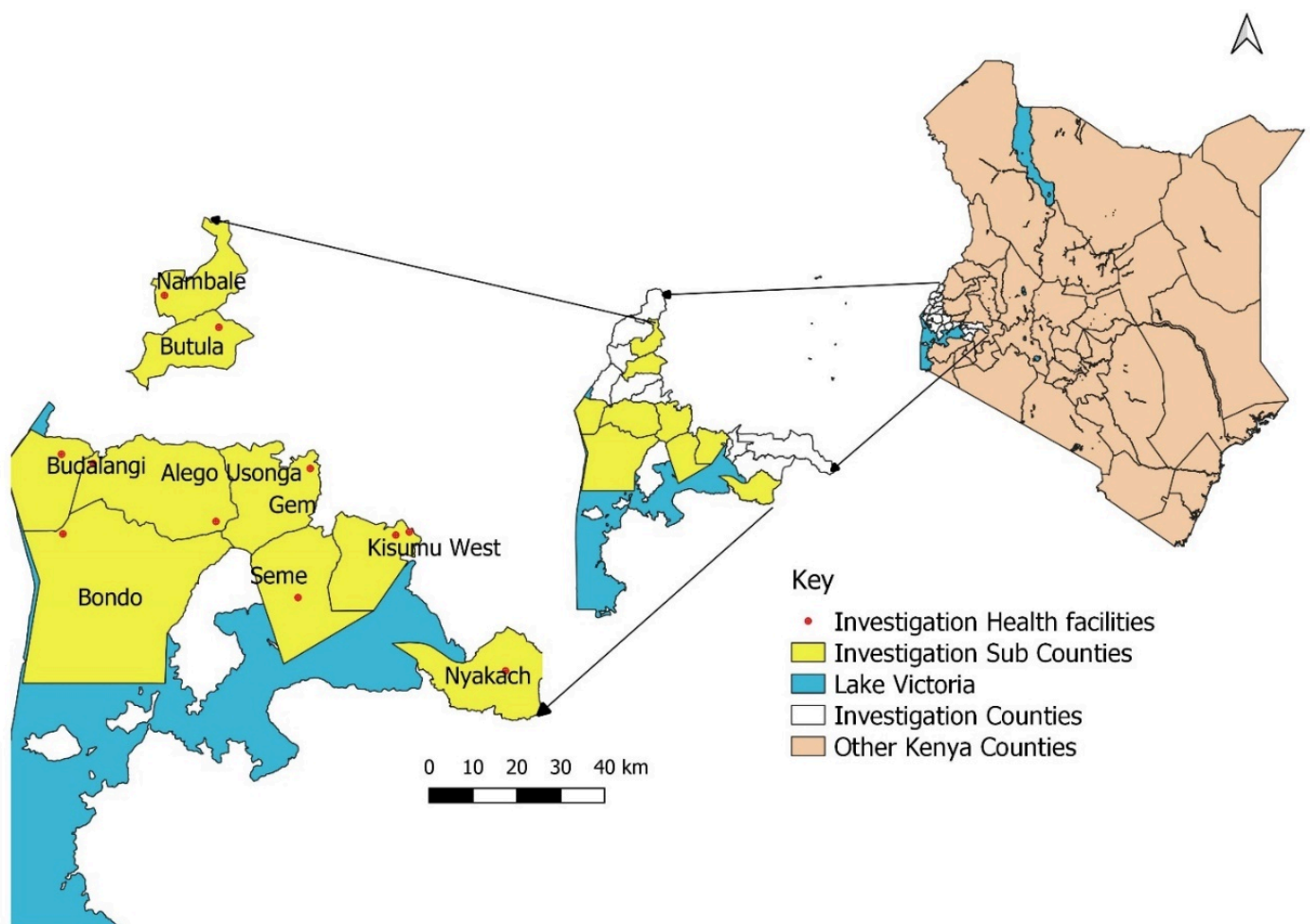


Figure 1

Map highlighting investigation sites for repeat malaria cases, Kisumu, Siaya and Busia, June21 –May 22.

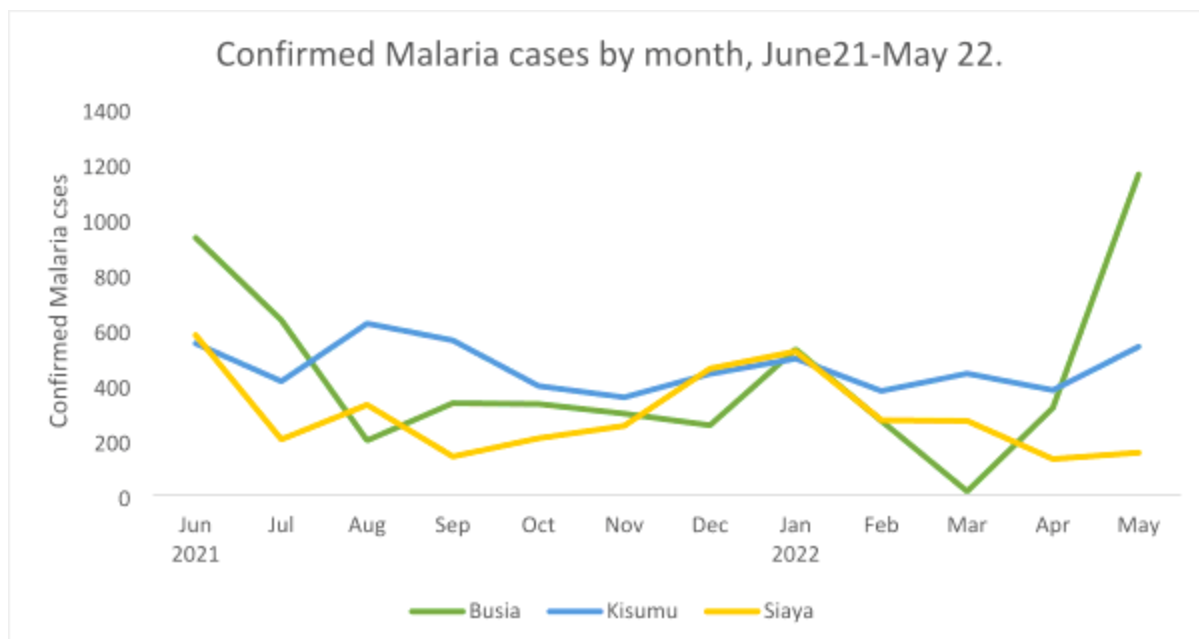


Figure 2

Map highlighting investigation sites for repeat malaria cases, Kisumu, Siaya and Busia, June21 –May 22.