Malaria Outbreak in Mbale: It's the Pits! A Case Study

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Abstract

Background: Malaria is a leading cause of morbidity and mortality in Uganda. In June 2019, the Uganda Ministry of Health through routine surveillance data analysis was notified of an increase in malaria cases in Bumbobi and Nyondo Sub-counties, Mbale District, which exceeded the action thresholds. We investigated to assess outbreak magnitude, identify transmission risk factors, and recommend evidence-based control measures.

Methods: We defined a confirmed case as a positive malaria result using malaria Rapid Diagnostic Test or microscopy from 1 Jan 2019 to 30 Jun 2019 in a resident or visitor of Bumbobi or Nyondo Sub-county, Mbale District. We reviewed medical records to develop a line list for descriptive epidemiology. In a case-control study, we compared exposures between 150 case-persons and 150 age- and village-matched asymptomatic controls. We conducted environmental and entomological assessments on vector dynamics and behavior.

Results: We identified 7,891 case-persons (attack rate [AR]=26%). Females (AR=36%) were more affected than males (AR=25%). The 5-18 year age group (AR=26%) was most affected.
The epidemic curve showed steady increase in malaria cases from March following intermittent rainfall from January with short spells of no rainfall up to June. In the matched pair case-control analysis, 95% (143/150) of case-patients and 49% (73/150) of controls had soil erosion control pits near their homes that held stagnant water for several days following rainfall (AOR=18, 95%CI=7-50); Active breeding sites were found near and within homesteads with *Anopheles gambiae* as the predominant vector.

Conclusion: Increased vector breeding sites due to erosion control pits sustained by the intermittent rainfall caused this outbreak. We recommended draining of pits immediately after the rains and increasing coverage for bed-nets.

Key words: Case Study, Malaria, *Plasmodium falciparum*, Outbreak, Uganda

Participant guide: Distribute to students

Learning Objectives

After completing this case study, the participant should be able to:

- Detect a malaria outbreak using ‘normal channels’
- Follow steps for outbreak investigations
- Develop a line list
- Perform descriptive epidemiology to inform a hypothesis
- Describe the role of an environmental assessment in the control of a malaria outbreak
- Discuss how to identify risk factors for an analytic study

This case study is based on an investigation conducted in June 2019 by Uganda Public Health Fellowship Program (UPHFP) fellows in Mbale District.

This case study was developed by Kadobera Daniel, Gloria Bahizi, Lilian Bulage, Benon Kwesiga, Stephen Ndugwa Kabwama, Alex Riolexus Ario and Julie Roberts Harris
in 2019

Do not read this page aloud

How to use this case study: Case studies in applied epidemiology allow students to practice applying epidemiologic skills in the classroom to address real-world public health problems. The case studies are used as a vital component of an applied epidemiology curriculum, rather than as stand-alone tools. They are ideally suited to reinforcing principles and skills already covered in a lecture or in background reading.

This case study has a facilitator guide and a participant guide. Each facilitator should review the Facilitator Guide, gain familiarity with the outbreak and investigation on which the case study is based, review the epidemiologic principles being taught, and think of examples in the facilitator’s own experience to further illustrate the points.

Ideally, participants receive the case study one part at a time during the case study session. However, if the case study is distributed whole, participants should be asked not to look ahead.

During the case study session, one or two instructors facilitate the case study for 8 to 20 students in a classroom or conference room. The facilitator should hand out Part I and direct a participant to read one paragraph out loud, then progressing around the room and giving each participant a chance to read. Reading out loud and in turns has two advantages. First, all participants engage in the process and overcome any inhibitions by having her/his voice heard. Second, it keeps the all participants progressing through the case study at the same speed.

After a participant reads a question, the facilitator will direct participants to answer the question by perform calculations, construct graphs, or engage in a discussion of the answer. Sometimes, the facilitator can split the class to play different roles or take different sides in answering the question. As a result, participants learn from each other, not just from the facilitator.

After the questions have been answered, the facilitator hands out the next part. At the end of the case study, the facilitator should direct a participant to once again read the objectives on page 1 to review and ensure that the objectives have been met.

Prerequisites: For this case study, participants should have received instruction or conducted readings in:

- Outbreak investigation
- Intermediate epidemiology (interpreting odds ratio, epidemic curves, etc.)
- Basics of malaria epidemiology

Target audience: Trainees in the Uganda Field Epidemiology Training Program / Public Health Fellowship Program, other Field Epidemiology and Laboratory Training Programs (FELTPs), public health students, public health workers who may participate in rapid needs assessments and others who are interested in this topic.

Level of case study: Intermediate or Advanced
Time required: Approximately 4 hours **Language:** English

Part I

In June 2019, the Uganda Public Health Emergency Operations Center (UPHEOC) at the Uganda Ministry of Health (MoH) received a call from an epidemiologist at the National Malaria Control Division (NMCD). The epidemiologist reported that 84 of the 112 districts in Uganda had ongoing malaria outbreaks. These outbreaks had begun as early as March, during the start of the annual rainy season.

According to the UPHEOC, this was an unprecedented situation! Even with the expected seasonal increases, this was unusually high compared to previous years. In addition, for all of them to happen at the same time was highly unusual. During the call with the UPHEOC, the NMCD epidemiologist warned that the whole country could be battling malaria outbreaks if the outbreaks continued to expand as projected.

<u>Question 1</u>:
What is an outbreak?

Malaria is a vector-borne disease transmitted by mosquitos of the *Anopheles* genus[1]. In Uganda, malaria is the leading cause of morbidity and mortality and is endemic in approximately 95% of the country[2]. Malaria transmission intensity is dependent on the vector (mosquito) population, favorable temperature ranges, and the presence of a malaria-susceptible population. The mosquito population itself depends on the existence of stagnant water, which is needed for breeding sites.

The NMCD is responsible for malaria prevention and control in Uganda, commonly carrying out activities such as distributions of Long-Lasting Insecticide treated Nets (LLINs), Indoor Residual Spraying (IRS), supplying anti-malarials, and development of treatment guidelines among other activities. They are also responsible for analyzing surveillance data, which are collected in the electronic District Health Information System 2 (DHIS2) database from the local public healthcare levels in the country. Ideally, malaria surveillance data should be analyzed by both the districts and by NMCD on a weekly basis. In June 2019, however, analysis had not been done routinely for the past six months.

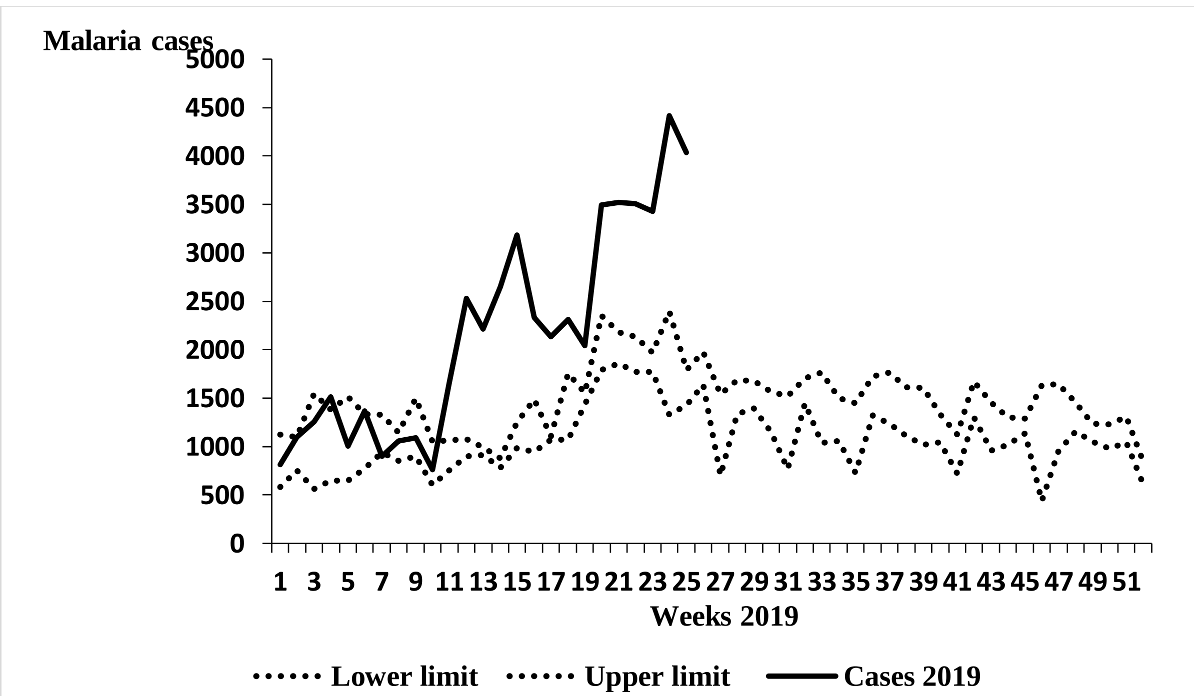
The National Task Force (NTF) in Uganda is responsible for emergency response and control of disease nationally. On hearing about the large number of districts identified as having outbreaks, the NTF recommended immediate investigations. Four fellows in the Uganda Public Health Fellowship Program (PHFP) were assigned to start the work, under the supervision of the NMCD.

<u>Question 2</u>:
List the steps of an outbreak investigation

The team noted that the outbreaks were so widespread that it would be impossible to investigate all of them. They discussed options and selected Mbale District for their initial investigation.

Mbale District is in the Eastern Region of Uganda on the slopes of Mount Elgon, with an estimated population of ~600,000 residents in 23 sub-counties. It is served by 68 health facilities and hosts the Mbale Regional Referral Hospital. At the time of the investigation, the prevalence of malaria in Mbale was 21%, which was higher than it had been for many years. Normal channel graphs clearly showed an outbreak occurring in Mbale district.

Figure 1. *Malaria Normal Channels, Mbale, Uganda, January-June 2019*



<u>Question 3</u>:
What is a normal channels graph?

<u>Question 4:</u>
How is a normal channels graph generated?

<u>Question 5:</u>
Based on the normal channels graph, when did the malaria outbreak begin in Mbale?

A rapid response team (RRT) was assembled, comprising four epidemiologists from PHFP, the NMCD surveillance officer, and a logistics person from the MoH. The team met quickly to discuss who else to bring to the field. The PHFP fellows did not have all the expertise needed. They discussed what they would need to do in the field, and what skill sets would be helpful to ensure they could conduct a successful investigation.

<u>Question 6</u>:
Besides those mentioned, who else might be included in the RRT? What are their roles?

The RRT planned to leave for the field on 30 June 2019. Before departing, the team prepared logistics and identified the required equipment. In addition, they met to agree on a case definition, to guide the case-finding process.

<u>Question 7</u>:
What case definition should be used during malaria outbreaks?
How would you define the start and end dates for case identification in Mbale?

Part II

On 1 July 2019, the Rapid Response Team (RRT) arrived at the district and immediately met with the District Health Team (DHT), including the District Health Officer (DHO), District Malaria focal person, Biostatistician, District Entomologist, and Health Management Information System (HMIS) focal person.

The DHO told the team that he had first realized that there was a problem when he received reports of stockouts of malaria rapid diagnostic tests and antimalarial drugs in early April. At the time, the DHO did not report the problem because he initially attributed it to late delivery of mRDTs and antimalarial stock to the district from National Medical Stores. According to the DHO, all subcounties in Mbale appeared to be experiencing unusually high numbers of cases, but the most affected seemed to be the subcounties of Bumbobi (population: 18,835) and Nyondo (population: 7,891). The RRT subsequently constructed sub county malaria channels which confirmed the DHO's statement. To work within the scope of available resources, the team decided to focus the investigation on those two subcounties.

On 2 July 2019, the entire team traveled to Bumbobi and Nyondo. The team visited five health facilities, where they reviewed outpatient records and developed a line list. They included all patients who had been diagnosed with malaria between 1 March 2019 and 30 June 2019. In total, 8,827 confirmed case-persons were line-listed.

Question 8:
Although the cases did exceed normal channels before March 2019, the team chose to identify all cases in Bumbobi and Nyondo starting in March. Why was this important?

Question 9:
How would you search for cases?

Part III

The large number of cases in the outbreak made it difficult to look quickly at the line list and understand the situation, as might have been possible for a smaller outbreak. Descriptive epidemiology was needed to understand which group(s) is/are most affected, in terms of person, place, and time, which could provide clues to the etiology or the modes of transmission.

Calculating attack rates and comparing them across different groups is an important aspect of descriptive epidemiology. Calculating these rates correctly is important for interpreting an outbreak situation appropriately. Because different groups – age groups, geographic regions, sexes – have different-sized underlying populations, relying only on the count (the number of cases) to understand who is most affected can be misleading. A particular group may have the highest number of cases, yet be the least affected, because their underlying population is so large.

Question 10:
Using the data in the table 1 below, calculate the attack rates by sub-county and parish, Jan 2019-June 2019. What were the two most-affected parishes?

Table 1: Attack Rates by Sub-county and Parish, Jan 2019-June 2019

Sub-county	Parish	Cases	Population	AR/100
Bumbobi	Busambe	2227	4221	53
	Bufuya	1542	3139	
	Bukhumwa	1436	4456	
	Bumbobi	1493	7020	
	Total	**6698**	**18835**	
Nyondo	Bubetsye	1374	3555	
	Nyondo	554	3131	
	Bufukhula	85	1205	
	Total	**2013**	**7891**	

Although the team attempted to identify subdistrict population data, they were not available. As a result, they calculated the attack rates by age and sex for all of Mbale District.

Table 2: Attack Rates by Sex and Age, Jan 2019-June 2019

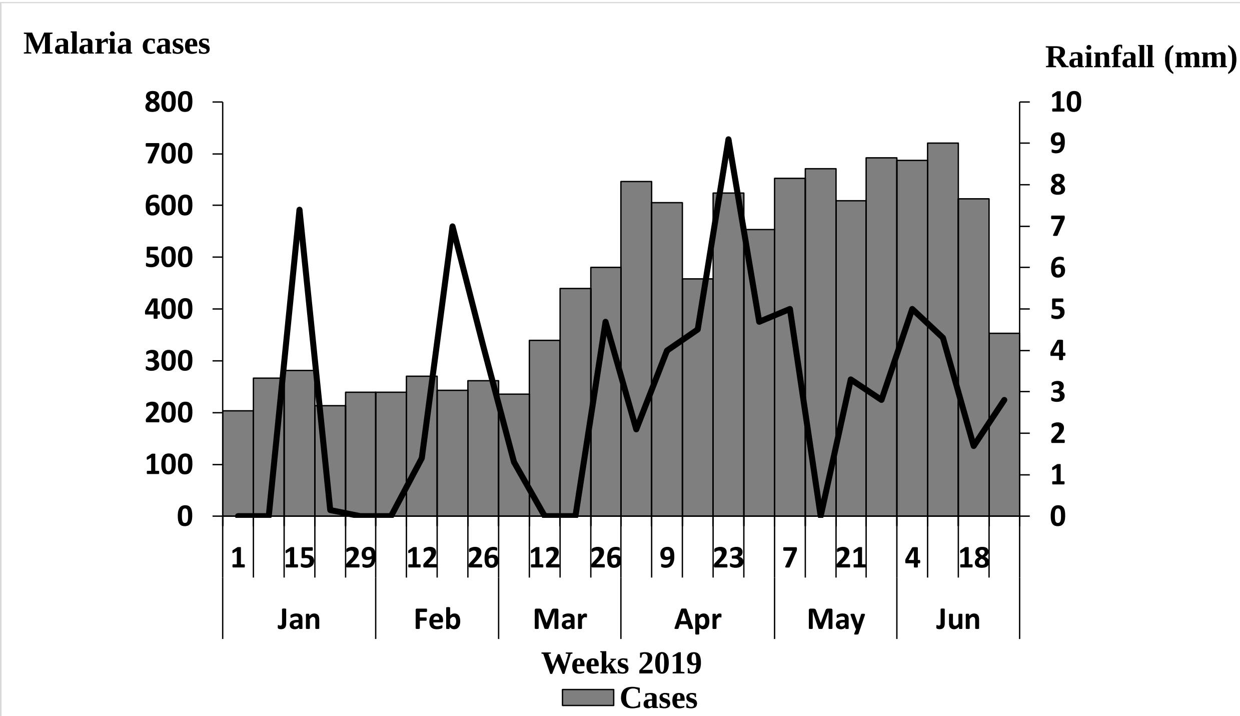
Variable	Cases	Population	AR/100
Sex			
Male	3,449	14,023	25
Female	5,378	15,320	36
Age			
<5	2,791	120,558	23
5 to 18	5,019	190,742	26
18+	3,702	254,700	14

Question 11:
What age group was most affected by the outbreak? What does it mean that women had a higher attack rate than men?

To understand the outbreak's onset and spread over time, the team developed an epidemic curve. An epidemic curve shows the frequency of new cases over time, usually using the date of onset of disease. An epidemic curve can be used to identify the most likely time or period of exposure that led to the outbreak and, sometimes, the likely mode of spread of the disease.

After calculating attack rates, the team decided to search for rainfall data to overlay with the epidemic curve. Malaria incidence is associated with previous rainfall, which can create mosquito breeding sites by leaving standing pools of water, and minimum temperature, which influences how quickly the malaria parasite matures into the mosquito (and can be passed to a human). For this reason, rainfall graphs are often overlaid on top of malaria epidemic curves.

Figure: Epidemic curve of the outbreak superimposed with weekly average rainfall (total rainfall (mm) in a week divided by 7 days, plotted at the median day of the week), Mbale District, 2019



Question 12: **Describe the rainfall pattern shown in the graph**.

<u>Question 13</u>: **Summarize the descriptive epidemiology for the outbreak in terms of person, place, and time.**

Part IV

The malaria cycle has three components: 1) the growth of the mosquito vector from egg to adult that becomes infected after it takes a bloodmeal from an infected person; 2) the development of the malaria parasite in the mosquito to a phase that is able to infect humans in the mosquito's next bloodmeal (and the survival of the mosquito to that time); and 3) the incubation period in the human host from the time of infection until the onset of malarial symptoms.

Because mosquitoes require standing water in which to deposit eggs, malaria outbreaks are strongly associated with rainfall. Models have shown that, under optimal conditions with a mean temperature of 25 C, a *minimum* of 38 days must elapse from rainfall and egg deposition to malaria cases in humans. However, given that conditions are not always optimal, the time period between rainfall and outbreaks is often closer to 50-60 days. As a result, malaria cases that occur a week or two after heavy rains are usually unrelated to those rains, but they may be related to rains that occurred ~7-8 weeks before[3].

Located on the slopes of a mountain, Nyondo and Bumbobi subcounties traverse an area of highlands (areas with steep hills that facilitate rapid runoff of water after rains), midlands (less hilly areas where rainwater often stops and stagnates in the gardens), and lowlands (the base of the mountains, which is flatter and mainly comprises sandy soils and swamps). On 11 July 2019, the team began an environmental assessment in Nyondo and Bubombi subcounties. They observed that rainwater streams from the highlands flowed through the midlands and down to the lower lands. The midlands, which hosted the farming community, had dug large "erosion control pits" in gardens close to the homesteads. These pits were meant to reduce the amount of post-rain erosion, which swept fertile soil away from the midlands and down to the lowlands and reduced the ability of the midlands residents to farm. However, erosion control pits also provided large standing pools of water after rainfall in the areas near homes. Because the rains were intermittent and not heavy, they successfully refilled the pits which kept the breeding sites active for long periods. In addition, the team identified multiple sites favorable for mosquito breeding along the roadside drainages, swamps, marram pits, and rock pools in the midlands. The team also noted that all households had at least one long-lasting insecticide-treated bednet (LLIN) in their house.

<u>**Question 14**</u>:

Of what significance was this environmental assessment in the investigation of the malaria outbreak?

Mosquitoes in Uganda comprise *Anopheles spp, Culex spp and Aedes. Anopheles gambiae* and *Anopheles funestus* are important vectors of malaria in Uganda. Of these, only female *Anopheles* spp can transmit malaria. They bite during the late evening outdoors and at night indoors. To identify whether or not people have such mosquitoes in their homes, pyrethrum spray catches (PSC) are often used. PSCs work by spraying an insecticide (pyrethrum) into the space (usually a home) and leaving a white sheet on the floor to collect the knocked-down mosquitoes[4]. These mosquitoes are then identified. PSC is usually conducted in the early morning. This captures for identification mosquitoes that likely had fed on household residents at night.

Twenty-two households from the 11 affected villages in Bumbobi and Nyondo were randomly selected from a list and visited to conduct PSCs. Mosquitoes collected were identified using morphological features under a microscope and identified by sex, species, and abdominal condition (fed, semi-gravid, or gravid). Gravid mosquitoes represent vector multiplication, while fed mosquitoes indicate possible transmission. In addition, larval scoops from stagnant water observed along the roadside and in the pits in the midlands were conducted, and indicated the presence of mosquito larvae and pupa, immature stages in the mosquito life cycle.

<u>Table 2</u>: Mosquitoes collected in households in Bumbobi and Nyondo subcounties

Anopheles gambiae	Male	0
	Female	37
Abdominal condition	Fed	25
	Semi gravid	4
	Gravid	8
Anopheles funestus	Male	0
	Female	8
Abdominal condition	Fed	8
	Semi gravid	0
	Gravid	0
Culex spp	Male	173
	Female	284

Question 15:
Comment on the findings in Table 2. What insight do these findings provide into the outbreak?

Question 16:
What additional entomological analyses could have been useful in this outbreak?

Question 17:
Based on what you know right now, what are some possible risk factors for this malaria outbreak?

Note: Ask the participant to mention as many possible risk factors as possible with justification of inclusion

Malaria outbreaks are often multifactorial, and are related to a combination of weather conditions, sanitation conditions, and insufficient use of protective clothing or bednets by humans. To identify the most relevant risk factors for the outbreak in Bumbobi and Nyondo, the investigators carried out hypothesis-generating interviews with 20 case-patients in the two most affected parishes. They developed a questionnaire that included possible risks factors for malaria transmission. Listed below are the exposures investigated.

Exposure	**%**
Kitchen located outside of main house (in the open air)	95
House had mud walls	85
Participated in evening outdoor activities	80
Having torn mosquito nets	71
Resided <500m from swamps/ditches/pits	60
Water logging around the house	50
Did not wear long clothes in the evening	50
Staying near over grown bush	50
No curtains on doors/windows	50
Did not have a mosquito net at home	29

Questions 18:
Explain each of the selected risk factors in the table in terms of association with malaria transmission. Are there other factors you think would have been important to include?

Instructors note: A number of these could have already been mentioned and justified in Question 17. Only focus on the variables that have not been highlighted previously.

Part V

The team planned a case-control study in Bumbobi and Nyondo to further study the risk factors for this outbreak. The initial questionnaire was modified to include the risk factors for which >50% of persons reported exposure, as well as any other factors that are well-known to be risk factors for malaria. For a malaria outbreak, it is good practice to always include a question about bednets, protective clothes, even if they didn't reach 50%. For example, having a mosquito net is no guarantee of its use, its integrity, or its sufficiency for the whole family. The investigators planned to enroll 150 cases and 150 controls. Investigators matched by neighborhood and age (±5 years). For children who were less than 5 years, a match could be ages 0 up to 5 years greater than their age.

Question 19:
Why do people match in a case-control study?

Question 20:
What are the disadvantages of matching? Do you agree that the cases and controls should have been matched in this study?

The four most affected villages (those with AR>30%) in Bumbobi and Nyondo subcounties were selected for the case-control study. For purposes of the case-control study, a case was defined as a positive malaria result using mRDT or microscopy or having taken antimalarials after a lab test from a public health facility from 1 March 2019 to 30 June 2019, in a resident or visitor of any of the 4 selected villages. A control was a resident of any of the 4 villages with no signs or symptoms of malaria and no evidence of a positive test for malaria at the time of onset for the corresponding matched case.

Cases were selected systematically using a village household listing obtained from the village leaders. Controls were selected randomly in the same village the case was found.

Question 21:
Compare the characteristics of a case-control study and a cohort study in the below table.

	Case-Control	**Cohort**
Sample size		
Costs		
Study time		
Rare disease		
Rare exposure		
Multiple exposures		
Multiple outcomes		
Progression, spectrum of illness		
Disease rates		
Recall bias		
Loss to follow up		
Selection bias		

Question 22:
Compare the characteristics of a case-control study and a cohort study in the below table.

**Recall bias is a potential problem in any retrospective study, including retrospective cohort studies, but less of a problem in prospective studies.

The team conducted the case-control study and calculated odds ratios with 95% CI for the risk factors evaluated. Results are shown in the figure below.

Table 3: Risk factors associated with malaria in affected sub-counties

Variable	Cases N(150) n_1 (%)	Control N(150) n_2 (%)	Matched OR (95% CI)
Sick household member before case onset	102 (68%)	13 (8.7%)	19 (8-46)
Wearing long clothes during evening hours	47 (31%)	108 (72%)	0.2 (0.08-0.3)
Presence of erosion control pits around home	143 (95%)	73 (49%)	18 (7-50)
Curtains on doors and windows	18 (12%)	55 (37%)	0.2 (0.1-0.4)
Time to bed daily (Before 9pm vs after 9pm)	58 (39%)	25 (17%)	0.3 (0.2-0.6)

Question 23:
What recommendations would you make, based on these findings?

Conclusion

This malaria outbreak in Mbale District was just one of the many malaria outbreaks that rocked Uganda in 2019. By the end of 2019, 87 of the 112 districts had reported malaria outbreaks, compared to only 11 districts reporting outbreaks in 2018.

While it wasn't possible to know precisely why so many districts were so affected in 2019, in Mbale, the case-control study indicated a strong association between the presence of erosion control pits (ECPs) near households in the midland region, and case status. The soils favorable for crop agriculture in the midlands attracted activity and settlement, but over time the uncontrolled erosion led to the fertile topsoil being washed from the midlands to the lowlands. Starting in 2006, in an effort to help the midlands population to retain their soil, local leaders encouraged residents to innovate mechanisms to stop the rampant soil erosion. The ECPs were the solution. During the rainy season, the ECPs helped retain the soil by reducing the speed of the rainwater pouring down from the highlands. When rains were heavy, it was thought that the ECPs actually disrupted the mosquito breeding cycle because the overflow washed the mosquito larvae and pupae downhill.

However, in 2019, the rains were much more intermittent and lighter in nature than in previous years. This allowed the ECPs to fill, but not overflow, which likely facilitated an enhanced mosquito breeding cycle.

The investigation team recommended the following:

- Draining of pits (ECPs) around households after the rains, to break the mosquito breeding cycle.
- Larviciding of common breeding sites, such as swamps
- Educating the communities about malaria preventive measures during peak transmission periods
- Need to use their epidemic channels more effectively. The moment those lines cross officials need to start inquiries and if they stay above the threshold for 2 weeks they need to send a team out what's happening
- Training more field epidemiologists to conduct regular analyses of the data and respond appropriately to control outbreaks early

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Competing interest

The authors declare that they had no competing interest

Author's contributions

DK - Led the writing process after collecting program data and drafted the case study; GB, LB, ARA, BK, SNK and JRH facilitated the case study development workshop, writing and revision of many drafts. All authors read and gave approval to the final case study for use and publication.

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Disclaimer

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