An Outbreak of Malaria Caused by Increase in Malaria Breeding Sites in Swamps

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Abstract

On 10 June 2019, routine analysis of malaria surveillance data at the National Malaria Control Division, Ministry of Health in Uganda revealed that there was an unusual increase in the number of malaria cases reported in the Oyam District. On 11 June 2019, the District Health Officer in Oyam District convened a meeting with the District Health Team (DHT) in which the District Biostatistician confirmed that the number of malaria cases had indeed exceeded the upper limit, starting in epidemic week 24 (approximately the week of June 10). The District Health Officer issued a formal request to the Ministry of Health for assistance in dealing with the malaria outbreak in Oyam. Two field epidemiology residents were assigned to work with the District Health Team to investigate the outbreak. The residents followed the steps in conducting vector borne disease outbreak investigations including preparation for field work, establishment of the existence of an outbreak by analyzing surveillance data, descriptive data analysis, hypothesis generation, conducting environmental and entomological assessments, conducting analytic studies with a focus on the utility of retrospective cohort studies as well as reporting findings.

This case study teaches trainees in Field Epidemiology and Laboratory Training Programs, public health students, public health workers who are interested or who may participate in vector borne disease outbreak investigation and response.

Key words: Case Study, Malaria, Outbreak investigation, Retrospective Cohort, Uganda

Participant guide: Distribute to students

Learning Objectives

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

1. Discuss the importance of analysis of malaria surveillance data
2. Construct and apply a good case definition
3. Discuss the importance of environmental and entomological assessments in vector- borne disease outbreaks
4. Compare cohort studies with case control studies as analytical study designs in outbreak investigations

This case study is based on an investigation of a malaria outbreak conducted by Maureen Katusiime, Gerald Rukundo and Steven N Kabwama in Oyam District, Uganda in 2019. The data and story were modified for the purposes of the case study.

This case study was developed by Steven N Kabwama, Julie Harris, Benon Kwesiga, Alex Ario, Lilian Bulage and Daniel Kadobera in December 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 in 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 performing calculations, constructing graphs, or engaging 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:
Topic 1: Study designs
Topic 2: Prospective and Retrospective Cohort Studies
Topic 3: Odds Ratios and Risk Ratios

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 vector- borne disease outbreak investigation and response.

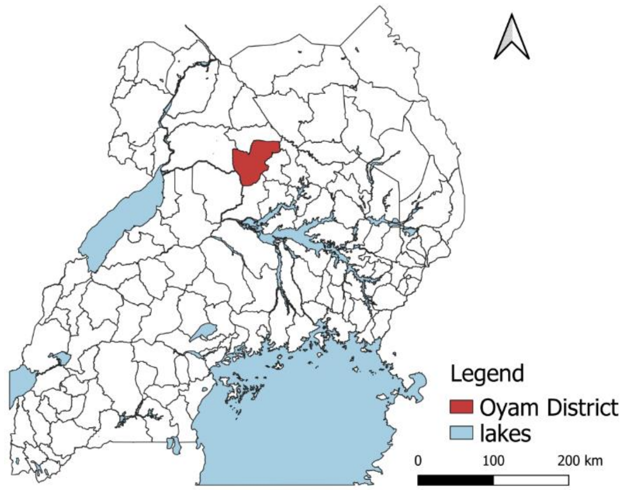
Level of case study: Intermediate or Advanced (Intermediate participants should have background in analyzing data from a two-by-two table and in interpreting data from tables.)

Time required: 3 hours
Language: English

Part I

On 10 June 2019, routine analysis of malaria surveillance data at the National Malaria Control Division, Ministry of Health in Uganda revealed that there was an unusual increase in the number of malaria cases reported in the Oyam District. Reports from the District Health Officer showed that the number of malaria cases reported in Oyam District increased from an average of 1,000 cases per week in May 2019 to almost 2,000 cases per week in June.

Oyam District, Uganda lies in Lango sub-region, in the northern part of the country, with a population in 2019 of ~425,000 persons. The district headquarters are approximately 78 kilometers (48 mi) west of Lira, the largest city in the area. The primary economic activities carried out in the district are subsistence agriculture and animal husbandry. Major crops include cotton, cassava, sweet potatoes, millet, pineapples, and bananas. Many people keep cattle, goats, sheep, pigs, chickens, and rabbits.



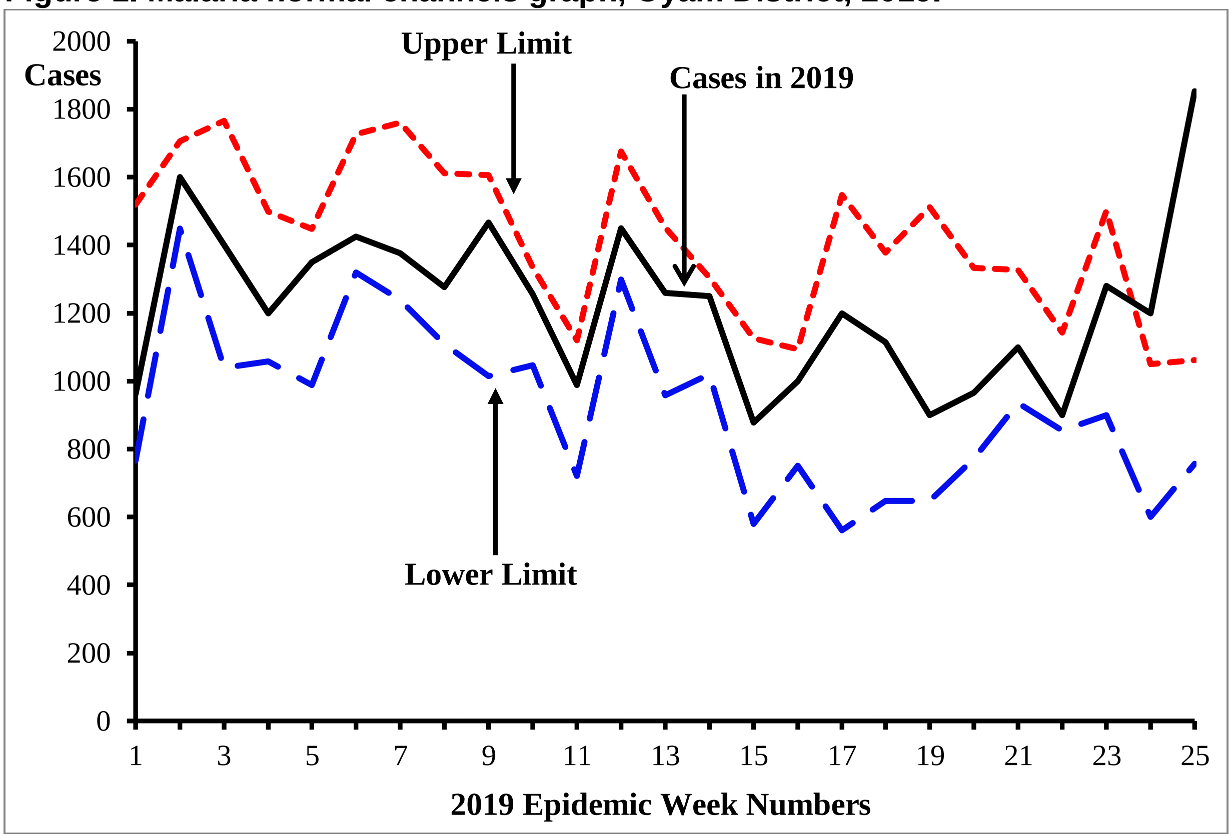
<u>Question 1</u>: What are some of the reasons we conduct routine analysis of malaria surveillance data?

<u>Answer 1</u>

Although fluctuations in the number of malaria cases throughout the year are expected, under normal conditions, these numbers remain within certain lower and upper limits, called *normal channels*. Normal channels are constructed by computing the 25th and 75th percentile of the number of cases for the respective weeks for the previous 5 complete years. The 25th percentile forms the lower limit while the 75th percentile is the upper limit. Thus, when the number of cases in each region over a given time period falls above the bounds of the normal channel, an outbreak may be occurring.

To understand whether or not the situation in Oyam District in June 2019 represented an outbreak, the team constructed a graph indicating the lower and upper limits of the expected number of malaria cases per week (normal channels) and the malaria cases per week for the year 2019.

Figure 1. Malaria normal channels graph, Oyam District, 2019.



<u>Question 2</u>: Interpret the malaria normal channel graph.

<u>Answer 2</u>

Part II

On 11 June 2019, the District Health Officer in Oyam District convened a meeting with the District Health Team (DHT) in which the District Biostatistician confirmed that the number of malaria cases had indeed exceeded the upper limit, starting in epidemic week 24 (approximately the week of June 10). The District Health Officer issued a formal request to the Ministry of Health for assistance in dealing with the malaria outbreak in Oyam. Two field epidemiology residents were assigned to work with the District Health Team to investigate the outbreak.

Neither of the two field epidemiology residents had conducted a vector-borne disease outbreak investigation before. To prepare for the field investigation, the residents started by reviewing literature on malaria, its mode of transmission, and its epidemiology in Uganda.

Malaria is endemic in most of Uganda; more than 90% of the population lives in an area at risk. Malaria accounts for about half of outpatient visits at health facilities, and two in every 10 hospital deaths in the country. Outbreaks can sometimes affect nearly everyone in a village.

Malaria is caused by *Plasmodium* parasites. *P. falciparum* accounts for 99% of malaria cases in Uganda. Human infections occur through bites from infected female *Anopheles* mosquitoes. *Anopheles* mosquitoes breed in fresh water in temporary pools, often those formed after rains. Even small pools such as those caused by animal hoofprints, road potholes, and irrigation can serve as breeding sites for mosquitoes. *Anopheles funestus* are more common in Northern Uganda, including in Oyam District during dry months, while *An. gambiae* can be found during the rainy season. These vectors feed exclusively on humans, and rest indoors after feeding. Interventions that have been effective in the control of malaria include the use of insecticide-treated nets (ITNs), which prevent mosquitoes from biting humans while they sleep and kills mosquitoes that land on the nets, and indoor residual spraying (IRS), which kills mosquitoes that rest on indoor walls sprayed by the insecticide.

Symptoms of malaria infection may include fever, tiredness, vomiting, and headache, approximately 10-15 days after the bite of an infected mosquito. Severe infection may lead to yellowing of the eyes (indicating liver failure), seizures, coma, and death.

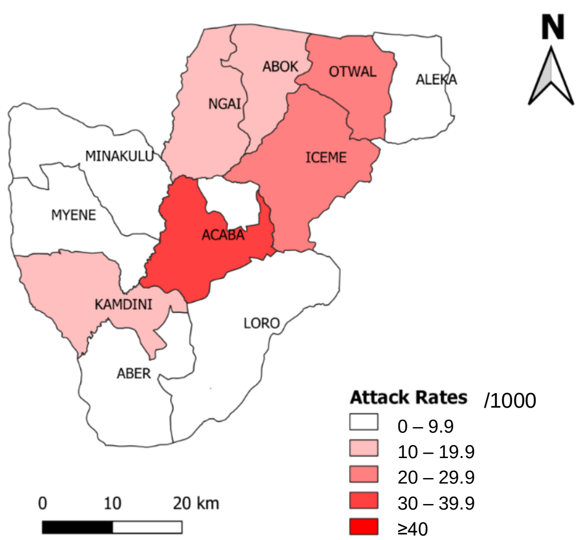
Malaria outbreaks occur annually in Uganda and are usually linked to the onset of the rainy season in March and July. During 2015-2016, northern Uganda experienced a large outbreak of malaria that affected more than 10 districts, including Oyam District and led to more than 20,000 cases and 150 deaths in less than 2 months.

On arrival in Oyam District on 24 June 2019, the two field epidemiology residents held a meeting with the District Health Team (DHT) at the District Health Offices. The District Health Officer, District Malaria Surveillance Focal Person, District Vector Control Officer, and District Biostatistician described an intense situation in the district, reporting that health facilities had been treating so many cases that they had run out of antimalarial drugs. After quickly reviewing the facility supply stock sheets, the team issued a request for emergency restocking.

Question 3: Do you agree that the team should have implemented public health actions (like ordering emergency restocking) this early in the investigation? Why or why not?

Answer 3:

The investigation team hypothesized that recent prolonged rainfall after the dry season might have contributed to the malaria outbreak by increasing malaria vector breeding sites in the area. Working with the District Biostatistician, the team compared the reported malaria attack rates (per 1000 population) across the sub-counties in Oyam District during epidemic weeks 23, 24 and 25 and plotted them on a map.



Question 4: What is an attack rate? Why are attack rates used instead of counts when comparing the burden of disease in different areas or age groups?

Answer 4

Question 5: Interpret the map above. Which areas are most affected by the outbreak? Which are least affected?

Answer 5

Question 6: Why do you think that different areas could have different attack rates during a malaria outbreak?

Answer 6

To identify cases, the team developed a working case definition. They defined a confirmed case as a positive result using a malaria rapid diagnostic test (mRDT) or microscopic examination of a thick blood film in a resident of Oyam District during epi weeks 23, 24, and 25 (June 3-23, 2019).

Question 7: What are the components of a case definition?

Answer 7

Question 8: Why do you think the team chose to use a case definition that did not include the symptoms of malaria?

Answer 8

The team noted that a study could be useful in identifying the reasons that the outbreak was occurring in Oyam District. However, the district was too large for them to cover with the available resources. They discussed focusing their efforts in a smaller region.

Question 9: Where would you recommend the team focus their efforts? Why?

Answer 9

Part III

The team decided to focus on Acaba sub-county for their investigation. With an attack rate of over 40%, they reasoned that any analytic study would be easiest to do there. If they chose to do a case-control study, cases would be easy to find. If they decided to do a cohort study, the outcome was common enough (>40% of the sub-county was infected!) that any cohort they chose would be likely to develop cases over the time period of the study.

However, they first wanted to conduct descriptive epidemiology to learn more about the cases and develop hypotheses. They worked with the District Health Officer and his team to conduct case-finding using health facility records. They developed a line list of malaria cases by reviewing outpatient records from all health facilities in Acaba sub-county. They abstracted data from the facility registers, including age, sex, date of onset of clinical symptoms of malaria, and parish of residence.

In total, they identified 9,235 malaria cases during 3-23 June 2019.

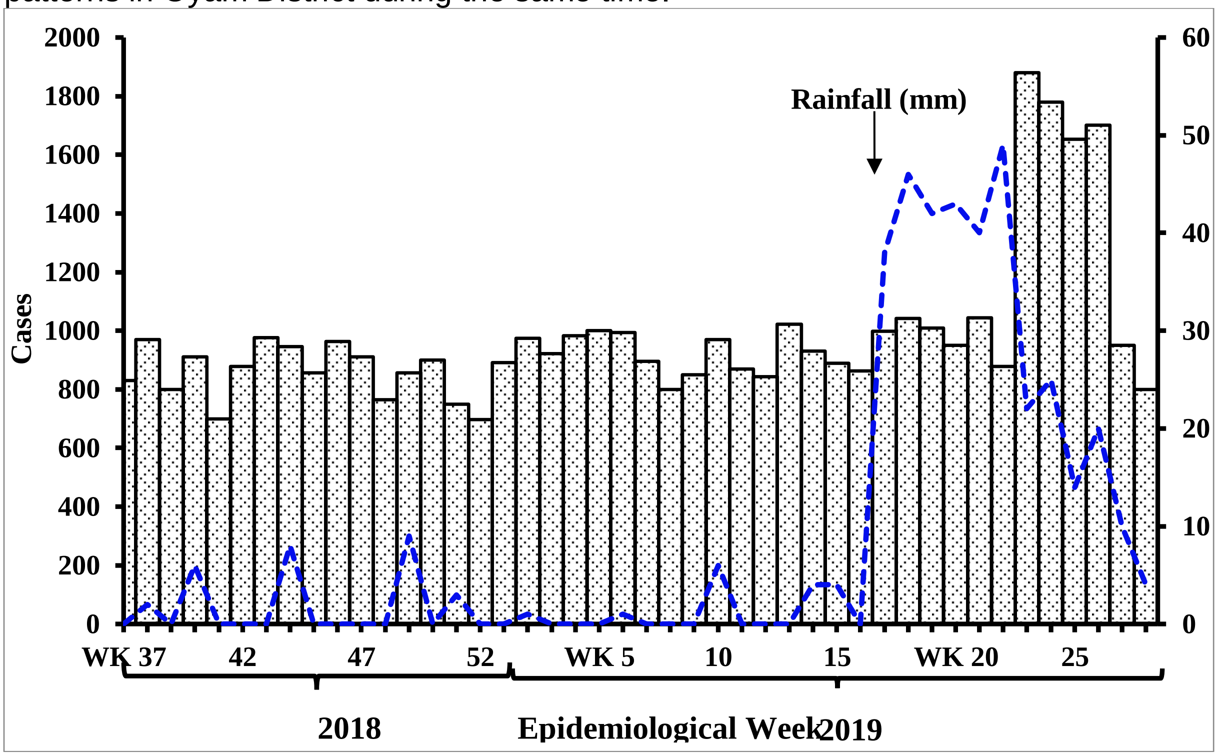
Table 1: Distribution of Cases in Acaba Sub-County by Sex, Age, and Parish

		Cases	Population	AR/100
Sex				
	Males	3,078	13,575	22.6
	Females	6,157	14,517	42.4
Age group (yrs)				
	<5	897	4,905	18.3
	5-17	2,942	10,571	27.8
	≥18	5,396	12,616	42.8
Parish				
	Obangangeo	2,793	5,867	47.6
	Dogapio	2,128	5,811	36.6
	Abanya	1,354	3,800	35.6
	Ogwangapur	1,070	3,735	28.6
	Atekober	1,493	6,892	21.7
	Anyeke	391	1,987	19.7
Total		**9,235**	**28,092**	**32.9**

Question 10:	Interpret the descriptive epidemiology data in the table.
Answer 10	

Rainfall patterns are strongly associated with malaria outbreaks. Models have demonstrated that a minimum of 38 days (but more often 50-60 days) are required between heavy rains and the onset of an outbreak [1]. This delay represents the time it takes for mosquito eggs to develop, for the young mosquito to take a bloodmeal from an infected person, the time for the malaria parasite to mature in the mosquito, and the time from that mosquito's next bloodmeal (in which an uninfected human becomes infected) until the parasite develops in the human and causes symptom onset.

The graph below shows the epidemic curve of the outbreak, overlaid with rainfall patterns in Oyam District during the same time.



<u>Question 11</u>: Interpret the epidemic curve. What pattern, if any, do you see between rainfall and the start of the outbreak in Oyam District?

<u>Answer 11</u>

<u>Question 12</u>: When conducting vector-borne disease outbreak investigations, it is important to identify the possible vector breeding sites. What other assessments do you think would be useful as part of the epidemiologic investigation?

<u>Answer 12</u>

Part IV.

The team decided to conduct an environmental assessment in Acaba sub-county, to better understand the factors that might have led to the outbreak. They traveled around the sub-county, observing the area to identify potential mosquito breeding sites such as standing water in empty containers and around homes, or standing water due to agricultural and other economic activities. The topography of Acaba sub-county is generally flat, characterized by swamps and streams that flow through it. The vegetation is mainly savannah grassland with bushes, except in areas occupied by human dwelling and crop farming. The photographs below display typical land in Acaba sub-county.

In addition to the environmental assessment, the team assessed adult indoor resting vector density in 40 households in two villages of Acaba sub-county. Indoor resting density represents the number of adult female mosquitoes collected per house over a specific period. The risk of malaria transmission would be eliminated at an indoor resting density of zero. During the investigation, the team calculated that the average indoor resting density of malaria vectors was 19 mosquitoes per household per night. This is considered a very high resting density.

Question 13: Why is it important to conduct an environmental assessment in vector-borne disease outbreak investigations? Why is it important to conduct an entomological assessment?

Answer 13

The entomological and environmental assessments suggested that water collection in swampy areas as a result of activities, such as rice farming, brick making, and sand mining created breeding sites for mosquitoes after rains. To further develop their hypotheses, the investigators interviewed 20 confirmed case-persons. They asked about potential risk factors for malaria transmission from April 29 – May 19, 2019 (Weeks 18-20). Key exposures explored included engagement in activities in or near areas favorable for mosquito breeding sites, wearing clothing protective against mosquito bites, and owning and using ITNs. The team also observed the surroundings of the case-patients' homesteads for containers with stagnant water, overgrown bushes, and proximity to potential or active breeding sites.

Question 14: What is the purpose of hypothesis generation during outbreak investigations?

Answer 14

During the hypothesis generation, the team learned that residents conducted multiple commercial activities in Obangangeo District. Many of the people they interviewed were involved in commercial activities such as brickmaking, rice-growing, and other activities, and reported that it was common to carry out these activities outdoors, directly on the swampy lands. The case-patients reported that mosquitoes had been very heavy that year, and that they were frequently bitten especially in the evenings. When the investigators tallied the results from the hypothesis-generating interviews, they found that nearly all of them had conducted some type of commercial activity in the swamps. When they asked about other risk factors, such as staying outdoors for more than 6 hours after 7pm, improper usage of ITNs, they also found some patients reporting these factors, although less often.

The team hypothesized that engaging in commercial activities in swamps late in the evening predisposed people to mosquito bites and subsequent infection with malaria. With their hypotheses in hand, the investigators proceeded to conduct an analytic study to identify specific risk factors for infection. The investigators selected Obangangeo parish for the analytic study. With nearly half of the residents infected, they would easily be able to include people with and without illness (and presumably with and without relevant exposures) no matter what study type they decided to conduct.

<u>Question 15</u>: Why do you think the investigators chose to conduct the analytic study in a single parish? What are the advantages and disadvantages of conducting the study in only one parish?

<u>Answer 15</u>

<u>Question 16</u>: What analytic studies can be considered? What are the advantages and disadvantages of each for the situation at hand?

<u>Answer 16</u>

Part V

The investigators decided to conduct a retrospective cohort study. In academic cohort studies, we are often taught that we can only evaluate the association of a single exposure with multiple outcomes. To do this, we are taught to select two groups: unexposed and exposed persons. Next, we follow those persons forward in time to see if they develop the outcome.

In reality, cohort studies can be used to assess multiple exposures. This is done in retrospective cohort studies all the time, such as in cohort studies of foodborne outbreaks associated with a social event, like a wedding. In these cohort studies, we enroll everyone at the wedding – or a random sample of people, if there are more than we need – and ask them about their food exposures at the wedding. This represents multiple exposures that we assess to evaluate their riskiness in causing the outcome, which is the foodborne illness.

However, this means that we can't divide people neatly into exposed and unexposed groups, because different people will have different exposure profiles across multiple factors. In these situations, we typically select a single exposure of interest to calculate the sample size. However, when we analyze the data, we evaluate multiple exposures for their association with the outcome.

With nearly 6,000 persons in its population, enrolling everyone in Obangangeo Parish as a cohort was out of the question. However, if the participants were selected randomly from the entire parish, they could be expected to be representative of the entire cohort.

To calculate their sample size, the investigators knew they needed to estimate several things. First, they estimate the ratio of exposed to unexposed persons in Obanbangeo, based on a single exposure that they felt would be most relevant as a risk factor. They selected 'living near standing water' as the risk factor of interest and estimated that approximately half of the persons in Obanbangeo would have this risk factor. This made the ratio of unexposed to exposed 1:1, or 1. In addition, they needed to estimate the proportion of unexposed persons (persons who didn't live near standing water) who had the outcome (i.e., developed malaria). They estimated that 25% of unexposed persons would develop malaria anyway. Finally, they needed to determine their effect size: how much more likely would it be that persons living near standing water would develop malaria, compared with persons not living near standing water? They reviewed the literature and estimated that a, person living near standing water would have 3.1 times the likelihood of developing malaria compared with persons not living near standing water.

Using OpenEpi, they were able to estimate that, with 80% power and 95% confidence limits, they would require a total of 128 individuals to enroll in a cohort study.

<u>Question 17</u>: Do you agree with the investigators' decision to use a retrospective cohort study rather than a case-control study?
Why or why not?

<u>Answer 17:</u>

<u>Question 18</u>: What measure of association would you use to analyze cohort study data? Why?

<u>Answer 18</u>

The investigators randomly selected 124 individuals in Obangangeo Parish, using a list of all residents in the parish that was provided by the community leaders. Obangangeo Parish has a population of 5,867 people. Each person on the list was assigned a number and a computerized random number generator was used to select 128 people. They interviewed the participants about their exposures during April 29 – May 19, 2019 (Week 18-20). Their case status during June 3-30, 2019 (Week 23-25) was assessed.

Table 2: Risk Factors for Malaria Infection, Cohort Study, Obangangeo Parish, 2019

Exposure	Ill	Not Ill	Risk Ratio (95% CI)
House located <500m from swamp			
Exposed	69	18	1.5 (1.1-2.0)
Unexposed	22	19	
Engaged in rice growing <500m from swamp			
Exposed	66	18	___ (1.0-1.8)
Unexposed	25	19	
Engaged in brick making <500m from swamp			
Exposed	68	18	___ (1.1-1.9)
Unexposed	23	19	
Engaged in sand mining <500m from swamp			
Exposed	69	21	1.3 (0.9-1.8)
Unexposed	22	16	
Engaged in rice growing, brick making or sand mining <500m from swamp			
Exposed	68	21	___ (0.9-1.7)
Unexposed	23	16	
Wears long-sleeved clothes in evening hours			
Exposed	30	20	0.8 (0.6-0.99)
Unexposed	61	17	
Slept under an ITN the previous night			
Exposed	31	29	___ (0.45-0.8)
Unexposed	41	64	

<u>Question 19</u>: Calculate the missing risk ratios.

<u>Answer 19</u>

<u>Question 20</u>: Interpret these results.

<u>Answer 20:</u>

Question 21: Compute the cumulative effect of the exposure and protective factors and fill in the table below

Risky exposures	**Ill**	**Not Ill**	**RR**	**95% CI**
None	9	11	REF	REF
One	10	5	0.68	(0.4 - 1.2)
Two	14	22	[__]	(0.6 - 2.2)
Three	6	12	1.4	(0.6 - 3.0)
Four	3	9	[__]	(0.6 - 5.4)
Five	2	10	[__]	(0.7-10.5)
Protective factors	**Ill**	**Not Ill**	**RR**	**95% CI**
None	22	48	REF	REF
One	26	19	0.5	(0.4 - 0.8)
Two	13	6	[__]	(0.3 - 0.7)

Answer 21:

Conclusion

The year 2019 was a particularly bad year for malaria in Uganda. Ultimately, over the year 21,000 persons were reported with disease and 80 deaths were attributed to malaria. In Oyam District*, after concluding the epidemiologic investigation, the team disseminated their findings to the district health team. The district health officials organized communication campaigns recommending that the public remove standing water around homesteads, wear long-sleeved clothes in the evenings, sleep under insecticide-treated nets, and stop conducting their commercial activities, such as brick making, rice growing and sand mining, in swampy areas. By July 2019, the number of malaria cases per week had dropped to within the normal ranges.

In Oyam District, the rainy season usually begins between February and March. However, during 2019, the rainy season did not start until the end of May. Because of the delay of the rainy season, people could not plant crops as they normally would in March and April, and instead engaged in other commercial activities, such as brickmaking. As these activities require water, they conducted the activities in or near swamps, which still retained some water even in the dry season. Engagement in these activities while the ground was still mostly dry created pits in which water collected after the rains began and made grounds that were conducive for mosquito breeding. The resulting malaria outbreak was thought to be partially attributable to the persistent presence of the pits and increased mosquito breeding.

Malaria is likely to continue to be a challenge in Uganda for many years. Proactive identification of risky behaviors and environmental conditions and implementation of appropriate interventions will be necessary to reduce and, ultimately, eliminate malaria in Uganda.

*Oyam District was a representative example, but the data and story were modified for the purposes of the case study

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Further Reading

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Author's contributions

SNK participated in the data collection and analysis, SNK led the writing process and developed the initial draft of the case study; DK, BK, LB, and ARA participated the case study development workshop and the writing process. JRH facilitated the case study development workshop, writing, and revision of the drafts. All authors read and gave approval to the final case study for use and publication.

Disclosure statement

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Disclaimer

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