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# Unexplained Haemorrhagic Fever in Rural Ethiopia

Zegeye Hailemariamm, Doreen Tuhebwe, Meeyoung Mattie Park, and Casey Daniel Hall


**African Case Studies in Public Health**

Participants' Guide

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PanAfrican Medical Journal

# Unexplained Haemorrhagic Fever in Rural Ethiopia

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## Abstract

This case study was written based on events of an outbreak investigation of an unfamiliar disease in Ethiopia during October–December 2012. Ethiopia did not have reports of similar cases in the 50 years prior to this outbreak. In this case study, we recapitulate and analyse this outbreak investigation based on data gathered from the community, health facility, and laboratory systems. It can be used to teach: 1) the outbreak investigation process; 2) selection of appropriate epidemiological design for the investigation process, 3) basic statistical analysis of surveillance data, and 4) principals of disease control. The target audiences for this case study are officials working in public health and public health trainees. It will take at most 3.5 hours to complete this case study. At the end of the case study, participants should be able to apply the principals of outbreak investigation and use surveillance data to respond to an outbreak in their country-specific context.

## How to Use the Case Study

**General instructions:** To conduct this case study in the classroom, the authors propose that the participant's guide be distributed one part at a time. Background material, including the appendices, should be distributed before the case study for review by the participants.

Participants should take turns reading the narrative aloud, paragraph by paragraph. Reading all paragraphs aloud and in turns has two advantages: first, everyone is given an opportunity to participate and get beyond the inhibition of having her/his voice heard in a large room; second, the whole class is given time to understand the issue and think about the answers.

The participants reading the question may try to answer it if s/he can; otherwise, it can be discussed as a group or completed as an exercise as the instructor's notes dictate. Instructor's notes are included in the instructor's guide for each question. Complete all reading and questions before the next part is distributed. Then the next participant continues and so on until the case study is over. Once the conclusion is read, re-visit the learning objectives – this reinforces the learning and provides an opportunity to clarify any remaining issues.

**Audience:** Officials working at the National Surveillance Department, Ministry of Health, Regional Surveillance Office, District Surveillance Office, District Head of Heath Department, and FETP/ Public Health trainees.

**Prerequisites:** Before using this case study, participants should have received lectures in outbreak investigation, application of epidemiological study designs, and Integrated Disease Surveillance & Response guidelines and have experience or be currently working in a health-related field, or contributing to the government health surveillance functions.

**Materials needed:** White board or flip chart and marker

**Level of training and associated public health activity:** Intermediate – Outbreak investigation

**Time required:** Approximately 3.5 hours

**Language:** English

# Participant's Guide

**Goal of Case Study:** To review and simulate an outbreak investigation for an unfamiliar disease in Ethiopia

**Learning Objectives** - After completion of this case study, the participants should be able to:

1. Discuss steps of an outbreak investigation
2. Develop a case definition of the disease
3. Consider ethical principles and their implications for procedures during an outbreak investigation
4. Examine the importance of laboratory surveillance systems in disease detection
5. Analyse surveillance data and interpret it
6. Propose appropriate measures of control and prevention of the disease

## Introduction

In November 2012 (epi week 48), in southern Ethiopia (Figure 1), a health worker at Jinka General Hospital in Jinka District managed a case of an unfamiliar disease that had symptoms of jaundice, extended abdomen, fever, and bloody vomiting. This case was a 4-year-old female from Village A. Several sporadic cases with the unfamiliar symptoms also presented to Jinka Hospital from Villages B and C, which are both located in Jinka District in the forested areas of Southern Ethiopia.

Because of the malaria-like symptoms and the endemic nature of malaria in the country, the health worker managed the cases with malaria treatment; however, the patients did not respond to the treatment.

Given the increasing number of sporadic cases of an unfamiliar disease presenting at the hospital and lack of response to malaria treatment, the health worker reported these cases of an unfamiliar disease to the District Surveillance Official (DSO) in November 2012 (epi week 49).


Figure 1. Blue flag marking the location of Jinka in South Omo, Ethiopia. Map created using Scribblemaps.

Question 1: If you were the DSO, what is the first action upon receiving the report about the unfamiliar disease from the health worker in Jinka Hospital? Why?

In order to verify the reports, the DSO visited Jinka Hospital and conducted an overview of the patient medical records. The records confirmed reports for 11 cases, including 1 death, that presented to the hospital with fever, jaundice, and in some cases bloody vomiting. The cases were all from Jinka district and of different age groups. Patients reported that the symptoms started in October 2012 (epi week 41).

As required by the Integrated Disease Surveillance & Response/Public Health Emergency Management (IDSR/PHEM) guidelines of information flow (Appendix 1), the DSO reported to the District Health Manager, who reported to the Regional Office, then to National Surveillance Office, up to the Minister of Health himself during the last week of March 2013 (epi week 13) [1,2]. Following these reports about the unexplained fever, jaundice, and sometimes vomiting of blood, the National Surveillance Office at the Ministry of Health (MoH) declared that there was "an outbreak of an unfamiliar disease," and an outbreak investigation was conducted during the first two weeks of April 2013 (epi weeks 14-15). The aim of the outbreak investigation was to characterise the outbreak and inform the source of the disease.

Question 2: List and discuss the steps of an outbreak investigation

Question 3: List the possible sources of information that can inform the investigation of this unfamiliar disease.

The Head of national surveillance and selected personnel to compose an investigation team. The team was made up of epidemiologists, laboratory personnel, veterinary officials and medical interns. Part of their responsibility was to conduct surveillance of the unexplained disease.

Question 4: Why do you think case finding was suitable for this scenario?

Question 5: What type(s) of epidemiologic study design should the team use to conduct the investigation? Why? Refer to Appendix 4 for a description of study designs.

Question 6. Develop case definitions for this disease for: 1) community-based surveillance by community members and 2) active case finding by health workers.

From the records at Jinka Hospital, the investigation team identified a total of 14 deaths with symptoms characteristic of the "unfamiliar disease" as of April 2013 (epi week 12). The National Surveillance Office was concerned with the magnitude and seriousness of the outbreak and directed the investigation team to identify the disease.

Due to the similarity between symptoms identified in the outbreak and liver disease (i.e. jaundice), the first hypothesis was that the illness may result from excessive methanol intake. However, laboratory results ruled out the assumption.

The investigation team had to employ the most suitable epidemiologic study design to describe the outbreak (Appendix 2) [3]. Investigators conducted active case searches from house to house using a standardized case definition and case investigation form (Appendix 3). The case definition used by the team was "a patient or unexplained death that presented with fever and jaundice, with or without blood vomiting, in Jinka district starting epi week 44 of October 2012" [2].

Question 7. What types of specimens might you collect to investigate this unfamiliar disease?

Question 8. What are the guiding principles of ethics when researching human subjects, and the ethical implications of collecting samples for this investigation?

Continue to next page →

## Part 1

In the months following April 2013, Hospital A provided supportive treatment for the identified cases. During September 2013, the investigation team collected 21 whole blood samples from cases having clinical manifestations typical of the outbreak and transported these samples to the virology laboratory at the Ethiopian Public Health Institute (EPHI). The samples were collected to investigate the underlying causative agent and to guide an appropriate outbreak response. The approval to complete data and sample collection was given from EPHI, the government organisation which has a full mandate to conduct epidemiological investigation and respond to any public health emergencies.

Given that some cases presented with haemorrhagic symptoms (blood vomiting), investigators also sent blood samples to the WHO Collaborating Centre for Haemorrhagic Fevers in Dakar, Senegal, for serological analysis. By epi week 38 of September 2013, 11 months after the first case had been reported in Jinka District, the laboratory results from Dakar confirmed that the outbreak was due to yellow fever. On receiving the results, the National Surveillance Office noted that "no cases of Yellow Fever had been reported in over 50 years." Alas, yellow fever had re-emerged in Ethiopia [4].

Question 9. What were possible challenges that delayed laboratory confirmation of yellow fever during this outbreak in Ethiopia?

Question 10. Provide recommendations to improve the turnaround time for disease confirmation.

Continue to next page →

## Part 2

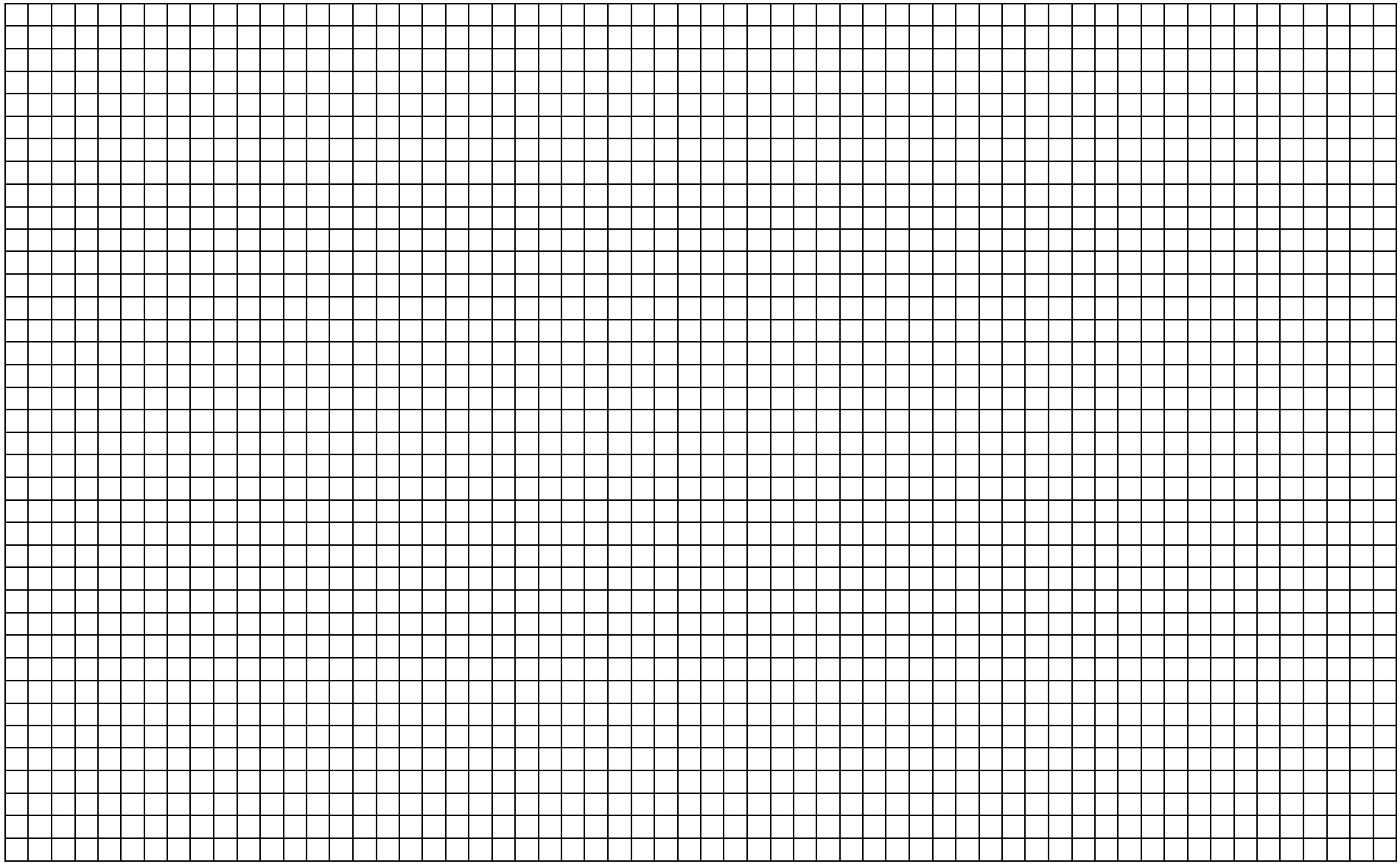
Following the confirmation of the yellow fever outbreak, the investigation team conducted extensive case finding. By October 2013, 141 cases and 43 deaths were recorded as shown below.

**Table 1.** Number of Cases of Yellow Fever by Epidemiological Week, Ethiopia, 2012 - 2013

| Epi Week | # of Cases | Epi Week | # of Cases | Epi Week | # of Cases |
|---|---|---|---|---|---|
| 46, 12 Nov 2012 | 0 | 12 | 8 | 29 | 0 |
| 47 | 0 | 13 | 7 | 30 | 0 |
| 48 | 0 | 14, 1 Apr 2013 | 13 | 31 | 0 |
| 49 | 1 | 15 | 5 | 32, 5 Aug 2013 | 0 |
| 50 | 1 | 16 | 3 | 33 | 0 |
| 51 | 4 | 17 | 0 | 34 | 0 |
| 52 | 4 | 18 | 5 | 35 | 0 |
| 1, 31 Dec 2012 | 2 | 19, 6 May 2013 | 2 | 36, 2 Sept 2013 | 0 |
| 2 | 0 | 20 | 19 | 37 | 0 |
| 3 | 4 | 21 | 12 | 38 | 0 |
| 4 | 3 | 22 | 10 | 39 | 0 |
| 5 | 3 | 23, 3 Jun 2013 | 3 | 40 | 1 |
| 6, 4 Feb 2013 | 3 | 24 | 0 | 41, 7 Oct 2013 | 0 |
| 7 | 4 | 25 | 5 | 42 | 1 |
| 8 | 3 | 26 | 1 | 43 | 0 |
| 9 | 3 | 27, 1 Jul 2013 | 0 | 44 | 0 |
| 10, 4 Mar 2013 | 4 | 28 | 1 | 45, 4 Nov 2013 | 0 |
| 11 | 6 | | | | |

Question 11. Given the data above, draw an epidemic curve using the graph paper below and interpret it. See next page for graph paper.

Instructions: Draw epicurve for data in Table 1 in the graph paper below. Label the graph appropriately.



Question 12. Calculate the sex specific attack rates for the disease in each age group and calculate the case fatality rate for the disease for each age group and interpret the results

**Table 2.** Number of Cases by Age Group and Sex in Jinka District, Ethiopia, Nov 2012 – Nov 2013

| Age Group | Population at Risk | | | Number of Cases | | | | Crude AR* | AR* | | Deaths | CFR[2] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | T | M | F | T | % | M | F | | M | F | | |
| 0-4 | 51,453 | 25,542 | 25,910 | 3 | 2.1 | 0 | 3 | 0.01 | | | 0 | |
| 5-14 | 107,134 | 53,184 | 53,950 | 15 | 10.6 | 8 | 7 | 0.01 | | | 2 | |
| 15-44 | 151,538 | 75,228 | 76,311 | 106 | 75.2 | 44 | 62 | 0.07 | | | 36 | |
| ≥45 | 42,290 | 20,994 | 21,296 | 17 | 12.1 | 8 | 9 | 0.04 | | | 5 | |
| Total | 352,415 | 174,948 | 177,467 | 141 | 100.0 | 60 | 81 | 0.04 | | | 43 | |

*Per 100 population at risk; T = total, M = male, F = female, AR = attack rate, CFR = case fatality rate

Question 13. Explain the implications of the attack and case fatality rate in the most highly affected age group.

Following the confirmation of yellow fever, the National Surveillance Officer (NSO) summarised the number of cases by district (Table 3).

**Table 3.** Distribution of Suspected Cases of Yellow Fever by District, South Omo Zone, November 2012 – October 2013

| District | Population | Cases | Percent |
|---|---|---|---|
| Bena-Tsemay | 65,992 | 19 | 13.5 |
| Jinka Town | 26,851 | 14 | 9.9 |
| Selamago | 34,293 | 2 | 1.4 |
| South Ari | 226,131 | 106 | 75.2 |
| Total | 353,267 | 141 | 100.0 |

Question 14. Using Table 3, calculate the incidence rate per 10,000 person per district and interpret the results.

Continue to next page →

## Part 3

Yellow fever is an acute and often fatal infectious disease caused by the yellow fever virus (YFV), a flavivirus transmitted in tropical and subtropical areas, mainly through the bite of infected *Aedes* spp. mosquitoes in Africa [5,6]. There are two types of yellow fever; the urban type i transmitted from human to human hosts and the jungle (zoonotic) type is transmitted from animal to human hosts.

In Ethiopia, the last outbreak of yellow fever occurred in 1962 (Appendix 4). As a consequence, yellow fever vaccination was not routinely administered in Ethiopia.

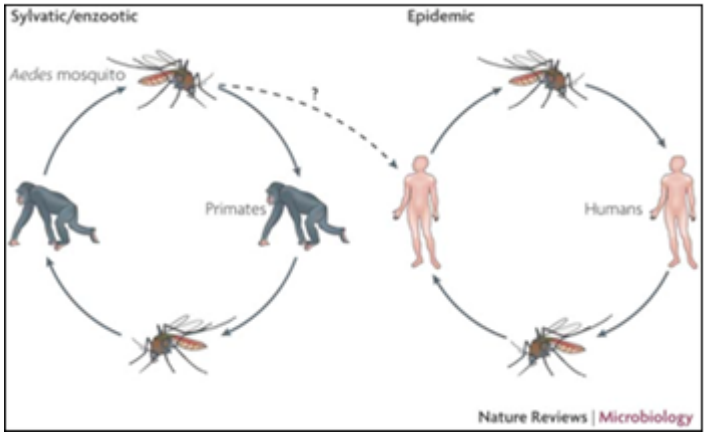



*Figure 2. Transmission cycle between humans, primates, and Aedes spp. mosquitos* [13].

Following the confirmation of a yellow fever outbreak, entomologists on the investigation team conducted an entomological assessment and collected mosquito larvae from the surroundings of the affected areas. A subsequent environmental assessment revealed that the affected areas were mostly in the forested southern parts of Jinka District in Ethiopia.

Results of this investigation showed that mosquitoes responsible for transmitting yellow fever were present in the vegetation cover, the main natural breeding site for the mosquito, near the affected villages. There was concern because human settlements had expanded into forested areas, setting the stage for mosquitoes to spread the disease between infected primates and humans.

Further interpretation of the epidemic curve showed that the number of cases peaked in the weeks following the rains. These revelations supported the fact that the human-animal-environment interactions in Jinka District sparked this yellow fever outbreak. A number of activities were initiated in order to control the outbreak.

Question 15. What public health actions needed to be executed following the re-emergence of yellow fever in Ethiopia?

Question 16. List the conditions that promoted re-emergence of Yellow Fever in Jinka District, Ethiopia.

Question 17. Why do you think yellow fever is a one health concern?

Continued on next page →

## Conclusion

There was genuine concern about the re-emergence of yellow fever, especially after 50 years of no cases. The 2012/2013 yellow fever outbreak in Ethiopia lasted for over 10 months (December 2012 – October 2013) with 141 recognised cases and 43 deaths (Appendix 5). This yellow fever outbreak was a typical example of a re-emerging disease documented in parts of the world. The local surveillance system in Ethiopia did not immediately detect the disease, in part due to inexperience in clinically diagnosing this condition and the unavailability of a locally-based laboratory diagnostic system for this disease. This event revitalised decision makers to focus attention on the surveillance and response towards yellow fever in the region.

The Federal Government of Ethiopia solicited support from other stakeholders, such as the World Health Organisation, to procure vaccine and insecticide as interventions to protect the at-risk population in the affected areas of Arkisha and Aykamer. The MoH implemented house-to-house indoor residual spraying and health education campaigns on the prevention of yellow fever, targeting the most affected areas as indicated by the surveillance information.

Based on outcomes of the investigation, the national and regional surveillance offices initiated yellow fever surveillance and increased work force capacity to detect yellow fever through training and construction of biosafety level 3 and 4 laboratories. Several program activities were implemented, such as routine vaccination for yellow fever, routine indoor residual spraying in high risk areas, and advocacy.

## Background Reading

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WHO. *District guidelines for yellow fever surveillance*. 1998. Geneva, Switzerland. resources

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# Acknowledgements

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This case study was developed by Zegeye Hailemariam (zegeyehailemariam@yahoo.com) and Doreen Tuhebwe (tuhereen@yahoo.com) in 2015 for the Ethiopia and Uganda FETPs, with review and input from Kelly Fletcher, Meeyoung Park, Casey D. Hall, and Scott McNabb of Emory University.

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# Appendices

## Appendix 1: IDSR/PHEM Guidelines [2]

The information and activities in the IDSR/PHEM Guidelines are intended for use by health managers and health staff at all levels of the health system at national, regional, zonal, woreda (i.e. districts in Ethiopia) and health facilities). These include:

- Public health /Health management teams
- PHEM staff
- Surveillance officers/focal points
- Health facilities

The Ethiopian Ministry of Health planned to update the guideline continuously based on changes in disease patterns and new issues that emerge during the implementation phase.

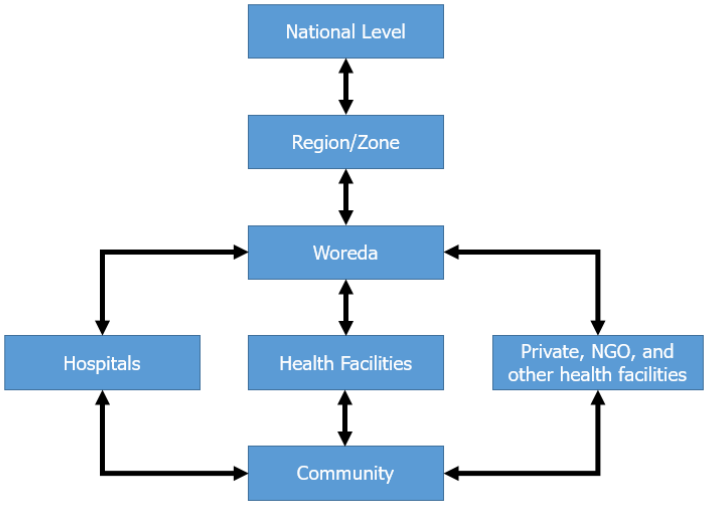
The activities and steps in the process of planning include:

- Identify and convene preparedness planning team(s)/experts from different sectors including partners
- Coordinate and integrate all response and recovery agencies/organisations in the planning process
- Identify needs required to respond to potential emergencies
- Discuss with partners to endorse and agree on their roles and responsibilities
- Develop plans, to prevent, protect against, respond to, and recover from natural and man-made disasters
- Prepare monitoring mechanisms and tools to ensure preparedness plan is operationalised
- Ensure the integration of the plan in the sector regular plan

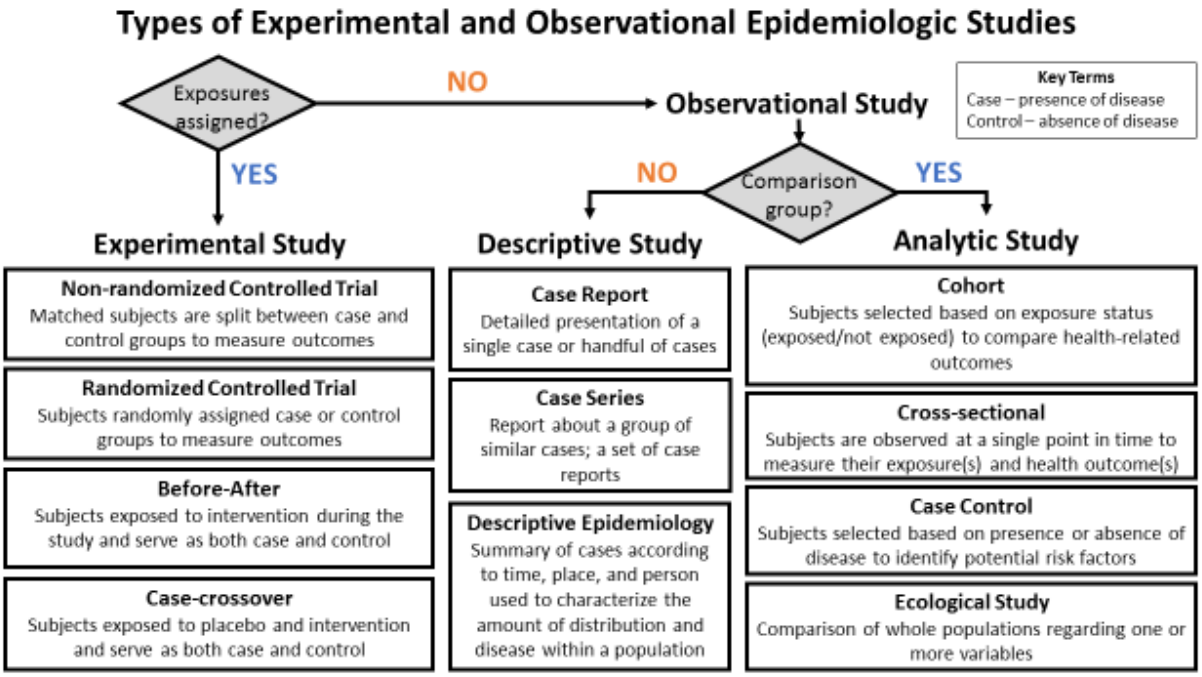
Reporting diseases and conditions under surveillance

- Ensuring reliable reporting of surveillance data throughout the country is important so that program managers, surveillance officers and other health care staff can use the information for action.
- The routine flow of surveillance data is usually from reporting sites to the next level up to the central level as indicated in Appendix 1.1 below. The community and health facilities, especially health posts, are the main source of information. The information collected from this site is compiled in standard forms, analysed and then forwarded, to the woreda health office.
- Woreda level uses standard formats to compile aggregate, and sends the data to the zone/region, which forwards to the central level. Feedback and information sharing will follow the same route.

## Appendix 1.1 – Flow of surveillance data and information from community to national level in Ethiopia [2]




## Appendix 2 – Epidemiologic Study Designs [7]



## Appendix 3: Case Investigation Form

| **1. PART ONE – BACKGROUND** | | | |
|---|---|---|---|
| 1.1 Age | 1.2 Sex<br>___ Male ___ Female | 1.3 Family size | 1.4 Woreda |
| 1.5 Kebele | | 1.6 Village | |
| 1.7 Occupation<br>___ A. Farmer<br>___ B. Housewife<br>___ C. Government employee<br>___ D. Private employee<br>___ E. Merchant<br>___ F. Student<br>___ G. Daily laborer<br>___ H. Other (specify): | | 1.8 Marital Status<br>___ A. Single<br>___ B. Married<br>___ C. Divorced<br>___ D. Widowed<br>___ E. Not applicable/child | 1.9 Level of Education<br>___ A. Illiterate<br>___ B. Elementary school<br>___ C. Secondary school<br>___ D. College and above |

| **2. PART TWO - KNOWLEDGE** | | |
|---|---|---|
| 2.1 Have you heard about yellow fever?<br>___ Yes (go to 2.1.1)<br>___ No (skip to 2.2) | 2.1.1 Where did you hear about yellow fever?<br>___ A. Friends<br>___ B. Family<br>___ C. Health extension workers<br>___ D. Health workers<br>___ E. Mass media/internet<br>___ F. Others (specify): | 2.2 How do you think yellow fever is transmitted?<br>___ A. By contacting sick person for yellow fever<br>___ B. Bite of mosquito<br>___ C. Natural<br>___ D. Others (specify): |
| 2.3 How can you prevent yellow fever?<br>___ A. Using ITN<br>___ B. Vaccination<br>___ C. Others (specify): | 2.4 What signs of yellow fever do you know?<br>___ A. Fever<br>___ B. Bleeding from the gums, nose, eyes, and/or stomach<br>___ C. Jaundice<br>___ D. Others (specify): | 2.5 What measures or advise can you share with family/friends if you or they get sick/show signs of yellow fever?<br>___ A. Go to health facility for treatment<br>___ B. Go to traditional healers for treatment<br>___ C. Go to holy water/religious places for treatment<br>___ D. Others (specify): |

| **3. PART THREE – CLINICAL PICTURE** | | |
|---|---|---|
| 3.1 Date of onset of symptoms | 3.2 Date seen at health facility | 3.3 Date of admission to health facility |

| 3.4 Signs and Symptoms | Yes | No | | Yes | No |
|---|---|---|---|---|---|
| A. Fever | | | J. Bleeding from the gums, nose, eyes, and/or stomach | | |
| B. Chills | | | K. Blood in the stool (black stool) | | |
| C. Headache | | | L. Bloody vomit (black vomit) | | |
| D. Anorexia | | | M. Kidney failure | | |
| E. Nausea and vomiting | | | N. Confusion | | |
| F. Jaundice | | | O. Seizures | | |
| G. Diarrhea | | | P. Coma | | |
| H. Muscle and join pains | | | Q. Others (specify): _____ | | |
| I. Abdominal pain | | | | | |

| 3.5 Specimen collected | 3.5.1 Result |
|---|---|
| ___ Yes (go to 3.5.1) ___ No (skip to 4.1) | ___ Positive ___ Negative ___ Pending |

| **4. PART FOUR – RISK FACTORS** | | | |
|---|---|---|---|
| 4.1 Travel history to other area<br>___ Yes (go to 4.1.1) ___ No (skip to 4.2) | | 4.1.1 Where? | 4.1.2 When? |
| 4.2 Contact history with disease person<br>___ Yes<br>___ No | 4.3 Contact history with disease animal<br>___ Yes<br>___ No | 4.4 Anyone with the same disease in the same family?<br>___ Yes<br>___ No | 4.5 Presence of other disease(s)<br>___ Yes, type: _____<br>___ No |
| 4.6 History of vaccination for yellow fever<br>___ Yes (go to 4.6.1) ___ No (go to 4.7) | | 4.6.1 Date (MM/YY) | 4.6.2 Check vaccination |
| 4.7 Anyone who visited you from other area before you got sick?<br>___ Yes (go to 4.7.1) ___ No (go to 4.8) | | 4.7.1 Where? | |

| 4.8 Availability of breeding sites for insects | 4.9 Long-lasting insecticide treated nets (LLINs) availability | 4.10 Utilisation of LLINS (observation) | 4.11 Presence of forest around residence place |
|---|---|---|---|
| ___ Yes<br>___ No | ___ Yes<br>___ No | ___ Yes<br>___ No | ___ Yes<br>___ No |

| 4.12 Work in the forest | 4.13 Frequent presence in the forest | 4.14 Presence of monkeys, other primates in the forest |
|---|---|---|
| ___ Yes<br>___ No | ___ Yes<br>___ No | ___ Yes |

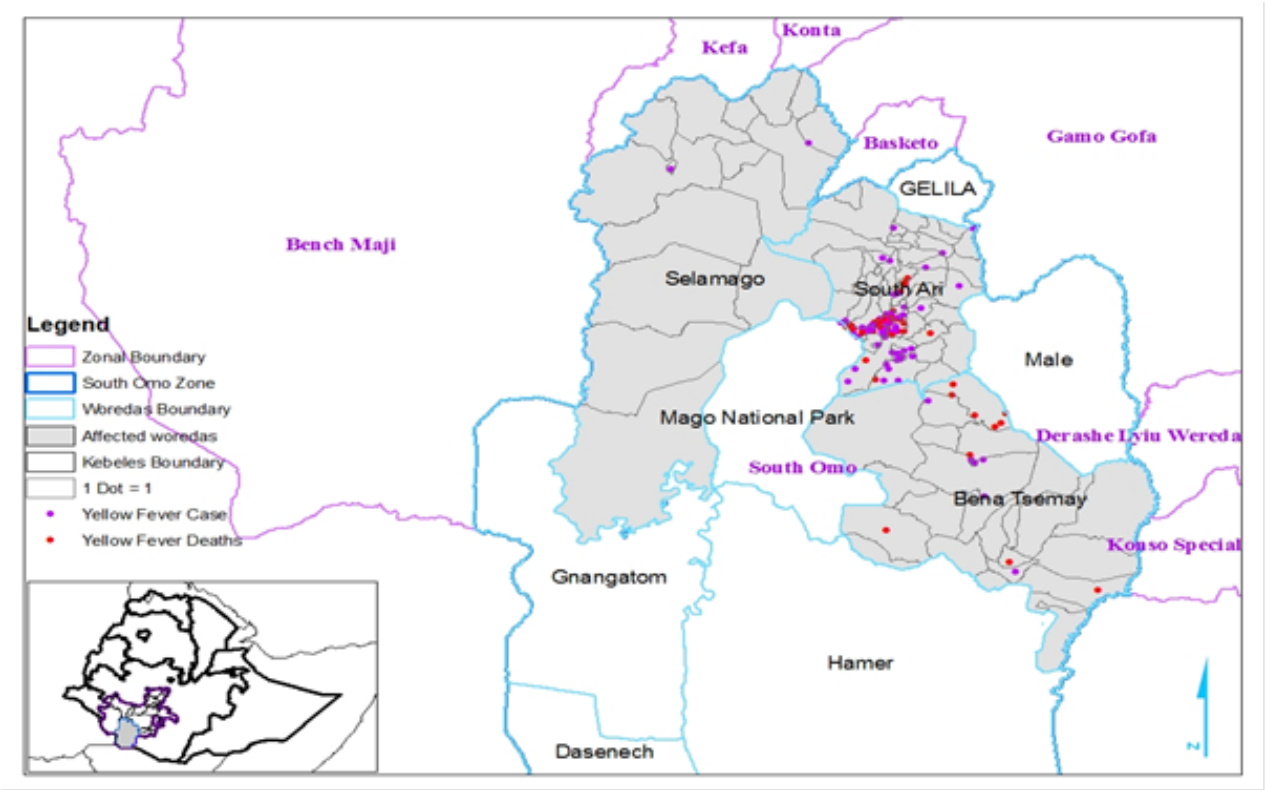
| | | |
|---|---|---|
| | | ___ No |

## Appendix 4: Background about Yellow Fever

Yellow fever is characterised by acute onset of fever, chills, headache, backache, generalised muscle pain, nausea, and vomiting. The clinical presentation ranges from asymptomatic to classical haemorrhagic fever and death. In most instances the clinical manifestation follows three phases; acute, remission and toxic phases. Most cases improve and recover within 4 to 5 days. Some cases will undergo temporary remission phase for 24-48 hours in which patients start to be relieved of symptoms. However, about 15% to 25% of cases enter into a toxic phase after 1 to 2 days of initial recovery [2].

YF is endemic in tropical areas of Africa, and Ethiopia is one of the YF transmission at-risk countries [5,8–10]. Different research and outbreak investigation reports showed that YFV had been circulating In Ethiopia [9,11,12]. From 1960-1962, there was a large outbreak of YF in different parts of Ethiopia, mainly around the Gamo Gofa, Jinka, Kaffa and Wollega areas, which affected approximately 100,000 persons and killed 30,000 (CFR: 30%). In this outbreak, adults were slightly more frequently affected than children while men were more affected than women [8]. Similarly, in 1966, YF reappeared in Arba-Minch, east of Lake Abaya, in an area unaffected by the outbreak of 1960, and affected 2,200 persons with 450 deaths [12]. There are two prevalent types of YF: Urban Yellow Fever, transmitted from human to human, Jungle (Zoonotic) Yellow Fever, transmitted from animal to human.

## Appendix 5: Distribution of cases and deaths of Yellow Fever in affected Kebeles by district - South Omo Zone, November 2012 – October 2013



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