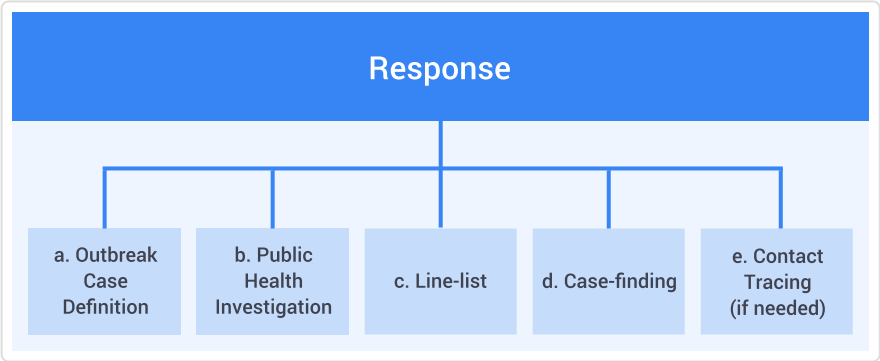
Response



Checklist

1. Define an outbreak case definition
2. Conduct Public Health Investigation
3. Organise a line-list
4. Develop a case-finding strategy
5. Implement contact tracing if needed

Key points

- When an outbreak or an acute public health event is confirmed (or in some cases suspected and awaiting laboratory confirmation) there is a need to enhanced surveillance and implement additional measures.
- Cases reported through IBS and EBS may only represent a small proportion of the total number of cases in the community. Therefore, additional measures are needed to find cases and collect more detailed information in order to support the wider public health response.

Note

A public health response to an outbreak or acute public health event, will also require additional pillars of response (for example, health operations, community mobilisation, logistics) but these are beyond the scope of this guidance. For more information on disease-specific control measures, see Communicable Disease Control in Emergencies.

> **Enhanced surveillance** describes the process for investigating, finding and recording more detailed information on cases identified using outbreak case definitions. It can also include active case-finding and tracing of contacts, to reinforce existing passive methods that may be in place.

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1. Define an outbreak case definition

What is it?

> An **outbreak case definition** is a revision of a regular surveillance case definition used in IBS. It specifies an additional, standard set of criteria to help decide if a person should be classified as having an epidemiological link to cases in the outbreak.
>
> As soon as an outbreak has been detected and confirmed (though the alert management steps) an outbreak case definition must be agreed upon, to support Public Health Investigation and line listing of cases.

How is it developed?

- The **four critical components** of outbreak case definitions include:
  a. Clear and easily understandable wording
  b. Reference to person, place, time, and any clinical features which can provide the epidemiological link to the outbreak
  c. May or may not include laboratory confirmation or serology
  d. Categorization by the degree of certainty regarding the diagnosis as "suspected", "probable", or "confirmed".
- Note that the suspect case definition includes clinical symptoms of the case that are compatible with the disease in question, though laboratory confirmation is negative (or pending result).
- This differs from the confirmed case definition where the laboratory test provides definitive evidence (regardless of clinical symptoms).
- Hence in outbreaks, there is a reliance on the suspect or probable case definition for tracking the evolution and magnitude of the outbreak in real-time, while laboratory specimens are

collected and processed. Suspect and probable cases will become confirmed cases upon testing positive in a laboratory. See Figure 2 for an example of the formulation and the use of outbreak case definitions.

What data to collect?

An outbreak case definition should include criteria for person, place, time, and clinical features. These should be specific to the outbreak under investigation (see Table 1). A checklist for developing outbreak case definitions is found below.

Table 1 Variables for outbreak case definitions

Element	Descriptive features	Examples
1. Person Describes key characteristics the patients share in common.	Age group Occupation	"children under the age of 5 years" "health care workers at clinic X"
2. Place Describes a specific location or facility associated with the outbreak.	Geographic location	"resident of Y camp or X district"
3. Time Specifies illness onset for the cases under investigation.	Illness onset	"onset of illness between May 4 and August 31, 2018"
4. Clinical features Can be simple and eventually include laboratory criteria in confirmed and negative case definitions.	Inclusion criteria	"shortness of breath and fever"
	Exclusion criteria	"persons with no previous history of chronic cough or asthma"
Laboratory criteria	Culture or serology results	Culture-positive for *Vibrio cholerae*

Case example: Components of the outbreak case definitions (Diphtheria, Ukhia and Teknaf refugee camps, Bangladesh, since November 8 2017)

- Person
- Place
- Time
- Clinical features

Confirmed: camp resident living in Ukhia or Teknaf reported as positive for toxigenic C. diphtheriae strain by a multiplex assay since November 8, 2017.

Probable: camp resident living in Ukhia or Teknaf with an upper respiratory tract illness with laryngitis or nasopharyngitis or tonsillitis AND sore throat or difficulty swallowing and an adherent membrane/ pseudomembrane OR gross cervical lymphadenopathy with onset since November 8, 2017.

Suspected: camp resident living in Ukhia or Teknafwith a clinical suspicion of diphtheria with onset since November 8, 2017. Includes case-patients that are unclassified due to missing values.

Checklist for developing the outbreak case definitions

- **Evaluate your data:** Use the data collected so far (e.g. from IBS) to understand the outbeak in terms of person, place and time. This may help you to suggest potential outbreak sources, modes of transmisison, and epidemiological links between cases suspected to be part of the outbreak.
- **Rapidly develop and apply outbreak case definitions with the right expertise:** Outbreak case definitions must be rapidly developed to classify all cases suspected to be part of the outbreak. Organize a team including an epidemiologist familiar with the local epidemiology and context. Consult definitions used in previous outbreaks of that disease in the same or similar settings as well as standardized definitions available from WHO.
- **Consider role of laboratory culture/serology versus rapid diagnostic tests (RDT):** RDTs for many diseases are not considered specific enough to accurately diagnose a patient (e.g. for cholera, RDT among several cases is used to produce an alert and culture is used to confirm the disease). Laboratory culture or serology is nearly always preferable for a confirmed case definition.
- **Make the outbreak case definitions visible on all tools:** Outbreak case definitions should be easily viewable on the case reporting form (WHO Outbreak Data Collection Toolbox) and any educational materials for reporters. The guiding principle is that persons reporting cases should be able to verify that the outbreak case definition is met.

2. Conduct a Public Health Investigation

What is it?

> A **public health investigation** describes a process for collecting detailed data through enhanced surveillance and additional field investigations.
>
> The aim is to develop hypotheses on the cause of an outbreak, the source of infection, and the mode of transmission, in order to inform a public health response.

We are using the term "Public health Investigation" instead of "Outbreak Investigation", as it refers to all hazards not just infectious disease.

When is it done?

- A thorough Public Health Investigation should be organised and conducted as soon as possible following confirmation of a disease outbreak or public health event.

Note there is a close relationship between a Public Health Investigation and a Risk Assessment.

- **Risk Assessment** aims to rapidly characterize the probability that an event will have a serious public health impact, and to help determine the actions needed to reduce this risk.
- **Public Health Investigation** aims to determine the cause of an outbreak, the disease transmission routes and potential for further spread, and to evaluate whether early control strategies appear effective.

In practice, an initial Public Health Investigation may overlap and be combined with a Risk Assessment and they often include the collection of similar information (e.g. both require sample collection to provide laboratory confirmation).

- A Public Health Investigation may need to be repeated, based on the nature of the public health threat. In Ebola, for example, a Public Health Investigation of each case will need to be conducted to document the source of transmission and to identify links to existing transmission chains. For cholera, public health investigations may only be needed for new

suspected cases reported in new geographic areas or in areas which have been declared to have ended transmission.

How is it done?

- The types of data collected during a Public Health Investigation will depend on the type of disease or event being investigated.
- The basic descriptive epidemiological principles of person, place and time should guide the types of data collected and the type of analysis conducted.
- The basic information to collect in each category is shown below in Table 5.
- Data initially collected by Public Health Investigations should also be systematically recorded and managed in the form of a line list.

Table 4 Variables for person, time, and place

Type	Variables	Rationale
Person	**Demographics** - Age and date of birth - Sex - Contact information **Exposure** - Occupation - Risk factors **Clinical** - Symptoms and signs of the case definition - Severity, complications, hospitalization - Interventions received (vaccination, etc.) **Laboratory** - Laboratory confirmation, subtype, antibiotic resistance	- Describe groups at risk - Verify that the case definition has been me - Characterize the disease - Produce hypotheses on the source and routes of transmission
Time	- Date of onset of symptoms - Date of reporting	- Construct an epidemic curve to monitor outbreak - Determine time of exposure
Place	- Address, place of residence - Travel history - School, workplace	- Analyze places of potential infection - Analyze places of potential transmission

How are the results analysed?

- The data collected in a public health investigation should be analysed based on the same descriptive epidemiology principles of person, place and time.

Interpret the time analysis results

- Look at the histogram and observe the shape of the epidemic curve. Draw conclusions about when exposure to the agent that caused the illness occurred, the source of infection and related incubation period. This helps to demonstrate where and how an outbreak began, how quickly the disease is spreading, the stage of the outbreak (start, middle or end phase) and whether control efforts are having an impact.
  - If the shape of the curve suddenly increases to develop a steep up-slope, and then descends just as rapidly, exposure to the causal agent was probably over a brief period of time. There may be a common source of infection. Point source
  - If exposure to the common source was over a long period of time, the shape of the epidemic curve is more likely to be a plateau rather than a sharp peak. Common source
  - If the illness resulted from person-to-person transmission, the curve will present as a series of progressively taller peaks separated by periods of incubation. Person-to-person

Interpret the place analysis results

- Use the map to:
  - Describe the geographic extent of the problem and identify high risk areas.
  - Identify and describe any clusters or patterns of transmission or exposure. Depending on the organism that has contributed to this outbreak, specify the proximity of the cases to likely sources of infection.

Dot map

Interpret the person analysis results

- Information developed from the person analysis is essential for planning the outbreak response because it describes more precisely the high risk group(s) for transmission of this disease or condition. For example, if yellow fever cases occurred in patients less than 15 years of age, then the immunization response would need to target children less than 15 years of age.
- Consider disaggregation by age, sex, other parameters (e.g. refugee status, immunization status)
- Consider collecting population denominators where available, and calculating attack rates to make population-weighted comparisions to identify high-risk groups

Develop hypotheses

- Use the results of the descriptive epidemiology analysis to formulate hypotheses to your stated objectives
    - What was the causal agent of the outbreak?
    - What was the source of infection?
    - What was the transmission pattern?
- These hypotheses should then be used to determine which control measures need to be implemented and to help guide the response.
    - How to modify the host response
    - How to control the source of the pathogen
    - How to interupt transmission

Use of data

Advanced

In later stages of an outbreak, you can use analytical epidemiology to test the hypotheses and determine the impact of control measures. Case-control studies are most commonly used in outbreak settings. Occassionally cohort studies are also used.

Advanced/Further reading

The extent of the investigation and will depend on what is already known about the control of the pathogen. Figure 4 provides a perspective on the extent of information gathering needed when faced with a known and unknown etiology (i.e., the latter including emerging infectious diseases or or a new condition) and a known and unknown mode of transmission (i.e. a previously known vehicle for transmission compared with a novel means of transmission).

Fig 4 The Level of data gathering necessary to enable investigation and control by etiology and transmission mode (Goodman, Buehler, and Koplan 1990)

(+) represents the amount of effort needed to investigate the source/transmission of the outbreak and control the outbreak. This is based on what is already known about usual sources of the disease, and the means of control from prior outbreaks. |

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3. Organise a line-list

What is it?

> **Note**
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> **Line-listing** refers to the organisation and management of individual level data on cases collected during an outbreak.

Why is it done?

- The main purpose of line listing is to support the ongoing analysis of epidemiological during the course of an outbreak.
- It should be thought of as a continuation of the initial analysis done at the start of an outbreak through a Public Health Investigation.

How is it done?

- Data should be collected systematically on all cases that meet the outbreak case definition using a standardised reporting form. This may be the same as the initial public health investigation form used at the onset. This can be collected using paper-based forms whilst out in the field, but they should be entered into an electronic database at the earliest possible interval to ensure the data is recorded accurately and reliably.

What data to collect?

- In many events - especially large-scale outbreaks with explosive transmission - surveillance needs often outstrip available capacity to collect and report data. It is therefore necessary to

decide on the minimal set of variables to guide control efforts. A comparison of the data collected for line-listing is shown in Box 1.

- Not all variables collected in a case investigation form need to be included in a line list. Depending on the type of event, not all cases necessarily need to be investigated using a case investigation form.
- For example, in cholera outbreak a case investigation form may only be needed to investigate initial cases or clusters, but not all may be required once transmission is confirmed in an area and the modes and risk factors well understood. In Ebola virus disease, however, all cases must be fully investigated using a detailed case investigation form so that the dynamics of transmission and links to existing cases can be fully documented and understood for each individual. In both these examples, however, all cases must be also reported using a line list for surveillance purposes, containing a smaller core subset of variables compared to the detailed case investigation form.

Line-list variables

Socio-demographic variables:

- Age
- Sex
- Address

Epidemiological variables:

- High-risk group (to be specified)
- Risk factors for disease
- Contact history with known cases
- Vaccination history
- Underlying conditions
- Severity of disease (hospitalization, complications, etc.)
- More information on place (e.g., GPS coordinates of village)

Laboratory variables:

- Confirmed (Y/N)
- RDT + / -
- Serotype / strain
- Antimicrobial resistance profile

4. Develop a case-finding strategy

Why is it done?

- Cases reported through IBS and EBS may represent only a small proportion of the total number of cases in the community.
- Therefore, some outbreaks also require a change in the way cases are found to enure all cases can be identified as quickly as possible.
- This is particularly important for diseases that are are highly-transmissible, and risk severe morbidity and mortality (e.g. cholera, EVD). These require the exhaustive identification of cases, so they can be isolated and treated, in order to interrupt community transmission.

What is it?

> **Note**
>
> **Active case-finding** involves searching for suspected cases in health facility records, or even going house-to-house to find additional persons who meet an outbreak case definition. Suspected cases are referred to a health facility, or if necessary, the household is quarantined and the patient is managed in place.
>
> **Passive case-finding** describes the usual process for reporting disease data by a health system, through the voluntary presentation of patients to health facilities. There is no active search for cases.

When is it done?

- Passive case-finding, through IBS and EBS, should continue. However, outbreak case definitions should be applied to IBS to ensure there are consistent sources of data.
- Healthcare workers must be aware of the new outbreak case definitions to ensure they can detect and notify of suspected cases as early as possible, through the screening of patients who present to health care facilities.
- However, this should be complemented by active case-finding strategies at the community level, to also identify and refer cases who are not able to access health facilities

How is it done?

The strategy developed for case-finding depends on:

- Characteristics of the disease or non-infectious hazard (transmissibility, risk of severe morbidity and mortality);
- Effectiveness of the routine surveillance system (completeness and timeliness of reporting, rural/remote locations, fragmented surveillance systems in emergencies);
- Receptiveness of affected communities (trust in healthcare facilities, fear caused by the outbreak, etc.).

Case Study

For example, during the 2014-6 West Africa Ebola outbreak:

- The pathogen was highly-transmissible in the community and had serious impact on morbidity and mortality;
- Surveillance systems in affected countries were unable to produce timely and complete data and detect outbreaks early enough, especially in the remote areas where it emerged;
- Community fear of visiting healthcare facilities was a problem during the early part of the outbreak.

- Active case finding can be conducted using one or more of the following methods shown in Table 2. In the example above, EVD employed all forms of active surveillance in Table 2.

Table 2 Active case finding methods

Method	Rationale	Challenges	Example use case
1. Rapid retrospective review of patient records in health facilities in area known or suspected to be affected	To identify patients meeting case definitions and yet undetected by surveillance When late detection of the outbreak is suspected	Time and labour-intensive Registers may not contain sufficient information to identify suspect cases.	At start of EVD outbreak to **retrospectively** assess whether any cases came villages not yet known to be affected
2. Daily phone calls to health facilities in area known or suspected to be affected or that are not routinely reporting as intended	To increase the vigilance and adherence by healthcare workers When reporting completeness and timeliness among health facilities is known to be low	Time and labour-intensive May inadvertently encourage delayed reporting instead of strong IBS or EBS	At start of cholera outbreak to **prospectively** assess whether any cases came villages not yet known to be affected
3. Daily data collection of data from new treatment centres set up to handle the outbreak caseload	To identify cases managed in treatment units for explosive outbreaks that have serious infection prevention and control concerns	Need to assure reporting practices (both the type of data and methods/channels of reporting) are harmonized with surveillance system	For all diseases with treatment units: cholera, EVD, hepatitis E, yellow fever, diphtheria
4. Systematic screening of patients presenting to existing health facilities	To identify outbreak-related suspect cases that continue to make contact with health system	Risk of double counting between health facilities and treatment unit Logistically intensive for a large number of healthcare workers and structures	Cholera, EVD, hepatitis E, plague, yellow fever
5. House to house search for cases in the community	To identify all cases in a limited geographical area To identify why cases are still occurring despite control measures in place	Logistically intensive for a large number of healthcare workers and structures May cause concern in community and patients may be hesitant about referral	Diseases with asymptomatic status (i.e., tuberculosis), high-risk diseases not well-captured by surveillance
6. Media release informing about	Identify cases as comprehensively as	Avoiding of panic/ overreaction, putting	Media releases during foodborne outbreaks

5. Contact tracing

What is it?

> Contact tracing refers to the identification and management of persons ("contacts") who may have come into close enough contact with another person infected by a communicable disease transmitted by aerosol or direct contact with bodily fluids, thereby putting put them at risk of infection.

- The aim is to identify contacts who become cases at the earliest possible opportunity, ensuring they can be promptly identified, isolated and treated and therefore helping to prevent the further spread of the disease.
- Contact tracing can be thought of as active case-finding *restricted to contacts* of known cases. For these diseases, close contacts have a much higher risk of developing infection compared to the general population.
- Exhaustive identification of contacts is necessary. They are informed of their exposure, and public health actions are taken to monitor their clinical and diagnostic status and limit their spread of the disease to their own contacts.

When is it done?

- Contact tracing is indicated for several highly infectious diseases transmitted by aerosol or direct contact with bodily fluids (see Table 3).

Table 3 Diseases typically requiring contact tracing

Diseases	Public health actions for cases and contacts	Isolation
Viral hemorrhagic fevers (EVD, Lassa, Marburg)	- Observations of symptoms for maximum length of incubation period among contacts	-Rapid isolation and treatment of contacts who develop symptoms
Cholera (initial cases)	- Antibiotic chemoprophylaxis of contacts who have not yet developed symptoms to prevent development of disease and limit spread	- No isolation but contacts self-report if they develop symptoms
Diphtheria	- Vaccination - Antibiotic chemoprophylaxis of contacts who have not yet developed symptoms to prevent development of disease and limit spread	- No isolation but contacts self-report if they develop symptoms
Measles (initial cases)	- Vaccination	- No isolation but contacts self-report if they develop symptoms
Meningococcal disease (initial cases)	- Vaccination Antibiotic chemoprophylaxis of contacts who have not yet developed symptoms to prevent development of disease and limit spread	- No isolation but contacts self-report if they develop symptoms
Tuberculosis	- Detailed screening (tuberculin skin testing or chest radiography) and chemoprophylaxis - Further periodic monitoring as deemed necessary (e.g. for MDR-TB or other high-risk situations)	- No isolation but contacts self-report if they develop symptoms

Quote

Contact tracing to support outbreak control for epidemic-prone diseases serves a different objective as compared to the identification of sexual partners of index cases of sexually-transmitted infections, or the identification of common exposures (water sources or shared food) sought through other types of case investigations.

How is it done?

- Close contacts can be defined as persons with very close and substantial contact with the case. The exact definition of a contact will depend on the disease but may include persons listed below.
- The date of last contact with the known case should be determined as precisely as possible, and used to calculate the number of day since last contact. Follow-up visits conducted for the remainder of the days remaining in the incubation period of the disease. Only after the incubation period has ended can the tracing of the contact end.
- If the date of the last contact with the case cannot be determined, then the contact should be followed for the full duration of the disease incubation period.

Types of contact

- Household members;
- Caretakers, friends, or coworkers with substantial close interaction (ex., close contact less than one meter away for over one hour during the five days prior to onset of disease);
- Healthcare workers who were exposed to secretions of the case;
- Persons who have had contact with blood/bodily fluid of the case;
- Persons who had any direct physical contact during time of illness;
- A baby who has been breastfed by the case.

The steps involved are outlined in Box 2.

Steps in contact tracing

The simplified steps in contact tracing include:

1. Develop a contact definition for the particular disease.
2. Interview the case (or a surrogate who knows about routine activities) to identify and list all contacts using the contact definition.
3. Immediately evaluate the contacts for the appearance of symptoms compatible with the disease.
4. Apply public health actions to contacts (depending on disease):
    - Preventative measures to contacts to prevent the development of disease (may include vaccination if unvaccinated, antibiotic chemoprophylaxis if no symptoms).
    - For some diseases, self-assessment and self-report in case of symptom development.
    - For some diseases, follow-up for the maximum incubation period from the date of exposure to monitor for development of symptoms.
    - Rapid isolation and treatment of contacts who develop symptoms and become cases.

What data to collect?

Contacts must first be identified and listed. Table 4 contains the typical variables for collection through an interview with the case or a surrogate. All of this data should be entered in a database linked to the case by the unique ID.

Table 4 Core variables for contact tracing

Category	Variable
Information on the case	
Person	- Unique ID - Name
Time	- Date of symptom onset
Place (case)	- Address - Village/town/block
Information on the contact	
Person	- Name - Sex - Age - Relationship to case - Healthcare worker - Mobile number
Time	Date of last exposure to case
Place	AddressVillage/town/block
Public health actions taken	If applicable [checklist] - Vaccination - Antibiotic chemoprophylaxis - Exclusion from work/school until end antibiotics - Self-assessment and self-report - Preferred means of follow-up (call, visit)

For follow-up of contacts over the maximum incubation period (e.g. 21 days for EVD, seven days for diphtheria), follow-up data will be collected (Box 4). Only the data relating to completion of the visit and presence of symptoms should be added to the database (bolded).

Table 5 Follow-up data for contacts

Category	Variable
Information on the contacts	
Person	- Name - Sex - Age - Completion of day X of Y follow-up call/visit
Time	- Date of last exposure to case
Place	- Address - Village/town/block
Symptoms	- List key signs/symptoms consistent with case definition, and check all that are present

References

Goodman, Richard A., James W. Buehler, and Jeffrey P. Koplan. 1990. "THE EPIDEMIOLOGIC FIELD INVESTIGATION: SCIENCE AND JUDGMENT IN PUBLIC HEALTH PRACTICE."*American Journal of Epidemiology*132 (1): 9–16.

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