



Chapter 5: Investigation of Healthcare-Associated Infection and Antibiotic-Resistant Pathogen Outbreaks Interim Version March 31, 2021

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CHAPTER OUTLINE

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PREFACE

This chapter reviews the key elements and steps involved in the response to a healthcare-associated infection (HAI) or antibiotic-resistant (AR) pathogen outbreak. The types of events addressed here include person-to-person (often due to deficient infection control practices) or point-source (e.g., contaminated medical products such as medications or devices) outbreaks. The information contained in this chapter can also be applied to investigations of toxins or chemicals in the healthcare setting, infection control breaches (see Supplement B), and sentinel cases of emerging pathogens. The overarching goal of HAI/AR outbreak investigations is minimizing patient harm by implementing effective control measures.

INTRODUCTION

5.0 Introduction

Collaboration between public health and healthcare is essential for an effective outbreak response. While healthcare settings are responsible for prevention and control practices on their premises, public health officials are responsible for ensuring the health and safety of



the population within their jurisdiction, including patients, visitors, and employees in healthcare settings. During an outbreak investigation, public health authorities may conduct or assist with data collection, epidemiological analyses, laboratory testing, infection control and environmental assessments, and provide recommendations to prevent disease transmission. The level of public health involvement and support will vary depending on the nature of the outbreak and available resources.

During an outbreak investigation, a systematic approach is necessary to determine the nature and scope of the problem, identify the etiologic agent, establish the existence of an outbreak, define the population at risk, determine risk factors and routes of transmission, implement appropriate control measures, and develop strategies to prevent future occurrences. See Box 5.1 for HAI/AR outbreak investigation resources. Overall goals of an outbreak investigation are listed in Box 5.2. Objectives for any outbreak and associated activities to be performed by epidemiology, infection prevention, and laboratory public health staff are listed in Table 5.1. Investigation-specific objectives can be developed based on goals and objectives listed in Box 5.2 and Table 5.1.

Box 5.1 HAI/AR Outbreak Investigation Resources

CDC Healthcare-Associated Infection (HAI) Outbreak Investigation Toolkit:

www.cdc.gov/hai/outbreaks/outbreaktoolkit.html

CDC Outbreaks and Patient Notifications: Resources for state health departments investigating healthcare-associated infection outbreaks and patient notifications:

www.cdc.gov/hai/outbreaks/outbreak-resources.html

CORHA: www.corha.org

Outbreak response and incident Management: SHEA guidance and resources for healthcare epidemiologists in United States acute-care hospitals¹

Box 5.2 Goals of an Outbreak Investigation

- Stop the outbreak as quickly as possible to protect patients
 - Ensure a rapid response with accurate information
 - Implement control measures that will halt transmission of disease and prevent additional cases
- Maintain the public's confidence
 - Recognize that patient safety is the primary focus
 - Consider how decisions might impact patient care and public perception
- Identify new risks
- Recognize new and under-appreciated risks associated with healthcare delivery. For example, the outbreak of *Mycobacterium chimera* associated with heater-cooler devices identified a new possible risk of these devices, and identification resulted in new recommendations to prevent heater-cooler related infections.^{2,3} Prevent future outbreaks
 - Identify systemic problems that might lead to additional patient harm



- Mitigate and support mitigation of gaps identified, both within a facility and more broadly

Table 5.1 Investigation Activities for Outbreak Response Objectives

Objective	Epidemiology	Infection Prevention	Public Health Laboratory
Identify mode of transmission and vehicle	<ul style="list-style-type: none"> • Obtain information on individual cases using any or all of the following: <ul style="list-style-type: none"> - Surveillance data; - Medical records; - Healthcare facility staff interviews; - Patient interviews. • Establish case definition on the basis of characteristics of pathogen, agent, or infection • Characterize cases by person, place, and time, and evaluate this descriptive epidemiology to identify patterns • Analyze exposure information comparing cases to develop hypotheses 	<ul style="list-style-type: none"> • Obtain information about healthcare practices and infection control practices that might help characterize the outbreak 	<ul style="list-style-type: none"> • Obtain and store clinical material or isolates • Perform confirmatory laboratory testing to confirm pathogen • Perform molecular testing when applicable and available to assess relatedness
Identify persons at risk and determine size and scope of outbreak	<ul style="list-style-type: none"> • Look back at clinical laboratory records and other relevant facility records to identify cases • Talk to facility staff to identify cases • Depending on nature of outbreak, take additional steps as warranted; examples include contacting other facilities, healthcare providers, and/or public health agencies to ask if they have cases (“call for cases”), or directly asking members of the public to contact the health department 		<ul style="list-style-type: none"> • Contact clinical laboratories to identify additional cases • Speed up referral and additional testing of outbreak pathogen
	<ul style="list-style-type: none"> • Complete descriptive analysis using summary 	<ul style="list-style-type: none"> • To determine any contributing 	<ul style="list-style-type: none"> • Evaluate results of all outbreak-



<p>Identify cause of outbreak</p>	<p>statistics, timelines, maps, epidemic curves, and other techniques to develop possible causes</p> <ul style="list-style-type: none"> • Review descriptive epidemiologic results combine with any analytical epidemiology results to develop the most likely explanation for the outbreak 	<p>infection control gaps, perform an on-site infection control assessment to include:</p> <ul style="list-style-type: none"> - On-site observations; - Facility staff interviews; - Review of infection control policies 	<p>associated cultures to highlight possible relations among isolates from clinical, environmental, and healthcare worker samples</p> <ul style="list-style-type: none"> • Work with appropriate regulatory authority to ensure that samples are collected and maintained with appropriate chain of custody. This will help the regulatory authority to take appropriate regulatory action
<p>Identify contributing factors and antecedents</p>	<ul style="list-style-type: none"> • Summarize information to identify confirmed or suspected contributing factors 	<ul style="list-style-type: none"> • Evaluate results of infection control assessment, taking into account the identification of agent and results of epidemiologic investigation, to identify contributing factors and antecedents 	<ul style="list-style-type: none"> • Summarize information about culture results from clinical, environmental, and healthcare provider samples
<p>Determine potential for ongoing transmission and need for control measures</p>	<ul style="list-style-type: none"> • Perform ongoing surveillance of pathogen, agent, or infection using public health surveillance systems, clinical laboratory data, and facility prospective surveillance • If outbreak appears to be ongoing, continue surveillance and consider additional investigation and gap mitigation 	<ul style="list-style-type: none"> • Re-assess infection control practices after gap mitigation has occurred • If deficient infection control practices identified or additional cases identified following gap mitigation, consider re-assessment of infection control practices 	<ul style="list-style-type: none"> • Maintain stored sample in case comparison needed to newly identified cases



CORHA Keys to Success

Initial Steps in the Investigation of Outbreaks

Initial steps that should be performed rapidly

- Complete initial steps within a brief time period. Use this information to develop plans for a more in-depth investigation when warranted.
- Begin by gathering readily available data from affected healthcare facility(ies), laboratories, and applicable public health surveillance systems.
- Confirm the diagnosis by obtaining and verifying clinical and laboratory information.
- Determine how the implicated agent was identified and request that specimens or microbial isolates be saved and made available for further testing. This should be done as soon as possible to avoid unintentional loss of the specimen(s).
- As needed, perform a literature review to understand clinical features, host factors, exposure pathways, environmental factors, and other characteristics associated with the pathogen, infection, or condition; for novel or unfamiliar situations, consult experts and partners (e.g., CDC).
- Develop a preliminary hypothesis.
- Establish objectives for the investigation that reflect overall goals of an outbreak investigation to identify hazards, stop the outbreak, maintain the public's confidence, and prevent future outbreaks.
- Consider investigation authority based on local regulations.

Preliminary control measures

- Consider the need for instituting preliminary control measures based on initial information and descriptions of potentially hazardous conditions or practices (e.g., reuse of single dose vials or other injection supplies).
- Perform a site visit and on-site infection control assessment early in the process when warranted, including when there is:
 - High potential impact to patients (e.g., high morbidity, mortality, ongoing exposure); or
 - Involvement of an outpatient facility or other setting that lacks internal resources for conducting a reliable internal assessment.

Requests for assistance

- Request assistance as soon as the need is recognized to allow for a rapid investigation at the level determined to be appropriate.

Evaluation

- Frequently re-evaluate outbreak response objectives, methods, and approach as findings accumulate. Questions to consider include: Does the data support the hypothesis? Does the hypothesis need to be revised? Is there a need for additional resources?



OUTBREAK INVESTIGATION AND RESPONSE STEPS

5.1 Outbreak Investigation and Response Steps

As described in Chapter 4, public health authorities typically detect outbreaks through the reporting of a suspected HAI/AR outbreak by healthcare or other partners, or via the monitoring of surveillance systems and routine communicable disease reporting.

What follows is a step-by-step guide for the investigation of an HAI/AR outbreak. Steps can be applied to other investigations, such as a suspected transmission event, sentinel cases of emerging pathogens, infection control breaches, and non-infectious toxin or chemical exposures. Although most steps in an outbreak investigation follow a logical process—from determining whether an outbreak exists to identifying and controlling the source—multiple steps often occur concurrently and not necessarily in a specific order. The steps are from the perspective of the public health agency. See Box 5.3 for the steps of an outbreak investigation. The healthcare facility might be concurrently implementing their outbreak response; coordination should occur with each step. A response should be appropriately rapid, but it is important to also ensure accuracy. Take the time needed to gather information, do background research, and gather initial data.

Box 5.3 Steps of an Outbreak Investigation

1. Perform an initial assessment
2. Verify the diagnosis
3. Assemble and brief the outbreak response team
4. Establish a plan and prepare for fieldwork
5. Confirm the presence of an outbreak
6. Establish case definition and classification criteria
7. Identify and count cases
8. Collect, organize, and analyze data
9. Perform an infection control assessment
10. Consider an environmental assessment
11. Recommend control measures
12. Interpret results
13. Monitor the outbreak until completion

Not all steps might be performed in every outbreak response. Steps might not be performed in order, and some steps might occur concurrently.

PERFORM AN INITIAL ASSESSMENT

5.1.1 Perform an Initial Assessment

5.1.1.1 Initial Information to be Gathered



When a cluster or suspected outbreak is detected, as much of the following information should be collected as possible, knowing that some information might not initially be available. Initial data gathering might include conversations with the facility, brief review of medical records if easily accessible, and brief review of public health surveillance data. Initial information can include:

- Specific pathogen, infection, or syndrome;
- Number of cases identified, types of cases (e.g., infections vs. colonization, occurring primarily in patients vs. patients and staff), and outcomes (e.g., number of deaths);
- Characteristics of the patients/affected population (e.g., dates of visits, procedures, surgery, admission/discharge, death, reason for admission, underlying conditions, symptoms and dates of onset);
- Type of setting and setting characteristics (e.g., if a skilled nursing facility, does the facility have multiple units, care for ventilated patients, etc.);
- Location of the cases (e.g., unit vs. facility-wide, type of unit)
- Any testing information available (e.g., laboratory name, dates of culture/testing, additional testing performed, methodology used);
- Date of detection of suspected outbreak;
- Known or expected background rate, if known;
- Descriptions of relevant care delivery practices to help gauge whether accepted infection control standards are being followed (e.g., for an outbreak involving injections, ascertaining whether single dose vials are reused for multiple patients and other injection preparation and administration practices);
- Information related to any possible medical product involvement (see <https://corha.org/wp-content/uploads/2019/06/CORHA-Medical-Product-Assessment-Questions.pdf>); and
- Measures already implemented (e.g., infection control measures, additional testing, notification of patients).

5.1.1.2 Determining the Level of Response

Information gathered in the initial assessment will guide the next steps, including determining if an investigation is warranted. Levels of response for a public health agency might include a full investigation and response, investigation by the facility with public health being kept informed, or receipt of the report only. An effective triage process should be established to determine an appropriate level of response and ensure public health investigations proceed when needed but not necessarily for all suspected outbreaks reported and clusters detected, although all should be tracked by public health. Full investigations can be resource-intensive for the public health agency and the facility and are not needed for all suspected outbreaks. Resource limitations should not be the sole factor in determining the appropriate level of response during an outbreak; additional staffing and expertise are usually available when the situation warrants (e.g., from other jurisdictions or departments within state or local public health or from federal public health partners such as CDC). Local regulations and authority to investigate should be considered when determining the level of response and are discussed more in Chapter 8.

A more comprehensive investigation and public health involvement should be considered when:



- Risk to patients is elevated, including potential for ongoing transmission, greater levels of harm (e.g., morbidity and mortality), vulnerability of the population at risk, potential for involvement of large numbers of persons, and identification of concerning infection control practices;
- Early implementation of proven control measures is time-sensitive (e.g., prophylaxis);
- Resources and experience level of the facility to conduct their own investigation is limited, including healthcare settings with less infection control capacity, such as outpatient settings;
- Previous facility responses to outbreaks have been sub-optimal; or
- There is a sentinel event, such as an unusual or novel organism or organism/infection combination, a suspected involvement of a medical product, or other situation in which even a single case should be investigated.

Ensure the triage and prioritization process is established in advance and applied equally. A best practice is to have criteria for investigation and apply as uniformly as possible, realizing that some judgement is needed and situations vary. The level of response might change as the investigation proceeds, and public health agencies should be flexible.

5.1.1.3 Initial Control Measures

A brief assessment of infection control practices should be performed when the initial information is gathered, often during the initial phone call with the facility. If there are practices that need to be corrected immediately, this recommendation should be given to the facility as part of the initial assessment. It is not necessary to wait for an on-site assessment for initial recommendations to be given. Infection control assessments and control measure recommendations are discussed in more detail later in the chapter.

5.1.1.4 Developing Hypotheses

To focus the investigation, the development of initial hypotheses about potential sources of the outbreak should occur early in the investigation process. After gathering initial information, it should be possible to develop one or more hypotheses of likely outbreak causes. Key steps to developing hypotheses include the review of what is known about the pathogen or infection, including previous outbreak investigations, as well as the review of the initial information gathered. Consider possible infection control breaches and medical product involvement early in hypothesis development, which can inform early control measures. Initial hypotheses can help direct the course of the investigation. Hypotheses should be re-evaluated, refined, and narrowed as the investigation proceeds.

Meanwhile in the Healthcare Facility...

Initial Assessment

At this step in the investigation, public health should be in contact with the healthcare facility. The facility might have performed the following at this point in the investigation (the level of investigation performed by the facility might vary among facilities and healthcare settings):

- Development of their own hypotheses for the cause of the outbreak;
- Implementation of infection control measures based on preliminary information; and/or



- Notification of their leadership of the suspected outbreak and reporting to public health.

VERIFY THE DIAGNOSIS

5.1.2 Verify the Diagnosis

Often at the time a suspected outbreak is detected, the diagnosis might not be clear, or in some cases might be incorrect. Early in the investigation, identify as accurately as possible the specific nature of the disease by ensuring that the diagnosis is correct, by evaluating for possible laboratory error as a basis for increased diagnoses, by evaluating possible changes in surveillance and case definitions, and by reviewing clinical findings and microbiological testing results.⁴ Information reviewed should include clinical features, timing of symptom onset or laboratory testing in relation to the suspected source, and biologic plausibility.

The laboratory serving the facility or healthcare setting should be involved in the investigation as soon as an outbreak is suspected. Any clinical material, specimens, microbial isolates, environmental samples, and medical products including medications and devices should be saved; the public health team should prioritize contact with the laboratory to ensure samples are not discarded, and when needed forwarded to public health laboratory as soon as possible. Retention of anything that might be tested as part of the investigation is increasingly important in the face of widespread use of culture-independent methods to detect specific microorganisms and drug-resistant genes. If an unusual microorganism is suspected in the outbreak, it is essential to confirm laboratory test results via a review of test methods or performing additional testing. Additional testing to confirm the diagnosis, identify possible resistance mechanisms, or assess relatedness via molecular methods should be considered, and can be done at the state public health laboratory or other reference laboratory.

Meanwhile in the Healthcare Facility...

Verify the Diagnosis

The facility might be concurrently performing the following:

- Reviewing their own laboratory results and medical record information to verify the diagnosis;
- Requesting assistance from public health to contact the laboratory, if external to the facility, to save isolates; requesting assistance from the public health laboratory to perform additional testing; and
- Proceeding with infection control measures to protect patients, including saving and cessation of use of suspected medical products if applicable.

ASSEMBLE AND BRIEF THE OUTBREAK RESPONSE TEAM

5.1.3 Assemble and Brief the Outbreak Response Team

The number and composition of the members of the public health outbreak response team will depend on the nature of the outbreak. Consider the need for staff with epidemiology,



data analysis, laboratory, infection prevention, and medical expertise. If multiple public health agencies are involved there will likely be multiple public health teams; the leading agency should be determined, and this agency provide facilitation and coordination for the response. The leading agency is referred to as the “coordinating agency” in this guidance. Roles assigned should include designation of the team lead. During the course of the investigation, the composition of the team might need to be modified. For complex or lengthy investigations, assess the availability of additional staff to backfill team members’ routine work. For specific information on team member roles, see Chapter 3.

Each entity involved in an outbreak response might have their own team. The leading team might be from the healthcare facility when public health is not directly involved or might be a team from a public health agency that coordinates with the healthcare facility team. Similar strategies for team composition can be applied to teams from the healthcare facility and other agencies, although specific members and roles might vary. Close collaboration and coordination is needed when multiple teams are involved during a multi-facility or multi-jurisdictional outbreak; this is described in additional detail in Chapter 7.

5.1.3.1 Partners

Multiple partners are likely to be involved during an outbreak investigation, a single public health agency and the healthcare facility at a minimum. Each involved entity should have a response team. Other partners involved might include state facility licensing agencies (supervisory staff and surveyors from the involved healthcare setting), law enforcement (local, state, or federal) if criminal action might be involved, professional oversight organizations such as pharmacy boards or clinician licensing boards (staff from licensing organization), or regulatory agencies such as the Food and Drug Administration (FDA).⁴ Facility teams should be involved on a daily basis; other partners might be a daily part of the team or might provide assistance for specific parts of the investigation.

If the investigation cannot be managed with local resources due to its scale, complexity or limited agency expertise, help should be requested sooner rather than later. Escalation might occur from local public health agency to state public health agency to CDC; in some cases escalation might be helpful to obtain additional opinions or perspectives, and in other cases it might be helpful to request additional resources and expertise. A specific type of escalation involves Epi-Aids, investigations of an urgent public health problem led by CDC. Epi-Aids can be requested by a state, tribal, or territorial public health authority, often a state epidemiologist. Typically Epi-Aids are rapid, short-term (1-3 weeks), onsite, technical assistance or investigations by Epidemic Intelligence Service (EIS) officers and other CDC subject matter experts. The focus of an Epi-Aid investigation is to assist partners in making rapid, practical decisions for actions to prevent and control the public health problem.⁵

5.1.3.2 Public Health Team Communication

Public health team members should participate in regular briefings. As the investigation evolves, consider bringing in additional team members as needed and as early as possible, such as communication staff if media attention is anticipated, or legal staff if legal questions are anticipated. The team lead should be open to assessing how their team members are managing workload; team members should be open with their team lead about workload and



priorities. Consider implementing an incident command system (ICS) to formalize roles and communications when a large response is anticipated, See Chapter 3 for more information on ICS. Should the investigation lead to media attention, ensure that public information officers are brought onto the team.

5.1.3.3 Communication Among Partners

The public health outbreak response team should coordinate with other entities involved in the response, including the healthcare facility, regulatory agencies, and other entities involved. It is essential to consider the roles and responsibilities of the affected healthcare facility and their staff, and to communicate early and regularly with the facility, including details of the outbreak response team's approach. The public health team should be aware of the multiple responsibilities of a healthcare facility outbreak response team, including their ongoing surveillance and other roles. It is helpful for the public health team to consider the following regarding communication with the healthcare facility:

- Determine the frequency and method of communication with the healthcare facility early in the investigation. In some cases daily calls can be helpful. Consider when to include the healthcare facility on public health calls, such as calls with CDC.
- Methods for sharing information should be discussed early, as some entities might have restrictions on methods of sharing.
- An early discussion of priorities, objectives, and steps of the investigation can help prepare teams across entities.
- Value expertise across the partners.
- Determine methods that can help support the healthcare facility in their response.
- When giving recommendations, consider including methods for implementation.

Public health and regulatory investigations should be coordinated. When both public health and regulatory agencies are involved in an investigation, it might be helpful to consider a coordinating public health agency and a coordinating regulatory agency, with management occurring among the two coordinating agencies. Because the investigations can occur in parallel, it is critical that information is shared rapidly and fully between public health and regulatory. Often in infection control breach investigations, regulatory agencies such as the state survey agency or professional licensing boards are brought into the investigation early and might be the initial investigating agency that notifies public health. Information sharing is usually guided by local and state regulations, and the coordinating public health agency should be familiar with these regulations. If needed, legal staff should be brought in early to ensure that information sharing regulations are followed. Typically, the regulatory agency is at the state level, and coordination with public health might necessitate a specific role for the state public health agency, even if a local public health agency is designated in the coordinating role. When sharing information with federal regulatory agencies, consider necessary authority and procedures for sharing.

Drug diversion investigations are a subset of major infection control breaches that involve notification of and coordination with law enforcement, including local and state law enforcement agencies, the Drug Enforcement Administration (DEA), and the FDA. Due to the coordination with multiple state and federal agencies, unless the local public health agency has broad expertise and capacity, these investigations are usually led by a state public health agency. Coordination at the CDC level might occur if the drug diversion has a national



component, such as a healthcare worker that has worked at healthcare facilities in multiple states. For more information on drug diversion investigations, see the CSTE Drug Diversion Toolkit: <https://www.cste.org/general/custom.asp?page=Drug-Diversion-Toolkit>.

Meanwhile in the Healthcare Facility...

Assemble and Brief the Outbreak Response Team

The facility might be concurrently performing the following:

- Assembling their own outbreak response team, depending on the healthcare setting, which might include a medical epidemiologist, an infection preventionist, environmental services department staff, clinical staff, laboratory staff, administrative leaders, communication staff, legal staff, and department leads for the affected facility areas;
- Communicating with their corporate staff, which in some cases include a medical epidemiologist and infection preventionist at the corporate level, and who might be an integral part of the outbreak investigation;
- Developing or refining internal communication protocols specific to this outbreak investigation; and
- Communicating directly with state and federal regulatory partners.



CORHA Keys to Success

Communication during an investigation

General communication strategies

- Develop agendas for meetings and calls with clear objectives and action items.
- Establish clear lines of communication internally and among points of contact for each partner involved.
- Train team members on basic communication skills. Communication during outbreaks is an opportunity to develop relationships; use this opportunity to be respectful and consider middle ground options. Establish an atmosphere of collaboration from the beginning.
- Establish a schedule of regular status updates across the involved partners based on the needs of the partners.

Within the agency

- Establish a system of regular briefings with the investigative team and others within the agency.
- Inform leadership early when an investigation begins and establish a plan for updating leadership.
- Involve experts, such as communication and emergency preparedness, as soon as it is determined their expertise might be needed.

With the involved healthcare facility(ies)

- Determine with the facility a clear plan for communication as early as possible, including frequency and methodology.
- Develop and clarify expectations of public health agency and facility roles and responsibilities early on.
- During each communication, establish a detailed plan for next steps including roles and responsibilities.
- Frequently update the facility with the progress of the investigation, including aggregate data summaries; facility staff often have epidemiology experience and can offer expertise.
- Consider in-person communication when tension is high. Public health agencies can improve relationships and help dispel tension through face-to-face meetings with involved healthcare facilities.

With other partners

- Determine a plan for communication during the investigation with all involved partners, including roles and frequency and method of updates. These plans might differ from communication among public health agencies and healthcare facilities.
- Communicate early with agencies, healthcare facilities, and partners if a publication or presentation might result from an investigation that might lend itself to communication with a wider audience upon conclusion. Establish leads for each potential product early in an investigation to avoid difficult conversations later in the investigation.



ESTABLISH A PLAN AND PREPARE FOR FIELDWORK

5.1.4 Establish a Plan and Prepare for Fieldwork

Based on the information gathered in the initial assessment, determine what information is still lacking and the steps to gather that information. The team should be prepared to formulate a plan quickly for next steps; assign tasks to team members. Gather information on the pathogen or infection and similar previous outbreaks; typically, this is done via a review of medical literature, review of previous outbreak reports, and consultation with experts.

When thinking through the steps of an investigation, always consider the utility and burden of each task. For example: will additional laboratory testing change the course of an investigation? Consider for each step if the results might impact the investigation; if a task will not impact the investigation or change public health recommendations, evaluate if that task is truly necessary.

A decision should be made whether a site visit to the healthcare facility should be performed and how rapidly the visit should occur, depending on the severity, scope, and potential for spread of the outbreak. Consider also the size of the public health team that will go on-site to the facility based on both the needs of public health and the facility. During infection control observations, smaller, more experienced teams might be prudent to minimize disruption to facility functions. Infection control visits can be paired with epidemiologic investigations, medical record reviews, and in-person public health/facility team meetings. Consider pairing trainees with more experienced team members. If multiple facilities are involved, consideration should be given to visiting all facilities involved; see Chapter 7 for more information on multi-facility outbreaks. Preparation might be needed ahead of the site visit, which should be considered early to avoid delays, including:

- **Access to medical records:** This often takes time if not already established, and steps should be taken as early as possible to begin the process to gain access to medical records. In some facilities this requires the help of information technology professionals. It can be helpful to involve infection preventionists, medical epidemiologists, or clinical staff partners to help communicate the urgency of an outbreak investigation. Requesting other types of records (such as infection or transmission-based precautions logs, facility maps, patient lists or staff lists) can be done in advance of a site visit.
- **Data collection tool development:** As discussed in Chapter 3, it can be helpful to develop data collection tools in advance of an outbreak, which can be modified for specific outbreak and pathogen types. Using standardized tools during an outbreak response ensures uniform data collection. Final versions of data collection tools specific to an outbreak should be created for the collection of any data, onsite or otherwise. This should be done in advance of a site visit when possible.
- **Determination of specific infection control observations:** Depending on the type of outbreak, the areas of the facility that should be visited for infection control observations will vary. Determine the specific observations to be performed ahead of a site visit, allowing for flexibility during the visit itself as new information is discovered.



For anticipated large responses, consider tracking staff time spent, as this information can be used to understand resource needs for future investigations.

Meanwhile in the Healthcare Facility...

Establish a Plan and Prepare for Fieldwork

As the public health outbreak response team prepares for possible fieldwork, the facility is preparing to have public health authorities in their facility. It is important that the public health team understand the burden of preparation involved for the facility. The facility might be doing the following:

- Preparing their team and staff for a possible visit from public health authorities;
- Preparing for a possible regulatory visit from state licensing agencies, although it is worth noting that these visits are usually unannounced; and
- Responding to public health requests for information, records, and access to records.

CONFIRM THE PRESENCE OF AN OUTBREAK

5.1.5 Confirm the Presence of an Outbreak

Just as the diagnosis needs to be verified, it is important to confirm the presence of an outbreak. See Chapter 4 for the definition of a suspected outbreak. Keep in mind:

- Some cases might be part of the outbreak, whereas others might be unrelated.
- Increases in cases indicating a suspected outbreak might be due to increased or changed local reporting procedures, changes in the case definition, increased interest reflecting local or national awareness, or improvements or other changes in diagnostic procedures.
- A single case might be treated as an outbreak for response purposes if the pathogen, pathogen/infection, or situation is unusual or it is a sentinel event.

Healthcare-related outbreaks might be a smaller part of a larger community-wide outbreak, which can be identified using public health surveillance data.⁴ In these situations, possible community-associated or other explanations for illness not associated with healthcare should also be investigated.

Pseudo-outbreaks (e.g., those caused by laboratory processing errors or contamination of clinical diagnostic equipment, such as bronchoscopes, without clinical illness) are important to investigate and control because they can lead to unnecessary antibiotic prescriptions, diagnostic procedures, and other potentially harmful interventions to patients. Consider a pseudo-outbreak when the pathogen identified does not match the patient's clinical picture, in particular when an investigation identifies breaches in practice that might indicate contaminated equipment (e.g., bronchoscopes, endoscopes) or substandard laboratory practices. Pseudo-outbreaks also represent opportunities to recognize and correct inadequate infection control processes (e.g., device reprocessing).⁴

Meanwhile in the Healthcare Facility...

Confirm the Presence of an Outbreak

The facility might be concurrently performing the following:

- Reviewing their own surveillance data;



- Communicating with colleagues in other facilities to determine if other facilities might be experiencing a similar situation; and
- Communicating with their laboratory to rule out the possibility of a pseudo-outbreak.

ESTABLISH CASE DEFINITION AND CLASSIFICATION CRITERIA

5.1.6 Establish Case Definition and Classification Criteria

A case definition is a set of clinical and/or laboratory criteria used to define inclusion as part of the outbreak. The case definition for outbreak investigation purposes can be different than surveillance case definitions and different than clinical criteria for diagnosis. A case definition includes:

- Clinical information about the disease (e.g., laboratory test results, symptoms, signs);
- Information about the location of possible exposure (e.g., intensive care unit, radiology suite, operating room, ward); and
- A defined time period during which exposure or onset occurred.⁴

In some situations, demographic characteristics of affected patients (e.g., age, race/ethnicity, sex, occupation) might also be a part of a case definition.

Initially, consider using broad criteria for the case definition, making it more sensitive. As additional evidence accumulates, the case definition can be refined and made more specific. The case definition should be based on the etiologic agent, if known, and can include clinically infected and colonized patients. It is important to remember that the “case” is the set of criteria, not a patient; in fact, in some situations a patient might represent more than one case. When counting cases, it is important to distinguish the number of cases and the number of patients, as these might be different, and both sets of information can be useful to understand the outbreak. See Box 5.4 for example case definitions.

A stratified case definition (e.g., confirmed vs. probable vs. possible [i.e., suspect], or confirmed vs. probable) can be applied to account for the uncertainty of certain diagnoses.

- Confirmed: Usually must have laboratory verification.
- Probable: Usually has typical clinical features and an epidemiologic link to confirmed cases but lacks laboratory confirmation.
- Possible (suspect): Usually has fewer of the typical clinical features or weaker epidemiologic links to confirmed cases.⁴

Cases might move from one classification to another as additional information becomes available. For example, a case might be temporarily classified as *probable* or *possible* while laboratory results are pending.

Box 5.4: Example Case Definitions

- A blood culture positive for *Pseudomonas aeruginosa* with <10 single nucleotide polymorphism (SNP) differences based on whole genome sequencing with culture date since January 1, 2019, in a patient that had at least one overnight stay in the ICU.



- A respiratory infection (symptoms of cough, sore throat, shortness of breath or increased need for oxygen) in a patient residing in Nursing Home X between February 1 and March 31, 2019.
- A positive PCR test for *Klebsiella pneumoniae* carbapenemase in any organism from any clinical site in a patient admitted to Hospital Y in any timeframe.

Meanwhile in the Healthcare Facility...

Establish Case Definition and Classification Criteria

Although in some situations a healthcare facility might be working to develop a case definition, in most circumstances this task is performed by public health. When a healthcare facility has the capacity to develop a case definition, the public health agency should work with the healthcare facility to develop a case definition that can be used by all entities.

IDENTIFY AND COUNT CASES

5.1.7 Identify and Count Cases

Identification of all cases is important to understand the scope of the outbreak and formulate accurate hypotheses for the cause of the outbreak. Cases can be identified both retrospectively and prospectively.

Retrospective case identification might involve the following methods:

- Reviewing laboratory records (e.g., microbiology logs to identify a specific pathogen, histopathology logs to identify invasive fungal infections);
- Reviewing facility surveillance records (e.g., infection prevention logs, National Healthcare Safety Network (NHSN) surveillance data);
- Reviewing other facility records, such as scheduling records, billing records, occupational health records, pharmacy records, radiology reports, admission/discharge records, or logs specific to the infection type (e.g., operating room logs to identify surgical site infections);
- Reviewing public health surveillance data (e.g., reportable conditions, public health reports);
- Interviewing facility staff (e.g., infection preventionists, medical epidemiologists, clinicians, laboratorians); or
- Reaching out to clinicians, other facilities, or public health agencies (a “call for cases”); this applies to retrospective and prospective case identification.

Prospective case identification involves identifying new cases as the outbreak unfolds.

Methods to consider for prospective case identification include:

- A call for cases, as described above;
- Notification of clinicians to raise awareness, ensure appropriate testing, and encourage reporting to the infection prevention or outbreak team when suspected cases are identified;
- Notification of laboratory staff to raise awareness, ensure appropriate testing, encourage reporting of cases, and ensure storage of clinical specimens or isolates appropriately to ensure further testing can be performed;



- Testing of patients at risk who might be colonized with specific pathogens (e.g., carbapenemase-producing carbapenem-resistant Enterobacteriaceae, group A *Streptococcus*) can identify additional cases.

Of note, cases might occur in healthcare workers, visitors, and community residents, as well as patients within a healthcare facility; consideration should be given to collecting information on these potentially exposed individuals depending on the pathogen or syndrome and likely exposures. For example, testing healthcare workers might also identify additional cases, but should only be done when consistent with the epidemiology and biologic plausibility.

Cases should be counted systematically, uniformly applying the developed case definition and stratification and classification. It is helpful to track all reported or detected cases, including those that might not meet the case definition. In that way, if the case definition is refined, and additional cases meet the case definition, this information will already be available. Methodology for tracking cases can be found in the next section.

Meanwhile in the Healthcare Facility...

Identify and Count Cases

The healthcare facility and public health should be collaborating to identify and count cases. At this step, the healthcare facility should be doing the following:

- Determining and implementing methodology to retrospectively and prospectively identify cases, including consideration for screening via testing when applicable;
- Notifying clinicians and laboratory staff within their facility to be alert for cases meeting the case definition;
- Consider if other facilities within their network might need to be notified;
- Consider a call for cases among networks depending on the likely hypotheses; and
- Track cases within the facility and be prepared to share information with public health.

COLLECT, ORGANIZE, AND ANALYZE DATA

5.1.8 Collect, Organize, and Analyze Data

5.1.8.1 Data Collection

Data collection refers to all the information gathered during the investigation, including patient-specific information gathered from medical records, information gathered during the review of logs and other facility records, information gathered during the case identification process, infection control assessments, laboratory information, and any other pieces of information relevant to the investigation. Data sources listed in the previous section to identify cases can also be used to collect data during the investigation; types of records are also listed in Box 5.5. Information can then be entered into a line-list, or a similar database, to allow for easy review.



Information should be gathered systematically, maintained in a consistent format with appropriate security safeguards, and compiled in a way that is easy to store, review, and interpret. The use of standardized data collection forms ensures that pertinent information is collected from all patients, medical records, and other sources for subsequent systematic analysis. In addition, the use of standardized data elements (e.g., same variable names and attributes) will enhance data sharing and comparisons of exposures between cases and controls and/or within different healthcare facilities/jurisdictions, if indicated. Although a paper tool will suffice when a few cases are involved, the development and use of a readily accessible electronic database can be invaluable to ensure all critical team members across entities have timely and salient information during large, complex, or multi-jurisdictional investigations.

Box 5.5 Healthcare Facility Records to Consider Reviewing during an Outbreak Investigation⁴

- Individual patient medical records
- Infection control dashboard
- Records that specify dates of precautions (e.g., contact, droplet)
- Central service or supply records
- Occupational health records
- Hospital billing records
- Operative notes
- Infection control assessment
- Pathology reports
- Interviews with physicians
- Pharmacy reports
- Log books
- Purchasing records
- Medical records
- Radiology reports
- Microbiology data
- Surveillance records

A standardized data collection tool will ensure that consistent, complete information is collected on all outbreak cases. This can be developed by the public health agency, or adapted from a tool available from CDC at www.cdc.gov/hai/pdfs/outbreaks/Response_Toolkit_Abstraction_Form-508.pdf. If a case-control study is begun to test various hypotheses, the same tool can also be used as a basis to collect information on control patients. The data collection tool is usually comprised of the following components:

- Patient identifying information, such as name, medical record number, admission date, admission source (admitted from emergency department, home, another facility [name of facility], etc.), discharge date and discharge status (discharged to home, transferred to another facility, deceased, etc.);
- Demographic information, including age and gender;
- Location information (e.g., room, unit, ward, floor, building; facility type or healthcare setting; single vs. multi-occupancy room);



- Clinical information, focused on simple, objective criteria to the extent possible: disease signs and symptoms allow investigators to verify that the case definition has been met; date of illness onset or specimen collection is needed to chart the time course of the outbreak and, when applicable, the incubation period; supplementary clinical information, such as illness duration and re-hospitalizations or patient death, help characterize the spectrum of illness; and
- Risk factor information tailored to the specific disease and situation under investigation.

A standardized data collection form should also be used in the event that patients need to be interviewed.

All private information that can be identifying in some way (both direct and indirect identifiers, including names, addresses, dates of birth, dates of admission/discharge/death, and anything that can identify an individual), must be protected from public disclosure. All members of the outbreak response team—epidemiologists, laboratorians, environmental health specialists, and healthcare personnel—must follow data security practices and comply with relevant state and federal laws, including the Health Insurance Portability and Accountability Act (HIPAA). Public health agencies should be familiar with their local laws as well as HIPAA and federal laws. This is discussed further in Chapter 8.

5.1.8.2 Organize Data and Perform Descriptive Epidemiology

Data collected using standardized methods should be organized systematically, typically initially using a line list, which typically involves using a spreadsheet so that data can be organized and sorted easily during initial review and analysis. The line list helps guide the outbreak investigation and permits rapid examination of exposures. For each case, collect and array the following types of information encompassed by the case definition:

- Location information: Location within the facility (e.g., room number, bed number, and adjacent rooms);
- Demographic information: Age, sex, race/ethnicity, and occupation, plus other relevant characteristics of the affected population or others at risk;
- Clinical information: Symptoms, signs, and laboratory tests (e.g., culture, serology, or polymerase chain reaction results); and
- Risk factor information: as per the specific disease in question.⁴

Once information is collected and organized, performing descriptive epidemiologic analysis is the first stage, which includes describing the data using tables, graphs, diagrams, maps, or charts to answer basic questions of what, when, where, among whom, and how much. Descriptive epidemiology provides a critical assessment of the status of the outbreak and often serves as the basis for determining further actions, such as implementing specific prevention and control measures, initiating environmental assessments, and conducting analytic studies to test specific hypotheses. In many investigations, descriptive epidemiology is enough to determine the likely outbreak cause with sufficient confidence.

The analytic approach used in any situation depends on multiple factors, including the circumstances specific to the outbreak (e.g., the pathogen, number and distribution of cases), staff expertise, structure of the investigating agency, and agency resources. Investigators are encouraged to use a combination of analytical approaches, as appropriate to the specific outbreak.



The first step in descriptive epidemiologic analysis is to describe the cases or patients,

Figure 5.1: Sample Timeline

	1/1	1/2	1/3	1/4	1/5	1/6	1/7	1/8
Patient 1		**		*				
Patient 2	**	*						
Patient 3							**	*

Legend: Blue boxes = time in facility; * = date of positive culture; ** = date of procedure

typically in a simple table that includes the numerator, denominator, and percent (or mean, median and range) for each characteristic (e.g., age, sex, risk factors). Additional tools to organize data include maps and timelines. Facility maps are often extremely helpful and can be used to create spatial pictures of patient locations and movement. Creating a timeline for each patient that includes exposures of relevance, testing dates, symptom onset, and patient locations, can also be very helpful to identify common factors and overlaps. See Figure 5.1 for a sample timeline. All components of descriptive epidemiology, particularly when combined with infection control assessments, can be used to develop refine and evaluate hypotheses regarding the cause of the outbreak. As described in Chapter 3, tools can be developed during the preparation phase to have on-hand ahead of an outbreak investigation.

In many outbreak investigations, it is helpful to prepare an epidemic curve (i.e., a histogram). The epidemic curve is used to depict the magnitude of the outbreak over time, provide clues about the pattern of spread, identify the current phase of the outbreak, evaluate effectiveness of control measures, identify outliers that might provide clues, distinguish epidemic from endemic disease, and deduce a probable time of exposure when an incubation period is known. Update the epidemic curve regularly to depict the status of the outbreak. Notable events, such as implementation of control measures, and specific characteristics of cases, such as genetic matches, can also be indicated on the epidemic curve.

5.1.8.3 Refining the Hypothesis

The development of the initial hypothesis should occur early in the investigation, using findings from the descriptive epidemiological analysis to refine hypotheses further. After an explanatory outbreak hypothesis has been developed, the next step is to evaluate its plausibility, typically using a combination of epidemiology, laboratory, and environmental evidence. From the epidemiologic point-of-view, hypotheses are evaluated by either (1) comparing the hypotheses with established facts or (2) using analytic epidemiology to quantify relationships and assess the role of chance.

The first method, simple comparisons, is likely to be sufficient when the leading hypothesis is supported by accumulated evidence in an obvious manner and to a degree that formal hypothesis testing is unnecessary. Additionally, control measures are often clear and can be implemented without the need for further epidemiologic studies and analysis. Many outbreaks do not have sufficient numbers of cases, or the likely cause of the outbreak is multi-factorial; in these situations, more complex analytic epidemiology might not help advance the investigation. However, when there is a clear hypothesis to be tested in the presence of sufficient number of cases and particular exposure(s) of interest, analytic epidemiology can be useful. Sometimes a case that has unique characteristics or risk factors can be helpful in developing or refining a hypothesis. Care should be taken in refining the case definition or



hypotheses based on outliers; in some situations outliers might provide useful clues to the cause of an outbreak, but they also can be red herrings that are not part of the outbreak at all.

5.1.8.4 Analytic Epidemiology

Analytic epidemiology can be used for hypothesis testing when conducting a healthcare outbreak investigation. The two most common types of analytic epidemiology studies used in field investigations are *retrospective cohort studies* and *case-control studies*. Additional information about each comprises Appendix A.

In healthcare investigations, analytic studies typically take the form of a case-control study. The frequency of exposure to a risk factor among a group of case-patients (e.g., persons with the condition of interest) is compared with the frequency of exposure to that risk factor among a group of controls (e.g., persons without the condition of interest). Controls must be selected carefully to limit bias. Two or more controls for each case-patient might be needed to provide sufficient statistical power.

However, analytic studies are labor-intensive and not always necessary to identify the likely source of an outbreak and to institute control measures in healthcare investigations. For example, a combination of laboratory evidence and observations of serious lapses in infection control practices that are known to be associated with transmission are frequently sufficient to recommend and implement control measures. The following considerations can influence the decision to conduct an analytic study:

- Will an analytic study add to what is already known about the cause of the outbreak or contribute to the control recommendations?
- Is the necessary technical and statistical support available?
- Is the number of cases large enough to power the analysis and support statistical inferences?
- Can enough controls be selected to minimize bias?
- Is information available for testing possible risk factors?⁷

A prerequisite to the conduct of an analytic study is having a sufficient sample of cases to power the statistical analyses. The key feature of analytic epidemiology is a comparison group, which enables epidemiologists to quantify the relationships between exposures and disease; contrasting the observed patterns (e.g., incidence rates and odds ratios) among case-patients or exposed persons with those among non-cases or unexposed persons. In this manner, investigators are able to test hypothesis with regard to the likelihood of those relationships being due to chance.

Meanwhile in the Healthcare Facility... ***Collect, Organize, and Analyze Data***

Different healthcare facilities and facility types might have different levels of capacity to collect, organize, and analyze data. Some facilities might perform the collection and organization of data, others might be able to perform analysis, such as timelines and epi curves. Some healthcare facilities rely on public health for all data collection and analysis. Public health should be sure to frequently communicate the results of analysis with the healthcare facility. The healthcare facility might be doing the following during this step:

- Collecting data on cases, or assisting public health to do so;



- Tracking information on cases within healthcare facility systems;
- Performing data analysis, or assisting public health to do so; and
- Responding to public health requests for additional data, facility maps, or other additional information.

PERFORM AN INFECTION CONTROL AND ASSESSMENT

5.1.9 Perform an Infection Control Assessment

Infection control assessments offer the opportunity for public health to understand risk factors that might have contributed to or resulted in an outbreak. In some cases, infection control assessments might be brief and conducted over the phone; however, in most cases, if an infection control assessment is needed, the best practice is for the public health outbreak response team to go on-site to the facility. When an on-site infection control assessment is not feasible, consideration can be given to performing a virtual assessment using video meeting applications; limitations to this approach include the subjective nature of what is chosen to be shown on video due to the chosen camera angle, and if facility preparations are done prior to the virtual visit, potential inaccuracies of true infection control practices might result.

Direct observation of infection control practices and other conditions on-site at the facility often results in identification of infection control breaches or other exposures that contributed to patient harm. Considerations for performing an on-site infection control assessment include:

- On-site visits provide the opportunity to interact with and interview key staff, tour relevant areas of the facility, and gain increased understanding of the conditions, layout, culture and common practices within an affected facility.
- On-site observations can be combined with on-site medical record reviews.
- If a regulatory agency is also performing on-site visits, these visits might be able to be performed jointly between the two agencies, allowing for additional information to both agencies and potential for decreased burden on the facility.
- Control measures can be recommended during an on-site visit.

Ideally the outbreak response team will have expertise in infection prevention to help conduct the facility walk-through and infection control assessments. An infection control assessment should be tailored to the type of facility, the population affected, and common case-patient exposures or other potential risk factors. However, it can be helpful in some instances to broaden the assessment to help with the identification of additional risk factors, unanticipated exposure pathways, and suboptimal practices. Consider the following areas of focus when preparing for and conducting on-site investigations:

- Prepare for the visit by reviewing scientific literature related to the key concerns involved with the outbreak.
- Assemble checklists and other audit tools in advance of the visit; maintain familiarity with locally available examples (e.g., those used in previous investigations) as well as the general and setting-specific tools available on the CDC website at: <https://www.cdc.gov/hai/prevent/infection-control-assessment-tools.html>.



- Assess whether actual practices deviate from recommended infection control practices and the facility's policies. Such discrepancies are best identified through a combination of direct observations and review of healthcare provider self-reported practices.
- Examine whether practices differ among healthcare providers.
- Observe key activities (e.g., medication preparation, care of vascular access, hand hygiene, adherence to isolation precautions, device and equipment reprocessing, environmental services, and respiratory therapy) related to suspicions about likely transmission pathways that might be involved in the outbreak.
- Consider taking photos when possible. Be aware of facility and public health internal policies; photos should not contain anything that can identify a patient. Photos of medical products during medical product investigations can be extremely helpful; think about using photos to document lot numbers and specific product information.
- Review key concerns with facility staff to help generate hypotheses about the source and mode(s) of transmission. Review challenges with maintaining good infection control practices, their thoughts on the root cause of the outbreak, and information that might not be documented in medical records.
- Review protocols and procedures to ensure they are up-to-date and followed consistently. Assess if actual practice matches written and verbal protocols and what is expected.⁴

In addition to direct observations, it is also important to talk with multiple staff about their routine infection control practices in detail, as sometimes it is not possible to observe each staff member; this additional step can identify gaps that might not be detected through observation alone. A good technique to approach observations and staff interviews is to emphasize that you would like to learn how they perform the task of interest; they have the expertise of how their facility functions.

Meanwhile in the Healthcare Facility...

Perform an Infection Control Assessment

Facilities with an infection preventionist or an infection prevention team will likely have performed an infection control assessment (or several) before the public health agency does. It is helpful for the public health agency team and the facility infection prevention team to work together and compare findings and beneficial to have duplicate infection control assessments between the facility and public health agency. Facilities that do not have infection control teams or an infection preventionist can benefit from an on-site public health assessment by receiving education during the visit. Facilities might be preparing ahead of the public health team arriving, and it can be beneficial to remind the facility that to help them, public health needs to observe actual, and not optimal, infection control practices.

CONSIDER AN ENVIRONMENTAL ASSESSMENT

5.1.10 Consider an Environmental Assessment

An environmental assessment is a systematic evaluation of environmental factors that might have contributed to an outbreak. The need for an environmental assessment is informed by the epidemiology and other findings from the investigation. Often, some form of environmental assessment is conducted as part of the on-site work and infection control



assessment, such as an assessment of environmental cleaning practices including observations and interviews of environmental services staff. The overall goal of the environmental assessment is to identify possible environmental risk factors that contributed to the outbreak, such as:

- Possible points of contamination and contact between the disease agent and vulnerable persons; or
- Environmental conditions conducive to microbial survival, growth, and transmission.

Environmental cultures are infrequently warranted and should only be obtained once a potential microbial source or reservoir has been identified and epidemiologically linked to outbreak cases. For example, air sampling in an operating room affected by construction might be pursued during the investigation of an outbreak of surgical site infections with *Aspergillus*. Since clinical laboratories may not be licensed or able to perform environmental testing, samples might need to be sent to a public health or reference laboratory. Additional information on the laboratory component of an environmental assessment can be found in Chapter 6. Methods used in the collection of environmental samples can influence the accuracy and interpretation of results, and therefore consultation with a laboratory experienced in environmental sampling is advised. Check with the laboratory regarding validated collection methods and supplies needed to collect environmental samples.

Meanwhile in the Healthcare Facility...
Consider an Environmental Assessment

Facilities with an infection preventionist or an infection prevention team will likely also have the capability to perform an environmental assessment. When environmental sampling is performed, the facility will be working with their laboratory to ensure sampling procedures are correct and ensure the laboratory has the capability to perform the testing. Often public health laboratories are needed for testing of environmental samples, and coordination between the clinical laboratory and public health laboratory is needed in this case.

RECOMMEND CONTROL MEASURES

5.1.11 Recommend Control Measures

Effective control measures are critical for stopping the outbreak and preventing recurrence. If appropriate disease control measures are known and available, they should be initiated as soon as possible, even before a full investigation is launched. Control measures are often recommended in various parts of the investigation, including during the initial assessment, when performing on-site assessments, and following the on-site assessment. In general, such measures are directed against one or more segments in the chain of transmission that are susceptible to intervention—agent, source, mode of transmission, portal of entry, host. See Chapter 2 for example scenarios. It is helpful to provide the facility with recommendations in writing, either as part of an infection control assessment form, or as a letter of recommendation. In some cases, flexibility in implementation can be helpful to the facility when patient safety is not compromised. Follow up with the facility to ensure that recommendations have been followed and prevention measures are in place; this might be



done in-person or via phone or email communication depending on the situation. Keep in mind that regulatory partners (e.g., state professional boards or the state healthcare facility licensing agency) might need to be informed of the investigation’s findings and recommendations, according to local regulations, and may exert oversight authority as part of the corrective actions. Practices can be difficult to change, and new practices might need to be used for a substantial time before they become routine. For independent outpatient offices or facilities, monitoring the implementation of preventive controls typically warrants heightened levels of attention.

In situations where there is potential imminent harm to patients, the on-site team should consider the following potential steps:

- Notifying leadership and legal staff within your agency;
- Notifying appropriate regulatory agency; and
- Taking immediate steps to ensure poor practices are immediately halted.

Teams should be aware of laws that allow for notifying appropriate agencies, and individual obligations for doing so; consult with legal staff when situations might be unclear.

Additional disease control measures beyond recommendations to the facility might also need to be implemented. In some situations, recommendations to the public, specific patient groups, or healthcare providers and healthcare facilities might be needed, such as product recalls, infection control recommendations to a broader group of facilities, or notification of the wider healthcare community if there is an event of significance or a patient population at risk. This is discussed in greater detail in Chapter 9.

Meanwhile in the Healthcare Facility...
Recommend Control Measures

Healthcare facilities will be working to implement recommended control measures, once received. Some measures might be in the process of implementation following the internal assessments conducted by the healthcare facility. The facility might find it beneficial to discuss with public health methods to implement recommendations.

INTERPRET RESULTS

5.1.12 Interpret Results

The outbreak response team is responsible for ensuring all available information is used to construct a coherent narrative of what happened and why. Investigators should consider their data critically and question the strength of causal associations while considering timing, dose-response, plausibility, and consistency of findings. When data elements support the primary hypothesis, strong conclusions can be drawn. The most successful investigations are rigorous and evidence-based, but also adaptable, with investigators able to innovate as circumstances demand. Haphazard investigations are unlikely to yield meaningful results. However, even well-executed investigations can be inconclusive. HAI/AR investigations are often marked by small sample sizes as well as the absence of complete records and the presence of confounders and common exposures.

Meanwhile in the Healthcare Facility...
Interpret Results



Healthcare facilities might be interpreting their own results, or reviewing results shared by the public health agency. Some facilities might have questions or other interpretations, or suggestions for other analyses. Review of the results among the public health agency, healthcare facility, and other involved entities can result in discussion and possible additional next steps. It is important to communicate findings and be open to discussion.

MONITOR THE OUTBREAK UNTIL COMPLETION

5.1.13 Monitor the Outbreak until Completion

5.1.13.1 Monitor the Outbreak

Assure that surveillance of ongoing cases continues, with information on any potential new outbreak-associated cases forwarded to epidemiologists in real time. Similarly, as investigators acquire information about exposures in other facilities, transfers to or from other facilities, or across state lines, they should promptly update the appropriate health authorities and consider whether any information indicates the outbreak might be multi-jurisdictional.

5.1.13.2 Re-Evaluate Hypotheses and Case Definitions

Ongoing review of investigation findings, including current case-patient lists, new laboratory data, updated epidemic curves, recent environmental assessment findings, can raise novel questions or help to answer existing questions related to an outbreak. Investigators should re-evaluate any hypotheses as well as case definitions and classifications as new information is gathered. This information, in turn, may lead investigators to modify existing prevention and control strategies or to adopt new strategies.

5.1.13.3 Ending the Investigation

When the likely cause of the outbreak has been determined and appropriate control measures have been put in place, the investigation can end and a monitoring period can begin. The duration of the monitoring period should be dependent on the specifics of the pathogen or infection type as well as the likelihood that prevention measures will be successful. Determining timeframes ahead of time can be helpful. Most outbreaks are considered over when two or more incubation periods of the etiologic agent have passed with no new cases. This arbitrary rule might not apply to clusters with low attack rates, and cases from some sources might appear intermittently for years.

Maintaining communication with the healthcare facility involved to make sure additional cases are not detected is critical for a period of time after the investigation is over. The duration of the continued monitoring will vary depending on the type of outbreak. Often this can be accomplished through monitoring of surveillance data reported to public health, or through the inclusion of a recommendation to the facility to report any new cases to public health for a defined period of time. Should additional cases be detected, additional investigation should be considered, beginning with an evaluation of the new cases detected. This may include assessing whether their exposure(s) is consistent with the previous patterns and conclusions and whether control measures are being implemented as recommended. Note that for outbreaks involving a common source, such as those involving a distributed medical



product and a long incubation or non-specific symptoms, it may not be feasible to continue counting cases. In these situations, emphasis should be placed on recall efforts (or the implementation of other recommended control measures) to stop new exposures and directing newly diagnosed case-patients to appropriate medical management. Ultimately, the decision to end an investigation depends on the gravity and scope of the outbreak and on the likelihood that it reflects an ongoing public health threat.

For larger or more controversial investigations, conducting a post-outbreak meeting among investigators to assess lessons learned and to compare notes on ultimate findings can be helpful. This is particularly important for multiagency investigations and is also discussed in Chapter 7. It is important for public health agencies to be open to feedback during and after the investigation. In smaller outbreak investigation or when agency resources do not allow for a post-outbreak meeting, public health agencies should still consider obtaining constructive feedback from partners, as well as self-evaluation. For information on performance indicators, see Chapter 10. A formal after-action meeting should:

- Identify potential sources and contributing factors to the outbreak and control measures that might be needed to prevent additional outbreaks at the facility or other facilities in general;
- Assess the effectiveness of outbreak control measures that were implemented, and barriers and difficulties in implementing them, as well as opportunities for improvements in future similar outbreaks;
- Assess whether further scientific studies should be conducted;
- Clarify resource needs, structural changes, or training needs to optimize future outbreak response;
- Identify barriers or factors that compromised the investigation and identify areas for improvement;
- Identify necessary changes to current investigation and control guidelines and development of new guidelines or protocols; and
- Discuss any legal issues that might have arisen and the need for new laws to strengthen response (see Chapter 8).

Meanwhile in the Healthcare Facility...

Monitor the Outbreak until Completion

During this step, healthcare facilities might be performing the following:

- Putting into place additional surveillance of the pathogen or infection;
- Continuing to monitor for additional cases, which might involve communication with the laboratory and providers;
- Continuing to communicate with public health when additional cases are detected;
- Performing internal reviews of their investigation of the outbreak; and
- Participating in after-action reviews involving public health and other involved agencies.



OTHER FOLLOW-UP ACTIVITIES

5.1.14 Other Follow-Up Activities

5.1.14.1 Summarize Investigation Findings, Conclusions, and Recommendations

Writing a final report of the investigation can be helpful to document your methods and findings, as well as any lessons learned, to inform future investigations and prevention needs. In some cases, this report can be brief or follow a standard format or template, in the case of a common outbreak type (e.g., influenza-like illness in a long-term care setting). Written reports should include the following components:

- **Background:** Including information about the outbreak setting, timing, and manner of detection;
- **Methods:** Including agencies involved in the investigation, case definition, details of investigative methods (e.g., record reviews, patient interviews, environmental assessments), types of patient specimens and environmental samples collected and tested, and a high-level summary of laboratory test methods;
- **Results:** Including number of persons exposed, sickened, hospitalized and deceased; key clinical findings; key laboratory findings including the number of patient specimens and environmental samples collected; key infection control findings; key environmental findings; any analyses performed; and any figures, graphs, and tables that supported the investigation;
- **Recommendations:** Including those put in place for abatement of the outbreak under investigation, any enhanced surveillance, and prevention of similar outbreaks; and
- **Conclusions:** Including etiologic agent, transmission route(s), contributing factors, successes and challenges, lessons learned, justifications for conclusions, and study limitations.

The complexity of the report will depend on the outbreak, and for smaller outbreaks a brief report might suffice. The final report is an excellent tool to provide education for newer staff, as well as a resource for future, similar outbreaks. Given that outbreak reports can be subject to the Freedom of Information Act or local information release laws, they should be written with public disclosure in mind. The reports should not identify individuals or other legally non-public information unless absolutely necessary; care should be taken to follow local laws. It is simpler to refrain from including this information rather than redacting it later. For unusual situations, investigations that are large, complex, or highly consequential, or investigations that can contribute to the general scientific knowledge, consideration should be given to publishing in the medical literature, either the Morbidity and Mortality Weekly Report or another journal that reaches the intended audience, public health or otherwise.

5.1.14.2 Distribute Report

Copies of the report should be shared with members of the investigative team, laboratories, healthcare facilities, and other partners involved in the investigation. Consideration should be given to distribution of the report more widely when needed in order to help inform and educate the public health and healthcare community to help prevent future outbreaks. The report is a public record and should be made available to members of the public who request it.



5

5.3.12

5.3.13

5.1.14.3 Policy Action

Information gained during an outbreak might identify the need for new public health or regulatory policy at the local, state, or federal level. Establishment of different oversight (e.g., inspection) practices, infection control standards, manufacturing practices, source controls, or surveillance and reporting procedures might be necessary. Reports of past outbreaks should be analyzed to determine whether multiple outbreaks support the need for new policy. Other public health and regulatory agencies also should be consulted to determine whether concurrence exists on the need for new policy. If so, the issue should be presented to the appropriate jurisdictional authority by using the appropriate policy development processes.

Meanwhile in the Healthcare Facility...

Other Follow-Up Activities

The healthcare facility might be in the process of writing their own internal report, which might take the form of a report, root cause analysis, after-action document, or other. Public health agencies should share their report with the facility. If a published report in the medical literature is being considered, the healthcare facility and public health should work collaboratively.

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Appendix A: Cohort and Case-Control Studies

Retrospective cohort studies

A retrospective cohort study—in which the investigator calculates incidence rates for the exposed and the unexposed—is the study of choice for an outbreak in a small, well-defined population. Generally, an exposure is considered a strong suspect if it meets the following criteria:

1. The incidence rate is high among those exposed.
2. The incidence rate is low among those not exposed, so the difference, or ratio, between incidence for the exposed and unexposed is high.
3. Most case-patients were exposed, so the exposure could “explain” or account for most, if not all, cases.

Relative risk

Commonly, the investigator calculates the relative risk (a.k.a. risk ratio) by dividing the incidence of disease in the exposed group by the incidence of disease in the unexposed group. When the two incidence rates are the same, the relative risk equals 1.0, and the exposure is not associated with disease. The larger the relative risk, the stronger the association between exposure and disease.

Statistical significance testing

When an exposure is found to have a relative risk different from 1.0, many investigators perform a chi-square or other test of statistical significance to determine the probability of finding an association as large or larger based on chance alone. This probability is called the *p*-value, and the smaller the *p*-value, the less likely it is that the observed association is due to chance. (A purely chance association is considered the “null hypothesis,” which must be disproved to demonstrate causality.) Generally, an acceptable *p*-value—commonly 0.05 or a 5% probability of a chance association—is specified in advance.

The chi-square test works well if the number of study participants is greater than about 30. For smaller studies, the Fisher Exact Test may be more appropriate. Although this statistic is tedious to calculate manually, it—like all of the statistical tests described here—can be calculated electronically via Epi Info or another computer program.

Statistical association between exposure and illness may reflect a causal link, but also may reflect confounding (interference by a third variable that distorts the association between cases and exposures), bias (any action that systematically distorts findings), or chance (a random, unpredictable occurrence that is not due to human intervention). Conversely, failure to achieve a *p*-value <0.05 due to a small number of cases, faulty sampling method, inappropriate selection of controls, or other factors cannot rule out an association with a potential source or exposure.

Confidence intervals

An alternative to the *p*-value is a confidence interval, a statistic that combines an interval estimate (i.e., the range of values estimated to contain the true value), with a probability statement that specifies the uncertainty associated with the interval estimate (i.e., the



uncertainty associated with the investigator's sampling methods). The typical 95% confidence interval for a calculated relative risk, for example, indicates that use of the same sampling method to select different case-patients and controls will yield a confidence interval that contains the true relative risk 95% of the time. Less variable data and larger sample sizes will tend to yield narrower confidence intervals and thus more precise estimates of the true relative risk.

Because a confidence interval provides more information than a p -value, many medical and epidemiologic journals prefer confidence intervals to p -value. However, in the outbreak setting, the difference may be irrelevant. If the objective of an outbreak investigation is to identify the source of pathogenic exposure, a relative risk and p -value may serve as well as a relative risk and confidence interval.

Case-control studies

In a case-control study, the investigator compares the exposure status of case-patients with a comparable group of persons without the disease under study ("controls").

Choosing controls

When designing a case-control study, one of the most important tasks is selecting the individuals who will comprise the control group. As mentioned above, the controls must *not* have the disease under study, but should otherwise represent the population in which the cases occurred.

Common control groups consist of:

- Patients admitted to the same hospital unit within the same timeframe.
- Patients undergoing the same medical procedure.
- Patients with the same underlying diagnosis that prompted hospital admittance (but without, of course, the HAI under study).

If the control group differs systematically from the case group, a true association between exposure and disease may be missed or a spurious association may be observed between a non-causal exposure and disease.

When designing a case-control study, other considerations include the number of controls to select per case and potential confounding due to factors associated with both the exposure and disease outcome that cause a spurious association. Sample size formulas are available to help determine the number of controls per case. Confounding can be controlled by matching cases and controls on the confounding factor during the selection process or during data analysis.

Often, the number of case-patients that can be enrolled in a study is limited by the size of the outbreak. For example, in a hospital, four or five cases may constitute an outbreak. Fortunately, potential controls are usually plentiful. In an outbreak of 50 or more cases, one control per case will usually suffice. In smaller outbreaks, two, three, or four controls per case may be feasible. However, including more than four controls per case is rarely worth the effort in terms of increased statistical power.



Odds ratios

In most case-control studies, the population is not well defined, and the total number of people exposed (or unexposed) to a suspected vehicle or source is not known. Without a proper denominator, incidence rates cannot be calculated.

Thus, for a case-control study, the odds ratio is the preeminent measure of association. Fortunately, for rare events, such as HAIs and most other outbreak-associated diseases, the odds ratio from a case-control study approximates the relative risk that would have been found if a cohort study had been feasible.

The odds ratio—the ratio of the odds of exposure among cases to that among controls—is calculated as $a/c \div b/d$ where:

a = the number of individuals who are both exposed and have the disease.

b = the number who are exposed and do not have the disease.

c = the number who are unexposed and have the disease

d = the number who are both unexposed and without the disease.

To test the statistical significance of the odds ratio, a chi-square test can be computed. However, it is important to remember that statistical significance is not proof of causality, as the observed result may be due to chance, bias or confounding.



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