

CHAPTER 5

Investigation & Control

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Preface

Chapter 5 offers a review of the key elements and steps involved in healthcare outbreak response. The chapter is arranged according to the steps typically followed in an outbreak investigation, recognizing that such steps may not occur in linear order and will depend on the precise nature and needs of the response. Chapter 5 also presents a review of the goals of a healthcare outbreak investigation and includes collections of resources to support and improve the healthcare-associated infection and antimicrobial resistance (HAI/AR) outbreak response.

5.0 Introduction

Collaboration between public health and healthcare is essential for an effective outbreak response. While healthcare settings are responsible for disease prevention and infection control practices on their premises, public health officials are generally responsible for ensuring the health and safety of the entire 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, epidemiologic analyses, laboratory testing, and infection control and environmental assessments, as well as provide recommendations to prevent disease transmission.^{1,2} 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. For example, outbreaks of invasive *Mycobacterium chimaera* infections among cardiothoracic surgical patients exposed to heater-cooler devices identified a newly recognized HAI risk and resulted in new recommendations to prevent these life-threatening infections from being transmitted during surgical procedures.^{3,4}

See Box 5.1 for HAI/AR outbreak investigation resources. The overall goals of an outbreak investigation are listed in Box 5.2. Objectives for healthcare outbreak response and associated activities to be performed by epidemiology, infection prevention, and public health laboratory staff are listed in Table 5.1. Investigation-specific objectives can be developed based on the goals and objectives listed in Box 5.2 and Table 5.1.

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Box 5.1 | Selected HAI/AR Outbreak Investigation Resources

CDC Healthcare-Associated Infections (HAIs). Outbreak Toolkit: <https://www.cdc.gov/healthcare-associated-infections/php/toolkit/outbreak-investigations-toolkit.html>

CDC Healthcare-Associated Infections (HAIs). About outbreak investigations in healthcare settings: <https://www.cdc.gov/healthcare-associated-infections/about/outbreak-investigations-in-healthcare.html>

CORHA: www.corha.org

Outbreak response and incident management: SHEA guidance and resources for healthcare epidemiologists in United States acute-care hospitals⁵: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7113030/>

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 and staff safety is the primary focus
 - Consider how decisions may impact patient care and public perception
- Recognize new and underappreciated risks associated with healthcare delivery
- Prevent future outbreaks
 - Identify systemic problems that may lead to additional patient harm
 - Mitigate gaps in infection control when identified and support mitigation of such gaps both within the facility and more broadly

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 suspected transmission events, sentinel cases of emerging pathogens, infection control breaches, and noninfectious 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 of the outbreak—multiple steps often occur concurrently and not

necessarily in a specific order. The steps covered here are from the perspective of the public health agency (see Box 5.3).² The healthcare facility may be concurrently implementing its own outbreak response activities, and coordination between that facility and the appropriate public health agency should occur with each step. A response should be appropriately rapid, but it is important also to ensure accuracy. Take the time needed to gather information, conduct background research, and gather initial data.

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Table 5.1 | Investigation Activities in Support of 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 outbreak case definition based on clinical profile or characteristics of the pathogen, agent, or infection. • Characterize cases by person, place, and time, and evaluate this descriptive epidemiology to identify patterns. • Analyze exposure information by comparing cases to develop hypotheses. 	<ul style="list-style-type: none"> • Obtain information about healthcare practices and infection control practices that may help characterize the outbreak. 	<ul style="list-style-type: none"> • Obtain and store clinical material or isolates. • Perform confirmatory laboratory testing to confirm pathogen and/or antimicrobial resistance. • 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 the nature of the outbreak, take additional steps as warranted; examples include contacting other facilities, healthcare providers, and/or public health agencies to ask if they have similar cases (“call for cases”) and directly asking members of the public to contact the health department. 	<ul style="list-style-type: none"> • Communicate/alert key stakeholders. 	<ul style="list-style-type: none"> • Contact clinical laboratories to identify additional cases. • Coordinate rapid referral and additional testing of outbreak specimens.

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Table 5.1 | Investigation Activities in Support of Outbreak Response Objectives

OBJECTIVE	EPIDEMIOLOGY	INFECTION PREVENTION	PUBLIC HEALTH LABORATORY
Identify the cause of outbreak.	<ul style="list-style-type: none"> • Complete descriptive analysis using summary statistics, timelines, maps, epidemic curves, and other techniques to develop a list of possible causes. • Review descriptive epidemiologic results combined with any analytic epidemiology results to develop the most likely explanation for the outbreak. 	<ul style="list-style-type: none"> • To determine any contributing gaps in infection control, perform an on-site infection control assessment to include <ul style="list-style-type: none"> - On-site observations - Facility staff interviews - Review of infection control policies 	<ul style="list-style-type: none"> • Evaluate results of all outbreak-associated testing to highlight possible relations among isolates from clinical, environmental, and healthcare worker samples. • Work with the appropriate regulatory authority to ensure that samples are collected and maintained with appropriate chain of custody. This will help the regulatory authority take appropriate regulatory action.
Identify contributing factors and antecedents.	<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 identification of the agent and results of the epidemiologic investigation, to identify contributing factors and antecedents. 	<ul style="list-style-type: none"> • Summarize information including appropriate metadata about testing results from clinical, environmental, and healthcare provider samples.
Determine the potential for ongoing transmission and need for control measures.	<ul style="list-style-type: none"> • Perform ongoing surveillance of the pathogen, agent, or infection using public health surveillance systems, clinical laboratory data, and facility prospective surveillance. • If the 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 are identified or if additional cases are identified following gap mitigation, consider re-assessment of infection control practices. 	<ul style="list-style-type: none"> • Maintain stored sample using established specimen retention criteria, in case a comparison to newly identified cases is needed.

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Initial Steps in the Investigation of Outbreaks

Initial Steps That Should Be Performed Rapidly

- Complete initial steps in the investigation within a brief time. Use this information to develop plans for a more in-depth investigation when warranted.
- Confirm the diagnosis by obtaining and verifying clinical and laboratory information. Alert and communicate with key stakeholders.
- Begin by gathering readily available data from the affected healthcare facility(ies), laboratories, and applicable public health surveillance systems.
- 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 the 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., the Centers for Disease Control and Prevention [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.
- Determine the 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 an 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, or ongoing exposure) should this be ongoing cases instead of exposure; you probably do not know exposure at this point.
 - Involvement of an outpatient facility or other setting that lacks internal resources for conducting a reliable 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.

Evaluations

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

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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 preliminary 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 may be performed in every outbreak response. There is no rule that steps should be performed in order, and some steps may take place concurrently.

- Characteristics of the patients or affected population (e.g., basic demographics and/or underlying conditions); timing and details of potential exposures such as visits, procedures, surgery, and admission/discharge; timing and details of symptoms, testing, diagnosis, hospitalization, or other follow-up care; and death
- 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., facility-wide vs. confined to a single unit or type of unit)
- Any testing information available (e.g., laboratory name, dates of culture/testing, additional testing performed, and methodology[ies] used)
- Information related to any possible medical product involvement (more information is available at <https://corha.org/wp-content/uploads/2019/06/CORHA-Medical-Product-Assessment-Questions.pdf>)
- Descriptions of relevant care delivery practices to help gauge whether accepted infection control standards are being followed (e.g., for an outbreak involving injections, determination of whether single-dose vials are reused for multiple patients as well as other injection preparation and administration practices)
- Measures already implemented (e.g., infection control measures, additional testing, and notification of patients)

5.1 Perform an Initial Assessment

5.1.1 Initial Information to be Gathered

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

- Specific pathogen, infection, or syndrome
- Number of cases identified, types of cases (e.g., infections vs. colonization and/or occurring primarily in patients vs. patients and staff), and outcomes (e.g., number of deaths)
- Known or expected background rate of cases, if known
- Date of detection of the potential outbreak

5.1.2 Initial Control Measures

A brief assessment of infection control practices should be performed when the initial information is gathered, often during the first phone call with the facility. If there are practices that need to be corrected immediately, this recommendation should be given to facility personnel as part of the initial assessment. Table 5.2 shows immediate control measures that could be followed. See Chapter 2, Table 2.2 for more examples that can inform initial steps; based on past experiences, specific interventions to address various situations are often known and should be considered for implementation, in advance of a more detailed investigation. Put another way, it is often not necessary to wait for a detailed on-site assessment for initial recommendations to be given. Infection control assessments and control measure recommendations are discussed in greater detail later in this chapter.

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TABLE 5.2 | Immediate Control Measures for Healthcare Outbreak Management*

TYPE OF TRANSMISSION SUSPECTED	SUGGESTED ACTION
Cross-transmission (transmission between persons)	Patient isolation and transmission-based precautions determined by infectious agent(s); certain scenarios may require closure of locations to new admissions
Airborne infection (e.g., tuberculosis or emerging viral pathogens)	Triage, detection, and patient isolation with recommended ventilation type (positive or negative air pressure)
Agent present in water, waterborne agent	Assessment of the premises' water system, liquid products, or medications; use of disposable devices in which reusable equipment is suspected
Contaminated medical product	Sequestering of product and a switch to an alternate product or suspension of affected procedure(s); file MedWatch report to FDA
Environmental reservoir	Review and enhancement, as needed, of cleaning and disinfection processes; interruption of suspected mode of delivery from environment to patient
Colonized or infected healthcare personnel	Review of facility policies and discussion of work restrictions, duty exclusions, treatment, personal hygiene, or other steps
Infection control breach posing risk of bloodborne or other pathogen transmission	Immediate cessation of risky practice until corrective action can be instituted; patient notification; assurance that occupational health staff are aware

*Adapted from Christensen BE, Fagan RP. Healthcare Settings. In: Rasmussen SA, Goodman RA, eds. *The CDC Field Epidemiology Manual*, Table 18.3.²

5.1.3 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 may include a full investigation and response, investigation by the facility with public health being kept informed, or other approaches. An effective triage process should be established to determine an appropriate level of response and to ensure public health investigations proceed when needed; furthering the investigation is not necessary for all reports of potential outbreaks, 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 potential outbreaks. On the other hand, 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 a situation needs them (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 the authority to investigate may also need to be considered when determining the level of response, as noted in Chapter 3.

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

- Risk to patients may be elevated and ongoing due to a potentially hazardous, unusual, or unsafe situation.
- Failure to intervene could result in preventable exposures, patient harm, or spread.
- There is potential for greater levels of harm (e.g., morbidity and mortality) due to vulnerability of the population at risk or involvement of a considerable number of persons.
- Early implementation of proven control measures is time-sensitive (e.g., prophylaxis).
- Resources and the experience level at the facility to conduct its own investigation is limited, such as in healthcare settings with less infection control capacity such as outpatient settings.
- The facility involved has a history of struggling to manage outbreak response activities in an independent or reliable manner.
- There is a sentinel event, such as an unusual or novel organism or an organism-infection combination, the suspected involvement of a medical product, or other situation in which even a single case warrants additional follow-up.



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

5.1.4 Developing Hypotheses

To focus response activities, it helps to develop an initial hypothesis about potential sources of the outbreak early in the investigation. As noted in section 5.1.2, after gathering initial information, it is often possible to determine likely causes based on previous outbreak reports and experiences. Key steps to developing hypotheses include a review of what is known about the pathogen or infection, including results of previous outbreak investigations involving similar settings or procedures. 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 point in the investigation, public health should be working with the healthcare facility. The facility may have already performed the following (levels of investigation performed at this point may vary among facilities and healthcare settings):

- Collection of initial information and development of hypotheses about the cause of the outbreak
- Implementation of infection control measures based on preliminary information and previous experiences involving similar types of outbreaks
- Notification of the facility leadership of the potential outbreak and reporting to the public health agency

5.2 Verify the Diagnosis

At the time a potential outbreak is detected, diagnosis of the disease may not yet be clear or, in some cases, may be incorrect. Early in the investigation, identify as accurately as possible the specific nature of the disease by ensuring that the diagnosis is correct; this can be done by investigating possible laboratory error or contamination as a basis for increased diagnoses, evaluating possible changes in surveillance and case definitions, and reviewing clinical findings and microbiological test results.² Information to be reviewed should include clinical features of the disease, timing of symptom onset, laboratory test results as they relate 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 that samples are saved and, if needed, forwarded to the public health laboratory as soon as possible. Retention of anything that may 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 additional testing. Additional testing to confirm a diagnosis, identify possible resistance mechanisms, or assess relatedness via molecular methods should be considered and can be done at the state or local public health laboratory or another reference laboratory.

5.3 Assemble and Brief the Outbreak Response Team

The number and composition of 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,

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Meanwhile in the Healthcare Facility...

Verify the Diagnosis

The facility may be concurrently performing the following:

- Reviewing its 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; and requesting assistance from the public health laboratory to perform additional testing
- Proceeding with infection control measures to protect patients, including saving suspected medical products and cessation of their use, if applicable

there will likely be multiple public health teams. A lead agency should be determined, and this agency will provide facilitation and coordination for the response. The leading agency is referred to as the “coordinating agency” in this chapter. Roles assigned should include designation of the team lead. During the investigation, the composition of the team may 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 may have its own team. The leading team may be from the healthcare facility, when public health is not directly involved, or 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 may vary. Close collaboration and coordination are needed when multiple teams are involved during a multifacility or multijurisdictional outbreak; this is described in additional detail in Chapter 7.

5.3.1 Partners

Multiple partners are likely to participate during an outbreak investigation. It is common for investigations to involve at least one public health agency along with the

healthcare facility in which the potential outbreak occurred. Each involved entity may have its own response team. In addition to public health and the healthcare facility, other partners may include state facility licensing agencies (supervisory staff and surveyors from the involved healthcare setting); law enforcement (local, state, or federal), if criminal action could be involved; professional oversight organizations such as pharmacy boards or clinician licensing boards (staff from the licensing organization); or regulatory agencies such as the US Food and Drug Administration (FDA).² Representatives from the facility and public health may participate in investigative activities on a daily basis and be involved in many aspects of the outbreak response; other partners may participate as team members less frequently or provide assistance for specific parts of the investigation.

If the investigation cannot be managed with local resources alone due to its scale, complexity, or limited agency expertise, help should be requested sooner rather than later. Escalation may move from the local public health agency to the state public health agency to CDC; in some cases, escalation may be helpful to obtain additional opinions or perspectives; in other cases it may 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.^{2,6}

5.3.2 Public Health Team Communication

Public health team members should participate in regular briefings. As an 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 team members are managing their workloads; team members should be open with their team lead about workloads 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 the ICS. Should the investigation lead to media attention, ensure that public information officers are added to the team.



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5.3.3 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 staff members at the affected healthcare facility and to communicate early and regularly with them, including sharing 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 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 healthcare facility staff members on public health calls, such as calls with staff at CDC.
- Methods for sharing information should be discussed early, as some entities may 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 staff members at 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 may be helpful to consider establishing two coordinating agencies—one public health and the other regulatory—with management responsibilities shared between the two coordinating agencies. Because investigations can occur

in parallel, it is critical that information be shared rapidly and fully between public health and regulatory agencies. In infection control breach investigations, a regulatory agency, such as the state survey agency or a professional licensing board, is often brought into the investigation early and, in fact, may be the initial investigating agency that notifies public health (see Supplement B for additional information regarding infection control breach investigations).

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 also be added to the team early to ensure that information-sharing regulations are followed. Typically, the regulatory agency is at the state level; coordination with public health may necessitate a specific role for the state public health agency, even if a local public health agency is designated as having the coordinating role. When sharing information with federal regulatory agencies, consider the 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 FDA. Given coordination with multiple state and federal agencies, unless the local public health agency has broad expertise and capabilities, these investigations are usually led by a state public health agency. Coordination at the CDC level may occur if the drug diversion has a national component, such as a healthcare worker who has worked at healthcare facilities in multiple states. For more information on drug diversion investigations, see Supplement B and the CSTE Drug Diversion Toolkit: <https://www.cste.org/general/custom.asp?page=Drug-Diversion-Toolkit>.

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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 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 those involved in communication and emergency preparedness, as soon as it is determined that their expertise may be needed.

With the Involved Healthcare Facility(ies)

- Determine with the facility a clear plan for communication as early as possible, including frequency and method.
- Develop and clarify expectations of public health agency and facility roles and responsibilities early.

- 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 their roles and the frequency and method of updates. These plans may differ from communication among public health agencies and healthcare facilities.
- Communicate early with agencies, healthcare facilities, and partners if a publication or presentation is anticipated to result from an investigation and may lend itself to communication with a wider audience upon the investigation's conclusion. Establish leads for each potential product early in an investigation to avoid difficult conversations later in the investigation.

With Patients and the Public

- Consider early in the investigation the need to inform patients and the public, and to re-evaluate this need frequently. This is described in detail in Chapter 9.

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Meanwhile in the Healthcare Facility...

Assemble and Brief the Outbreak Response Team

The facility may be concurrently performing the following:

- Assembling its own outbreak response team, depending on the healthcare setting, which could 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 its corporate staff, which in some cases includes a medical epidemiologist and infection preventionist who may be an integral part of the outbreak investigation
- Developing or refining internal communication protocols specific to this outbreak investigation
- Communicating directly with state and federal regulatory partners

5.4 Establish a Plan and Prepare for Fieldwork

Based on data gathered in the initial assessment, determine what information is still lacking and what steps should be followed to gather that information. The team should be prepared to formulate a plan quickly for the 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 the medical literature, review of previous outbreak reports, and consultation with experts.

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

Depending on the severity, scope, and potential for spread of the outbreak, decide whether a site visit to the healthcare facility should occur and how soon that visit should be scheduled. Also consider the size of the public health team attending the site visit based on both the needs of public health and the facility. During infection control observations, deployment of small, more experienced teams may 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 multifacility outbreaks.

Some preparatory actions may need to take place early, ahead of the site visit, to avoid delays, including the following:

- **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 of gaining 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; the tools can be modified for specific outbreak and pathogen types. Using standardized tools during an outbreak response ensures uniform data collection and supports case definition development and case finding efforts (as described in sections 5.6 and 5.7). 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.



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- Determination of specific infection control observations: Depending on the type of outbreak, areas of the facility that should be visited for infection control observations will vary. Determine 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, facility staff members are preparing to host public health authorities at their facility. It is important that the public health team understand the burden of preparation involved for the facility. The facility may be doing the following:

- Preparing its 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
- Responding to public health requests for information, records, and access to records

5.5 Confirm the Presence of an Outbreak

Just as the diagnosis needs to be verified, it is important to confirm the presence of an outbreak. Keep in mind the following:

- Some cases may be part of the outbreak, whereas others may be unrelated.
- Increases in cases indicating a potential outbreak may be due to increased or changed local reporting procedures, changes in case definition, increased interest reflecting local or national awareness, or improvements or other changes in diagnostic procedures.

- A single case may be treated as a potential outbreak for response purposes if the pathogen, pathogen-infection combination, or situation is unusual or is a sentinel event.

Healthcare-related outbreaks may be a smaller part of a larger community-wide outbreak, which can be identified using public health surveillance data.² In these situations, possible community-associated or other explanations for illness not associated with healthcare should also be investigated.

Pseudo-outbreaks can manifest as an increase in diagnosed infections, often without clinical illness, which stem from laboratory processing errors or contamination of clinical diagnostic equipment such as bronchoscopes. Likewise, changes to surveillance methods can result in a spike in disease reports for a particular condition or pathogen. These situations are important to investigate. For example, an incorrect diagnosis can lead to unnecessary procedures, antibiotic prescriptions, and other potentially harmful or costly interventions. Consider a pseudo-outbreak when the pathogen identified does not match the clinical picture (e.g., patients do not have typical symptoms or compatible imaging findings). If a pseudo-outbreak is suspected, investigations may identify improper selection or contamination of materials used for specimen collection or deficiencies associated with reprocessing equipment involved in obtaining specimens (e.g., bronchoscopes or endoscopes).² Substandard laboratory practices or changes to surveillance practices should also be considered.

Meanwhile in the Healthcare Facility...

Confirm the Presence of an Outbreak

The facility may be concurrently performing the following:

- Reviewing its own surveillance data
- Communicating with colleagues at other facilities to determine whether other facilities are experiencing a similar situation
- Communicating with its laboratory to rule out the possibility of a pseudo-outbreak

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5.6 Establish Case Definition and Classification Criteria

An outbreak case definition is a set of standardized criteria used to categorize patients. For outbreak investigation purposes, case definitions can be different from surveillance case definitions and different from clinical criteria for a diagnosis. A case definition typically includes:

- Clinical information relevant to the disease or condition (e.g., symptoms and signs) and/or laboratory information (e.g., diagnostic test results)
- Information about the location of possible exposure (e.g., intensive care unit, radiology suite, operating room, or ward)
- A defined time period during which exposure or onset occurred²

In some situations, demographic characteristics of affected patients may 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; avoiding cases that might be unrelated is important when trying to identify causes. 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” designation references the set of defined criteria based on person, place, time, and other characteristics in the case definition and classifications (see below). The term “case” does not reference the patients themselves; in fact, in rare situations a single patient can represent more than one case (e.g., if the patient becomes infected serially within the outbreak period). When counting cases, it is important to distinguish the number of cases and the number of patients, as these may differ, 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 degree of uncertainty.

- 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 cases²

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

Box 5.4 | Example Case Definitions

- *Pseudomonas aeruginosa* isolated from a blood culture with a culture date after January 1, 2019, collected from a patient who spent at least one night in the ICU in Hospital X, with <10 single nucleotide polymorphism (SNP) differences from the outbreak strain based on whole genome sequencing (WGS).
- Presence of at least two of the following symptoms: cough, sore throat, shortness of breath, or increased need for oxygen in a resident while residing in Nursing Home X between February 1 and March 31, 2022.
- A positive PCR test for *Klebsiella pneumoniae* carbapenemase in a specimen collected at any clinical site from a patient admitted to Hospital Y in November 2021.

Meanwhile in the Healthcare Facility...

Establish Case Definition and Classification Criteria

Although in some situations, a healthcare facility may 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 partners.

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5.7 Identify and Count Cases

Identification (and classification) of cases is important for several reasons. Case finding helps investigators confirm the presence of an outbreak, formulate accurate hypotheses for its cause, and direct resources to affected patients and institutions. The approach to finding and enumerating cases can reflect the stage of the investigation, similar to how a case definition can be adjusted over time to make it broad initially and then more specific (see previous section). Finding and counting cases in a comprehensive manner can support efforts to identify and evaluate potential risk factors. Once the cause of the outbreak has been determined, it may be less important (and could pose an unnecessary burden) to identify and account for every single related case.

Cases can be identified both retrospectively and prospectively. Retrospective case identification may involve the following methods:

- Reviewing laboratory records (e.g., microbiology logs to identify a specific pathogen or histopathology logs to identify invasive fungal infections)
- Reviewing facility surveillance records (e.g., infection prevention logs and/or 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 condition and public health reports)
- Interviewing facility staff (e.g., infection preventionists, medical epidemiologists, clinicians, and laboratorians)
- Reaching out to clinicians, other facilities, or public health agencies (a “call for cases”)—applicable to both 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 may be colonized or infected with specific pathogens (e.g., carbapenemase-producing carbapenem-resistant Enterobacterales, group A *Streptococcus*, or hepatitis C virus) to identify additional cases

Note that the pool of potentially exposed individuals may extend to healthcare workers, visitors, and even community residents, depending on the pathogen or syndrome and likely exposures. In general, testing of healthcare workers is only done when consistent with the epidemiologic picture and biologic plausibility.

Meanwhile in the Healthcare Facility...

Identify and Count Cases

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

- Determining and implementing methodology to identify cases retrospectively and prospectively, including consideration of screening via testing when applicable
- Notifying clinicians and laboratory staff within the facility to be alert for cases meeting the case definition
- Considering whether other facilities within the facility's network need to be notified
- Considering a call for cases among networks depending on likely hypotheses
- Tracking cases within the facility and being prepared to share information with public health

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Cases should be counted systematically, uniformly applying the developed case definition, stratification, and classification. As noted earlier, in some instances the approach can be adjusted (e.g., made less meticulous) after the cause of the outbreak has been determined. It can also be helpful to track all reported or detected cases, including those not meeting 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 following section.

5.8 Collect, Organize, and Analyze Data

5.8.1 Data Collection

Data collection refers to all information gathered during an investigation, including patient-specific data gathered from medical records, information amassed during the review of logs and other facility records, data collected during the case identification process, infection control assessments, laboratory results, and any other pieces of information relevant to the investigation. Data sources used to identify cases (listed in the previous section) can also be used to collect data during the investigation; types of records are listed in Box 5.5. Information can be entered into a line list or 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 and/or 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 multijurisdictional 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 or droplet)
- Central service or supply records
- Occupational health records
- Hospital billing records
- Operative notes
- Infection control assessment
- Pathology reports
- Interviews with physicians
- Pharmacy reports
- Logbooks
- 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 (<https://www.cdc.gov/healthcare-associated-infections/media/pdfs/Response-Toolkit-Abstraction-Form-508.pdf>).

If a case-control study is begun to test various hypotheses, the same tool can be used to collect information on control patients. A standardized data collection form should also be used in the event patients need to be interviewed. The data collection tool usually comprises 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.), and discharge date and discharge status (discharged to home, transferred to another facility, deceased, etc.)

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- Demographic information, such as age, sex/gender, and race/ethnicity
- Location information (e.g., room, unit, ward, floor, and building; facility type or healthcare setting; and single vs. multi-occupancy room)
- Clinical information focused on simple, objective criteria to the extent possible: disease signs and symptoms that allow investigators to verify that the case definition has been met; date of illness onset or specimen collection needed to chart the time course of the outbreak and, when applicable, the incubation period; supplementary clinical information, such as illness duration and rehospitalizations or patient death, which help characterize the spectrum of illness
- Risk factor information tailored to the specific disease and situation under investigation
- Other information (e.g., insurance status, socioeconomic characteristics) not covered above that could identify healthcare disparities or issues relating to health equity

As described in Chapter 3, section 3.8.3, information that can be used to identify a patient 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.

5.8.2 Organize Data and Perform Descriptive Epidemiology

Data collected using standardized methods should be organized systematically. Initially, this is accomplished

with the aid of a line list,² 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:

- Demographic information: age, sex/gender, race/ethnicity, and occupation, plus other relevant characteristics of the affected population or others at risk
- Location information: location within the facility (e.g., room number, bed number, and adjacent rooms)
- Temporal information: examples include dates of illness onset, diagnosis, admission, discharge, procedures
- Clinical information: symptoms, signs, and laboratory test results (e.g., culture, serology, or polymerase chain reaction [PCR] results)
- Risk factor information as it relates to the specific disease in question²

Once the information is collected and organized, performance of descriptive epidemiologic analysis is the first stage; this includes describing the data using tables, graphs, diagrams, maps, or charts to answer the 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 sufficient to determine the likely outbreak cause with sufficient confidence.

The analytic approach used in any situation depends on multiple factors, including circumstances specific to the outbreak (e.g., the pathogen and number and distribution

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



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of cases), staff expertise, structure of the investigating agency, and agency resources. Investigators are encouraged to use a combination of analytic approaches, as appropriate to the specific outbreak.

The first step in a descriptive epidemiologic analysis is to describe cases or case-patients, typically in a simple table that includes the numerator, denominator, and percent (or mean, median and range) for each characteristic (e.g., demographics, exposures, and risk factors). Additional tools used to organize data include maps and timelines. Facility maps are often extremely helpful and can be used to create spatial images of patients' locations and movements. Creating a timeline for each patient that includes exposures of relevance, testing dates, symptom onset, and patient locations can also be helpful to identifying 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 and stored ahead of the 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 the effectiveness of control measures, identify outliers that may provide clues, distinguish an 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.

5.8.3 Refining the Hypothesis

Development of the initial hypothesis should occur early in the investigation, using findings from the descriptive epidemiologic analysis to refine the hypothesis further. After an explanatory outbreak hypothesis has been developed, the next step is to evaluate its plausibility, typically by using a combination of epidemiology,

laboratory, and environmental evidence. From the epidemiologic point of view, hypotheses are evaluated either by comparing a hypothesis with established facts or by 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 the accumulated evidence in an obvious manner and to the 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 analyses. Many outbreaks do not have a sufficient number of cases or a predicted cause of the outbreak is multifactorial; in these situations, more complex analytic epidemiology may not help advance the investigation. However, when there is a clear hypothesis to be tested in the presence of a 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 hypothesis based on outliers; in some situations, outliers may 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.

5.8.4 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 can be found in 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 (i.e., persons with the condition of interest) is compared with the frequency of exposure to that risk factor among a group of controls (i.e., persons without the condition of interest). Controls must be selected carefully to limit bias. Two or more controls for each case-patient may be needed to provide sufficient statistical power.

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Analytic studies are labor-intensive and are not always necessary to identify the likely source of an outbreak or 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 disease 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 a sufficient number of controls be selected to minimize bias?
- Is information available for testing possible risk factors?

Meanwhile in the Healthcare Facility...

Collect, Organize, and Analyze Data

Different healthcare facilities and facility types may have different capacities to collect, organize, and analyze data. Some facilities may perform the collection and organization of data, whereas others may also be able to perform analyses such as timelines and epidemic (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 analyses with the healthcare facility. The healthcare facility may 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 the public health agency to do so
- Responding to public health requests for additional data, facility maps, or other additional information

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 inclusion of a comparison group, which enables epidemiologists to quantify the relationships between exposures and disease by contrasting observed patterns (e.g., incidence rates and odds ratios) among case-patients or exposed persons with those among non-case-patients or unexposed persons. In this manner, investigators can test a hypothesis regarding the likelihood of those relationships being due to chance.

5.9 Perform an Infection Control Assessment

Infection control assessments offer the opportunity for public health to understand risk factors that may have contributed to or resulted in an outbreak. In some cases, infection control assessments may be brief and conducted over the phone; for example, as part of the initial assessment (section 5.1). In many cases, however, the best practice is for the public health outbreak response team to make a site visit to the facility that includes an on-site infection control assessment. If this is not feasible, consideration can be given to performing a virtual assessment using video meeting applications.⁷ Unfortunately, limitations to this approach exist. Video views may be restricted to the selected camera angle, and potentially inaccurate assessments of true infection control practices may result if facility preparations are put in place prior to the virtual visit.

Interviews and discussions with both managers and frontline staff can help identify areas of concern and help focus infection control audits and other forms of assessment related to the environment of care, procurement and handling of equipment and supplies, or environmental factors that could have contributed to the outbreak. Direct observation of infection control practices and other conditions at the facility often results in the identification of infection control breaches or other exposures that contribute to patient harm. Considerations for performing an on-site infection control assessment include the following:

- On-site visits provide the opportunity to interact with and interview key staff, tour relevant areas of the

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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 conducting on-site visits, visits could be consolidated into joint (public health–regulatory) agency visits, which would provide greater information to both agencies and the 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, which will aid the facility walk-through and infection control assessment. 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 aid 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 of such items (e.g., those used in previous investigations) as well as general and setting-specific tools made available on the CDC website: <https://www.cdc.gov/healthcare-associated-infections/php/toolkit/icar.html>.
- Assess whether actual practices deviate from recommended infection control practices and facility 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; give priority to observing staff who were most closely involved in providing care for the case–patients.
- 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 may be involved in the outbreak.

- Consider taking photographs 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 disease source and mode(s) of transmission. Review challenges with maintaining good infection control practices, facility staff members' thoughts on the root cause of the outbreak, and information that may not be documented in medical records.
- Review protocols and procedures to ensure that they are up-to-date and have been followed consistently. Assess if actual practice matches written and verbal protocols and what is expected.²

In addition to direct observations, it can be helpful to talk with multiple staff members about their routine infection control practices in detail, as sometimes it is not possible

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 to compare findings, and it is beneficial to have duplicate infection control assessments between the facility and the 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 may prepare ahead of the arrival of the public health team; it may be beneficial to remind the facility that to help them, public health personnel need to observe actual, not optimal, infection control practices.

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to observe each staff member; this additional step can identify gaps in infection control that may 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 different staff members perform the task of interest since approaches may vary.

5.10 Consider an Environmental Assessment

An environmental assessment is a systematic evaluation of environmental factors that may have contributed to an outbreak. The need for an environmental assessment is informed by epidemiologic 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 that includes observations and interviews with environmental services staff. CDC has specialized tools available to help guide environmental assessments when investigating outbreaks involving waterborne pathogens or outbreaks caused by certain fungi such as *Aspergillus* and mucormycetes.^{8,9}

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
- 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 the outbreak cases. For example, air sampling in an operating room that may be affected by its construction may be pursued during the investigation of an outbreak of surgical site infections with *Aspergillus*.⁹ Since clinical laboratories may not be licensed or able to perform environmental testing, samples may need to be sent to a public health, environmental, 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 be able to perform an environmental assessment. When environmental sampling is performed, the facility will work with its laboratory to ensure that sampling procedures are correct and the laboratory has the capability to perform the testing. Often public health laboratories are needed for testing environmental samples, and coordination between clinical and public health laboratories is needed in this situation.

5.11 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 can be recommended at various times throughout an 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, or host. See Chapter 2, section 2.3, 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 may be done in person or via phone or email communication, depending on the situation.

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Keep in mind that regulatory partners (e.g., state professional boards or the state healthcare facility licensing agency) may 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 may need to be used for a substantial time before they become routine. For independent outpatient offices or facilities, monitoring implementation of preventive controls typically warrants heightened levels of attention.

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

- Notifying leadership and legal staff within your agency
- Notifying the appropriate regulatory agency
- Taking immediate steps to ensure that patient risk is mitigated (e.g., poor practices are immediately corrected, procedures are suspended, or ward or unit is closed to new admissions)

Teams should be aware of laws that allow for notifying appropriate agencies as well as individual obligations for doing so; consult with legal staff when situations may be unclear. See Chapter 8 for more information related to notification of patients, stakeholders such as providers and healthcare facilities, and the general public.

Additional disease control measures beyond recommendations to the facility may also need to be implemented. In some situations, recommendations to the public, specific patient groups, or healthcare providers and healthcare facilities may 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.

5.12 Interpret Results

The outbreak response team is responsible for ensuring that all available information is used to construct a coherent narrative of what happened and why.

Meanwhile in the Healthcare Facility...

Recommend Control Measures

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

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



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5.13 Monitor the Outbreak until Completion

5.13.1 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. Likewise, as investigators acquire information about similar cases, exposures or adverse conditions at other facilities, or transfers of case-patients to or from other facilities or across state lines, investigators should promptly update the appropriate health authorities and consider whether any information indicates that the outbreak may be multijurisdictional.

5.13.2 Re-evaluate Hypotheses and Case Definitions

Ongoing review of investigation findings, including current case-patient lists, new laboratory data, updated epidemic curves, and recent environmental assessment findings, can raise novel questions or help answer existing questions related to an outbreak. Investigators should re-evaluate 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.

5.13.3 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 to be over when two or more incubation periods of the etiologic agent have passed with no new cases. This arbitrary rule may be difficult to apply in some situations (e.g., infections with long or variable incubations).

Maintaining communication with the healthcare facility involved to make sure additional cases are not detected

is critical for some time after the investigation is over. The duration of continued monitoring will vary depending on the type of outbreak. Often this monitoring can be accomplished by reviewing surveillance data reported to public health or through inclusion of a recommendation to the facility to report any new cases to public health for a defined time. Should additional cases be detected, additional investigation should be considered, beginning with an evaluation of the new cases. This may include assessing whether exposure(s) of these cases is consistent with previous patterns and conclusions, and whether control measures are being implemented in the manner recommended. Note that for outbreaks involving a common source, such as those involving a distributed medical product with a long incubation or nonspecific symptoms, it may not be feasible to continue counting cases. In these situations, emphasis should be placed on recall efforts (or implementation of other recommended control measures) to stop new exposures and on 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 investigations 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. A formal after-action meeting should include the following:

- Identify potential sources and contributing factors to the outbreak and control measures that may need to be addressed to prevent additional outbreaks at the facility or other facilities in general.
- Assess the effectiveness of outbreak control measures that were implemented, barriers and difficulties in implementing these measures, and opportunities for improvements in future similar outbreaks.

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- Identify barriers or factors that compromised the investigation and identify areas for improvement.
- Identify necessary changes to current investigation protocols and practices.
- Clarify resource needs, structural changes, or training required to optimize future outbreak responses.
- Discuss any legal issues that may have arisen and identify options for addressing these.
- Assess whether further scientific studies should be conducted.

Meanwhile in the Healthcare Facility...

Monitor the Outbreak until Completion

During this step, the healthcare facility may be performing the following:

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

- **Methods:** Including agencies involved in the investigation, case definition, details of investigative methods (e.g., record reviews, patient interviews, and environmental assessments), types of patient specimens and environmental samples that were collected and tested, and a summary of laboratory testing methods
- **Results:** Including numbers of persons exposed, sickened, hospitalized, and deceased; key clinical findings; key laboratory findings, including numbers of patient specimens and environmental samples that were collected; key infection control findings; key environmental findings; any analyses that were 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
- **Conclusions:** Including the 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; for smaller outbreaks, a brief report may suffice. The final report is an excellent tool to provide education for newer staff and a resource for future, similar outbreak investigations. 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 provide other legally nonpublic 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 general scientific knowledge, consideration should be given to submitting the report for publication in the medical literature, either in the *Morbidity and Mortality Weekly Report* or a peer-reviewed journal that reaches the intended audience—public health or otherwise.

5.14.2 Distribute the Report

Copies of the report should be shared with members of the investigative team, laboratories, healthcare facilities, and other partners involved in the investigation.

5.14 Other Follow-Up Activities

5.14.1 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 that may inform future investigations and prevention needs. In some cases, this report can be brief or follow a standard format or template, such as 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





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Consideration should be given to distributing the report more widely 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.

5.4.3 Policy Action

Information gained during an outbreak may 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 may 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 may be in the process of writing its own internal report, which could 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 agency 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 unexposed—is the study of choice for an outbreak in a small, well-defined population. Generally, an exposure is strongly suspected if it meets the following criteria:

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

Relative risk

Commonly, the investigator calculates the relative risk (a.k.a. the 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 than that 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 the

other statistical tests described here—can be calculated electronically using Epi Info or another computer program.

The statistical association between exposure and illness may reflect a causal link, but it 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, a faulty sampling method, an 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., a 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*-values. 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.

Appendix A: Cohort and Case-Control Studies

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, controls must *not* have the disease under investigation, 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 or condition under investigation)

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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