Chapter 2: Fundamental Concepts of Healthcare-Associated Infections and Antimicrobial Resistant Pathogens Surveillance and Outbreak Response
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PREFACE

Outbreaks in healthcare settings represent a breakdown in practices designed to prevent transmission of disease. Often, outbreaks are the result of a failure to follow basic (or "core") infection control practices, at the point where healthcare is delivered. Outbreaks also result from contaminated products, such as medications or devices, entering a medical facility and exposing patients. Protecting patients from acquiring a healthcare-associated infection (HAI) or antimicrobial resistant (AR) pathogen is a critical aspect of patient safety. Patients seek healthcare as a means of maintaining or improving their health. When, as an unintended consequence of healthcare, an infection occurs or colonization with an AR organism results, it can be a significant event for the patient, one that is shaped by a patient's health status, understanding, emotions, and social context.[1] Trends in our understanding of HAIs and healthcare-associated pathogens including AR pathogens and trends in healthcare delivery have changed the landscape of how public health agencies and healthcare facilities collaborate to prevent and respond to outbreaks. As HAI/AR surveillance improves and outbreaks are recognized earlier, the public health and healthcare community increases its capacity to prevent HAIs and healthcare outbreaks and improve outcomes for patients. The ultimate goals are to rapidly detect and control HAIs, interrupt transmission of healthcare-associated pathogens, and stop outbreaks

INTRODUCTION

2.0 Introduction

This chapter reviews the fundamentals in healthcare and public health surveillance and healthcare outbreaks that have impacted the detection, investigation, and control of HAI/AR outbreaks. Public health practice in the field of HAI/AR has changed dramatically over the last few decades, influenced by changes in settings where healthcare is delivered, evolving laboratory techniques, and emerging pathogen resistance to antimicrobials. Expertise and capacity to respond to HAI/AR outbreaks has increased among public health agencies. Public health agencies, healthcare settings, and partner organizations all work together prevent and respond to HAI/AR outbreaks.

HAIs are infections acquired or related to a healthcare setting or related to receipt of medical care and are one of the leading causes of unnecessary death and avoidable. They are a serious threat to public health, and each year millions of patients are affected by HAIs worldwide; in 2011, a U.S. prevalence survey estimated 721,800 HAIs in acute care hospitals.[2] An HAI is considered to be an infection *associated* with healthcare delivery in any setting. This term reflects the inability to always determine with certainty where the pathogen is *acquired* because patients might be colonized (i.e., microorganisms on or in a person without causing a disease) or exposed outside the healthcare setting, and patients frequently move among different settings within a healthcare system.[3] HAIs might appear after discharge, and HAI transmission can involve visitors and healthcare personnel in addition to patients.[4]

Antimicrobial resistance occurs when pathogens develop the ability to defeat the antimicrobials designed to kill them. Infections caused by AR pathogens are difficult, and sometimes impossible, to treat. Transmission is impacted not only by increasing numbers of infections, but also increases in people who are colonized which serves as an important reservoir for transmission. In most cases, AR infections require extended hospital stays, additional follow-up doctor visits, and costly and toxic alternative treatments. AR has the potential to affect people at any stage of life, as well as the healthcare, veterinary, and agriculture industries, making it one of the world's most urgent public health problems. Each year in the U.S., more than 2.8 million people are infected with antibiotic-resistant bacteria, and at least 35,000 people die as a result.[5] Over recent decades, we have seen the landscape of AR pathogens change as new antibiotics are developed, healthcare delivery changes, new patterns of AR emerge, and laboratory detection of AR pathogens advances. As novel AR pathogens emerge, it is important to maintain progress for the prevention of all AR pathogens.

Throughout the guidance, we refer to "HAI/AR outbreaks," which include outbreaks that involve infections that meet the definition of an HAI, infections/colonizations of AR pathogens, and infections/colonizations of other pathogens that are associated with healthcare. Since public health HAI/AR programs often respond to outbreaks that extend beyond traditional HAIs and AR pathogens solely within healthcare settings, the guidance also includes consideration for outbreaks of pathogens that we typically think of as being healthcare-associated but also found in community settings (e.g., non-tuberculous *Mycobacteria* in a nail salon, *Pseudomonas* spp. associated with hot tub exposure), outbreaks in healthcare settings associated with exposures to noninfectious chemical and other toxic agents, outbreaks that include healthcare-associated and community cases, and situations that might require investigation even prior to an outbreak occurring (e.g., medical product contamination, serious infection control breaches). The term "HAI/AR outbreaks" is used throughout the guidance but is inclusive of these other outbreak types.

The primary intended audience of this guidance is public health agencies at the federal, state, and local levels; however, the guidance can also be useful for healthcare professionals, healthcare facilities, and other partners responding to HAI/AR outbreaks. It is important to acknowledge the work involved in responding to and preventing HAI/AR outbreaks occurs across the healthcare-public health continuum; healthcare institutions and providers, public health and government agencies, and other partners working in this arena form a large community of professionals collaborating on the same goal: infection prevention and disease control.

TRENDS IN HEALTHCARE

2.1 Trends in Healthcare

2.1.1 Healthcare Settings

The term healthcare setting represents a broad array of services and places where healthcare occurs, including but not limited to acute care hospitals, urgent care centers, rehabilitation centers, nursing homes and other long-term care facilities, outpatient clinics, specialized outpatient services (e.g., hemodialysis, dentistry, podiatry, chemotherapy, endoscopy, and pain management clinics), outpatient surgery centers, pharmacies, and any other location where medical care is provided. In addition, some healthcare services are provided in private offices or homes. The National Quality Forum (NQF) defines a healthcare setting as follows: "Any facility or office, including a discrete unit of care within such facility, that is organized, maintained, and operated for the diagnosis, prevention, treatment, rehabilitation, convalescence or other care of human illness or injury, physical or mental, including care during and after pregnancy."[6]

Within each type of setting, specific locations or services might be the focal point of an epidemiologic investigation. Acute care hospitals are complex organizations that can have multiple specialized areas for triage and emergency care, inpatient and outpatient surgical procedures, management of immunosuppressed populations (e.g., oncology or transplant recipients), rehabilitation services, and intensive care units. The type of healthcare delivered within a healthcare setting can vary widely depending on the community; rural areas often have different capacities than urban areas for a given healthcare setting type. An understanding of the types of patients and clinical services provided in a given setting and given jurisdiction is crucial for recognizing infectious disease transmission risks. Problems identified within a healthcare setting also can be related to use of medications or devices that became contaminated at the point of manufacture or other locations outside the setting of interest.[4]

Selected healthcare settings, definitions and characteristics, and staff public health agencies will typically interact with can be found in Table 2.1.

Table 2.1. Selected Healthcare Settings: Definitions, Characteristics, and Staff with whom Public Health Might Interact

Healthcare Setting	National Quality Forum (NQF) and Centers for Medicare and Medicaid Services (CMS) Definitions [6,7,8]	Additional Characteristics	Public Health Interactions with Healthcare Setting Staff
	NQF: Healthcare services that do not require a	This broad designation includes	For clinics, often public health will interact

Ambulatory Care Settings	hospital admission. These may be provided in an ambulatory surgery center, clinician office, or clinic/urgent care setting.	any outpatient setting of medical care where a patient is not admitted.	directly with an office manager or clinicians. For outpatient procedure centers, public health might interact with clinicians, a manager, or in some cases with an infection preventionist.
Ambulatory Surgery Centers (ASCs)	NQF: Setting where outpatient surgical services are provided. CMS: A facility where certain surgeries may be performed for patients who aren't expected to need more than 24 hours of care.	A type of ambulatory care where surgical services are provided. Some centers are located within a hospital or hospital complex but are licensed separately. Others are stand-alone centers. Public health authorities usually reserve the term ASC for Medicare-certified facilities. The term office-based surgical practice is usually applied to less-regulated entities such as oral or plastic surgery practices.	Public health might interact with an infection preventionist when one is available; sometimes this might be a hospital infection preventionist or an infection preventionist that is affiliated with the center. Public health might also interact with center administration (manager or executive level) or clinicians.
Critical Access Hospitals (CAHs)	CMS: A small facility located in a rural area more than 35 miles (or 15 miles if mountainous terrain or in areas with only secondary roads) from another hospital or critical access hospital. This facility provides 24/7 emergency care, has 25 or fewer inpatient beds, and maintains an average length of stay of 96 hours or less for acute care patients.	Critical access hospitals are acute care hospitals that meet specific criteria as defined by CMS.	Typically, public health will interact with a staff member that fulfills several duties, including that of an infection preventionist. Other staff members might include those found in an acute care hospital (see Acute Care Hospital).
Urgent Care Centers	NQF: Setting in which urgent care services are provided. Urgent care services are medically	Urgent care centers are a type of ambulatory care.	Often public health will interact directly with an office manager or clinicians.

	necessary services which are required for an illness or injury that would not result in further disability or death if not treated immediately, but require professional attention and have the potential to develop such a threat if treatment is delayed longer than 24 hours.		
End-Stage Renal Dialysis Facilities/Dialysis Centers	NQF: Setting in which dialysis services are furnished to patients.	Dialysis facilities might be stand-alone centers or associated with a hospital complex. Often dialysis facilities are part of large corporations.	Often public health will interact with an office manager, clinical manager, or an infection preventionist (that might have other duties). Sometimes public health might also interact with executive administration.
Home Health Agencies	NQF: Limited part-time or intermittent skilled nursing care and home health aide services, physical therapy, occupational therapy, speech-language therapy, medical social services, durable medical equipment (such as wheelchairs, hospital beds, oxygen, and walkers), medical supplies, and other services that are provided to a patient in his/her home or place of residence. CMS: An organization that provides home health care, defined as healthcare services and supplies that patients receive in their home under a plan of care established by a provider.	Many but not all Home Health Agencies are designated Medicare-certified by CMS.	Public health typically has fewer interactions with home health agencies than other healthcare settings. When public health does interact, it will typically be with a clinical manager.
Hospice	NQF: Palliative services provided to terminally ill patients and their families/caregivers in the patient's place of residence or in an inpatient facility.	Many but not all Hospice practices are designated Medicare-certified by CMS.	Public health typically has fewer interactions with home health agencies than other healthcare settings. When public health does

	CMS: An organization that is primarily engaged in caring for people who are terminally ill. Hospice care involves a team-oriented approach that addresses the medical, physical, social, emotional, and spiritual needs of the patient.		interact, it will typically be with a clinical or facility manager.
Acute Care Hospitals (ACHs)	NQF: Setting in which healthcare services, including but not limited to, diagnostic, therapeutic, medical, surgical, obstetric, and nursing are provided, by or under the supervision of physicians, to patients admitted for a variety of health conditions.	There are a variety of hospitals types that might include specialty hospitals (e.g., cancer hospitals, orthopedic hospitals, pediatric hospitals), academic and community hospitals, etc. Two hospital types are specifically described in this table: critical access hospitals and long-term acute care hospitals.	Typically, public health initially interacts with an infection preventionist. Other staff might include quality and risk management, clinical staff (e.g., nurses, physicians, pharmacists, therapists), executive administrative staff (e.g., chief medical or nursing officer), laboratory staff, administrative staff (e.g., medical records staff), facilities management (e.g., environmental services), and other specialty staff depending on the outbreak
Inpatient Rehabilitation Facilities (IRFs)	CMS: A hospital, or part of a hospital, that provides an intensive rehabilitation program to inpatients.		Public health will often interact with the infection preventionist initially but might also interact with other staff similar to an acute care hospital.
Long-Term Acute Care Hospitals (LTACHs)	CMS: Acute care hospitals that provide treatment for patients who stay, on average, more than 25 days. Most patients are transferred from an intensive or critical care unit. Services provided include comprehensive rehabilitation, respiratory therapy, head trauma		Public health will often interact with the infection preventionist initially but might also interact with other staff similar to an acute care hospital.

	treatment, and pain management.		
Nursing Homes (NHs)/Skilled Nursing Facilities (SNFs)	NQF: Setting in which healthcare services are provided under medical supervision and continuous nursing care for patients who do not require the degree of care and treatment which a hospital provides and who, because of their physical or mental condition, require continuous nursing care and services above the level of room and board. CMS: A nursing facility with the staff and equipment to give skilled nursing care and, in most cases, skilled rehabilitative services and other related health services.	Although there are technical differences between the terms "nursing home" and "skilled nursing facility", these terms are sometimes used interchangeably. Some skilled nursing facilities can provide additional skilled care, such as ventilator or central line care. Skilled nursing facilities providing ventilator care are sometimes referred to as vSNFs.	If there is an infection preventionist or a staff member that fulfills some duties of an infection preventionist, public health will initially likely interact with them. Public health might also interact with nursing home administrators or nursing managers as an initial point of contact.
Long-Term Care Facilities (LTCFs)	NQF: A variety of services that help people with health or personal needs and activities of daily living over a period of time. Long-term care can be provided in the community or in various types of facilities, including but not limited to nursing homes, skilled nursing facilities, rehabilitation facilities, and assisted living facilities. CMS: Services that include medical and non-medical care provided to people who are unable to perform basic activities of daily living, like dressing or bathing. Long-term supports and services can be provided at home, in the community, in assisted living, or in nursing homes. Individuals may need long-term supports and services at any age.	Long-term care encompasses nursing homes, skilled nursing facilities, and assisted living facilities (ALFs). Medical care delivery in ALFs is highly variable and entails models that include on-site staffing, home health agencies and individual resident arrangements with community-based clinics and providers. Note also that group homes are another setting in the LTCF spectrum where persons, many with chronic medical needs, live in a congregate setting.	Depends on facility type, as described elsewhere in the table.

Outpatient Clinics		Outpatient clinics (such as a medical practice) are not typically licensed as a facility. A rural health clinic is a type of outpatient clinic that is licensed through CMS and/or state regulatory bodies.	Often public health will interact directly with an office manager or clinicians.
Dental Settings		Dental settings encompass outpatient locations where oral and dental care is provided. Typically, dental settings are not licensed but the providers are licensed through the appropriate state agency.	Public health will most often interact directly with an office manager or clinicians.

2.1.2 Healthcare Delivery

Healthcare delivery has changed dramatically in recent decades. Hospital stays have decreased[9] with healthcare moving more toward outpatient settings. Between 2000 and 2016, the numbers of traditional institutional providers, such as hospitals and skilled nursing facilities, decreased or remained flat despite a growing and aging US population. Meanwhile, there was substantial growth and increased specialization among outpatient providers and other forms of long-term care such as assisted living facilities.[10] As another example, many types of surgeries have shifted from inpatient settings to ambulatory surgery centers, hospital outpatient departments, and office-based surgical practices.[11] The number of long-term acute care facilities and skilled nursing facilities with ventilator care has grown as healthcare improves and people who need critical care live longer. Additionally, increasing healthcare delivery across national borders, such as medical tourism, has affected potential for disease transmission across borders.[12]

The changing healthcare delivery landscape requires public health agencies to be nimble when responding to outbreaks; each healthcare setting has unique characteristics and associated patient populations unique risks that result in a wide variety of outbreaks. Infection prevention needs for healthcare settings have similarly changed over time, and infection prevention resources available for healthcare facilities can vary widely.[13,14]

2.1.3 Regulation and Oversight

With growth and changes in healthcare delivery, regulations related to the prevention of healthcare-related infections have also expanded. A full description of regulatory changes impacting healthcare is outside the scope of this guidance. Laws and standards emphasizing infection prevention and antimicrobial stewardship stem from efforts at the federal, state and even local levels. Federal agencies such as the Centers for Medicare and Medicaid Services (CMS), Food and Drug Administration (FDA), and Occupational Safety and Health Administration (OSHA) play significant roles from a regulatory point of view. Other agencies such as the Centers for Disease Control and Prevention (CDC) generate recommendations and standards that heavily influence healthcare regulation. Of note, core infection control practices are established by CDC's Healthcare Infection Control Practices Advisory Committee (HICPAC) and can be found here: https://www.cdc.gov/hicpac/recommendations/core-practices.html. Accrediting organizations provide participating healthcare facilities with a structure for achieving regulatory requirements and other quality standards. State level agencies license many types of healthcare facilities and take an active role in enforcement. Although regulations and requirements for infection prevention are established for some healthcare settings, not all settings have clear requirements or active oversight. Likewise, even facilities that are generally subject to federal and state regulations do not all have clear standards governing the organization or staffing of their infection prevention and control programs; some of those that do are still working toward meeting newly established requirements. For example, CMS implemented requirements for infection prevention and antibiotic stewardship in nursing homes in November 2016 with a rolling 3-year set of requirements.[15] Regulations affecting infection prevention, HAIs, AR, and antimicrobial stewardship can be found here: (1) apic.org/Advocacy/Regulations/ and (2) apic.org/cms/.

Increasing requirements and regulations have led to more attention on trends and prevention of HAIs, leading to additional resources put toward these efforts in healthcare facilities and public health agencies. HAI rates are now publicly available by specific hospital and nursing home and can be found here: (1) https://www.medicare.gov/hospitalcompare/ and (2) https://www.medicare.gov/nursinghomecompare/.

TRENDS IN SURVEILLANCE

2.2 Trends in Surveillance

2.2.1 Overview

In 1963, Alexander Langmuir defined disease surveillance as "the continued watchfulness over the distribution and trends of incidence through the systematic collection, consolidation and evaluation of morbidity and mortality reports and other relevant data"; dissemination of data should be to "all who need to know".[16] The current World Health Organization (WHO) surveillance definition is "An ongoing, systematic collection, analysis and interpretation of health-related data essential to the planning, implementation, and evaluation of public health practice."[17] Public health agencies, healthcare facilities, and many other partner organizations conduct disease surveillance for purposes as described by Langmuir and the WHO. Here we describe trends in HAI/AR surveillance for public health agencies and healthcare settings that have influenced outbreak detection and response.

2.2.1.1 Public Health Surveillance and Healthcare-Associated Infections and Antimicrobial Resistance Program Development

Widespread public health surveillance of HAIs and healthcare-associated pathogens including AR organisms is a relatively new endeavor. Historically healthcare facilities have performed surveillance for conditions and responded to outbreaks within their walls. In recent years, public health has taken a greater interest in the surveillance of infections that occur within healthcare settings. Advancements in medical care have led to new infection-related healthcare risks. Additionally, although scientists have been aware of AR since the discovery of penicillin and introduction of the first antimicrobials for clinical use, the sulfonamides, it has only been recently that public health has begun surveillance for healthcare-related AR organisms. Dramatic improvements in HAI/AR surveillance and outbreak response have been made within the last decade, including public health experience and expertise. Public health funding specifically for these conditions is relatively new, with major funding streams for state and local public health adding HAI and AR activities to more traditional public health communicable disease activities, such as foodborne, zoonotic, and vaccine-preventable diseases (e.g., CDC Epidemiology and Laboratory Capacity [ELC] cooperative agreement and Emerging Infections Program [EIP] beginning in 2009, part of which was provided through the American Recovery and Reinvestment Act); expanded funding for infection prevention in public health and antimicrobial resistance activities have been added to ELC in more recent years, including approximately $85 million for healthcare Infection Control Assessment and Response (ICAR) as part of the Domestic Ebola Supplement to ELC distributed by CDC to 49 states and 6 local health departments in March 2015.[18] As a result, state public health reporting laws have expanded to include additional HAI/AR reportable conditions over the last decade. The novel SARS-CoV-2 virus pandemic has already had substantial effects on public health activities, public health funding, and healthcare systems. For example, many HAI/AR programs have received an influx of funds and staff support. However, whether the COVID-19-related investments will be sustained and at what levels is not yet know.

2.2.1.1.1 Reportable and Notifiable Diseases and Conditions

State, territorial, tribal, and local public health agencies establish lists of diseases and conditions for public health surveillance that are reportable by healthcare providers, healthcare facilities, and/or laboratories, including HAI and AR pathogens; reporting is mandatory. Reporting criteria include how to report, to whom, and the time frame. Reports might be pathogen-specific or based on infection type or other criteria. Reporting to public health ideally is via a web-based reporting system and/or automatic generation from electronic medical records or laboratory information systems. Systems that rely on phone calls, mail, or fax are still used in some circumstances (e.g., a phone call might be required for urgently reportable conditions in redundancy with web-based or electronic reporting) but can be slower and more labor-intensive. Isolates or clinical material are often required to be submitted in conjunction with the report; required samples are sent to public health laboratories for storage and/or additional testing. This type of required reporting uses personal identifiers and enables the states to identify cases where immediate disease control and prevention is needed. Each state has its own laws and regulations defining what diseases and conditions are reportable. The list of reportable diseases and conditions varies among states and over time; public health agencies typically evaluate these lists periodically for any needed changes to be responsive to emerging pathogens and shifting priorities. Reporting requirements by state can be found at www.cste.org/group/SRCAQueryRes.

State, territory, and some local public health agencies share de-identified data with CDC based on the nationally notifiable disease list found here:

https://wwwn.cdc.gov/nndss/conditions/. Data is reported via the CDC National Notifiable Diseases Surveillance System (NNDSS). It is voluntary that notifiable cases be reported to CDC by state and territorial jurisdictions (without direct personal identifiers) for nationwide aggregation and monitoring. Regular, frequent, timely information on individual cases is considered necessary to monitor trends, identify populations or geographic areas at high risk, formulate and assess prevention and control strategies, and formulate public health policies. The list of notifiable diseases varies over time and by state. The list of national notifiable diseases is reviewed and modified annually by the Council of State and Territorial Epidemiologists (CSTE) and CDC. Every national notifiable disease is not necessarily reportable in each state. In addition, not every state reportable disease or condition is national notifiable.

Most HAI conditions and some pathogen-specific data are reported separately from the NNDSS into a long-standing CDC-developed surveillance system, the National Healthcare Safety Network (NHSN). Requirements for NHSN reporting have been established by CMS nationally, and additional state requirements vary among states; some states require reporting and others do not.

2.2.1.2 Surveillance within Healthcare Facilities

Many healthcare facilities perform their own surveillance, in addition to performing surveillance activities to meet reporting requirements for public health purposes. How surveillance is performed within a facility varies widely. In hospitals this is typically performed by infection preventionists or infection prevention teams whereas in other facility types surveillance might be performed by healthcare personnel with multiple duties. In recent years, many healthcare facilities have moved toward using data mining within electronic health records to identify conditions of interest to infection prevention. Modules within electronic health record systems designed to monitor possible infections are available, can show useful aggregate information on dashboards, and can be timesaving and more comprehensive than manual reviews, which are subject to human limitations. However, these systems are not always feasible for all healthcare systems and facility types, and in some situations manual reviews might be more effective or necessary. Some healthcare facilities rely heavily on notification of outbreaks by astute clinicians. Public health should be aware of surveillance systems used within healthcare facilities in their jurisdiction, including barriers facilities might experience in implementing surveillance systems and limitations of various systems. As public health surveillance has improved, the burden on healthcare facilities for reporting to public health has increased. It is critical that infection prevention programs have adequate resources to complete infection prevention tasks across the spectrum, including surveillance, outbreak detection and response, and active prevention of infections.

2.2.2 Public Health Surveillance Systems

Public health surveillance systems rely on surveillance case definitions to count cases systematically and consistently. Surveillance case definitions might differ from case definitions developed during an outbreak, which might be more specific for the purposes of counting outbreak cases; outbreak case definitions are described in Chapter 4. A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance, which enables public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.[19] Reporting of conditions associated with healthcare settings might be population-based or facility-based. Reporting of HAIs is usually facility-based; reporting of AR pathogens might be population-based or facility-based.

Other surveillance systems not described here might be employed in limited jurisdictions. HAI/AR programs should understand surveillance systems within their agency and explore ways to partner or capitalize on opportunities to use other surveillance and monitoring systems.

2.2.2.1 Population-Based Surveillance

Population-based surveillance involves identifying cases that meet a specific surveillance definition within a defined population. Typically in public health, the population under surveillance is the population of residents of a certain jurisdiction, such as a state or a county. Often in public health HAI/AR programs, population-based surveillance includes conditions that are diagnosed with specific laboratory testing (e.g., CRE, *Clostridioides difficile*, etc.) and is based on the pathogen identified. Reporting of these conditions within a population is typically performed by clinical laboratories, either via each individual case or lists of cases, such as via electronic laboratory reporting, although in some jurisdictions providers and healthcare facilities might also report cases.

Routine public health surveillance of HAI/AR conditions is relatively new. In foodborne surveillance, AR tracking has occurred since 1996 following establishment of the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS), which tracks changes in the antimicrobial susceptibility of selected enteric bacteria found in ill people (CDC), retail meats (FDA), and food animals (US Department of Agriculture [USDA]) in the U.S.[20] Tracking of healthcare-related AR pathogens was established much more recently. With the increases in public health funding to state and local HAI/AR programs as described above, state and local public health agencies have drastically increased capacity to perform pathogen-specific surveillance of AR and other organisms associated with healthcare, such as carbapenem-resistant organisms (CRE, *Pseudomonas aeruginosa* [CRPA], *Acinetobacter baumannii* [CRAB]), MRSA, *C. auris*, and *C. difficile*. Pathogen-specific surveillance might be performed as facility-specific surveillance (i.e., reported by certain healthcare facility types only) or on a population level. Increasing capacity of public health laboratories to receive isolates and clinical material and perform additional specialized testing (e.g., polymerase chain reaction [PCR], whole genome sequencing [WGS]) has allowed public health agencies to focus surveillance and prevention efforts on specific subsets of AR organisms, such as carbapenemase-producing (CP)-CRE. In 2016, CDC established the Antibiotic Resistance Laboratory Network (AR Lab Network), which includes labs in 50 states, four cities, and Puerto Rico, including seven regional labs and the National Tuberculosis Molecular Surveillance Center. The AR Lab Network supports nationwide lab capacity to rapidly detect AR.[21]

Surveillance of other organisms that are of interest to HAI/AR programs but do not fall into the category of AR organisms, are often tracked using population-based surveillance practices. Such organisms might include non-tuberculous mycobacteria (NTM), *Legionella,* and group A *Streptococcus* and might be within the purview of some HAI/AR programs, or the HAI/AR program might coordinate with other communicable disease programs for surveillance within healthcare facilities. Surveillance activities frequently identify cases or outbreaks needing investigation in settings other than healthcare such as nail salons and tattoo parlors, or elsewhere in the community.

2.2.2.2 Healthcare Facility-Based Surveillance

For some conditions, surveillance occurs at the healthcare facility level rather than the population level. HAIs are typically reported using healthcare facility-based surveillance practices, meaning that each healthcare facility will report conditions for their facility. Pathogens might be reported using healthcare facility-based surveillance or population-based surveillance as described above. The system most often used for reporting using healthcare facility-based surveillance is the CDC-developed NHSN.

In 1970, CDC launched the National Nosocomial Infections Surveillance System (NNIS), a collaborative surveillance system among CDC and hospitals, who voluntarily reported "nosocomial" infections (now termed HAIs) into the system.[22] In 2005 NHSN was established, which combined the NNIS with the Dialysis Surveillance Network and the National Surveillance System for Healthcare Workers (NaSH).[23] Similar to the NNIS system, NHSN facilities report HAI surveillance data for aggregation into a single national database. Beginning decades ago with 300 hospitals in NNIS, NHSN now encompasses approximately 25,000 medical facilities including acute care hospitals, long-term acute care hospitals, psychiatric hospitals, rehabilitation hospitals, outpatient dialysis centers, ambulatory surgery centers, and nursing homes, with hospitals and dialysis facilities representing the majority of facilities reporting data. Infections can be risk-stratified based on facility type, including specific hospital types such as pediatric, cancer, teaching, etc. Facilities report HAIs based on state mandates, CMS requirements, or voluntarily and usually use NHSN for reporting; 34 states and the District of Columbia, as well as CMS, mandate reporting to NHSN.[24,25] See Box 2.1 for conditions that can be reported into NHSN.

Some jurisdictions might choose to implement both healthcare facility-based and population-based surveillance for some conditions; for example, acute care hospitals might be required to report CRE via NHSN and clinical laboratories all cases of CRE throughout a jurisdiction on a population level. Population-based surveillance will capture all cases; facility-based surveillance will capture only cases within that facility type and will miss community cases. However, the benefit of facility-based surveillance is that analyses can focus on a particular facility type or specific facility, allowing for more granular information within that setting and development of more directed infection prevention efforts. Both surveillance methods have their advantages and using both methods can provide a clearer picture of HAIs and pathogens associated with healthcare within a jurisdiction and facility.

State and local health departments can access NHSN data based on local authority for regional, state, and local surveillance purposes, including identifying facilities in need of prevention assistance. Information on NHSN can be found here: https://www.cdc.gov/nhsn/.

NHSN data is used for national-, state-, and local-level analyses, and for targeted prevention initiatives by healthcare facilities, states, regions, quality groups, and national public health agencies.[26,27] Nationally, CDC has used NHSN-reported HAIs to develop the AR dataset of the

Patient Safety Atlas, which allows the user to quickly customize maps and tables by filtering datasets to show AR data by geographical area, facility type, phenotype, HAI type, and time period.[26] Position statements from CSTE have established both *C. auris* and CP-CRE (*Escherichia coli*, *Klebsiella* spp., and *Enterobacter* spp.) as nationally notifiable conditions in 2017 and 2018, respectively; CSTE position statements can be found at https://www.cste.org/page/PositionStatements.

Box 2.1 Reporting into the National Healthcare Safety Network (NHSN): Conditions and Healthcare Settings

Conditions that can be reported into NHSN

Healthcare-associated infections
- Central line-associated bloodstream infections
- Surgical site infections
- Catheter-associated urinary tract infections
- Ventilator-associated events
- Dialysis events

Pathogens
- *Clostridioides difficile*
- Carbapenem-resistant Enterobacteriaceae
- Methicillin-resistant *Staphylococcus aureus* (bloodstream infections)
- SARS-CoV-2

Antimicrobial use and resistance
Blood safety errors
Healthcare process measures
- Healthcare personnel influenza vaccine status

Infection control adherence rates

Healthcare settings that can report into NHSN

Acute care hospitals
Critical access hospitals
Inpatient rehabilitation facilities
Long-term acute care hospitals
Nursing homes
Outpatient dialysis facilities
Ambulatory surgery centers
Inpatient psychiatric facilities

2.2.2.3 Other Surveillance Systems

Although the two main surveillance systems for HAI and healthcare-associated pathogen reporting are population-based and healthcare facility-based, there are other systems that can support monitoring and outbreak detection. Each system has advantages and limitations, might be employed in some jurisdictions but not others, and are not a replacement for the two main surveillance systems.

2.2.2.3.1 Emerging Infections Program: Healthcare-Associated Infections – Community Interface

The healthcare-associated infections community interface (HAIC) component of the CDC Emerging Infections Program (EIP) engages a network of 10 state health departments and their academic medical center partners to help answer critical questions about emerging HAI threats, advanced infection tracking methods, and antibiotic resistance in the U.S. Data gathered through the HAIC plays a key role in shaping future policies and recommendations targeting HAI prevention. Activities include surveillance of invasive *Staphylococcus aureus* infections, AR Gram-negative organisms (Multi-Site Gram-Negative Surveillance Initiative [MuGSI]), *Candida* bloodstream infections, and *C. difficile*, as well as HAI and antibiotic use prevalence surveys across healthcare settings. Data gathered by each state health department might be population-based, facility-based, or sentinel, and can be used at a local level. For more information on HAIC activities within EIP, please visit: www.cdc.gov/hai/eip/index.html.

2.2.2.3.2 Antimicrobial Resistance Laboratory Network (AR Lab Network)

As described previously, laboratory capacity is critical for the detection of AR organisms, from clinical to public health laboratories. The establishment of the AR Laboratory Network in 2016 led to expansion of healthcare facilities' and public health agencies' capabilities to accelerate detection of emerging AR threats and support coordinated local responses to prevent their spread. The network includes public health laboratories in 50 states, four cities, and Puerto Rico, seven of which serve as more comprehensive regional labs, as well as a National Tuberculosis Molecular Surveillance Center. This network infrastructure provides much-needed capacity for public health and healthcare to rapidly detect emerging AR threats, rapidly respond at state and local levels to contain any transmission, and increase understanding of AR trends and emerging threats.[21] Regional laboratories provide additional testing when state/local laboratories do not have capacity, which at the time of this writing includes advanced testing for *Acinetobacter*, *Candida*, *C. difficile*, CRE, colistin resistance among extended-spectrum beta-lactamase (ESBL)-producing organisms, *Mycobacterium tuberculosis*, *Neisseria gonorrhoeae*, *Salmonella*, and *Streptococcus pneumoniae*. Regional laboratories which detect organisms and mechanisms of public health interest alert laboratories and epidemiologists who can implement public health actions to prevent transmission. The AR Laboratory Network assists each local jurisdiction with AR surveillance, and the network as a whole also functions as a surveillance entity with the capacity to provide information on national trends and detect outbreaks. More information on the AR Lab Network can be found here: https://www.cdc.gov/drugresistance/solutions-initiative/ar-lab-network.html.

2.2.2.3.3 Sentinel Surveillance

Sentinel surveillance occurs among a group of healthcare facilities or settings (or other reporting entity) selected to report cases of a specific disease. This is in contrast to population-based surveillance, which collects data across an entire population. In sentinel surveillance, reporting occurs from only a carefully selected group of healthcare facilities. It is typically used when population-based surveillance is not feasible or practical. Healthcare facilities selected should have a high probability of seeing cases of the disease under surveillance, as well as clinical expertise and laboratory capability needed to detect the disease. Data collected can be used to monitor trends and disease burden, and if facilities selected are most likely to see the disease, can also be used to detect emerging diseases. Emerging diseases can be missed if they occur outside the sentinel system.[29] Sentinel surveillance has been used for AR pathogens in limited circumstances, such as AR pneumococcal disease[30] and has the potential to be applied in other situations as well.

2.2.2.3.4 Syndromic Surveillance

Syndromic surveillance was developed in the context of a need for the early detection of a large-scale release of a biologic agent. Since that time, it has been used for a variety of surveillance activities, often short-term event-based surveillance, although it is also used for sustained surveillance activities.[31] Syndromic surveillance definitions rely on a constellation of symptoms (i.e., “syndrome”) for reporting. For this reason, syndromic surveillance is a sensitive, but not specific, surveillance system. Since HAI/AR surveillance relies heavily on a laboratory component, syndromic surveillance is not often used in HAI or AR pathogen surveillance. Jurisdictions that perform syndromic surveillance could consider how such systems might complement or enhance their standard approaches to healthcare-related outbreak detection.

2.2.2.3.5 Regulatory Monitoring Systems

Public health communicable disease staff should consider working with regulatory partners to understand their unique surveillance systems and reporting requirements. Regulatory partners, including state licensing agencies and CMS at the federal level, typically have systems in place to receive reports of adverse events; information gathered through these systems can help to identify risks for communicable diseases in healthcare settings. For example, starting in 2016, CMS issued expanded guidance requiring accrediting organizations and state survey agencies to report serious infection control breaches to state health departments.[32] In addition, agencies and professional boards that receive reports of drug diversion events record these in systems that ideally could be used by public health communicable disease staff to identify situations needing investigation to assess patient infection risks.

2.2.2.3.6 Administrative Databases

Some jurisdictions have access to administrative databases, such as hospital discharge databases, that can be used for surveillance purposes, including case finding. These types of databases might be used to supplement other surveillance systems, such as comparisons with population-based or facility-based systems to ensure complete case finding.

2.2.3 Impact of Advances in Laboratory Methods on HAI/AR Surveillance

The progress of microbiological and molecular testing technology over recent decades has dramatically impacted HAI/AR surveillance. Advances in testing have led to increased detection of specific organisms of interest to public health, as well as to healthcare facilities implementing specific infection control measures to prevent transmission. Over the years, the expansion and refinement of DNA-based molecular techniques such as pulsed-field gel electrophoresis (PFGE), PCR typing, and multilocus sequence typing (MLST) have been applied to the surveillance of healthcare-associated pathogens, enhancing case detection and the detection and investigation of outbreaks.

Most recently, the use of PCR typing to identify resistance mechanisms and organisms has had a significant impact on public health activities. Surveillance of carbapenem-resistant organisms relies on the detection of carbapenemases to identify cases of the highest public health import, and with the advent of the AR Lab Network, CP-CRE can be quickly identified, which assists epidemiologists in a rapid response to prevent spread. In some jurisdictions, CP organisms might be the only carbapenem-resistant organisms reportable, which relies on advanced laboratory testing for detection. Screening of patients for AR organisms as part of the containment response also relies on PCR typing. Perhaps the most significant advancement has been the use of WGS, which can detect differences among organisms down to the single nucleotide. The application of WGS to surveillance data in real time can identify related organisms and outbreaks, and when coupled with epidemiologic data can pinpoint the spread of organisms through healthcare and community settings. Although WGS is not widely applied to healthcare-associated pathogen data yet, it is likely to play a big role in the future.

Another area of laboratory advancement is the increasing use of culture-independent testing (CIDT) in healthcare settings, often as a part of a panel of tests. CIDT is performed directly on clinical material, leading to identification of organisms and mechanisms without the availability of an isolate. Positive CIDT results (e.g., *Klebsiella pneumoniae* carbapenemase [KPC], MRSA, vancomycin-resistant *Enterococcus* [VRE], *C. difficile*) without an accompanying isolate provide a challenge to public health when outbreaks are detected, as isolates are not available on which to perform additional identification and typing for case linkage.

CDC laboratory protocols for the detection of antimicrobial resistant and healthcare-associated pathogens can be found here: https://www.cdc.gov/hai/settings/lab/lab_settings.html.

2.2.4 Quality and Usefulness of Surveillance Data

2.2.4.1 Uses of Surveillance Data

Surveillance data can be used to examine long-term patterns and trends of HAIs and AR organisms, as well as to identify sudden changes in disease occurrence that might signal an outbreak or infection control breach that needs investigation. Public health and healthcare partners can rapidly respond to individual cases of high-consequence organisms, leading to immediate infection prevention interventions to prevent transmission. When additional epidemiologic information is collected on cases, data can be used to characterize groups at greatest risk for a disease, informing prevention efforts. HAI surveillance data can indicate specific facilities that might need additional support to prevent infections. Data can help identify prevention priorities and provide information for resource allocation, including for future prevention of disease and effectiveness of prevention efforts over time. Analyzed data provides information to generate hypotheses and determine further in-depth studies.

2.2.4.2 Completeness and Quality of Data

Although national, state and territorial, and local capacity for detection and surveillance of HAIs and AR organisms has improved considerably in the past decades, surveillance of every case is incomplete for several reasons:

1) HAI definitions might not be uniformly applied and are subject to human error;
2) HAIs might not be identified post-discharge;
3) HAIs identified post-discharge (regardless of whether or not identified by another facility or in the community) might not be reported;
4) Patients and community residents might be colonized with an organism that is not detected, and therefore cases go unrecognized;
5) Not all types of infections can be diagnosed with routine laboratory testing; and
6) Laboratories and health-care providers may fail to report to a public health agency.

The scope of possible under-reporting for population-based healthcare-associated pathogens is unknown. Since the syndromes, as well as the signs and symptoms, of infections can be quite varied even for a specific pathogen, and asymptomatic colonization is often included in pathogen-based surveillance, it is challenging to determine what proportion of cases are missed. It can be helpful to ensure complete reporting with validation consisting of laboratory audits or requesting line lists of all cases periodically to compare with reported cases. Electronic laboratory reporting can also help with data quality when reporting systems are evaluated for completeness of reporting.

It is worth noting that HAIs reported to NHSN are validated in some jurisdictions to enhance data completeness and quality. Validation usually includes systematic identification of facilities and medical records for review, comparison to other data sources when available, and review of facility processes for reporting. CDC provides guidance to public health departments embarking on validation efforts, found here: https://www.cdc.gov/nhsn/validation/index.html. Healthcare facilities can also perform their own validations, and CDC guidance for facilities can also be found on this website. Errors identified by such validations (in particular under-reporting) indicate that validations can be critical for accurate HAI reporting, although validations undertaken by public health are resource intensive, and require staff expertise and time to perform validations.[33,34]

2.3 Trends in Outbreak Detection and Response

Improvements in HAI/AR surveillance and expansion of public health HAI/AR programs have increased the detection of and capacity to respond to healthcare-related outbreaks. For example, $85 million of increased funding to 55 state/local public health agencies as part of domestic Ebola response activities in 2015 led to improvements among state and local HAI/AR programs including staffing for outbreak response (96% of funded programs hired additional staff for this purpose), on-site infection control assessments (83%), investigative tool development (78% developed new tools), and outbreak-related laboratory capacity (91%).[18] The context of improved outbreak detection and response includes novel and non-traditional medical care leading to new healthcare infection risks; shifting healthcare settings for patient care, primarily toward outpatient care; increased funding for public health HAI/AR programs leading to increased expertise in outbreak response, infection control, AR containment, and antimicrobial stewardship; increased capacity of public health and clinical laboratories to detect organisms of public health interest and provide advanced laboratory testing such as molecular methods; and increasing collaboration among public health, healthcare facilities, and partners. The novel SARS-CoV-2 virus pandemic, still underway at the time of this writing, has had, and will continue to have, an enormous impact on public health and healthcare systems, the full scope of which is not yet known. As this field continues to evolve, collaboration among public health and healthcare remains critical to the success of outbreak response.

As more experience is gained, the understanding of the scope of the wide variety of outbreaks that might be investigated by HAI/AR public health programs is also emerging. Healthcare settings are widely variable in the type of care delivered, patient susceptibility to infections, infection risks, and infectious pathogens likely to be present. As noted above in section 2.1.1.1, healthcare settings range from acute care hospitals with broad variability among internal care locations (e.g., operating rooms, neonatal intensive care units, oncology wards, burn units), long-term care facilities, as well as a diverse array of outpatient facilities covering everything from acupuncture clinics to ambulatory surgery centers.[10] Outbreaks can be related to medical products, encompass multiple facilities and healthcare settings, span healthcare and community settings, or result from drug diversion and other unique circumstances. A vast number of agents have been implicated in HAI transmission scenarios; these include a constantly evolving list of bacteria, fungi, viruses, parasites, and prions. HAI outbreaks can be caused by pathogens that are common in the community or by pathogens that are rarely observed outside of healthcare environments and specific patient populations.[4] Health department tracking of healthcare outbreak response activities is relatively new and still evolving. One recent assessment found 6665 response activities were recorded by health departments in calendar year 2016 with the majority (78%) involving long-term care facilities.[18] Much of this routine outbreak response activity pertains to investigation and control of gastrointestinal and influenza-like illnesses in nursing homes. Superimposed on this baseline, we see a wide range of more complex and challenging healthcare outbreak response activities.[35-40]

2.3.1 Modes of Transmission

Classically, outbreaks have been characterized based on the mode of transmission using terms such as point-source or person-to-person. Often the pathogen identified provides a clue as to the most likely method of transmission. For example, a group A *Streptococcus* outbreak is more likely to be person-to-person, whereas an unusual pathogen identified in a cluster of bloodstream infections across multiple healthcare facilities is more likely to be point-source. In healthcare-related outbreaks, person-to-person is often the most common, and can occur from patient-to-patient directly, patient-to-healthcare worker and vice versa (often resulting in patient-to-patient spread), and person-to-person via contamination of the environment or shared equipment. Infection control breaches are usually the cause of person-to-person spread within healthcare facilities. Point-source outbreak examples include contaminated medical equipment or medical products including medications and devices (including situations where contamination occurs at the point of manufacture, the point of distribution, or within the facility), and environmental point sources (such as *Legionella* contamination of a water feature, *Aspergillus* spread via air handling breaches, or mold contamination of hospital linens). The physical environment in healthcare settings is an important source of pathogen transmission that can result in infection or colonization; the environment can be conducive to certain pathogen types (such as molds or hydrophilic bacteria in sink drains or ice machines), and human interactions with the environment can result in transfers of pathogens between a healthcare worker or patient and environmental surfaces.

In some cases, point-source and person-to-person transmission can overlap, for example when a healthcare worker with group A *Streptococcus* colonization spreads infections to patients during the course of wound care or peripartum care or delivery. Likewise, a healthcare worker infected with a bloodborne pathogen (HIV, hepatitis B, hepatitis C) can spread their infection to patients when diverting medications (usually opioids as a result of reusing or tampering with medications and injection equipment. A thorough epidemiologic investigation is needed to identify a healthcare worker as a possible point-source, as this situation needs to be handled delicately in close collaboration with the healthcare facility.

It is also helpful to keep in mind that pseudo-outbreaks can also be identified; pseudo-outbreaks are important to investigate and are discussed more in Chapter 5.

Early in an investigation, investigators should consider all possible sources and modes of transmission when forming hypotheses and organizing data collection.

2.3.2 Outbreak Types Based on Etiology

The specific pathogen(s), along with type of infection, body site, and relationship to procedures, provide clues to investigators about possible modes and sources of an outbreak, as well as potential control measures that can be implemented even prior to investigation completion. Consideration of the following outbreak types, along with modes of transmission described above, and healthcare setting described below, early in the investigation can assist with hypothesis generation and investigation direction.

2.3.2.1 Based on Pathogen

Most HAI/AR outbreaks are identified based on a specific pathogen cluster. When an increase in a specific pathogen is identified, or a unique, unexpected pathogen is identified, this can indicate a possible outbreak and further investigation is warranted. Suspect a possible outbreak when cases of a specific pathogen are clustered based on epidemiologic links, such as within the same unit, after the same procedure, occur close in time, or when the pathogen is rare enough that it is unlikely to have caused multiple sporadic infections without a common source. In Colorado in 2012, the first identified New Delhi metallo-beta-lactamase (NDM)-producing CRE was found to be part of a larger hospital outbreak during the investigation of a single case.[41]

As laboratory techniques for assessing isolate relatedness have improved, outbreaks have been able to be identified based on specific pathogen characteristics, as illustrated in the example of the NDM outbreak described. Whole genome sequencing (WGS) has allowed for greater discrimination and more accuracy when determining if something is an outbreak or counting cases during an outbreak investigation. The use of WGS for outbreaks of common pathogens, such as group A *Streptococcus*, helps to determine if cases identified are truly part of an outbreak. As WGS becomes used more widely, identification, investigation, and response to outbreaks will improve.

The regional and even global spread of specific pathogens forces public health and healthcare to consider outbreak response not only on a local level but also on regional, national, and global scales. Although public health agencies are unlikely to investigate them as outbreaks, understanding transmission of emerging pathogens provides context for local communities to determine outbreak investigation priorities. What is endemic in one region might be novel upon appearance in another region; public health agencies and healthcare facilities should understand their regional epidemiology as well as the wider epidemiology of emerging pathogens that might enter their region as novel situations. For example, examination of clonal lineages of carbapenem-resistant *Klebsiella pneumoniae* in Europe identified four clonal lineages with high transmissibility within hospital environments and spread among hospitals within a country was more frequent than between countries.[42] This information can be applied to infection prevention priorities within a jurisdiction. Understanding the global spread of *Candida auris* provided context for the emergence of *C. auris* within the U.S., which informed recommendations and guidance for *C. auris* among U.S. jursidictions.[43]

2.3.2.2 Based on Infection Type

Outbreaks based on the type of infection, such as bloodstream infections or surgical site infections, when a pathogen is unknown or when multiple pathogens are involved are less common than outbreaks identified based on a specific pathogen. Although both etiology and infection type are clues to the reason for an outbreak, in some cases both clues might not be available. Other examples of this type include outbreaks of an unknown respiratory infection or an undiagnosed gastrointestinal illness. However, an outbreak based on infection type should be considered when the overall rates of specific infection types are higher than expected or occur within a defined patient population that might be susceptible to certain types of infections, such as patients receiving dialysis or patients undergoing a specific procedure. An example of this type of outbreak was identified in dialysis patients among three hemodialysis facilities during 2015-16 when increases in bloodstream infections due to *Serratia marcescens* and *Pseudomonas aeruginosa* were noted. The cause was noted to be pooling and regurgitation of waste fluid at the recessed wall boxes that house connections for dialysate components and the effluent drain located at dialysis treatment stations, along with infection control practices that allowed healthcare worker hands to become contaminated at the wall boxes.[44] Another clue to identifying a mixed-pathogen outbreak can be the type of pathogens involved; in this example, both pathogens frequently contaminate water, and therefore investigation of possible water sources can help direct the course of the investigation.

2.3.2.3 Other Etiologies

Non-infectious etiologies might also result in an outbreak within a healthcare setting and should be investigated with the same investigative steps described in this guidance for infectious disease outbreaks. A good example of a non-infectious condition causing outbreaks needing investigation is toxic anterior segment syndrome (TASS). TASS is an uncommon post-operative inflammatory reaction following eye surgeries involving the anterior segment, such as cataract extraction; the cause is a non-infectious substance that has entered the anterior segment of the eye resulting in toxic damage to intraocular tissues. Investigations of TASS outbreaks have resulted in the identification of poor infection control practices and endotoxin contamination of shared products as possible causes of outbreaks.[45,46] Other examples of non-infectious outbreaks within the healthcare settings include infant morbidity and mortality following intravenous vitamin E,[47] aluminum toxicity following use of dialysis machines with electric pumps with aluminum-containing parts,[48] and carbon monoxide poisoning during surgery related to anesthesia circuits.[49]

2.3.3 Outbreak Types Based on Setting

The specific healthcare or non-healthcare setting of the outbreak has a large impact on the investigation and response. Some healthcare settings are more prone to certain types of outbreaks than others. Additionally, the need for public health assistance among healthcare facilities and facility settings can vary. For example, dialysis facilities are more likely to see bloodstream infection related outbreaks than gastrointestinal outbreaks due to the nature of the healthcare provided. Similarly, nail salons and tattoo parlors are more likely to have outbreaks of skin and soft tissue infections. The changing landscape of healthcare discussed earlier in the chapter impacts the trends of types of outbreaks that occur. Understanding these different settings when investigating HAI/AR outbreaks is crucial to understanding likely risk factors and etiologies.[4] Examples of healthcare settings and types of outbreaks are shown in Table 2.2.

Table 2.2: Outbreak Examples Based on Healthcare Setting (*adapted from: Rasmussen SA, Goodman RA (editors). (2018) The CDC Field Epidemiology Manual. Chapter 18.*[4])

Setting or Procedure	Exposure or risk factor	Pathogens or conditions	Investigation and response considerations
General	Infected or colonized persons (healthcare personnel, patients, visitors); contaminated	Organisms spread by contact (e.g., *Staphylococcus aureus*, AR Gram-negative bacteria, *Clostridioides*	Containment strategies as per CDC guidance*

	environmental surfaces	*difficile*, group A *Streptococcus*)	
General	Serious, high-risk infection control breaches	Bloodborne pathogens (HIV, hepatitis B, hepatitis C)	Consideration for patient notification, including considerations for bloodborne pathogen testing and prophylaxis
General	Contaminated water sources (e.g., sinks, ice machines, whirlpool bathtubs and hydrotherapy locations), aqueous medication preparation areas, or any device that generates mist	Hydrophilic organisms (*Legionella, Pseudomonas, Acinetobacter, Serratia, Stenotrophomonas,* non-tuberculous mycobacteria)	Epidemiologic investigation and infection control assessment focusing on water sources
General/injections	Contamination of medications at the point of production (manufacture or compounding)	Environmental organisms (Gram-negative bacteria, fungi)	Syndromes often reflect the mechanism of transmission (e.g., infections at an injection site)
General/injections	Contamination of medications at the point of delivery (healthcare facility)	Gram-negative bacteria, Gram-positive bacteria, fungi, bloodborne pathogens (HIV, hepatitis B, hepatitis C)	Assessment of injection safety practices
General/injections	Diversion of medications (narcotics, related medications) by healthcare personnel	Bloodborne pathogens (HIV, hepatitis B, hepatitis C)	Assessment of medication safety practices; epidemiologic investigation focusing on healthcare personnel
General/point-of-care (POC) testing involving capillary blood sampling	Reuse of single-patient lancing devices or contaminated monitoring devices	Bloodborne pathogens (HIV, hepatitis B, hepatitis C)	Assessment of infection control practices focusing on blood glucose monitoring or other POC testing
General/surgical procedures	Contamination of surgical wounds from sources: healthcare workers,	Varied, includes environmental pathogens (Gram-negative pathogens,	Assessment of infection control practices related to surgical procedure,

	environment, inadequately sterilized instruments	fungi, mycobacteria), colonized healthcare workers (*Staphylococcus aureus*, group A *Streptococcus*), antimicrobial resistant pathogens	sterilization, and perioperative practices
General/endoscopy	Endoscope reprocessing errors or device design problems that prevent adequate cleaning and disinfection	multidrug-resistant organisms (particularly with duodenoscopes); upper-and lower-respiratory tract infections (e.g., bronchoscopes); pseudo-outbreaks of nontuberculosis mycobacteria	Infection control assessment focusing on endoscope use and reprocessing
Transplant units	Dust exposure or air-handling problems for severely immunocompromised patient populations (e.g., during building construction or renovation)	Fungi including *Aspergillus* and mucormycoses	Review of air handling systems, construction processes; typical scenario is invasive mold infections in a bone-marrow transplant unit
Hemodialysis clinics	Lapses in injection safety, maintenance of dialysis machines, or vascular access care	Bloodborne pathogens bloodstream infections with varied bacterial/other pathogens	Review all dialysis infection control processes
Dental clinics	Biofilm formation in inadequately maintained dental unit waterlines; inadequate cleaning and sterilization of dental surgical instruments	nontuberculous mycobacteria infections; bloodborne pathogens	Review of dental clinic infection control processes, water sources, sterilization practices
Laboratory	Specimen collection, handling, or culture-related activities that might put laboratory workers at risk	Brucellosis, tularemia, coccidioidomycosis, bloodborne pathogens (HIV, hepatitis B, hepatitis C)	Evaluation for unintentional laboratory staff and other healthcare personnel exposures to bloodborne pathogens through

			needlesticks and splashes to mucous membranes; evaluation for tularemia or brucellosis processing
Laboratory	Contamination of microbiological specimens during collection, handling, or culture	Pathogens vary	Pseudo-outbreaks resulting in inappropriate invasive diagnostic procedures, antibiotic prescriptions, or extended hospitalizations

* https://www.cdc.gov/hai/containment/index.html

2.3.3.1 Single-Facility Outbreaks

The most common type of healthcare-related outbreak identified is a single-facility outbreak. This type of outbreak is easier to identify than a multi-facility outbreak. Infection control breaches within a facility can result in person-to-person transmission as well as point-source outbreaks involving shared equipment, supplies, or environmental reservoirs. Infection control lapses are often the cause of single-facility outbreaks. In a review of outbreak investigations occurring in outpatient settings in Los Angeles County, it was found that 16 (57%) of 28 outbreaks were suspected to be due to lapses in infections control.[50] In an example of a point-source outbreak related to lapses in infection control, contamination of laundry with *Rhizopus microspores* (a zygomycete) due to substandard washing, drying, and storage resulted in cases of pulmonary and cutaneous infections.[51]

2.3.3.2 Multi-Facility Outbreaks

Multi-facility outbreaks can result from person-to-person transmission when patients are transferred among healthcare facilities, or from a point-source such as medical product contamination. Multi-facility outbreaks can be challenging to identify, absent timely and complete reporting to public health and recognition of the potential for patient sharing, common healthcare staff providing care across multiple facilities or contamination of a medical product. This type of outbreak is typically identified when public health agencies receive similar outbreak reports from multiple facilities, when public health agencies identify an outbreak across facilities using surveillance or laboratory data, or when a healthcare facility performs its own outreach to other healthcare facilities.

2.3.3.2.1 Local Multi-Facility Outbreaks

Local multi-facility outbreaks are more likely to be due to person-to-person spread related to the transfer of patients among facilities within a jurisdiction. These types of outbreaks often result from the combination of infection control breaches and poor communication between the transferring and receiving facilities. Less common scenarios might include local product contamination when a medical product is locally distributed, such as with a local compounding pharmacy, drug diversion by a healthcare worker that works at multiple facilities, or medical equipment contaminated locally and shared across multiple facilities.

2.3.3.2.2 Widespread Multi-Facility Outbreaks

In some situations, multi-facility outbreaks might be more widespread across multiple jurisdictions, states, or countries. This might occur under circumstances when a pathogen is transmitted across multiple facilities, often related to patients transferring among facilities without facility-to-facility communication and poor infection control practices, or when an outbreak source moves across jurisdictions, such as a healthcare worker infected with a bloodborne pathogen that transmits the infection to patients across multiple healthcare facilities and states,[52] or a contaminated medical product is distributed to a wide region.

As laboratory techniques, public health-healthcare facility relationships, and HAI/AR surveillance have improved over recent decades, the chance of finding an outbreak from product contamination has similarly improved. Reports of large-scale, high profile outbreaks as a result of product contamination have increased in recent years, including outbreaks of fungal meningitis resulting in severe morbidity and mortality[53] and fungal endophthalmitis[54] leading to severe vision complications, both associated with widespread distribution of compounded medications, and an outbreak of invasive *Mycobacterium chimaera* following cardiac surgeries associated with contaminated heater-cooler devices.[55,56] Additional information to assist with the investigation of medical product-related outbreaks can be found here: https://www.corha.org/resources/corha-interim-potential-medical-product-related-infection-outbreak-assessment-questions/.

2.3.3.2.3 Outbreaks Related to International Travel

Outbreaks related to medical care outside the U.S. are included here with other multi-facility outbreaks; oftentimes, these outbreaks are identified following reports from multiple healthcare settings that evaluated and treated patients upon their return to the U.S. These outbreaks might initially be investigated similarly to multi-facility outbreaks. The detection relies on astute clinicians who might recognize that patients with infectious complications following overseas healthcare or procedures might indicate a larger problem. Since this type of outbreak typically manifests with sporadic cases appearing across multiple states, reporting even a single case related to international travel to CDC is critical to outbreak recognition. Medical care as part of international travel may be incidental to an injury or other acute condition. However, increasingly, medical care is itself the impetus for overseas travel.[12] A recent example of an outbreak associated with medical tourism involved Verona integron-encoded metallo-beta-lactamase (VIM)-producing carbapenem-resistant *Pseudomonas aeruginosa* infections; 11 cases occurred among medical tourists who traveled to a hospital in Mexico for bariatric surgery and subsequently presented for care in multiple facilities around the US.[57]

2.3.3.3 Healthcare Facilities as a Sentinel for Community Outbreaks

Similar to the previous section, a healthcare facility such as an acute care hospital might identify a suspected outbreak in which the source is outside their facility. Broadly, healthcare facilities can serve as sentinel sites for detecting outbreaks occurring in the larger community. For example, an emergency room or urgent care center might detect multiple cases of gastrointestinal illness associated with a community setting or event. A healthcare facility might detect an outbreak in an assisted living residence or independent living center, which might not have the capacity to recognize an outbreak. A hospital might detect an outbreak associated with outpatient care, such as multiple infections following a procedure performed in a clinic setting. Healthcare facilities might also experience outbreaks that reflect unique circumstances in the communities they serve.

For example, an outbreak of imipenemase metallo-beta-lactamase (IMP)-producing organisms occurred within a long-term-care facility during a larger community outbreak of extended-spectrum ß-lactamase (ESBL)-producing organisms.[58] Similarly, during a large U.S. outbreak of *Salmonella* Tennessee associated with peanut butter, an outbreak of the same pathogen occurred within a hospital neonatal intensive care unit (NICU) as the result of poor infection control practices; it was postulated that the initial introduction was via a visitor or healthcare worker who acquired *Salmonella* as part of the national outbreak.[59]

2.3.4 Investigation of Serious Infection Control Breaches

The conditions underlying outbreaks are sometimes identified in the absence of identified infections. For some types of infection control breaches, patients might have been exposed to serious risks that might not be immediately apparent. A prime example is the reuse of a syringe for multiple patients, which carries risks for transmission of bloodborne pathogens, which have long incubations and symptoms that can be subtle, variable, or altogether absent. Serious infection control breaches can be identified from internal audits and observations or survey activities conducted by state survey agencies or accrediting organizations. CMS introduced a policy in 2014 that indicates that surveyors who identify serious infection control deficiencies should relay these concerns to public health for evaluation, including considerations for patient notification.[32] Investigations of infection control breaches involve infection control observations, recommendations to the facility to improve practices, and assurance of mitigation of gaps. Increasingly, these situations are being investigated using similar methodology to other outbreak investigations. In some situations, the response to infection control breaches involves notification of patients and their potential risk for bloodborne pathogens or other infections. The investigation and response to infection control breaches, including exposures associated with drug diversion and tampering, are discussed more in Supplement B.

In this chapter we reviewed healthcare settings and healthcare delivery and associated trends, public health HAI/AR surveillance, and trends in outbreak delivery and response. In subsequent chapters, these topics will be applied to outbreak detection and response and will be explored in greater depth.

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