Research Gaps in Patient and Healthcare Personnel Safety

Priority Research Questions to Drive Improvements

From CDC's Division of Healthcare Quality Promotion (DHQP) | **2024**

CDC
U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

A Foreword from Acting Director, Mike Bell, MD

CDC wants zero healthcare-associated infections (HAIs) in the United States. Many say it's impossible. After supporting more than 160 public and private organizations and investing more than $500 million in innovative solutions for health care since 2016, we're closer than we've ever been. But for the 1 in 31 hospital patients and 1 in 43 nursing home residents who have at least one HAI on any given day, there is still so much important work to be done.

Finding innovative solutions for patient and healthcare worker safety is a primary driver for CDC and my division, the Division of Healthcare Quality Promotion (DHQP). We began CDC's Prevention Epicenters Program in 1997 as a way to work directly with a network of academic medical centers to address important scientific questions regarding HAIs, antimicrobial resistance, microbial ecology, and other healthcare-associated adverse events. We have expanded these investments through the Antimicrobial Resistance Solutions Initiative, growing networks of research collaborators like CDC Prevention Epicenters, Modeling Infectious Diseases in Healthcare (MInD Healthcare), Safety and Healthcare Epidemiology Prevention Research Development (SHEPheRD), and Project Firstline.

Through world-class data and expert research, we've continued to champion innovation while responding to outbreaks, a pandemic, and a changing healthcare workforce. Our collaborations have resulted in new prevention approaches (like the use of chlorhexidine to prevent infections), uncovered new pathogen reservoirs (like sink drains in patient rooms), and answered mysteries at the molecular level (like disease markers for *C. difficile* infections). These advances are wonderful, but there's more to be done.

We know that future research will help us continue this progress, as well as prevent infections that we can't prevent just yet. We hope this list of unanswered questions will improve safety and quality in health care in the next 5 years and will drive progress against threats like HAIs, antimicrobial resistance, and sepsis. We're hopeful that researchers and partners will join us in accelerating this critical science and investing alongside the agency for patient and healthcare worker safety, using this list to inform decisions such as grant funding and strategic planning.

Thank you all for your dedication and contribution as we work together to ensure safe health care and continue to extend the impact of our work around the world.

Mike Bell, MD
Acting Director
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention

Contents

4 Background

6 Research Gaps for Epidemiology and Drivers of Infections and Antimicrobial Resistance

6 Microbial ecology/microbiome
7 Determinants of infection and transmission
8 Healthcare personnel

9 Research Gaps for Health Equity

10 Research Gaps for Prevention of HAIs and Associated AR

10 Built environment
11 Antibiotic use and stewardship
12 Pathogen reduction
12 Pathogen transmission
12 Microbial assessment
12 Economic analyses and long-term care
13 Non-ventilator associated pneumonia
13 Prevention effectiveness

14 Research Gaps for Surveillance, Data, and Metrics

14 Outbreak detection and forecasting
15 Surveillance methods in low- and middle-income countries
15 Wastewater surveillance
16 Advancing quality measurement
17 Applied genomics

Suggested Citation: CDC. Research topic areas and questions for the understanding and prevention of healthcare-associated infections, associated antimicrobial resistance, and healthcare personnel harms: Priorities of the Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, 2024. Atlanta, GA: U.S. Department of Health and Human Services, CDC; 2024.

Background

This report is intended to help investigators, funders, state and local health departments, and patient advocates understand key priority research questions for health care.

The prevention of healthcare-associated infections (HAIs) and antimicrobial-resistant (AR) infections is a mixed story of progress and setbacks with a long path ahead. Until 2019 there was progress from earlier in the decade in reducing several device- and procedure-related HAIs, including central line-associated bloodstream infections (CLABSIs), catheter-associated urinary tract infections (CAUTIs), and major surgical-site infections, all of which are important causes of patient harm, including sepsis, and death. In addition, from 2012 through 2017 there were decreases in five of seven HAI-associated antimicrobial-resistant bacterial pathogens; however, from 2017–2019, progress in the declines of three of these pathogens stalled. Moreover, beginning in 2020, and continuing in 2021, there was a reversal in progress with COVID-19-related increases in CLABSIs, CAUTIs, and methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia events. There were also increases in six of the seven HAI-associated antimicrobial-resistant bacterial pathogens. In addition, the COVID-19 pandemic severely threatened the safety and well-being of healthcare personnel in ways never witnessed previously. Finally, the COVID-19 pandemic highlighted longstanding public health and infection-related disparities. While disparities in HAI and associated AR, and healthcare personnel safety, are known to exist, they are woefully under-studied and remain largely unaddressed.

DHQP's healthcare RESEARCH and INNOVATIONS have resulted in:

More than **$500 million** invested since 2016.*

**Work supported through CDC annual appropriations and emergency supplemental funding. Learn more about these investments: https://ARinvestments.cdc.gov/*

600+ funding awards for healthcare-centric projects with **160+ partners** in the U.S. and around the world.

Networks of research collaborators, including CDC Prevention Epicenters, Modeling Infectious Diseases in Healthcare (MInD-Healthcare), Safety and Healthcare Epidemiology Prevention Research Development (SHEPheRD), and Project Firstline awardees.

DHQP's investments have resulted in public health advances such as:

- Assessing the impact of enhanced disinfection strategies, such as UV light emitters, on pathogen transmission from patient rooms.[1]
- Estimating the burden of sepsis in the United States for the first time to drive advances and reduce incidence.[2]
- Uncovering potential disease markers for *C. difficile* infections to aid clinical diagnosis, treatment, and preventing transmission.[3]
- Improving treatment for patients with cystic fibrosis by studying their lung microbiomes.[4]
- Installing specialized inkjet printers in public health labs nationwide to provide on-demand susceptibility testing for new antibiotics.[5]
- Establishing a network of nursing homes in 8 states to rapidly characterize infectious diseases in residents and staff to inform infection prevention and control strategies.[6]
- Identifying contaminated sink drain P-traps in patient rooms as possible modes of transmission in healthcare facilities.[7]
- Reducing unnecessary antibiotic use by testing patient-tailored computerized prompts that calculate a patient's risk for antimicrobial-resistant infections.[8]
- Using mathematical modeling to assess the potential effectiveness of different interventions to stop the spread of germs in intensive care units.[9]
- Establishing the Healthcare-Wastewater Antimicrobial Network (H-WARN) to detect antimicrobial resistance threats in healthcare facility water.[10]
- Using virtual reality to educate healthcare workers on infection prevention topics, including hand hygiene in neonatal intensive care units, reprocessing shared equipment, and ordering of nursing tasks to reduce contamination.[11]

At CDC, DHQP conducts and funds research and innovation designed to address HAIs and AR that are potentially preventable but lie beyond the reach of current prevention strategies.

The Division of Healthcare Quality Promotion (DHQP), CDC, conducts and funds research and innovation designed to move beyond the HAIs and associated AR pathogens already prevented, to those not yet prevented but potentially preventable, and those that lie beyond the reach of current prevention strategies.

This report is intended to help investigators, funders, state and local health departments, and patient advocates, understand some of the key priority research questions that exist in late 2023. We believe that answers to these questions will help the nation and world make important progress in protecting patients and healthcare personnel. This is not a comprehensive list of all research questions that DHQP considers important to advance patient and healthcare personnel safety. Instead, these priorities reflect a federal public health perspective intended to maximize returns on investments made in the next 1–3 years, to achieve actual prevention in 4–5 years. We believe that addressing these questions will reduce infections and resulting complications, like sepsis, and, save lives. It should also be noted that while there are some questions included that specifically focus on health equity, we believe that many of the questions set forth here have important health equity considerations.

In partnership with, 1) Duke University and University of North Carolina; 2) Harvard University; 3) Washington University; 4) Georgia Institute of Technology; 5) HP Inc.; 6) Ohio, Rhode Island, Georgia, Maryland, Michigan, Oregon, Pennsylvania, and Wisconsin; 7) University of Virginia; 8) University of California, Irvine and Harvard University; 9) The University of Utah; 10) The University of Utah, Rush University Medical Center, as well as collaborators in the Atlanta metro area; 11) Yale New Haven Health System, University of Nebraska Medical Center, Massachusetts General/Brigham, Emory University.

Research Gaps for Epidemiology and Drivers of Infections and Antimicrobial Resistance

Microbial ecology/microbiome

Recent advances in the use of advanced molecular detection including high throughput biological analyses have opened a window to understanding dynamic interactions between antimicrobial-resistant HAI pathogens and the human host. Through these early insights, it is clear we need to further understand and apply emerging scientific fields of study to prevent antimicrobial-resistant HAIs in the context of colonization as well as the natural resistance to colonization and infection afforded by the intact human microbiome.

Questions in this domain include:

- What is the natural history of colonization and infection with an antimicrobial-resistant pathogen in different populations or communities, how is the natural history affected by socioeconomic factors, and what is the role of microbiota-based interventions or novel approaches (such as phage and other decolonizing agents, vaccines) in reducing microbial load of colonization, risk for colonization, or risk for infection with antimicrobial-resistant pathogens? For example:
  - What is the association between cumulative antibiotic exposure (e.g., over the prior year) and risk of sepsis, antimicrobial-resistant infection/colonization, and *Clostridioides difficile* infection (CDI)?
  - What are determinants of colonization duration?
  - What are risk factors for progressing from colonization to infection?
  - Does decolonization or reducing the burden of colonization with a particular antimicrobial-resistant pathogen prevent transmission and/or infection and infectious complications like sepsis?

Photo Credit: CDC's Public Health Image Library

- Are there interventions, e.g., live biotherapeutics, that reduce the risk of colonization with antimicrobial-resistant pathogens?
- Are infected persons more effective vectors of antimicrobial-resistant pathogens than colonized persons?
- What changes in pathogen burden and/or infection risk can be used to assess and compare the impacts and efficacy of decolonization agents in studies supporting FDA approval?

- What are methodologies for colonization screening (e.g., environmental testing, passive surveillance for clinical isolates, active screening through collection of stools or rectal swabs) that will drive prevention in healthcare facilities that have high rates of colonization/infection with antimicrobial-resistant pathogens?
- What are the best approaches to adapt culture-dependent and -independent diagnostic methods to environmental sources and associated animal vectors that may drive rates of community-associated or -onset infections?
- Is point-of-care testing for targeted multidrug-resistant pathogen colonization possible and implementable?

Inpatient healthcare settings provide a 'perfect storm' for transmission.

Determinants of infection and transmission

Transmission is a foundational driver of antimicrobial-resistant HAI pathogen spread and infection rates. Modern healthcare settings, especially inpatient healthcare settings, provide a 'perfect storm' for transmission with the proximity of highly contagious and vulnerable patients, cared for in highly complex clinical environments. Meanwhile, increasing rates of infection due to antimicrobial-resistant pathogens in community settings provide increasing pressure for transmission in healthcare delivery settings.

Questions in this domain include:

- What are the determinants of infection/pathogen transmission (e.g., ESBL-producing Enterobacterales, *C. difficile,* MRSA) in different community and healthcare settings?
- Why are rates of selected community-associated AR infections (e.g., ESBL-producing Enterobacterales) increasing?
- How does the prevalence of antimicrobial-resistant pathogens in the community influence rates of HAI/AR infections and infectious complications, like sepsis in healthcare facilities?

Photo credit: Tolu Jethro Bade, Envizage Concepts

Healthcare personnel

The COVID-19 pandemic caused unprecedented strain on individual healthcare workers as well as health systems and demonstrated the inextricable link between healthcare personnel and patient safety.

Questions in this domain include:

- What workplace-associated events or conditions pose the greatest threat to the safety and well-being of healthcare personnel?
- How do we measure and track workplace-associated adverse events in healthcare personnel?
- What are the effects of healthcare personnel staffing levels and burnout on healthcare personnel safety?
- What are the optimal staffing ratios and combinations of personnel types that allow sustained effective care delivery in the various settings where health care is delivered?
- How do factors that affect healthcare personnel safety and well-being, such as staffing level and burnout, affect patient safety?
- How do we reduce or eliminate workplace-related conditions or events that threaten the safety and well-being of healthcare personnel?
- What are better, more effective, cost–effective, acceptable, and feasible ways to train frontline HCP domestically and in low- and middle-income countries (LMIC) on IPC practices?

Photo Credit: FatCamera / E+ via Getty Images

Research Gaps for Health Equity

Research priorities should include health disparity considerations.

Although several topics are listed here, nearly all the other topic areas that are part of this priorities list include health disparity considerations that should be addressed. Nonetheless, specific stand-alone priority areas include the following.

Questions in this domain include:

- What is the relative contribution of individual-level (e.g., poverty) versus facility-level (e.g., receiving treatment at an under-resourced facility) socioeconomic characteristics to the risk of developing a healthcare-associated infection or infection with an antimicrobial-resistant pathogen?
- Do healthcare facilities located in areas with higher social vulnerability have higher rates of infection/colonization with antimicrobial-resistant pathogens and/or higher rates of AR than facilities in areas with lower social vulnerability?
- What specific sub-populations (e.g., race/ethnicity, disability status, sex) or conditions (e.g., payor/insurance status, rurality, poverty, etc.) are more likely to experience worse outcomes for example, sepsis, from healthcare-associated infections and/or infections with resistant pathogens?
- What are individual-level (both patient and clinician) characteristics and modifiable factors (drivers) associated with health disparities in antibiotic prescribing quality across the spectrum of care?
- How should health equity considerations be incorporated into antibiotic stewardship implementation?

Research Gaps for Prevention of HAIs and Associated AR

Photo Credit: CDC Project Firstline

History has shown repeatedly how many HAIs that were previously thought to be inevitable could be prevented, once proven strategies were implemented in a consistent manner, facilitated by sound guidance and clinically meaningful measurement. Thus, building the evidence base for the strategies to prevent HAIs and associated AR is foundational to realized prevention.

Built environment

The buildings in which modern health care is delivered constitute the patient care environment. This includes all fixtures and furniture, the water supplied and drained away, even the air circulated down corridors and hallways and into patient and procedure rooms. These environments can either promote or interrupt effective care, and can become contaminated, either from pathogens that usually colonize and infect patients, or more environmental-adapted organisms that can fill the role of opportunistic pathogens.

Questions in this domain include:

- What are design and organizational factors that make it easier for healthcare personnel to take correct actions?
- Are there ways to engineer the built environment to reduce risks of pathogen contamination and transmission?
- Are there ways to change processes of care to reduce the risks of environmental contamination and pathogen transmission?
- What are approaches that will best enhance our understanding of pathogen persistence and survival in healthcare environments (including surfaces, fomites, and water/wastewater systems) to inform transmission risks?

Antibiotic use and stewardship

Antibiotic use is the other foundational driver of antimicrobial-resistant HAI pathogen spread and infection rates. Great strides have been made in making antibiotic stewardship a common resource both across hospitals and many other patient care settings. Meanwhile, the measurement of antibiotic use has advanced, and yet more can and needs to be done in both areas.

Questions in this domain include:

- What are the most effective, cost–effective, acceptable, and feasible strategies to reduce inappropriate use and overuse of antibiotics in low- and middle-income countries in acute care settings (e.g., prospective audit and feedback, pre-approval authorization, retrospective audit)?
- What are the clinical outcomes among patients with COVID-19 who received antibiotics compared to those who did not?
- What are ways to expand best practices and implement interventions to improve antimicrobial prescribing by high prescribers and/or in high-prescribing settings?
- What are ways to use the National Healthcare Safety Network (NHSN) data on antimicrobial use, resistance, and infections to inform, implement, and assess stewardship interventions?
- Which antibiotic stewardship interventions are most effective in reducing colonization or infection with multidrug-resistant pathogens?
- Which antibiotic stewardship interventions are most effective in reducing other antibiotic-related adverse events?

Photo Credit: SDI Productions / iStock / Getty Images Plus via Getty Images

Pathogen reduction

Pathogen reduction involves the use of agents that decolonize patients to various degrees, whether it be in the human gut, nasal, oropharyngeal, or skin sites. Early evidence suggests it is a promising strategy for both preventing infection in the recipient and preventing transmission.

Questions in this domain include:

- Is there a way to modify the microbiome to reduce the risk of colonization with multidrug-resistant organisms pathogens?
- Which products and strategies for pathogen reduction are most effective in reducing colonization or infection and infectious complications like sepsis with multidrug-resistant pathogens?

Pathogen transmission

Hand hygiene by healthcare personnel, environmental cleaning, correct reprocessing of shared devices, and selective use of isolation including cohorting and barrier precautions (i.e., gloves, gowns) remain the primary proven tools for preventing transmission, and yet are difficult to implement and can have low levels of personnel and patient acceptance.

Questions in this domain include:

- How long do specific pathogens retain infectivity when suspended in air of varying humidities and temperatures?
- What is the optimal air quality in various parts of healthcare facilities to reduce transmission of respiratory infections?
- What is the most ideal implementation and prioritization of current tools (e.g., hand hygiene, barrier precautions, masking, environmental cleaning) to prevent transmission of pathogens within and between healthcare facilities, considering clinical effectiveness, cost, acceptability of the intervention to different patient and clinician communities, and ease of implementation? For example, are there circumstances where gowns do not add significant value to gloves and/or hand hygiene in preventing transmission? Or are there better ways to implement barrier precautions that would reduce transmission?

Microbial assessment

Advanced molecular detection has much to offer prevention of HAIs and AR, and yet still needs to be further tailored to meet the unique needs in this area.

Questions in this domain include:

- What are the optimized culture-dependent and culture-independent microbial community analysis methods to improve pathogen detection and inform infection prevention and control measures?

Economic analyses and long-term care

Although primary prevention typically offers great economic value, demonstration of this value is critically important in an era of rising costs with constrained resources.

Questions in this domain include:

- What is the cost-benefit relationship between different practices to prevent MDRO transmission (pathogen burden reduction vs. enhanced barrier precautions and other transmission-based precautions) in long-term care settings?
- What are the most effective reimbursement or incentive methods to financially support implementation of infection control in long-term care settings?

Non-ventilator associated pneumonia

Pneumonia is a major threat to patient safety in hospitals and other healthcare facilities and can contribute to significant patient harm, including sepsis. Most research has focused on preventing pneumonia associated with mechanical ventilation; however, data show that non-ventilator-associated pneumonia is a more common cause of patient harm, and less is known about how to prevent these infections.

Questions in this domain include:

- What are the risk factors and microbial causes that account for the greatest etiologic fraction of non-ventilator associated pneumonia in U.S. hospitals and long-term care settings?
- Based upon increased understanding of major risk factors and microbial causes, what is the best way to prevent non-ventilator-associated pneumonia in hospitals, taking into account clinical effectiveness, cost, acceptability of the intervention to different patient and clinician communities, and ease of implementation?

Prevention effectiveness

Prevention effectiveness is the systematic assessment of the impact of public health policies, programs, and practices on health outcomes by determining their effectiveness, safety, and costs.

Questions in this domain include:

- How can bundled implementation science be modeled to determine relative contributions of each component?
- What are the individual and relative contributions of specific interventions in IPC bundles (e.g., colonization screening, PPE, environmental cleaning)?
- What are the highest impact interventions in IPC bundles?
- What are the cost and reimbursement barriers to the implementation of infection control and healthcare personnel protections in outpatient, residential care, and home health settings?
- What is the prevention effectiveness of regular implementation of masks for source control of respiratory pathogens for different groups (i.e., patients, HCP, or both) during respiratory virus season on absenteeism, HCP infections, and hospital-acquired viral respiratory infections?

Photo Credit: FatCamera / E+ via Getty Images

Research Gaps for Surveillance, Data, and Metrics

Spanning traditional public health surveillance, a rapidly evolving healthcare IT landscape, and advanced genomics, the available tools for measuring the challenging complexities of HAIs and evolving AR are growing. Yet key questions remain to realize and coordinate the benefits of these tools.

Outbreak detection and forecasting

Although HAI and AR outbreaks, as well as changes in their epidemiology, remain primarily detected by clinical observations of increased or unusual/severe cases, modern genomic-based applications has recently demonstrated their ability to anticipate epidemiologic changes of public health importance; for example, ongoing strain characterization of SARS-CoV-2.

Questions in this domain include:

- Can facilities and units at greater risk of specific types of outbreaks be identified in advance?
- What methods can identify transmission events and ecological drivers of disease, such as methods to detect pathogen strain diversity?
- What are ways to use genomics to interpret and stratify laboratory and epidemiological data regarding pathogen trajectories in health care?

Surveillance methods in low- and middle-income countries

Domestic surveillance for antimicrobial-resistant pathogens using data generated from clinical cultures is benefitted by a rather narrow range in the culturing intensity and laboratory proficiency. However, across international settings there can be a much greater range in these factors leading to biased measurements that can undermine surveillance.

Questions in this domain include:

- Taking into account the major variation in diagnostic capacity, what are optimal (e.g., balancing feasibility and value/meaningfulness) surveillance methods for antimicrobial-resistant pathogens (e.g., longitudinal point-prevalence surveys (PPS), rapid repeated PPS, with or without support from regional resources) and HAI definitions in LMIC settings?

Wastewater surveillance

Having long proven its value in polio surveillance, community-wide and healthcare facility wastewater surveillance advanced remarkably during the COVID-19 pandemic. Given how HAI AR pathogens frequently colonize the human gut, there is reason to hope that the benefits of wastewater surveillance can be extended to address AR in HAI pathogens.

Questions in this domain include:

- How can wastewater surveillance for antimicrobial-resistant pathogens be used to improve infection prevention and control in healthcare facilities?
- Does wastewater surveillance for antimicrobial-resistant pathogens help prevent infections with antimicrobial-resistant pathogens in people?

Photo Credit: CDC and The Ohio State University

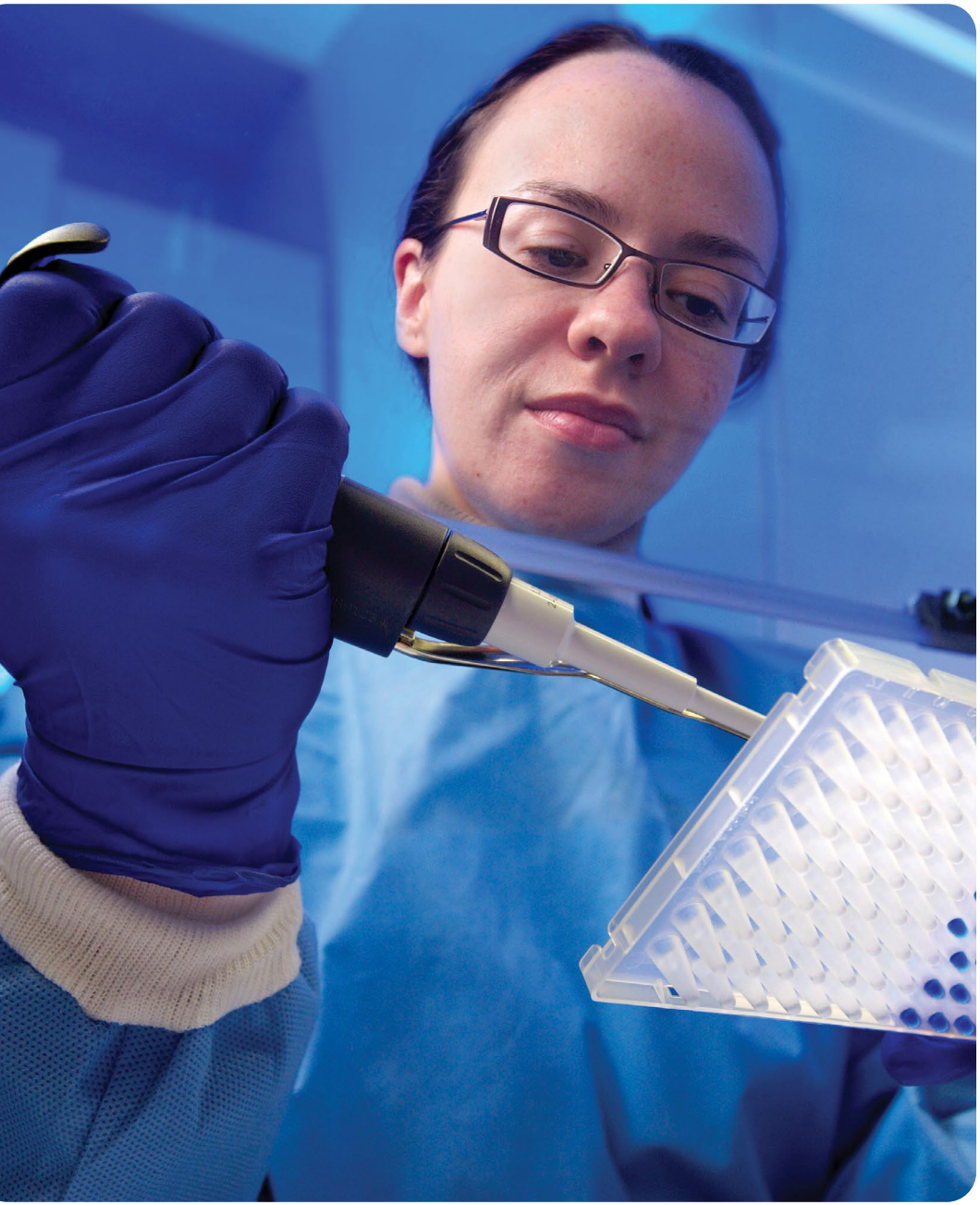

Photo Credit: CDC's Public Health Image Library

Advancing quality measurement

As noted above, previous successes in the prevention of HAIs and associated AR have been made possible by proven prevention practices paired with clinically meaningful measurements. DHQP surveillance systems, working together and supported by payor incentives for reporting and performance, have proven successful and yet require ongoing study to meet the challenges of an evolving healthcare landscape.

Questions in this domain include:

- How do we continue to measure progress in HAI/AR prevention as goals increasingly become tied to quality improvement targets?
- Has the adoption of HAI/AR quality measures improved patient safety and successfully prevented infections, infectious complications like sepsis, or deaths?
- Has the adoption of HAI/AR quality measures reduced disparities in the rates of infections or other HAI/AR-related adverse outcomes for patients based on demographic or socioeconomic characteristics?
- How do we determine which events in health care should be subject to surveillance and/or quality measurement?
- What measurement gaps exist for health equity indicators in DHQP HAI/AR surveillance data?
- How do we evaluate the effectiveness of new or existing surveillance or clinical quality measures?
- How do we determine when a measure is no longer useful for improving patient safety?

Applied genomics

Unlike some public health areas where pathogens are limited to a few species and point sources prevail, the most appropriate application of genomics to HAI and associated AR prevention is much more complex and further study is needed to reach the maximum benefit from this technology.

Questions in this domain include:

- What is the current landscape of genomic applications across clinical health care and public health laboratories?
- What are best practices and standardized approaches for leveraging genomics for HAI/AR outbreaks, surveillance, diagnosis, prevention, and containment in healthcare settings?

For more information, please contact:

Centers for Disease Control and Prevention
Phone: 1-800-CDC-INFO (232-4636)
Web: https://www.cdc.gov/hai/

Publication Date: April 2024

CS 347886-A