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GLOBAL INFECTION PREVENTION AND MANAGEMENT IN HEALTHCARE

VOLUME 2

Infection prevention and control and antimicrobial stewardship

Editors: Massimo Sartelli, Federico Coccolini, Fausto Catena and Leonardo Pagani

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GLOBAL INFECTION PREVENTION AND MANAGEMENT IN HEALTHCARE

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Editors

ISBN: 978-88-943799-3-8
FIRST PUBLISHED on 18 November 2024

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Global Alliance for Infections in Surgery

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Contents

Volume 2

Infection prevention and control and antimicrobial stewardship

Volume 2

Infection prevention and control and antimicrobial stewardship

Chapter 41

Hand hygiene in hospital settings

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Introduction

Hand hygiene in hospital settings is a key element of infection prevention and control that impedes the transmission of Healthcare-Associated Infections (HAIs) among people who work, stay, and even visit the hospital. The most common types of HAIs are bloodstream infection (CLABSI), pneumonia (VAP), urinary tract infection (CAUTI), and surgical site infection (SSI). They are caused by pathogenic microorganisms such as viruses, bacteria and fungi which are often considered as multidrug resistance microorganisms (MDRO).
Infections can spread similarly in community settings; however, they generally do not have the same potential for widespread and result in severe outcomes as in healthcare environments, especially in hospital settings. The hands of healthcare workers can serve as vectors for the transmission of pathogenic microorganisms which can instigate infections among patients, patients to healthcare workers, healthcare workers to patients, and among healthcare workers themselves. Implementing hand hygiene, including regular handwashing is universally identified as the single most important strategy in preventing the spread of infectious agents.
HAIs pose a significant public health challenge. Studies have demonstrated that healthcare workers have considerable difficulties maintaining appropriate hand hygiene compliance. This condition can lead to a higher risk of Healthcare-Associated Infections (HAIs) and their associated morbidity, mortality, and healthcare costs. The high prevalence emphasizes the urgent need for effective infection control measures.
Hand hygiene remains one of the most important interventions for reducing the transmission of healthcare-associated infections in hospital settings, yet many barriers are placed on its full implementation. This paper aims to provide a comprehensive overview of the importance of hand hygiene in hospital settings, the barriers to effective hand hygiene practices, and the strategies to improve the compliance of hand hygiene programs.

The concept of hand hygiene in different settings

Hand hygiene is a broad term that encompasses various methods for cleaning the hands, including the use of soap and water or alcohol-based hand rubs. These practices are essential for removing transient microorganisms that can be acquired through contact with contaminated surfaces, patients, or other sources within the healthcare environment. Contaminated hands can serve as a vehicle for the transfer of pathogenic bacteria, viruses, and fungi which increase the risk of spreading infectious diseases moreover an outbreak.
In community settings, hand hygiene is typically only required before eating, after using the restroom, or when hands are visibly soiled. Multidrug-resistant microorganisms (MDROs) such as methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase (ESBL), and vancomycin-resistant

Enterococcus (VRE) are less likely to be encountered in everyday community environments. Hospitals have a much higher concentration of pathogens including Multidrug-resistant Microorganisms and more vulnerable patients compared to community settings. Hospitals house many patients with active infections and compromised immune systems nearby. Many invasive procedures are performed in hospitals, creating opportunities for pathogens to enter the body. Healthcare workers who frequently move between patients are potentially spreading pathogens if proper hand hygiene is not performed.

Hand hygiene for healthcare workers

WHO Guidelines on Hand Hygiene in Health Care provide a thorough review of evidence on hand hygiene and specific recommendations for implementation. These guidelines are designed to be implemented in all healthcare settings, including hospitals, clinics, and home care. They emphasized the importance of ensuring consistency with their recommendations while allowing for individual adaptation according to local regulations, settings, needs, and resources.

The "Five Moments for Hand Hygiene" framework provides a comprehensive and evidence-based approach to hand hygiene practices in healthcare settings. This framework emphasizes the key points in the patient care process where healthcare workers should perform hand hygiene to interrupt the chain of pathogen transmission and prevent the spread of healthcare-associated infections.

1. **Before touching a patient**. Performing hand hygiene before direct patient contact is crucial to protect the patient from harmful microorganisms that may be present on the healthcare worker's hands.
2. **Before performing an aseptic procedure**. Proper hand hygiene before engaging in aseptic tasks, such as inserting a catheter or dressing a wound, is essential to prevent the introduction of pathogens and ensure a sterile field.
3. **After potential exposure to body fluids**. Performing hand hygiene immediately after any contact with body fluids, or after the removal of gloves, is necessary to prevent the transmission of infectious agents.
4. **After touching a patient**. Hand hygiene after direct patient contact is vital to protect the healthcare worker and prevent the transfer of pathogens to other patients or the healthcare environment.
5. **After touching the patient's surroundings**. Cleaning hands after contact with patient-related equipment or the immediate patient environment is important to avoid the spread of microorganisms.

Hand hygiene technique with hand rub (20 – 30 seconds) steps are the following:

1. Apply a palmful of the product in a cupped hand, covering all surfaces.
2. Rub hands palm to palm.
3. Right palm over left dorsum with interlaced fingers and vice versa.
4. Palm to palm with fingers interlaced.
5. Backs of fingers to opposing palms with fingers interlocked.
6. Rotational rubbing of left thumb clasped in right palm and vice versa.
7. Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa.

Hand hygiene technique with soap and water (40 – 60 seconds) steps are the following:

1. Wet hands with water.
2. Apply enough soap to cover all hand surfaces.
3. Rub hands palm to palm.
4. Right palm over left dorsum with interlaced fingers and vice versa.

5. Palm to palm with fingers interlaced.
6. Backs of fingers to opposing palms with fingers interlocked.
7. Rotational rubbing of left thumb clasped in right palm and vice versa.
8. Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa.
9. Rinse hands with water.
10. Dry thoroughly with a single-use towel

The number of opportunities for hand hygiene depends largely on the process of care provided. Inflating the number of hand hygiene opportunities per hour of care may increase the risk of poor performance. Even if hand hygiene compliance is high, the technique applied may be inadequate. Healthcare workers often fail to cover all surfaces of their hands and fingers and wash their hands for very short periods.

Despite the well-established importance of hand hygiene in infection prevention and control, numerous studies have consistently reported suboptimal compliance among healthcare workers, with adherence rates often falling significantly below the desired levels across various healthcare settings globally. Research has also uncovered variations in compliance rates among different healthcare roles, with nurses generally demonstrating higher adherence compared to physicians and other healthcare workers.

The issue of poor hand hygiene compliance among healthcare workers is a complex and multifactorial problem with various contributory elements. Workload and staffing levels have been identified as significant factors impacting adherence, with studies demonstrating that healthcare workers are less likely to comply with hand hygiene protocols during periods of high workload and understaffing. This association highlights the importance of maintaining adequate staffing levels and managing workloads to enable healthcare workers to prioritize hand hygiene practices.

In addition to workload, the availability and accessibility of hand hygiene supplies, such as soap, water, and alcohol-based hand rubs, also play a crucial role in determining compliance. In resource-constrained settings, the lack of access to these essential hand hygiene products can pose a significant barrier to consistent adherence.

Moreover, the lack of comprehensive training and education programs for healthcare workers has been identified as a major contributing factor to suboptimal hand hygiene practices. Insufficient knowledge and skills regarding proper hand hygiene techniques, the rationale behind the recommended practices, and the importance of hand hygiene in infection control can all negatively impact adherence.

Frequent handwashing and use of alcohol-based hand rubs are essential for infection control in healthcare settings, these practices can have unintended consequences on the skin health of healthcare workers. Repeated exposure to hand hygiene products, particularly handwashing with soap and water, can lead to skin irritation, dryness, and damage to the skin's protective barrier. Some healthcare workers may hold the belief that handwashing with soap and water is superior to the use of alcohol-based hand rubs, even though both methods are equally effective in eliminating a wide range of pathogens when performed correctly.

Hand hygiene for patients

Hand hygiene for patients is a fundamental but often forgotten part of infection prevention within the hospital environment. Patients may contaminate themselves, other patients, visitors, and environmental surfaces with pathogens. Studies have shown that improving hand hygiene compliance among patients may reduce infection rates at the unit level. Vancomycin-resistant enterococci (VRE) and methicillin-resistant

Staphylococcus aureus (MRSA) infection rates have been found to decrease significantly after the intervention of patient hand hygiene.

Patients can be encouraged to practice good hand hygiene and remind the healthcare workers to perform it as well before treating them. Good hand hygiene from the patient improves the second layer to decrease HAIs, making it more rounded in practice. The challenges are similar to hand hygiene for healthcare workers including lack of awareness or knowledge, skin irritation, and inadequate facilities or resources.

Conclusion

Hand hygiene implementation programs are critical and evidence-based interventions that significantly reduce healthcare-associated infections (HAIs) and improve patient safety in hospital settings. Multiple studies have demonstrated that when hand hygiene compliance increases, particularly from already high levels to even higher levels, there is a corresponding decrease in HAI rates. The impact of these programs extends beyond infection reduction. They have been shown to decrease mortality rates, reduce antibiotic use, and generate substantial cost savings.

Importantly, the most effective hand hygiene programs utilize a multimodal approach, as recommended by the World Health Organization (WHO). This strategy includes system change, training and education, evaluation and feedback, reminders in the workplace, and fostering an institutional safety climate. Such comprehensive programs have led to significant and sustained improvements in hand hygiene compliance across various healthcare settings including hospital settings.

Despite the clear benefits, hand hygiene compliance remains suboptimal globally. This underscores the ongoing need for robust implementation programs. Moreover, the COVID-19 pandemic has further highlighted the critical role of hand hygiene in preventing disease transmission, making these programs more relevant than ever.

In conclusion, hand hygiene implementation programs are not just beneficial but essential in hospital settings. They represent a high-impact, cost-effective strategy to significantly reduce HAIs, improve patient outcomes, and promote a culture of safety in healthcare. Healthcare workers should prioritize the implementation and continuous improvement of comprehensive hand hygiene programs as a cornerstone of their infection prevention and patient safety efforts.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 42

How to educate healthcare workers on hand hygiene

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Introduction

Hand hygiene is one of the cornerstones of infection prevention and control (IPC) within healthcare settings and plays a pivotal role in preventing many healthcare-associated infections (HAIs). These infections not only contribute to patient morbidity and mortality but also impose significant financial burdens on health systems globally. The importance of hand hygiene is universally recognised; it is a critical and cost-effective intervention for reducing HAIs and antimicrobial resistance (AMR).

However, adherence to hand hygiene practices among healthcare workers remains suboptimal, and many barriers contribute to this challenge. Within the context of multimodal strategies, hand hygiene practices can be enhanced through education and training initiatives. Evidence evaluating the impact of educational programs has demonstrated improved adherence to hand hygiene practices. Huang observed increases ranging from 16.3 to 24.5 percentage points in the proportion of nurses following hand hygiene guidelines after an educational intervention, whilst those without the intervention showed no change or a decrease of 4.1 percentage points. Higgins noted that hand hygiene adherence increased twofold, from 42% to 84%, following the implementation of an e-learning hand hygiene game intervention in contrast to no intervention.

This chapter addresses the need for comprehensive hand hygiene education for healthcare workers and patients, which is one essential part of improving compliance and, consequently, patient outcomes. By delving into the historical evolution of hand hygiene practices, from Semmelweis's discovery in the 19th century to the development of the WHO multimodal strategy, this chapter explores how practices have been shaped by scientific advancements and behavioural insights and how education can continue to play a role. In doing so, we aim to equip educators and healthcare leaders with the tools and knowledge necessary to foster a culture of safety that prioritizes hand hygiene education, in support of HAI prevention and the establishment of a more resilient health system capable of withstanding future emerging health threats.

Understanding hand hygiene

Many factors influence the causal pathway in the development of HAI. One of them is the absence of hand hygiene at certain critical moments. Hand hygiene can break the chain of infection; it has been acknowledged as one of the cornerstones of IPC programmes and contributes to combat the risk of AMR. Hand hygiene guidelines, tools and an ongoing plethora of research in this area exist to ensure that any touch in healthcare is clean and safe.

If a timeline of hand hygiene improvement advances were to be presented, it would start circa 1847 with Semmelweis's (1818–1865) landmark discovery of the causal association between hand hygiene and sepsis in post-partum women and then jump 150 years to the late 1990s and the seminal work of Didier Pittet in Geneva, who demonstrated the value of a multifaceted approach to improving hand hygiene. The "Geneva model" put a multimodal behaviour change strategy in the context of hand hygiene on the map. Behavioural science informed a shift from unimodal to multimodal for greater chances of success. The most visible part of the strategy was the "talking walls" and placement of alcohol-based handrub at the point of care, but education and training, monitoring and feedback and safety climate also formed key elements.

This history continues to influence present-day guidelines and approaches. In 2009, the WHO published the first global guidelines on hand hygiene in health care that continue to provide definitive guidance for training and education initiatives. In 2017, many of the authors of these guidelines contributed to a new handbook on hand hygiene for medical professionals that provided recommendations based on the latest evidence.

In 2024, training and education are both core components of IPC programmes, and are also solutions to achieving the WHO IPC vision by 2030. Lack of knowledge, suboptimal performance, and poor motivation to undertake hand hygiene can increase the risk of infection.

Guidelines and policies on hand hygiene historically addressed the "what" – what needs to happen to address known barriers and protect people from harm. Indeed, hand hygiene improvement approaches in the last century largely relied on a mantra that could be described as "teach it and they will do it" with training and education relied on as the lever for behaviour change. This changed in the 2000s when informed by a growing body of knowledge, there was acknowledgement that modifying the hand hygiene practices of healthcare professionals is a complex undertaking, influenced by multiple determinants and the importance of the interdependent influences of biology, environment, education, and culture, as well as individual, institutional, and community factors when designing behavioural interventions. The WHO guidelines cited lack of self-efficacy, peer influence, lack of feedback and cues to action, and poor organizational culture as the key characteristics that contribute to suboptimal adherence. The impact of the environment, including the design and lack of supplies that hinder correct health behaviours, was also positioned as a determinant of low compliance. In addition, the guidelines drew attention to reported barriers such as time constraints and the belief that hand hygiene interrupted workflow, perceived skin irritation from products, and complacency and forgetfulness.

Anderson *et al.* have further articulated the barriers, using a human factors lens. These include delayed feedback between the omission of hand hygiene and the consequence in terms of infectious outcome, the lack of connection in the mind of the healthcare worker with a positive result, time pressure and high cognitive workload, the lack of consistent, inbuilt IPC cues and the historical design of the healthcare environment that fails to make it easy to perform hand hygiene at the point of care. The invisibility of microbes in particular has a strong impact on the cognitive aspect of performing hand hygiene and the absence of a visible danger in the mind of healthcare workers contributes to the health behavior problem. All of these aspects should influence health worker training and education.

Ensuring that guidelines move from the 'shelf' to implementation in the real world, therefore requires a behaviourally grounded and evidence-based strategy that targets all of the known barriers.
To recap, the aforementioned multimodal improvement strategy has five elements, one of which is most relevant to this chapter.

1. The infrastructure & resources available to perform hand hygiene, including water, sinks, and hand sanitisers.
2. People are trained in why, when and how for hand hygiene.
3. Checks in place to monitor whether it is being/can be performed at the right time & in the right way & timely feedback so that corrective action can be addressed.
4. Reminding people to perform hand hygiene, at the right time and in the right way.
5. A culture within a care facility that values hand hygiene, especially the support of managers and supervisors.

Any aspect of hand hygiene improvement can be strengthened through the use of a multimodal lens which means systematically asking the following questions.

1. What resources, infrastructures or supplies are required to facilitate optimal practices?
2. Who needs to be trained and/or educated to address the identified gap – how will this happen and who will undertake the training and education?
3. How have you become aware that practices need to be improved – how will you know that an improvement has taken place?
4. How will you publicize action on specific measures and promote improvement and best practices in this area?
5. How will you make and maintain this as a healthcare facility priority and engage senior leaders/managers/champions and opinion leaders over time?

Educational strategies for hand hygiene must be part of broader, multimodal efforts that address diverse barriers, including environmental, cultural, and organizational factors. A singular focus on education alone is insufficient for sustained improvements across healthcare settings. Instead, integrating education with other interventions—such as infrastructure enhancements, monitoring, feedback, and fostering a supportive safety culture—is essential for widespread, long-term change.

Designing an effective hand hygiene education programme

To effectively implement hand hygiene training for healthcare workers (HCWs), a stepwise approach is essential. The process begins with a needs assessment and baseline evaluation to identify current gaps and tailor training to the local context and specific needs of healthcare staff. Practical, participatory training methods—such as incorporating hand hygiene into daily workflows or using role-playing—can reinforce key actions during critical moments of patient care. WHO guidelines provide tools and action plans for facilities at different stages of hand hygiene education, whether starting from scratch or enhancing existing programs. Evaluation through audits, surveillance reports, and ongoing feedback ensures continuous improvement and sustained adherence.
The WHO Guidelines for hand hygiene in healthcare, 2009 highlight that educational interventions should consider cognitive learning, psychomotor, and affective skills, and to work towards including higher levels of

taxonomy such as that by Bloom which deals with synthesis and analysis, as well as lower levels of knowledge, comprehension, and application.

Education for healthcare professionals must be grounded in theoretical frameworks that explain the drivers of behaviour and determinants of sustaining change. These frameworks provide critical insights into what motivates healthcare workers and how to support sustained adherence to best practices. By incorporating these principles, educational interventions can be more effective in promoting hand hygiene improvement and fostering a culture of safety in healthcare facilities learning theories emphasize the need for training that is directly relevant, practical, and engaging. Healthcare professionals are adult learners, meaning that they prefer education that is problem-centred and immediately applicable in the clinical setting, particularly at the patient's bedside. Incorporating real-life scenarios, case studies, and interactive learning activities not only keeps the learners engaged but also helps to build hand hygiene into their automatic behavior for specific clinical situations. This approach ensures that learning is directly connected to their daily responsibilities, enhancing engagement, retention and application of hand hygiene practices in the clinical setting.

Behavioural change models such as the theory of planned behaviour (TPB) are instrumental in structuring education programs. The TPB suggests that intention, influenced by attitudes, subjective norms, and perceived behavioural control, predicts behaviour. In hand hygiene education, this model helps to understand the factors that shape healthcare professionals' decisions to follow guidelines consistently. By addressing beliefs about the importance of hand hygiene and aligning it with organizational norms, the programme can provide a stronger commitment to behavior change.

The health belief model (HBM) can further enhance hand hygiene education by addressing perceived susceptibility and severity. Healthcare professionals may intellectually understand the risks associated with HAIs, but an education programme grounded in HBM would emphasize the personal and professional impact of a lack of adherence to hand hygiene best practices. By highlighting the consequences of patients acquiring HAIs that could arise from non-compliance, educators can instill stronger motivation for change and adherence to hand hygiene guidelines.

The social-cognitive theory, outlines five key elements essential for behavior change: knowledge, goals, expectations, encouragement, and barriers. In the context of hand hygiene, knowledge includes understanding the risks of transmission and understanding the risk-based construct of zones and critical sites and the five moments for hand hygiene

. Goals are the desired outcomes and necessary changes to achieve them, while expectations involve knowing what changes are needed and what will result once they are accomplished. Encouragement provides the support and motivation required to foster behavior change, while barriers represent the obstacles that healthcare professionals must overcome. Bandura's theory emphasizes the role of observational learning and imitation in behavior acquisition. Hand hygiene practices are often influenced by peers, positive deviants and strong and positive leaders. Education programs can leverage this by incorporating role models or peer/team leaders who exemplify best hand hygiene practices. Observing respected colleagues adhering to hand hygiene guidelines reinforces behavioural change, making it more likely to become a part of their routine.

Additionally, social learning theories such as Vygotsky's "zone of proximal development" emphasise the importance of scaffolding in learning. As individuals progress in hand hygiene education, continued guidance ensures they develop the necessary skills before moving to more advanced levels. Maintaining a supportive learning environment is crucial for fostering ongoing improvement.

Effective hand hygiene education must integrate theoretical underpinnings, addressing cognitive, psychomotor, and affective skills while fostering long-term behavioral change through practical, engaging, and context-

specific learning. Combining these educational strategies with behavioral change models and social learning theories ensures sustainable improvement and supports a culture of safety in healthcare environments.

Engaging patients and their loved ones in hand hygiene improvement is crucial, as it supports the overall effort to maintain a safe healthcare environment. By educating patients on hand hygiene, healthcare workers can empower them to not only protect themselves but also to contribute to the adherence to best practices within the healthcare setting.

One effective way to involve patients is through the use of educational materials. When these resources are carefully crafted in plain language, they can significantly improve patient understanding and encourage active participation in infection prevention. This involvement can extend beyond self-care; for instance, where appropriate, patients can be encouraged to observe and provide feedback on healthcare workers' hand hygiene practices, such as compliance with WHO's "Moment 1" (before touching a patient). Even a small act, like thanking a healthcare worker for cleaning their hands, can reinforce the culture of hand hygiene and promote accountability.

For this involvement to be successful, support and encouragement from healthcare workers are essential. Training both patients and staff at the same time to embrace this new collaborative role is key. Educating patients on any IPC practices should be integrated into broader healthcare initiatives to ensure both parties are prepared to take on their responsibilities effectively.

In addition to observing healthcare workers, patients' own hand hygiene practices are critical. For example, post-surgical patients may unintentionally play a role in transmission of microorganisms from their own skin to the surgical site. Loveday *et al*. implemented a successful patient-centered hand hygiene initiative that included face-to-face education, hand wipes, information cards, and staff protocols. Continuous monitoring and feedback further improved patient compliance, demonstrating the effectiveness of this comprehensive approach. These efforts resulted in a marked increase in patient hand hygiene compliance.

WHO's World Hand Hygiene Day has highlighted the importance of patient involvement with campaigns such as "Patients Have a Voice Too," which emphasizes the role of patients as active participants in hand hygiene practices. In addition, the Association for Practitioners in Infection Control and Epidemiology (APIC) patient hand hygiene toolkit provides practical steps for integrating patient education into healthcare settings.

Working with patients and their loved ones on this issue not only strengthens IPC but fosters a collaborative environment where healthcare workers and patients work together to achieve safer care. Consistent reinforcement of this approach can improve patient outcomes.

Country story – Successful hand hygiene education programmes and lessons learned

The Australian experience with hand hygiene education, led by the National Hand Hygiene Initiative (NHHI), has provided key insights into successful training programs, challenges across different healthcare settings, and innovative approaches to improving hand hygiene compliance.

One of the successes was its sustained, national-level approach that standardised hand hygiene practices across both public and private healthcare institutions. By mandating participation as part of hospital accreditation, the programme ensured high engagement. Over eight years, more than 1.9 million healthcare workers completed the NHHI's online learning modules, leading to a marked improvement in hand hygiene compliance rates. For example, compliance increased from 63.6% in 2009 to 84.3% in 2017, resulting in significant reductions in healthcare-associated *Staphylococcus aureus* bacteraemia (HA-SAB).

The initiative also leveraged train-the-trainer programs to build local expertise, further improving compliance and maintaining the program's longevity. The Australian experience demonstrates that tailoring hand hygiene education to different healthcare environments, such as hospitals, clinics, and long-term care facilities, is crucial for success. In acute care settings, the program targeted high-risk areas, such as intensive care units and emergency departments. This sector-wide approach helped embed hand hygiene in daily clinical practice, ensuring that compliance became a priority across various healthcare services.

However, several challenges remain. The initiative identified lower compliance rates before touching a patient (moment 1), suggesting that healthcare workers were more focused on self-protection than on the prevention of infection transmission to patients. Addressing this gap requires enhanced education focused on changing mindsets regarding patient protection.

Australia introduced the HHCApp mobile, a web-based application used for real-time hand hygiene auditing. This tool allowed auditors to provide immediate feedback to healthcare workers, increasing efficiency by reducing manual data entry and promoting prompt educational interventions. The use of the mobile device for auditing saved 50% of the auditors' time compared to traditional methods, further enhancing data accuracy and promoting better compliance. Another innovative practice was integrating hand hygiene compliance into the Royal Australasian College of Surgeons credentialing process. All surgical trainees were required to complete hand hygiene training before sitting for professional examinations, embedding these practices into the professional development of future healthcare leaders.

Australia's NHHI serves as a model for how structured, large-scale initiatives can foster long-term behavioural changes in hand hygiene compliance through standardised education. By utilizing theoretical models of behaviour change, engaging diverse healthcare settings, and leveraging technology, the programme sets new standards for IPC that can be replicated globally.

Future directions in hand hygiene education

The future of hand hygiene education for healthcare workers could leverage emerging technologies and innovative educational approaches to enhance both learning outcomes and long-term compliance. Emerging technologies such as artificial intelligence (AI), virtual reality (VR), and gaming platforms are reshaping training methods by moving away from traditional didactic teaching toward more reflective and interactive approaches. These technologies offer participatory, rather immersive, and learner-focused experiences, potentially improving hand hygiene compliance through interactive and engaging content.

Simulation-based training is becoming increasingly important, as it offers realistic clinical scenarios that allow learners to practice and refine their hand hygiene skills in a controlled environment. The role of e-learning and online platforms continues to grow, offering flexible and self-paced options that accommodate the varying schedules of healthcare professionals. Gamification and mobile apps further enhance engagement and retention by transforming learning into interactive and enjoyable experiences. However, although brief educational interventions have demonstrated immediate benefits, there is still a lack of research on the long-term impact of emerging technologies and their effectiveness in improving hand hygiene performance and preventing HAIs over time. Sustainability remains a key challenge, as single training sessions often result in temporary improvement. Continuous and ongoing training, coupled with real-time feedback from electronic monitoring systems and hand scanners, is essential for maintaining high compliance and ensuring that healthcare workers stay up-to-date with evolving hand hygiene guidelines. Future research should explore the long-term effects of these educational interventions to ensure sustained improvements in hand hygiene

practices across healthcare settings. In addition, future studies need to evaluate the long-term impact of hand hygiene training strategies that measure the effectiveness of various teaching methods over time.

Conclusion

In summary, this chapter underscores the critical role that hand hygiene education plays in reducing healthcare-associated infections and fostering a culture of safety within healthcare settings. It traces the evolution of hand hygiene practices, from Semmelweis's early historical milestones to the development of evidence-based, multimodal improvement strategy, emphasizing how education serves as a a cornerstone for promoting best hand hygiene practices Effective hand hygiene education is not a singular effort, it requires a comprehensive, behaviourally informed approach that integrates cognitive, psychomotor, and affective skills. The implementation of multimodal strategies is essential for overcoming the complex barriers that healthcare workers encounter in adhering to hand hygiene best practices. Training programmes must be interactive, context-specific, and grounded in solid theoretical foundations, ensuring that healthcare workers can immediately apply their knowledge in clinical settings. Furthermore, the utilisation of behaviour change models, is critical for structuring educational interventions that address the psychological and social factors influencing healthcare workers' decisions.

Looking ahead, the future of hand hygiene education lies in the integration of innovative technologies, such as simulation-based learning, artificial intelligence, and e-learning platforms. However, sustained improvement will only be achieved through multimodal, organization-wide interventions that include continuous healthcare worker education as well as other change interventions.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 43

Epidemiological aspects of healthcare-associated infection

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Introduction

Healthcare-associated infections (HAIs) are a threat to patients' safety and an increasing problem in public health, due to their morbidity, mortality, costs and social-psychological distress to infected patients and their relatives.

HAIs are infections acquired by patients during their stay in a hospital or another healthcare setting, including long-term care facilities, ambulatory care centers, and outpatient settings. Therefore, HAIs should not be present or in incubation at the time of admission, and first appear 48 hours or more after hospital admission, or within 30 days after having received health care.

The most frequently reported types of healthcare-associated infections are respiratory tract infections, surgical site infections, urinary tract infections, bloodstream infections and gastrointestinal infections, with *Clostridioides difficile* infections representing almost half of the gastrointestinal infections.

In the European Union and European Economic Area (EU/EEA) each year more than 3.5 million cases of HAIs are estimated to occur, leading to more than 90 thousand deaths and corresponding to approximately 2.5 million disability-adjusted life years (DALYs), a burden estimated to exceed the cumulative burden of other infections including influenza and tuberculosis in the EU/EEA.

Moreover, HAIs represent a public health problem for the burden of antibiotic-resistant bacteria that they carry out. Indeed, in 71% of cases, HAIs are due to antibiotic-resistant bacteria, including bacteria resistant to last-resort antibiotics, such as carbapenem-resistant *Enterobacterales*.

The reason why many efforts are intended to tackle HAIs is that Up to 50% of HAIs are estimated to be preventable. Therefore, the application of infection prevention and control measures in healthcare settings is essential to prevent HAIs.

Epidemiological data

The most recent prevalence survey of HAIs was conducted in Europe in 2022-23. Twenty-eight EU/EEA countries and three Western Balkan countries (Kosovo, Montenegro and Serbia) participated in the third ECDC point prevalence survey (PPS) of HAIs and antimicrobial use in European acute care hospitals.

Data from a total of 1,623 hospitals were submitted to the European Centers for Disease Control (ECDC). Of these, 309,504 patients from 1,332 hospitals were included in the final European sample for analysis.
Data from a single ward were collected on a single day. The final results correspond to 293,581 patients from 1,250 European hospitals.
In this PPS, the prevalence of patients with at least one HAI was 7.1%, ranging from 3.1 to 13.8% by country. Correcting for results of national validation studies, the adjusted prevalence of patients with at least one HAI was estimated at 8.0% (95% confidence interval: 6.6–9.6%).
According to this prevalence, there were an estimated total of 93,305 (95% CI: 76 427–111 899) patients with at least one HAI on any given day, 4.3 million (95% CI: 3.1–5.8 million) patients with at least one HAI and 4.8 million (95% CI: 3.1–5.8 million) infection episodes per year in the period 2022 to 2023 in acute care hospitals in the EU/EEA.
Additionally, in this PPS, the most frequently reported types of HAIs were respiratory tract infections (29.3% of the total, including pneumonia 19.0%, COVID-19 7.0% and other lower respiratory tract infections 3.3%), urinary tract infections (19.2%), surgical site infections (16.1%), bloodstream infections (11.9%) and gastrointestinal infections (9.5%), with *C. difficile* infections accounting for 62.1% of the latter and 5.9% of all HAIs.
Of note, 26% of HAIs were present on admission. Around twenty-six percent of HAIs present on admissions were surgical site infections (SSIs).
Among the overall HAIs, at least one microorganism was isolated in 60.8% of HAIs, ranging from 51.5% in pneumonia and lower respiratory tract infections to 87.4% in bloodstream infections.
The commonest organisms were: *E. coli* (12.7%), *Klebsiella* spp. (11.7%), *Enterococcus* spp. (10.0%), *SARS-CoV-2* (9.5%), *S. aureus* (9.0%), *C. difficile* (8.0%), *P. aeruginosa* (7.9%), coagulase-negative staphylococci (5.8%), *Candida* spp. (4.7%), *Proteus* spp. (3.2%), *Acinetobacter* spp. (3.2%) and *Enterobacter* spp. (3.0%).
However, other less common but nonetheless epidemiologically important microorganisms were identified, including *Serratia* spp.*, Stenotrophomonas maltophilia* and *Aspergillus* spp., that accounted for1.4%, 0.8% and 0.3% of all microorganisms, respectively.
Regarding the site of infection, the predominant groups of microorganisms were Gram-positive cocci in surgical site infections and bloodstream infections, *Enterobacterales* in urinary tract infections, viruses (mainly SARS-CoV-2) and gram negatives including *Enterobacterales* and non-fermentative organisms, in respiratory tract infections, and *Clostridioides difficile* in gastrointestinal tract infections.
The main problem of HAIs is represented by antimicrobial resistance and therefore to treat them with appropriate antimicrobial therapy. In this PPS, methicillin resistance was reported in 23.7% of *S. aureus* isolates, a decrease from 31.0% in the ECDC PPS 2016–2017. Among *Enterococcus* spp., vancomycin resistance was reported in 15.6% of isolates, with a higher rate in *E. faecium* (28.7%) *versus E. faecalis* (4.9%).
Enterobacterales reported 34.7% and 9.3% resistance to third-generation cephalosporins and carbapenems, respectively. Resistance to carbapenems among *P. aeruginosa* and *Acinetobacter baumannii* was reported in 29.7% and 82.9% of isolated strains, respectively.
Of course, resistance rates greatly differed by country, and overall European antimicrobial resistance (AMR) percentages were largely influenced by the data of a few countries reporting large numbers of isolates with AMR.
As a further aim of the PPS, prevalence and indication of antimicrobial use was assessed. These findings represent an important element for planning and implementing effective antimicrobial stewardship programs.
On the day of the survey, 35.5% of patients, i.e. 104,303 out of 293,58, received at least one antimicrobial agent, with an average of 1.34 agents per patient receiving antimicrobials: 72.6% of patients received one antimicrobial agent, 22.4% received two agents, and 5.4% received three or more agents (up to a maximum of nine antimicrobials agents for two patients).

The main route of administration of antimicrobials was parenteral (80.4%) and the reason for antimicrobial use was documented in the medical records for 82.7% of prescriptions.
The indication for antimicrobial use was in 70.3%, 26.2% and 3.6% for a community-acquired infection, for a hospital infection, and for an infection acquired in a long-term care facility, respectively. About fifteen percent of prescriptions were done for surgical prophylaxis, which was done for more than one day in 48.3% of cases, whereas the proportion of single-dose surgical prophylaxis was 32.4% better than the 26.8% in 2016–2017 PPS.

Risk factors for the most common HAIs

Healthcare-associated pneumonia (HAP)

Healthcare-associated pneumonia (HAP) is one of the most common nosocomial infections and is associated with significant clinical and economic burdens, such as long-term hospitalization, high medical costs, and increased morbidity and mortality. Worldwide, its incidence ranges from five to more than 20 cases per 1,000 hospital admissions and from 2.5 to more than 6.1 cases per 1,000 patients not admitted to the intensive care unit (ICU).
The main risk factors ascertained in epidemiological studies include older age and preexisting lung diseases, such as chronic obstructive pulmonary disease (COPD), asthma, interstitial lung disease, or multiple organ system disorders that increase the risk of HAP. Other risk factors for HAP include aspiration, intubation, and mechanical ventilation (MV).
In a population-based retrospective cohort study of adult patients who were hospitalized for more than 3 days between January 1, 2016 and December 31, 2018, in South Korea. older age, male sex, asthma, COPD, other chronic lower respiratory diseases, CKD, and poverty were associated with the incidence of HAP. Additionally, clinical factors, such as tube feeding, suctioning, positioning, MV, and ICU admission, increased the risk of HAP. In terms of the hospital environment, hospital type, beds-to-nurse ratio, hospital room type, and ward with caregivers were associated with the incidence of HAP.
Aspiration is a critical factor for the occurrence of HAP. The most important reservoir of Gram-negative bacilli that can ascend and colonize the respiratory tract is the stomach. In a prospective observational study, patients who used acid-suppressive medications were more likely to develop HAP than were patients who did not (5% *vs.* 2%). Moreover, the risk for pneumonia was significantly increased with proton pump inhibitors, but not with histamine 2-blocking agents.
The intensive care unit (ICU) is a setting with the highest incidence of HAP, due to the risk posed by intubation in ventilated patients (ventilator-associated pneumonia, VAP). Even though the incidence of ICU-acquired pneumonia, mainly VAP has decreased significantly in recent years possibly due to the generalized implementation of preventive bundles, the exact incidence of VAP is difficult to establish due to the diagnostic limitations and the methods employed to report rates.
Data in the literature strongly support the relevance of intubation, not ventilatory support, in the development of HAP in ICU patients. Endotracheal intubation is an independent risk factor with multiple associated factors such as:

- Micro aspiration around the endotracheal tube.
- Length of ventilation.
- Abnormal swallowing function.
- Secretions pooled above the endotracheal tube.

Indeed, the endotracheal tube is a foreign body that can be easily colonized by biofilm-producing bacteria. Pathogenic bacteria can form a glycocalyx biofilm on the tube's surface that protects them from both antibiotics and host defences. This can become a contributing factor to the recurrence of infection and treatment failure, as well.

Surgical site infections (SSI)

A "Surgical Site Infection" (SSI) is defined as an infection following surgery at the incision site or in its immediate vicinity. From a strictly epidemiological point of view, for the purpose of their surveillance, surgical site infections are divided into superficial, deep and involving organ/space.

"Superficial" surgical site infections are so-called because involve only the skin and subcutaneous tissue at the incision site; they occur within 30 days of surgery. The so-called "deep incisional" infections involve the deep structure of the incision site (for example muscle bands) and occur within 90 days of surgery.

Organ/space infections affect the structures underlying the muscle bands manipulated during surgery and occur within 90 days of surgery.

Complete definitions of surgical site infections are available on the Centers for Disease and Prevention (CDC) website.

Surgical site infections occur in approximately 0.5% to 10% of surgical procedures, depending on the type of surgical procedure and the degree of contamination, the physical status score of the patient according to the American Society of Anaesthesiologists (ASA) score, and the duration of the intervention itself. These parameters concur in defining the National Nosocomial Infections Surveillance (NNIS) index.

The incidence density of in-hospital surgical site infections per 1,000 postoperative patient days ranges from 0.1 to 5.7%. Of note, up to 71% of surgical site infections occur after hospital discharge, making valid post-discharge surveillance systems necessary to assess the real burden of SSI in terms of public health.

From an economic point of view, SSIs are responsible for additional costs, increased length of stay, increased rate of re-operation and re-admission, and finally an increase in mortality rates. It is estimated that in the United States SSI costs up to 10 billion dollars per year.

Factors associated with surgical site infections include but are not limited to, advanced age, immunosuppression, obesity or malnutrition, diabetes, smoking, the presence of an infection at another site before surgery, the effectiveness of antimicrobial prophylaxis, the presence of foreign materials, previous radiation therapy that has caused tissue damage, and the degree of wound contamination.

While factors such as age and previous tissue damage or the presence of non-removable foreign bodies are not preventable, many other factors can be avoided with appropriate preventive measures.

Prevention strategies for surgical site infections can be classified as preoperative, intraoperative, and postoperative.

The main preoperative strategies include an optimal approach to hair removal, nasal decolonization in *Staphylococcus aureus* carriers, antimicrobial prophylaxis, and the use of a "checklist" to ensure adherence to best care practices.

Regarding hair removal, evidence shows that it is a risk factor for surgical site infection; if it is absolutely necessary, it should be done with a clipper and not with a razor, and it should be performed in the preoperative waiting area and not in the operating room.

Nasal decolonization with mupirocin is associated with a significantly lower rate of surgical site infections in cardiothoracic and orthopedic surgery related to prosthetic implantation.

The administration of antibiotic prophylaxis is recommended by all guidelines; those of the World Health Organization recommend the administration of prophylaxis within 120 minutes of the incision, depending on

the half-life of the antibiotic used, but for antibiotics with a short half-life it is generally practiced within 60 minutes of the incision.
The guidelines recommend not continuing with the administration of prophylactic antibiotics after the closure of the surgical wound.
Finally, the use of a "checklist" such as the "WHO's surgical safety checklist", which includes 19 points, can improve adherence to best practices by reducing the incidence of surgical site infections. The most important intraoperative measures include the use of chlorhexidine in alcohol solution for antisepsis of the surgical field and the maintenance of normothermia during the surgical procedure.
Current guidelines recommend that surgical site antisepsis be performed with a product that contains alcohol (a potent bactericidal antiseptic but without persistent activity) and an antiseptic. Chlorhexidine gluconate plus alcohol has been shown to be more effective in preventing surgical site infections than povidone-iodine in aqueous solution, and a meta-analysis of randomized clinical trials and 29,000 participants showed that skin preparation with chlorhexidine gluconate was associated with fewer infections than povidone-iodine (4.8% *vs.* 6.7%, $p<0.001$).
More recently, in a multicenter, cluster-randomized, investigator-masked, crossover, noninferiority trial, 3360 patients were enrolled and randomly assigned to either use povidone iodine or chlorhexidine gluconate, each formulated in alcohol. The findings of this trial demonstrated that povidone-iodine in alcohol as preoperative skin antisepsis was non-inferior to chlorhexidine gluconate in alcohol in preventing SSIs after cardiac or abdominal surgery.
Regarding normothermia, skin warming systems and heated intravenous fluids should be used to maintain core body temperature at normal levels compared to a sudden drop in temperature due to surgery. A systematic review of the literature demonstrated that using warm air devices to prevent intraoperative hypothermia increased the risk of surgical site infections from 13% (without the device) to 4.7% (with the device) ($p=0.008$).
The main postoperative measures include maintaining and monitoring blood glucose levels regardless of diabetic status and the application of negative pressure wound dressings. In a meta-analysis of 15 randomized clinical trials, strict glycemic control (blood glucose <150 mg/dL) compared with conventional control (blood glucose >150 mg/dL) was associated with lower rates of surgical site infections (9.4% *versus* 16%, $p<0.001$).
Finally, in a meta-analysis of 23 randomized clinical trials involving 2547 patients undergoing various surgical procedures, the use of negative pressure wound therapy was associated with lower rates of surgical site infections compared with conventional wound dressings. (9.7% *versus* 15%, $p<0.001$).

Central line-associated bloodstream infections (CLABSI)

A central line-associated bloodstream infection (CLABSI) occurs when a patient has:

- clinical signs of infection, e.g. fever, rigors, altered mental status, hypotension, and no alternate source of bloodstream infection;
- a positive blood culture from a peripheral vein with any one of the following: catheter tip/segment culture that matches organism grown from blood; at least threefold higher number of organisms grown from the catheter *versus* the peripheral blood culture on simultaneously drawn culture; growth from the catheter-drawn blood culture occurs at least two hours before growth of the same organism from a percutaneously-drawn blood culture.

CLABSIs often occur in patients being treated in intensive care units (ICU) and is a leading cause of death in ICU patients. CLABSIs result in the death of thousands of people each year and increases healthcare costs by billions of dollars. In the United States, 80,000 episodes of CLABSI are diagnosed annually and are associated with increased mortality and elevated economic costs (39,000 US dollars per episode).

Based on the route of entry of bacteria, causes of CLABSI can be distinguished into:

- extraluminal: pathogens migrate along the external surface of the catheter from the skin entry site. This infection often occurs within 7 days of insertion;
- intraluminal due to hub contamination, migration along the internal surface of the catheter. This infection more commonly occurs >7 days and is due to intraluminal colonization;
- secondary BSI: when bacteria from another source in the body infect the blood;
- infusate contamination: introduction of pathogens from fluids infused through the catheter system.

In a systematic review of observational studies including 23 studies out of 654 identified, a meta-analysis analyzed 9 risk factors including total parenteral nutrition (TPN), chemotherapy, monolumen and bilumen catheters, days of catheterization, immunosuppression, kidney disease and diabetes mellitus. The risk factors found to increase the probability of developing CLABSI were TPN, multilumen devices, chemotherapy treatment, immunosuppression and the number of days of catheterization. On the other hand, monolumen devices presented a lower likelihood of triggering this infection.
In this review, the most frequent microorganisms isolated in CLABSIs were Gram-positive cocci, the most prevalent being coagulase-negative Staphylococci, thereby indicating possible colonization by skin flora of the patient or secondary to manipulation of the device by different health care professionals.

Catheter-associated urinary tract infections (CAUTI)
Urinary tract infections (UTIs) are one of the most common healthcare-associated infections. In 2003, 70%–80% of UTIs were attributable to the presence of an indwelling urethral catheter (CAUTI). In a 2019 analysis, over 5 years, CAUTIs decreased in proportion to non–device-associated UTIs but still made up an average of 44% of these infections per year among the hospitalized patients included in the study.
The use of urinary catheters is very common in emergency departments and hospitals worldwide; they remain one of the most common medical devices experienced by adults, often without an appropriate clinical indication to justify the risk compared to the benefit.
In a cross-sectional study conducted in 726 hospitals across 34 states in the United States, data on 434,207 catheter-days over 1,400,770 patient-days were collected, a total of 1,099 CAUTIs were observed (2.5 per 1,000 catheter-days, and a population-based rate of 7.8 per 10,000 patient-days). Approximately 30%-40% of catheters in non-ICUs were placed without an appropriate indication.
It has been calculated that 12%–16% of adult hospital inpatients will have an indwelling urethral catheter at some point during admission. Of patients who have a urinary catheter placed in the hospital, up to half are placed in patients who may not have an appropriate indication for a urinary catheter.
Among the main risk factors for CAUTI, the duration of catheterization is one of the most important, with a daily risk of development of bacteriuria ranging from 3% to 7% when an indwelling urethral catheter remains in situ. Additional risk factors for CAUTI include female sex, older age, and not maintaining a closed drainage system.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 44

Environmental hygiene in hospital settings

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Introduction

Healthcare-associated infections (HAIs), especially those caused by antibiotic-resistant bacteria, pose an important threat to public health worldwide. A significant proportion of HAIs is estimated to be preventable by the application of Infection Prevention and Control (IPC) measures, including environmental hygiene practices that, as part of a multimodal strategy, are one of the eight core components of an effective IPC strategy. Among the core components for the prevention of infections, the World Health Organization (WHO) recognizes that healthcare activities should be undertaken in a hygienic environment that facilitates practices related to the prevention and control of HAIs and Antimicrobial Resistance (AMR).
Environmental microbial contamination in healthcare settings plays a key role in the exogenous transmission of microorganisms involved in the HAIs and AMR spread. Environmental hygiene comprises all aspects of the healthcare environment that are not the patient or the healthcare workers themselves and includes both technical - cleaning and disinfection of surfaces, air and water control and management, sterilization and device reprocessing, waste management and laundry – and human components - best practice implementation, staff management, and environmental services departments' structural organization and healthcare workers' education and training. The application of effective practices is crucial for patients' and healthcare workers' safety.
The aim of the present chapter is to provide an overview of the role of environmental hygiene in hospital settings with a special focus on environmental cleaning and disinfection. For additional information, readers are encouraged to refer to the reported references for further details.

Environmental transmission of HAIs

Environmental contamination - especially of high-touch surfaces in the patient's room, reusable care devices, and of indoor air - plays a significant role in the transmission of pathogens related to HAIs. Given the number of critical patients admitted, the characteristics of healthcare activities performed, and the complexity of hospital surfaces and of medical equipment and devices, the hospital environment is subject to harbour potential pathogens. Environmental hygiene strategies are implemented for the prevention of exogenous transmission of pathogens in hospitals. Particularly, several microorganisms - including vancomycin-resistant enterococci (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii*, *Clostridioides difficile*, *Pseudomonas aeruginosa* and other multidrug-resistant Gram-negative bacilli and fungi spores too - can persist in the environment for extended periods, also after cleaning and disinfection, and serve as vehicles of transmission and dissemination in the hospital setting. The degree of infection risk for patients from

inadequately cleaned and disinfected rooms, surfaces and devices, is determined by survival characteristics of individual species or strains on surfaces and, of course, by the patient's susceptibility. Generally, the survival times of microorganisms vary considerably based on factors such as temperature, humidity, and surface type in healthcare settings.

Furthermore, other characteristics of microorganisms including the capacity to form biofilms, are important factors that promote the persistence of the microorganism in the environment, in the surfaces and in reusable medical equipment thus favouring the transmission in the hospital setting. Biofilms act as a reservoir for pathogens including multidrug-resistant microorganisms and their elimination requires different approaches. Some scientific evidence has demonstrated that biofilms also interfere with cleaning and disinfection practices, also of reusable surgical equipment and medical devices. In fact, this matrix shields the resident cells from desiccation, chemical perturbation, and invasion by other bacteria, and confers reduced susceptibility to antibiotics and disinfectants. Failure to control biofilms increases the risk of HAI. It has been reported that biofilm-related infections reoccur in 65% - 80% of cases. New technologies such as self-disinfecting surfaces or continuous room disinfection systems may reduce or disrupt biofilm formation. However, at present, there are no recommendations with regard to choosing a self-disinfecting surface based on the results of studies conducted to analyse the ability of these materials to disrupt biofilms and/or inactivate microbes present in biofilms.

Increasing evidence suggests that indoor air quality together with contaminated surfaces is an important potential source for transmission of pathogens in hospitals. Air contamination may lead to the spread of HAIs especially among susceptible patients such as, for example, those affected by serious haematological diseases or transplant recipients. Particularly, it has been reported that microbial contamination of the surgical site is a necessary precursor of surgical site infections and air is a potential vehicle of infection. Microorganisms can contaminate directly the wound or can land on exposed surfaces and subsequently be transferred into the wound. To reduce microbial air contamination, heating, ventilation and air conditioning systems, are used; however, the effectiveness of these systems can be undermined by their poor management and the incorrect behaviour of the surgical team and, in this context, air microbiological control monitoring can represent a useful tool to assess air quality in operating theatres, as part of the clinical audit. The same monitoring can be useful in other critical areas. Additionally, sink drains and other wastewater drainage sites are universally contaminated with potential pathogens. Wastewater drainage sites provide optimal conditions for biofilm formation and plasmid-mediated sharing of resistance genes. In fact, there are plausible mechanisms by which organisms in these sites can be disseminated to environmental surfaces that are commonly touched and to patients and personnel.

Environmental cleaning and disinfection and IPC

One strategy to effectively prevent and control infection in healthcare settings is environmental cleaning. Environmental cleaning is part of standard precautions, which should be applied to all patients in all healthcare facilities. Environmental cleaning and disinfection represent one of the three pillars of IPC strategies in healthcare settings together with standard precautions and the application of good practices in invasive procedures. Environmental cleaning is addressed explicitly within the core component 8 "Built environment, materials and equipment for IPC at the facility level" defined in the Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level by the WHO. Additionally, other core components include important aspects for the implementation of environmental

cleaning and disinfection, such as core component 2 “IPC guidelines”, core component 3 “IPC education and training” and core component 6 “Monitoring/audit of IPC practices and feedback”.
Scientific evidence demonstrated that in the healthcare setting the main source of pathogens is the patient's endogenous flora; however, between 20% to 40% of HAIs are caused by cross-infection via the hands of healthcare workers contaminated as a result of contact with the patient, their body fluids, and surfaces in the patient’s surroundings. Although it is difficult to assess whether an infection came from the patient’s environment or from another source, appropriate hand hygiene and environmental cleaning and disinfection are fundamental strategies that can prevent the transfer of microorganisms to healthcare workers, visitors and susceptible patients. It has been reported that poor hand hygiene is one of the main drivers of HAIs acquisition among patients. Appropriate hand hygiene practices can reduce HAIs by up to 50%, however, the remaining proportion needs to be addressed and, in this contest, environmental hygiene intervention may play an important role. In any case, infection transmission is multifaceted and generally involves the complex interplay between a pathogen, a host and their environment, including humans, requiring multifaceted strategies to prevent their transmission. The use of multiple interventions as well as an overall multimodal approach to IPC activities and programs is recommended, for both outbreak and routine settings.
Several important inter-related environmental cleaning and disinfection strategies are used to reduce the risk of HAIs. The multimodal approach to environmental cleaning and disinfection in healthcare facilities, based on the bundled approach of the REACH (Researching Effective Approaches to Cleaning in Hospitals) trial, encompasses five key strategies: the product and approach used for cleaning and disinfection, technique, education and training, audit and feedback, and communication. The REACH multicentre randomised trial demonstrated that the cleaning and disinfection bundle reduce significantly the incidence of healthcare-associated vancomycin-resistant enterococci infections.
Important contextual factors are likely to play a role in the effectiveness of infection prevention strategies, including organizational culture, governance, support, resources, risk appetite, and motivation and capacity to change.
Few studies, especially high-quality randomized controlled trials, have been conducted in order to evaluate the role of healthcare environmental hygiene interventions in the reduction of patient colonization and HAIs. A systematic review has been recently published to review the scientific evidence on the efficacy of interventions in the hospital environment to reduce patient colonization with multidrug-resistant microorganisms and to prevent HAIs. The review highlights that, although there is a great heterogeneity in terms of the types of interventions performed and their quality, over half of the studies demonstrated a significant decrease in colonization or HAI. Thus, these results are indicative of the importance of environmental hygiene in the healthcare setting in order to reduce HAIs and thus improve patient safety.

Advancements and challenges in hospital cleaning and disinfection

One of the challenges of effective hospital cleaning and disinfection is represented by the fact that the disinfected surfaces rapidly become re-contaminated. Thus, it is necessary to develop and validate in healthcare settings new technologies that can provide continuous decontamination of occupied spaces between two cleaning operations. These technologies include antimicrobial surfaces or coatings that provide continuous decontamination of surfaces - eg, copper surfaces, organosilane-quaternary ammonium compounds that bind to surfaces - and light- or gas-based technologies that provide continuous decontamination of surfaces and air - eg, far-ultraviolet-C light or high-intensity visible light, hydrogen peroxide gas.

Particularly, antimicrobial surfaces, including copper-containing surfaces, are now being used in both new hospital construction and as covering material for high-touch surfaces in order to decrease the bacterial burden on surfaces. Copper surfaces reduce microbial burden compared to control surfaces in healthcare facilities but, future research should focus on measuring the effectiveness of using copper in contact surfaces and the reduction of HAIs and on the long-term effect, given theoretical concerns that bacteria will develop copper resistance.

Furthermore, some scientific evidence suggests good antimicrobial and sporicidal hydrogen peroxide activity, especially in wards with severe environmental contamination levels and endemic cases of infections with multidrug-resistant organisms.

Environmental hygiene is essential for all types of healthcare facilities, from hospitals and long-term care facilities to home care environments. Another challenge is to address particular settings with vulnerable patients as the nursing home environment. The nursing home residents have a high prevalence of colonization with multidrug-resistant organisms and the shared environment with vulnerable patients can facilitate intra- and interfacility transmission of HAIs and AMR. In this setting, future studies should be conducted in order to further explain the role of environmental contamination and thus evaluate methods to improve cleaning and disinfection practices.

Recently, “no touch” methods of terminal room disinfection have been developed such as ultraviolet light (UV) devices and hydrogen peroxide (HP) systems. A recent review report that most, but not all clinical trials of UV devices and HP systems for terminal disinfection demonstrated a reduction of colonization/infection in patients subsequently housed in the room. Copper-coated surfaces were the only “self-disinfecting” technology evaluated by clinical trials. The results of these clinical trials were mixed. The evidence is strong enough to recommend the use of a “no-touch” method as an adjunct for outbreak control, mitigation strategy for high-consequence pathogens (e.g., *Candida auris* or Ebola), or when there is an excessive endemic rate of multidrug-resistant organisms. Thus, additional research and clinical trials are strongly recommended.

More recently, self-disinfecting surfaces with incorporated antimicrobial substances have been proposed to support or replace either no-touch or conventional cleaning, and they represent an emerging research topic in continuous and rapid development. These innovative collective protective measures have several advantages over the other cleaning strategies because, following contact, they can kill most microorganisms, preventing their spread to other HAIs by healthcare personnel’s hands. The integration of antimicrobial agents into polymers with intrinsic antimicrobial activity has currently garnered significant interest for their potential to prevent microbial colonization.

One of the main areas of concern is the possible linkage between biocide usage and antibiotic resistance in bacteria. Particularly, inappropriate usage or low concentrations of a biocide may act as a stressor while not killing bacterial pathogens, potentially leading to antimicrobial resistance. Recent evidence suggest that in almost 90% of the outbreaks in which a pathogen was isolated, its susceptibility to the disinfectant used was not determined, and interestingly, when it was assessed, in most cases the pathogen turned out to be highly resistant to the disinfectant. Furthermore, in the future should be important to further explore the relationship between the consumption of disinfectants and the development of resistance also seeking a balance for their more sustainable and safer use.

Conclusion

Environmental hygiene in hospital settings plays a crucial role in the prevention and control of HAIs and AMR. Ensuring healthy indoor environmental quality is a critical aspect of patient safety and protecting healthcare

workers and visitors, avoiding HAIs and AMR spread. Increasing evidence related to new technologies supporting environmental hygiene strategies have been published; however, there is considerable uncertainty regarding the effectiveness of these technologies in real-world settings and for some aspects also concerns about safety.

Competing interests

The authors have no financial and non-financial competing interests to declare.

Acknowledgments

The chapter has been prepared on behalf of the Italian Study Group of Hospital Hygiene (GISIO, National Coordinator Martina Barchitta) of the Italian Society of Hygiene, Preventive Medicine and Public Health (SItI, President Roberta Siliquini). We thank all members of the GISIO-SItI and particularly Antonella Agodi, Roberto Albertini, Gerardo Altamura, Angelo Baggiani, Tatjana Baldovin, Annalisa Bargellini, Aida Bianco, Giovanni Boccia, Beatrice Casini, Maria Luisa Cristina, Daniela D'Alessandro, Osvalda De Giglio, Leila Fabiani, Pasqualina Laganà, Andrea Maugeri, Maria Teresa Montagna, Stefania Paduano, Cesira Pasquarella, Elena Righi, Giancarlo Ripabelli, Luisa Sodano, Stefano Tardivo, Marina Tesauro, Elena Vecchi, Licia Veronesi, Costanza Vicentini, Arianna Vitale, Raffaele Zarrilli, Carla Zotti, for their contribution.

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Chapter 45

Impact of healthcare-associated infections

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Introduction

Healthcare-associated infections (HcAIs) are a significant cause of illness and death worldwide and are primarily linked to catheter-associated urinary tract infections (CAUTIs), central-line–associated bloodstream infections (CLABSIs), surgical site infections (SSIs) and ventilator-associated pneumonia (VAP). HcAIs typically occur in patients more than 48 hours after their hospital admission and are not present or incubating upon their arrival in the health care setting. Approximately 1 in 30 to 1 in 10 hospitalized patients develop HcAIs, with intensive care units accounting for 9–20% of these cases. HcAIs contribute to higher rates of morbidity, mortality, and increased healthcare costs. The prevalence of HcAIs varies across different countries, with rates of 6.5% in Europe and 4% in the United States, while rates reach 9.0% in Asia, and around 16% in developing nations. In Africa, the rate of HcAIs is twice that of developed countries.

Various measures exist to estimate the impacts of disease; while a significant proportion of the scientific literature in the field of infectious diseases attempts to address their consequences on human health, other estimates are also applied to highlight the proportion that infectious diseases can affect human health, human economy and the ecology. Measures estimating the impact of healthcare-associated infections (HcAI) in the literature include burden on health (such as morbidity, mortality, extended length of stay, rehospitalization), healthcare costs, impact on healthcare systems (such as bed and departmental occupancy, healthcare workforce capacity), impact on the ecology (such as increase of antimicrobial resistance), as well as costs of prevention (**Table 1**). Nevertheless, measuring the true impact of these infections is not always a feasible task. It is often difficult, if not impossible, to control for all factors and confounders, in order to derive the true association between an infection and an outcome. One prominent example is measuring attributable mortality, ie. death directly attributed to an infection.

The aim of the current article is to provide a brief overview of the different impacts of HcAI on human health, healthcare services and healthcare costs.

Table 1. Measures of impact of healthcare-associated infections.

Measures	Examples
Disease / Health burden	Mortality (associated, attributable), morbidity, length of stay, rehospitalization, quality of life
Healthcare costs / Economy	Prolonged length of stay, additional hospitalizations, medical interventions, antimicrobial treatment
Healthcare system capacity	Bed occupancy, department occupancy, loss of healthcare workforce
Ecology	Antimicrobial resistance
Cost of prevention	Need for additional measures

Measures of impact of HcAIs

Morbidity/Mortality

Available evidence has shown that HcAIs, particularly those involving multidrug-resistant organisms, have a high mortality rate. In-hospital mortality was higher among patients with HcAIs compared to those without HcAIs. In-hospital mortality is higher in ICU patients, reaching as high as 51% in VAP, 29% in CLABSI, and 19% in CAUTI. Specific factors independently associated with HcAI-related death in the ICU vary and include the type of infection, reason for hospitalization, length of stay (LOS), older age, length of device use, and comorbidities.

HcAIs also significantly impact the LOS in hospitals. The LOS for patients with HcAIs was nearly double that of uninfected patients, with these cases staying an average of 8-12 days longer than the controls. In China, additional LOS due to HcAI has been recorded to reach 34 days (IQR 23-45 days).

The effects of disease on quality of life are difficult to estimate, especially in relation to hospital-related diseases. Appropriate data and controls are needed, to allow for accurate measurements and comparisons that depict the true burden of disease on objective metrics of quality of life. A modeling study published in 2016, used ECDC data to estimate the burden of six HcAIs (healthcare-associated pneumonia, UTI, neonatal sepsis, primary bloodstream infection SSI, and *Clostridium difficile* infection) in relation to Disability-Adjusted Life Years (DALYs). The DALY is a composite aggregate measure of health and well-being that pertains to the incidence of the disease, the disabilities associated with the disease complications, as well as the estimated years of life lost. The above study showed that the total burden of these six HcAIs was higher than that of all other surveyed infections, whereas pneumonia and BSI, although not among the most frequent HcAIs recorded, accounted for the largest part of the total burden of 2.5 million DALYs attributable to these infections. An additional, often intangible effect of HcAIs on quality of life includes the burden of disease on family and society, such as the need for caregiving, and absence from work of patients and family.

Healthcare costs

HcAIs not only increase morbidity and mortality rates but also place a substantial financial strain on the healthcare system, being associated with increased healthcare costs. This observation is supported by numerous studies from both developing and developed countries. The higher costs can be attributed to either direct or indirect costs; direct costs are related to prevention, diagnosis, and management, whereas indirect costs are related to healthcare capacity requirements, healthcare workforce burden, and productivity losses related to the disease.

In the United States, the estimated annual cost of treating HcAIs ranges from $28.4 to 45 billion, posing a significant burden on public health resources. Among US hospitals, specific costs per HcAI (in 2009 US Dollars) were estimated at $11,000-56,000 for CLABSI, $80,000-324,000 for VAP, $1,200-4,799 for CAUTI, and $2,200-6,700 for SSI. In Europe, costs exceed 7 billion euros annually, due to HcAIs that cause 16 million additional hospitalization days each year. Although there is extensive data on the costs of HcAIs from developed nations, applying this data to developing countries may not be appropriate for extrapolating safe conclusions. Moreover, the financial costs associated with HcAIs are often poorly documented and inconsistently reported in low- and middle-income countries. Taking these shortcomings into account, a systematic review of African studies among 14 countries with available data, estimated total financial costs of $13 billion in 2022. Of note, 77% of total costs were attributed to premature deaths, whereas healthcare costs accounted only for 5.6% of financial losses in African countries, with an estimated cost of $500 per infection. Another noteworthy observation from this study is that infrastructure and healthcare costs related to HcAIs were much lower in LMICs compared to other countries, signifying the geographical disparities in the prevention and control of HcAI.

Healthcare system capacity

Appropriate prevention and management of HcAIs carry several requirements, including patient isolation and/or cohorting, staff cohorting, departmental changes, material resources, as well as managerial, functional and operational adjustments. Often, the occupancy of healthcare facilities is overburdened to a degree that doesn't allow for patient isolation and staff cohorting. Reduced funds may hamper the application of protective measures and the use of protective equipment.

An often-overlooked dimension is that of increased operational requirements for HcAI prevention and management, which may result in healthcare workforce overburdening and reduced productivity. Examples include continuous surveillance and reporting, specialized microbiological methods and personnel, increased staffing to meet isolation and cohorting needs, specialized waste management procedures, infrastructure and facilities, application and monitoring of novel performance measures, etc.

Ecology

It is established knowledge that the physical environment and appropriate infrastructure impact the occurrence of HcAIs. Other environmental factors, such as air and water pollution, and sanitation, are also associated with increased risk for infections. Conversely, though, only limited data document the effects of HcAI on the environment. Among the most studied fields is the association of infectious risks with biomedical waste management in healthcare facilities. However, other environmental risks can also occur due to waste management; for example, increased HcAIs in a healthcare setting or a geographical area, require increased use of personal protective equipment, which should be in turn appropriately disposed of. This leads to increased operational requirements, but also to a need for strict waste management procedures which entail the risk of environmental pollution.

In addition, the majority of HcAIs require antimicrobial treatment, often with extended-spectrum and last-line agents, which carry a significantly wider ecological effect compared to narrow-spectrum antimicrobials. Exposure of humans to antimicrobials leads to shedding antimicrobial agents and their metabolites into the environment, thus facilitating the survival of antimicrobial-resistant microbial populations in the soil, water and air, which, in turn, may serve as predominant pathogenic and non-pathogenic agents in animals and humans in the community. This One Health concept consists of an emerging target of global efforts to decrease the burden of HcAIs and antimicrobial resistance inside and outside healthcare facilities.

Prevention

A significant proportion of HcAIs are likely preventable through adherence to infection control and prevention measures. Therefore, the impact of HcAIs cannot be estimated without taking into account the costs for applying appropriate measures for prevention. In addition, the nature, intensity, extent and costs of preventive measures needed, as well as healthcare system capacity and priorities, are directly related to the baseline frequency (incidence) of HcAIs.

Thousand-hundreds of HcAIs could be prevented, by implementing comprehensive, evidence-based infection control strategies, thus; saving thousands of lives and billions of dollars. Similarly, conducting surveillance studies on the incidence, clinical burden and economic impact of HcAIs is essential for their prevention and management. Access to published data on the clinical and economic impacts of HcAIs is pivotal, in order to raise awareness among healthcare workers and policymakers. However, in 2010, a World Health Organization survey revealed that only 16% (23/147 countries surveyed) of developing countries had a functioning national surveillance system, with remarkable differences and heterogeneity between low- and middle-income countries.

When estimating the cost and benefit of prevention, it is necessary to address the question, of to what degree can HcAI be actually prevented. A 2011 study among US hospitals estimated that the application of bundled interventions could lead to a twice-fold reduction for all HcAIs; specifically, a reduction of 18-66% for CLABSI, 38-55% for VAP, 17-69% for CAUTI and 26-54% for SSI.

A systematic review evaluating the impact of HcAI in Africa identified lack of water, sanitation and hygiene (WASH) as important risk factors for HcAI. To this end, it was estimated that the provision of WASH and additional basic measures (eg. environmental cleaning) wherever necessary, and a subsequent significant decrease (~50%) of HcAI, was associated with a significant reduction both in HcAI rates but also in a significant benefit-cost ratio ranging between 1.6 to 8.6 (depending on the range of economic metrics evaluated, ranging from healthcare savings to healthcare costs, productivity costs and premature deaths).

Conclusion

HcAIs pose a significant global health burden, leading to increased morbidity, mortality, and financial strain on healthcare systems. The prevalence of HcAIs varies globally, with different factors affected by geographic, resource and financial determinants. The impacts of HcAIs extend beyond individual patient outcomes, affecting hospital resources, workforce capacity, and healthcare costs. The cost burden on nations and healthcare systems is staggering, however, these financial estimates are less clear in developing nations, where infrastructure and prevention resources are often insufficient.

Ecologically, HcAIs contribute to antimicrobial resistance, compounding the problem of infection control both inside and outside healthcare facilities. Waste management, antimicrobial overuse, and environmental pollution from healthcare facilities highlight the broader ecological impacts of these infections. Nonetheless, HcAIs are preventable through adherence to evidence-based infection control measures, which can significantly reduce infection rates and associated consequences.

In conclusion, tackling the issue of HcAIs requires a multifaceted approach that includes prevention, surveillance, and global cooperation. By investing in prevention strategies, improving infrastructure, and ensuring adequate healthcare system capacity, the burden of HcAIs can be substantially reduced, saving lives and healthcare costs worldwide.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 46

Healthcare-associated infections and antimicrobial resistance

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The importance of antimicrobial resistance in HAI

Healthcare-associated infections (HAIs) represent a significant global health challenge, leading to increased morbidity, mortality, and healthcare costs. These infections, acquired during the provision of healthcare, often occur in patients who are already vulnerable due to illness or medical interventions. The emergence and spread of antimicrobial resistance (AMR) further complicate the management of HAIs, as many pathogens responsible for these infections have developed resistance to commonly used antibiotics. This growing threat undermines the effectiveness of treatment, placing immense pressure on healthcare systems worldwide. In this chapter, we explore the epidemiology of HAIs, the mechanisms driving AMR, and the strategies needed to combat both, aiming to provide a comprehensive understanding of this pressing issue.

Between 2000 and 2015, global antibiotic consumption in humans rose by 65%, while usage in animals is projected to increase by 11.5% from 2017 to 2030. If current trends continue, worldwide antibiotic consumption could surge by 200% before 2030.

Antibiotic-resistant bacteria have significantly increased the global burden of healthcare-associated infections (HAIs), posing heightened health risks, particularly in developing countries. Their continuous emergence and evolution have rendered many conventional antibiotics ineffective, leaving only a limited set of last-resort treatments for managing multidrug-resistant (MDR) HAIs. In 2017, the World Health Organization (WHO17) identified twelve priority antibiotic-resistant pathogens requiring new treatment options. The updated statement classifies as the critical group high-risk pathogens such as MDR *Acinetobacter baumannii*, carbapenem-resistant *Enterobacteriaceae* resistant to cephalosporins and carbapenems. These pathogens, along with the notorious 'ESKAPE' group (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species), exhibit both multidrug resistance and high virulence, especially in the healthcare environment.

Gram-negative bacteria among HAI, focus on carbapenem resistance

Resistant Gram-negative bacteria are a major concern in healthcare-associated infections (HAIs) due to their ability to evade many commonly used antibiotics. Pathogens such as *Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii,* and *Escherichia coli* frequently cause HAIs like pneumonia, bloodstream infections, and urinary tract infections. Their resistance to critical antibiotics, including carbapenems and third-generation cephalosporins, makes treatment options limited and often less effective. This resistance contributes to higher morbidity, mortality, and healthcare costs, underscoring the urgent need for effective infection control measures and antimicrobial stewardship in healthcare settings.

European surveillance of AMR from HAI highlights countries such as Greece, Romania, Serbia, and Italy, with the highest rates of CRE ranging between 16.7 and 43.7%. On the contrary, countries such as Finland, Iceland, and Lithuania have virtually no CRE among HAI.

Between 2015 and 2017, over 5,000 healthcare facilities monitored adult healthcare-associated infections (HAIs), reporting over 300 thousand pathogens isolated from HAIs. Surgical site infections (SSIs) accounted for the most significant proportion of pathogens (43%), followed by catheter-associated urinary tract infections (CAUTIs) at 29%, central line-associated bloodstream infections (CLABSIs) at 25%, and ventilator-associated pneumonia (PVAPs) at 3%. *Escherichia coli* was the most frequently reported pathogen, making up nearly 18% of all cases, followed by *Staphylococcus aureus* (12%) and *Klebsiella* species (9%).

Carbapenem resistance was found in 6.9% of *Klebsiella* spp. 6.2% of *Enterobacter* spp. in 0.7% of *E. coli* and in 20.2% of *Pseudomonas aeruginosa*, whereas in a similar study during the 2011-2014 period, carbapenem resistance was found in 11.3% of *Klebsiella* spp. 3.0% of *Enterobacter* spp. in 1.3% of *E. coli* and in 28.4% of *Pseudomonas aeruginosa* increasing resistance in all but *Klebsiella* spp.

Some centers have reported alarming rates of enterobacterial resistance to carbapenems, recorded bloodstream infections 2016-2021 with an average CRE rate for *K. pneumoniae* of 23.1% ranging from 8.1 to 47.4%, notably, the lowest rates were during the initial phase of the COVID pandemic. For *E. coli* isolate, CRE was considerably lower (1.5%), although ESBL was recorded on average in 38.2% and was unaffected during the pandemic period.

In California from 2014-2017, the incidence of CRE-derived HAI was, on average, 3.1% for *Enterobacteriaceae*, although *Klebsiella* spp. showed the highest, with 7.2% of the isolates being CRE.

A meta-analysis of *Pseudomonas aeruginosa* isolates from Ethiopia revealed that the overall multi-drug resistance (MDR) rate in *Pseudomonas aeruginosa* was 80.5% (95% CI: 66.25–93.84). Subgroup analysis by infection type and year of publication revealed that *P. aeruginosa* from healthcare-associated infections showed higher resistance to ceftazidime (94.72%) compared to isolates from mixed healthcare-associated infections (70.84%) and surgical site infections (57.84%). Resistance to gentamicin was highest during 2018–2020 (73.96%) but declined in 2021–2023 (42.69%) and 2015–2017 (29.82%).

A multicenter study from Iranian hospitals showed that CRE among HAI was 21.1% for *Klebsiella* spp. and 5.1% for *E. coli* isolates from 2017 through 2019. Resistance to carbapenems for *Pseudomonas* spp. was 26.3%, and for *Acinetobacter* spp.—34.5% during the same period. Also, a larger study of 940 Iranian hospitals in 2018 found CRE isolates in 57.8% of *Klebsiella* spp., 21.4% of *E. coli*, and *Pseudomonas* spp. and *Acinetobacter* spp. CR was documented.

Among the pediatric population, carbapenem resistance (CR) prevalence is generally lower than in adults. Data from the National Healthcare Safety Network (2011–2014) showed carbapenem resistance rates of 1.8% for *Klebsiella* spp., 2.6% for *Enterobacter* spp., 1.9% for *E. coli*, 8.2% for *Acinetobacter* spp., and 15.5% for *Pseudomonas* spp. These rates are notably lower than those reported in the adult population.

Between 2013 and 2016, a study conducted in an Italian intensive care unit revealed significant resistance patterns among Gram-negative bacteria. Resistance to third-generation cephalosporins (cefotaxime or ceftazidime) was found in 52.3% of *Klebsiella pneumoniae* isolates and 30% of *Escherichia coli* isolates. Additionally, carbapenem resistance (imipenem, meropenem, ertapenem) was observed in 91.6% of *Acinetobacter baumannii* and 28.5% of *Klebsiella pneumoniae* isolates. Multidrug-resistant (MDR) phenotypes were detected in all *Pseudomonas aeruginosa* isolates, as well as in 91.6% of *Acinetobacter baumannii*, 40% of *Escherichia coli*, and 52.3% of *Klebsiella pneumoniae* isolates. Furthermore, resistance to colistin was noted in 4% of *Klebsiella pneumoniae* isolates.

As Bunduki and colleagues highlighted in their meta-analysis, reliable reports on antimicrobial resistance from African countries are limited. The prevalence of extended-spectrum beta-lactamase (ESBL)- producing enterobacteria was found to range from 50% to 70%. Additionally, carbapenem resistance (CR) in *Enterobacter* spp. was reported at 9.8%, with few centers documenting resistance in *Klebsiella* spp. and *E. coli*. This raises concerns about potential underreporting and the need for more comprehensive surveillance.

Carbapenem resistance among Gram-negative bacteria, particularly in healthcare-associated infections (HAIs), is a growing global concern. High resistance rates are observed in pathogens like *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, with some regions reporting rates as high as 90% of MDR. While pediatric populations show lower resistance than adults, the overall trend reveals increasing resistance, especially in high-risk areas. Combating this rise is crucial as multidrug-resistant (MDR) organisms become more complicated to treat, posing significant challenges to healthcare systems worldwide.

Resistant Gram-positive bacteria among HAI

Staphylococcus aureus and *Enterococcus* species are significant causes of healthcare-associated infections (HAIs) due to their ability to colonize patients in medical settings. *S. aureus*, especially methicillin-resistant *S. aureus* (MRSA), frequently causes surgical site and bloodstream infections, as well as ventilator-associated pneumonia. *Enterococcus* species, including vancomycin-resistant enterococci (VRE), are linked to catheter-associated urinary tract infections (CAUTIs) and bloodstream infections. Both pathogens are known for their antibiotic resistance, complicating treatment, increasing hospital stays and costs, and raising mortality rates, making them key targets for infection control.

There was virtually no change for Gram-positives during two periods reported to the CDC; MRSA was found in 52.6% *vs.* 48.4% for 2015-17 and 2011-14, respectively. *Enterococcus faecium* resistant to vancomycin 83.8% *vs*. 82.1% or 2015-17 and 2011-14, respectively. Some groups, such as Shahnaz Rimaz *et al.*, have reported a low prevalence of MRSA (<10%) contrasts by high rates of vancomycin-resistant (VR) *S. aureus* (2.4%) with a similar pattern for non-*aureus Staphylococci* were VR ranges from 1.0-17% furthermore the also reported 63% of VRE among their *Enterococcus* HAI isolates.

In pediatric patients (including ICU, neonatal, and non-ICU), the prevalence of MRSA was 29.1%, and VRE was less than 1% for the National Healthcare Safety Network report during 2011–2014.

MRSA isolates from CLABSI between oncologic and non-oncologic patients differed significantly (45.6% *vs.* 57.0% respectively, $p<0.001$). There were no significant differences between isolates of VRE between those two groups of CLABSI patients.

Fluconazole resistance and emerging MDR *Candida* species

A multicenter study from India showed that candidemia was more frequent among COVID-19 patients hospitalized in critical care compared to non-COVID patients. Also, mortality between these two groups was statistically higher among COVID-19 patients. Interestingly, 17% of candidemias were caused by *Candida auris*.
Fluconazole resistance has increased considerably, leading to the predominance of fluconazole-resistant (FR) *Candida* sp. exemplified by Siopi *et al.* A steady increase in FR C. paraphimosis and *C. auris* predominated among candidemia isolates in 2020 through 2023 in a Greek hospital, leading to higher mortality.
Systematic reviews of *Candida parapsilosis* candidemia report mortality rates ranging from 17.5% to 46.8%, with resistance rates exceeding 10% in some regions. There is also clear evidence that the proportion of candidemia cases caused by *C. parapsilosis* has increased over time.
Over the last decade, *C. auris* outbreaks have been reported across all WHO regions. Given *C. auris*'s potential for outbreaks, the emergence and spread of multidrug-resistant (MDR) strains, and the difficulties in identifying and eradicating it in healthcare settings, it is critical to assess the effectiveness and feasibility of prevention and control measures based on known risk factors. *C. auris* candidemia is associated with overall mortality rates between 29% and 62%, with 30-day mortality ranging from 23% to 67%. Resistance to fluconazole is alarmingly high, ranging from 87% to 100%, while resistance to voriconazole is between 28% and 98%. Amphotericin B resistance rates vary from 8% to 35%, and echinocandin resistance ranges from 0% to 8%.

Specific healthcare-associated infections and AMR

Healthcare-associated infections (HAIs) occur when patients develop infections while receiving treatment in healthcare facilities such as hospitals, clinics, or long-term care centers. The five most common types of HAIs are pneumonia, urinary tract infections (UTIs), bloodstream infections (BSIs), surgical site infections (SSIs), and gastrointestinal (GI) tract infections. These infections frequently affect intensive care unit (ICU) patients. They can be caused by external devices, such as ventilators and catheters (leading to ventilator-associated pneumonia, catheter-associated UTI, and central-line-associated BSI) or endogenous sources, such as GI tract infections. Preventing HAIs relies on strict infection control measures, including hand hygiene, proper sterilization techniques, and appropriate use of antibiotics.

Surgical site infections

The National Healthcare Safety Network reported that during 2015-2017, SSI were the most frequent HAI recorded. *S. aureus* was the most frequently isolated pathogen, with 41.9% expressing methicillin resistance. *E. coli* was the second most frequently isolated pathogen, with 18.2% expressing ESBL and 0.6% being CRE. Enterococcal infections followed, with 55.6% showing vancomycin resistance and *Pseudomonas* with 9.1% CR.
In a multicenter study from Ethiopia, *Enterobacteriaceae* associated with SSI showed high levels of resistance to ertapenem (32.9%), amikacin (24.3%), imipenem (20.3%), and meropenem (17.6%). In that study, the multidrug-resistant (MDR) frequency of *Enterobacteriaceae* ranged from 84.5 to 94%. There are substantial complications around an SSI by an MDR organism; CRE has been associated with a median global hospital stay of 45 (IQR 26-67) days and a median global cost of hospitalization between €29,946 (IQR 15,405-47,749).

Central line-associated bloodstream infections

Multidrug-resistant (MDR) pathogens play a critical role in central line-associated bloodstream infections (CLABSIs), posing a significant challenge in healthcare settings. These resistant organisms are often more difficult to treat due to their resistance to multiple antibiotics. MDR pathogens in CLABSIs lead to higher morbidity, mortality, and healthcare costs, as treatment options are limited and more complex

The Korean National Healthcare-Associated Infections Surveillance System recorded that the rates of BSIs and CLABSIs significantly increased during the COVID-19 pandemic compared to the pre-COVID-19 period in large-sized hospitals. In contrast, these rates significantly decreased in small to medium-sized hospitals. The causative organisms changed between those two periods: a reduction in *S. aureus* and an increase in *Klebsiella* spp.

A study from Kuwait identified an MDR profile in 88.6% of *Acinetobacter* species and 81.4% of *Pseudomonas* species. The mortality rate among patients with bloodstream infections (BSIs) was 63.15%, notably higher than reported in other studies. MRSA is present on average in 49.5% of all *S. aureus* CLABSI in acute care hospitals but its presence increases to 77% in long-term care facilities.

Catheter-associated urinary tract infections (CAUTIs)

E. coli was the number one cause of CAUTI in acute care hospitals, oncology wards, and rehabilitation centers and was the second leading cause in long-term care facilities. A high proportion of isolates exhibited extended-spectrum beta-lactamase (ESBL) production and resistance to carbapenems. ESBL-producing *Klebsiella* spp. were identified in an average of 19.4% of isolates among non-LTCF (long-term care facility) CAUTIs, but this figure was more than double in LTCF patients (48.2%). However, in some centers, antimicrobial resistance (AMR) is at alarming rates, with 100% resistance to ceftriaxone among *Klebsiella* spp. and *E. coli* isolated from CAUTIs, and 10–57% of those isolates being carbapenem-resistant.

Ventilator-associated pneumonia (VAP)

A Japanese study found that *Pseudomonas aeruginosa*, followed by methicillin-resistant *Staphylococcus aureus* (MRSA), were the most frequently isolated pathogens. Risk factors for AMR included chronic renal disease, a history of antibiotic-resistant pathogen (ARP) infection or colonization within the past year, bedridden status, and tube feeding, all of which on average resulted in a two-fold increase in risk. In the USA, *Pseudomonas aeruginosa* in pVAP (probable ventilator-associated pneumonia) has been described with carbapenem resistance ranging from 26.3% to 61.4% and piperacillin-tazobactam (PIP/TAZ) resistance ranging from 21.7% to 34.8%. MRSA was found in 46.3%, and carbapenem resistance was seen in 23.3% of *Klebsiella* spp. isolates.

Conclusion

In conclusion, antimicrobial resistance (AMR) significantly exacerbates the global healthcare challenge posed by healthcare-associated infections (HAIs). The emergence of multidrug-resistant organisms complicates treatment, increasing morbidity, mortality, and healthcare costs. Gram-negative bacteria, particularly *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, exhibit alarming resistance to carbapenems, while Gram-positive pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) contribute to severe HAIs like surgical site infections (SSIs) and catheter-associated infections. Additionally, the growing prevalence of resistant fungal pathogens, like *Candida auris*, further complicates infection control.

Effective infection control measures, antimicrobial stewardship, and continued global surveillance are crucial to mitigate the spread of these resistant pathogens. The urgency of developing new antimicrobial therapies cannot be overstated, as AMR continues to threaten healthcare systems worldwide. Addressing this multifaceted challenge requires a collaborative, global approach to safeguard patients and ensure the sustainability of modern healthcare.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 47

Implementing infection prevention and control in hospital settings

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Introduction

Many professional societies in the healthcare field, as well as national and international institutions, recommend evidence-based measures to prevent the transmission of microorganisms and healthcare-associated infections (HAIs). However, adherence to these recommended infection control and prevention (IPC) measures remains inadequate and an increase in adherence continues to be a primary goal.
In recent years, the importance of IPC has increased significantly due to the global rise in antimicrobial resistance, which increasingly limits the effectiveness of treatment for many HAIs. While the introduction of technical innovations can support IPC to some extent, behavioral change among healthcare workers (HCWs) plays a far more crucial role in improving IPC. The implementation of practices such as WHO-recommended hand hygiene, specific infection prevention measures and outbreak prevention and control requires not only the attention of healthcare staff but also the adoption of measures that are not yet always standard in routine care. Factors such as time constraints and lack of knowledge are often cited as reasons for non-compliance with these guidelines. However, various studies have shown that IPC measures can be successfully implemented to enhance patient safety. Most implementation projects in hospitals have been initiated in intensive care units and surgical departments, with fewer taking place in regular wards or outpatient care. The experience gained from these projects has been valuable for further theoretical analyses and implementation projects. However, it should be noted that the success of an intervention in one area does not guarantee success in another. For example, the success of Pronovost *et al.*'s intervention to reduce central line-associated bloodstream infection (CLABSI) in US hospitals could not be replicated in UK hospitals.
Therefore, implementation should always be considered as an individual project for each department, unit, or ward, requiring careful planning that takes into account the specific characteristics of the environment and intervention as well as additional factors that are crucial for implementation.
This chapter outlines the most important aspects of implementing IPC measures in hospitals.

Theoretical approaches

Implementation is the process of translating a method, measure, concept, or strategy into routine practice within an organization or system in order to achieve a desired result.

It involves various phases, including planning, execution, monitoring, and evaluation to ensure that intended benefits are realized.

The implementation of clinical guidelines or organizational processes and workflows in hospitals is particularly challenging, as hospitals are complex organizations in which multiple practices and unforeseen events have to be coordinated. Therefore, implementation in hospitals requires careful consideration of various factors, including resources, stakeholder engagement and organizational culture.

Concretely, in ICP the goal of implementation is to successfully transfer evidence-based IPC measures into routine patient care with the goal of increasing patient safety by reducing the transmission of microorganisms and HAI.

A special feature of the implementation of IPC measures – as generally in the implementation of prevention measures – is the understanding that evidence-based IPC practices do not show their benefits immediately. This aspect, described as 'delayed gratification,' can affect HCWs' motivation to change their behavior concerning the sufficient integration of IPC measures into daily routine.

In this context, the RN4CAST study described interesting results: A Europe-wide survey on rationing-prone activities of nursing staff showed that when prioritizing patient care activities, oral care for ventilated patients was cited as an activity that was more likely to be omitted than, for example, pain management or treatments and procedures – practices for which results of the handling are often immediately recognizable.

The fact that symptoms of an acquired HAI appear later also contributes to the fact that no negative effects of IPC measures that are omitted are immediately obvious to HCWs. Frey and Schulz-Hardt describe this lack of immediately recognizable negative consequences as a contribution to so-called learned carelessness, which can lead to HCWs not implementing measures and thus setting an unfavorable example for others.

A failure to immediately recognize the effect of an action in practice may also lead to a failure to recognize the importance of this action in theory. More than two decades ago, Pittet described the barriers to appropriate hand hygiene. One reason for not performing it was the statement by HCWs that "patient needs take priority over hand hygiene". As recommended in these two publications and many others as well, to achieve better care, the implementation of actions frequently neglected in patient care must continue to be the goal. The authors of the European RN4CAST study describe measures such as improved documentation, organization of care, sufficient time, and adequate staffing as a help in this regard; Pittet also emphasizes the importance of strategies to increase the visibility of positive outcomes, such as regular feedback, training, and the collection of infection statistics, as well as the interactivity of various tools in the sense of multimodal, multidisciplinary strategies.

Meanwhile, the field of implementation has developed significantly. Various theoretical approaches and frameworks have been created to support and explain implementation, with some overlap in content. In 2009 Damschroder *et al.* brought together different theories of implementation and created the Consolidated Framework for Implementation Research (CFIR) specifically for the implementation of research findings in health services. The framework provides a comprehensive, theoretically grounded framework for effective implementation. It helps researchers and practitioners identify and understand the factors that influence the success or failure of implementation activities in different contexts, even in an environment as complex as a hospital. The authors identified five domains with specific constructs that can help or hinder implementation success in different ways:

1. "Intervention characteristics" domain. This domain refers to the characteristics of the intervention itself, such as complexity and adaptability, but also to the source and evidence of the intervention. For example, a complex intervention that requires a high level of training and new technologies may be difficult to implement. However, if the intervention is adaptable and can be customized to the specific circumstances of

a ward or department, the likelihood of successful implementation increases. Implementation can also be more successful if the stakeholders involved consider the intervention to be useful.

2. "Outer setting" domain. This domain includes external factors such as political guidelines, financial incentives, social norms, or a competitive situation resulting from peer pressure, which can also affect the success of implementation. Also, the extent to which an organization is networking with other external organizations favors the implementation of new practices.
3. "Inner setting" domain. This domain focuses on the characteristics of the organization, such as culture, leadership, and resources. In hospitals or wards with a strong culture of safety, a culture of continuous learning and improvement, and committed leadership, new guidelines are more likely to be successfully implemented. Conversely, in an organization with limited resources and a lack of leadership support, implementation efforts may be hampered.
4. "Characteristics of the individuals involved" domain. This domain considers the characteristics and beliefs of the individuals involved in implementation, such as knowledge, attitudes, and self-efficacy. For example, if HCWs are convinced of the benefits of a new guideline and feel competent to implement it, implementation is more likely to succeed.
5. "Process of implementation" domain. This domain deals with the steps and strategies taken to introduce the intervention, such as planning, implementation, and monitoring. A targeted implementation process might include the formation of interdisciplinary teams to support the introduction of a new practice and provide regular feedback. This structured approach can improve the acceptance and implementation of the practice.

In 2022, a revised version of the CFIR was published with additional constructs, including critical events such as the COVID-19 pandemic in the "outer setting" domain, in such a way that new constructs can be traced back to the original CFIR to ensure longitudinal consistency.

With more specific relevance to IPC, Trivedi *et al.* published strategies for preventing HAI in acute-care settings as part of the SHEA/IDSA/APIC Practice Recommendations in 2023. The authors provide a broad overview of various implementation models and concepts, enabling the reader to understand the different approaches and theories and to select the appropriate model for a planned implementation project. The authors also emphasize that the success of an implementation always depends on the context in which the implementation takes place, considering local factors such as operational support, experience, willingness to change, and safety culture and that in a specific healthcare setting for a given intervention, a detailed implementation plan is necessary for success.

As a pragmatic strategy for the implementation in everyday clinical practice, the WHO recommended the concept of a multimodal strategy. This concept was initially recommended for the improvement of hand hygiene and was later also part of WHO's core components for IPC programs.

WHO's multimodal strategy offers a clear, standardized structure for planning and realizing implementation projects. It defines five components:

1. system change to facilitate best practice;
2. education and training of healthcare workers and key stakeholders;
3. monitoring of practices, processes, and outcomes and the provision of timely feedback;
4. improved communication (e.g. reminders in the workplace or videos);
5. change in culture by fostering a climate of safety.

Various studies have shown that this multimodal strategy, while not a formal implementation framework like CFIR, nonetheless provides a practical and effective structure for improving IPC in diverse settings.

Practical approach

Before and during, but also in the post-interventional evaluation of an implementation project, all theoretical aspects listed above help support implementation.
The following is a chronological presentation of a possible application of these aspects and thus of the optimization of an implementation project in the context of improving IPC in the hospital setting.

Before implementation
Detailed planning is necessary before implementing an IPC intervention. This includes analyzing needs, involving relevant stakeholders, ensuring the availability of resources and training, and developing a monitoring system and effective communication. The intervention must be based on evidence-based practices and consider cultural and behavioral factors to ensure that it can be successfully implemented in the long term.

Identifying deficits in IPC
Before implementation, gaps in IPC measures should be identified. Ongoing surveillance or prevalence surveys offer opportunities for the identification of IPC gaps. Outcome data, such as infection rates, as well as process data, such as data on compliance with IPC measures or the consumption of alcohol-based hand rub, can be collected. In some areas of the hospitals such as ICUs or stationary surgical wards, outcome data may be easily collected. In other areas, such as ambulatory care or the emergency department, process indicators are more helpful in detecting deficits in IPC.
In particular, comparing a hospital or ward's own data with regional, national or even international data permits a quick interpretation of the situation.

Willingness to change
Once a problem in IPC has been identified, the question arises as to what extent the department or ward recognizes a need for action and to what extent the so-called readiness for change exists in a department or ward. As described by Weiner, organizational readiness refers to organizational members' commitment to change and change efficacy to implement organizational change. In other words, it represents how ready an organization or individuals are to successfully accept and implement change and is therefore a key factor in the implementation of IPC in hospitals. The assessment of this readiness can be performed by questionnaires or interviews with individuals of the intervention's target group, which is resource-intensive but helpful in getting a sufficient overview of the initial situation before possible implementation. Another option for assessing this readiness can be a presentation on the IPC deficits identified in the department or ward and then assessing the reaction of HCWs present.
Conducting a pilot phase of implementation can also provide helpful information about the readiness for change – as well as for other aspects of the feasibility of the intervention.

Implementation team
Ideally, the implementation should be organized and led by a multidisciplinary team consisting of leading nursing and medical staff, HCWs and IPC link personnel from the ward or department, IPC experts, and other key stakeholders, depending on the intervention. Are there champions in the department or ward who could support the implementation? Intrinsically motivated champions play an essential role in implementation. According to Shaw, a distinction should be made between project champions, who are associated with specific projects, and organizational change champions, who promote change for an entire organization and will have more influence on success than project champions. Damschroder *et al.* also point out that the effectiveness

of champions is influenced by the hospital's or department's organizational culture with its shared values, norms, attitudes, and behaviors that shape daily work and interactions among hospital staff. Several studies have shown that positive organizational culture is associated with patient safety and quality of care. As a major factor in organizational culture, leadership plays a particularly important role in IPC activities. As described by Saint *et al.*, successful leaders cultivate a culture of clinical excellence, focus on overcoming obstacles, inspire, and think strategically while acting locally.

Planning the intervention

A successful IPC intervention in hospitals should focus on specific IPC measures that are practically implementable and flexible enough to address the specific needs of the setting (see also above: CFIR domain 1 "Intervention characteristics"). Different departments (e.g., intensive care, surgery, emergency department) have general but also specific IPC requirements, and therefore, interventions should be tailored accordingly.
IPC measures should be evidence-based to ensure that they are actually effective. In recent years, IPC bundles have become widely successful in the hospital setting. To prevent a specific HAI, three to five key evidence-based IPC measures should be combined in a bundle to increase the impact of the intervention.
Adherence to IPC measures may be supported by the use of a checklist in which key measures are summarized and, therefore, easier to follow. In addition, checklists help to promote the intervention, support the evaluation, and also, when the checklist must be filled out and signed by individual HCWs, increase individual commitment and responsibility. A checklist could, for example, be created for catheter insertion or daily assessment of device necessity.
Consideration should be given to measurable outcomes of an intervention to analyze its impact but also to show the self-efficacy of all those involved during the implementation process. Relevant data for the selected process or outcome indicators should always be obtained before the start of the intervention as a baseline value. It is also beneficial to formulate a specific goal to be achieved, e.g., a specific hand hygiene compliance percentage.
Ideally, the intervention should adopt a multimodal approach to ensure that organizational and behavioral aspects have been taken into consideration. As mentioned above, this approach has been recommended by the WHO multimodal strategy and combines several measures to increase effectiveness.
Example of using the WHO multimodal strategy for improving adherence to an aseptic technique for dressing changes in surgical patients:

Component 1 (System change to facilitate best practice):

- Will all dressing materials, instruments and, if necessary, sterile gloves and swab tubes be available and easily accessible?
- Ideally, will dressing sets be available? Or a dressing trolley?
- Is the dressing trolley, or the dressing room, or the patient area where the dressing is changed equipped with alcohol-based hand rub dispensers?
- Is there a waste bin nearby for the dressing removed?

Component 2 (Education and training of healthcare workers and key stakeholders):

- Who is the target group among HCWs in the surgical department that is to be trained?
- Do other stakeholders, in administration, for example, also need to be trained to make them aware of the need to procure dressing materials and hand rub dispensers?
- What form should the training take? Is it possible to provide practical training using a model?

Component 3 (Monitoring of practices, processes, and outcomes and providing timely feedback):

- When can repeated audits be carried out during dressing changes to assess the implementation of the aseptic technique?
- In addition to individual feedback during the audit, how often can structural feedback on the audit results be provided?
- Who should participate in these feedback events?
- Are there different ways to communicate the feedback?
- How in-depth will the feedback be? Will the results of the audits also be used for the ongoing discussion of further improvements?
- Is data on SSI collected? If so, to what extent are these rates reflected in the department?

Component 4 [Improved communication (e.g. reminders in the workplace or with videos)]:

- How can the content and developments of the implementation be communicated effectively to all HCWs of the target group?
- What kind of supporting material could be created and by whom?

Component 5 (Culture change by fostering a climate of safety):

- Do the senior surgeons and senior nurses support the implementation? Are they present during feedback meetings? Do they perhaps take over the management or moderation of the feedback events?
- Is there a culture of learning that allows HCWs to address IPC measures that have not been realized? How can this culture of learning be introduced or supported?
- Is there also support at the hospital level, for example in facilitating the procurement of necessary materials?
- Will successes in the implementation process be acknowledged?
- Is it possible to engage patients with regard to HCWs' hand hygiene?

During implementation

The implementation phase is the operational phase in which the strategies are put into practice, with the introduction of measures being an important action at the beginning of the intervention. However, continuous evaluation and adjustment are also helpful for the success of the implementation. Regular audits, compliance monitoring, and infection rate analyses provide information on the effectiveness of the intervention. Based on feedback and evaluation data, the measures should be reviewed regularly and adapted to meet any newly identified challenges or simply to introduce better methods for integrating the IPC intervention into the existing workflow. HCWs may be involved in the implementation process to increase the sense of ownership and participation e.g., through suggestions for optimization or focus groups.

Initial successes in the implementation of the measures should be acknowledged and the recognizable self-efficacy of the HCW should be communicated to further promote the implementation of the IPC measures.

After implementation

After active implementation has been completed, an evaluation should be made of which results could be achieved with the intervention and how these results can be maintained in the future. The evaluation of the implementation project by the HCWs involved may also be useful. In addition, all evaluation results will be helpful for future implementations.

Conclusion

IPC should be more deeply integrated into daily patient care. Various studies have demonstrated that implementing IPC measures in hospitals is both feasible and effective. For successful implementation, strategies must follow a multimodal approach and be tailored to the specific needs of each hospital area. Theoretical frameworks and models provide valuable support in the planning, execution, and evaluation of IPC initiatives. Organizational factors and a strong safety culture are essential for sustainable and successful IPC implementation. Therefore, active support from both clinical and non-clinical leadership is crucial.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 48

Infection prevention and control: certainties and controversies

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Rationale for infection prevention and control

Healthcare-associated infections (HAIs) are infections acquired by patients while receiving healthcare. They appear during or after hospitalization of the patient who was not incubating the infection on admission to the hospital. Hundreds of millions of people are affected by HAIs each year worldwide. They threaten patient safety by representing the most prevalent adverse events experienced in hospitals, impacting morbidity, mortality, and quality of life, and dramatically increasing the cost of care to health systems worldwide with region-specific differences. They include hospital-acquired pneumonia (HAP), surgical site infection (SSI), urinary tract infection (UTI), catheter-associated bloodstream infection (BSI), and gastrointestinal infections, mainly with *Clostridioides difficile* infections. Up to 50% of HAIs are estimated to be preventable. The application of infection prevention and control (IPC) measures in healthcare settings is essential to prevent HAIs with a wide range of public health initiatives to reduce their high burden.

The ancient work of Ignác Semmelweis in the 19th century about the prophylaxis of puerperal fever, bacterial postpartum infections, and invasive infections in newborns illustrated one of the first epidemiological proofs for the prevention of HAIs by hand washing. His attempt to obtain a favorable collective change in behavior for hand hygiene among Vienna Medical University students in maternity represented a method to implement a safe patient culture. Nonetheless, his intransigence drove him to fail to achieve his objective despite a clear lifesaving intervention. His unsuccessful attempt to implement a patient safety initiative has allowed to his worthy successors in IPC to learn lessons of a successful intervention, especially in terms of feasibility and acceptability.

The integration of hand hygiene with alcohol-based handrubs has gone through different stages of multidisciplinary validation based on evidence of their effectiveness in real life. This remains the most effective preventive strategy to reduce HAIs. Modern campaigns to sustain improvement in compliance with hand hygiene, coincide with a reduction of nosocomial infections and methicillin-resistant *Staphylococcus aureus* (MRSA) transmission. The control of cross-transmission for multidrug-resistant Gram-negative bacteria by alcohol-based handrubs use slightly seems also efficient. The promotion of bedside antiseptic handrubs largely contributed to the increase in compliance for each opportunity in various situations of healthcare worldwide, contributing to reducing HAIs, especially for those involving the implantation of medical devices. Nowadays, various base-evidence IPC interventions have shown dramatic efficiency in reducing the incidence of HAIs in real-life settings whereas lots of healthcare practices are sustained despite the absence of formal proof of their effectiveness in preventing healthcare-associated infections. Continuous improvement in care

requires ongoing monitoring of the effectiveness and safety of medical procedures. This enables a more accurate assessment of the relevance in real-life situations of interventions and treatments that have already proved their effectiveness in clinical trials.

Surveillance programs for healthcare-associated infections

Individual actions of healthcare staff to control HAIs are not enough. A previous collective effort is crucial to know the local, regional, national and international incidence of each type of HAI and be able to assess the impact of relevant interventions in hand hygiene or other IPC strategies. The establishment of intensive surveillance programs is strongly associated with a reduction in all HAIs since the end of the 20th century. Many efforts have been made over the last few decades in the field of IPC to enable the essential WHO core components for the prevention and control of HAIs to be integrated into the hospital surveillance system. These effective programs included multidisciplinary and organized surveillance and control activities, active surveillance programs, a trained and effectual infection control physician or pharmacist, an infection control nurse per 250 hospital beds, and a system to report infection rates to surgeons and intensivists. In recent years, the collaboration of the IPC team was expanded to include an antimicrobial stewardship physician, a clinical microbiologist, and a pharmacist to control the consumption level, the prompt and relevance of antimicrobials prescription to improve patient safety by increasing clinical success of HAIs management and fighting the spread of antimicrobial resistance among pathogens and environmental microbes. Nonetheless, drug monitoring has not yet been proven to allow better clinical success but only decreases related-dose adverse events. Thanks to this strong organization, monitoring of HAIs brings several advantages, including training of staff in the prevention and control of HAIs, investigation and control of outbreaks, monitoring of staff health to prevent staff-to-patient and patient-to-staff spread of infection, advice on isolation procedures and infection control measures, infection control audit including inspection of waste disposal, laundry and kitchen, and monitoring and advice on the safe use of antibiotics. The spread of hand hygiene with alcohol-based handrubs among healthcare and medical staff has helped to combat the spread of MRSA colonization, cross infection, and HAIs rates among patients admitted at hospitals and requiring invasive medical or surgical procedures. Consequently, monitoring hand hygiene adherence and providing healthcare staff with feedback are of paramount importance. Then this surveillance system helps to build a safety culture and is a prerequisite to delivering trends data, changing behavior, adapting education to sociocultural context, strengthening performance feedback, and promoting an institutional safety climate using checklists.

Implementation strategies for preventing healthcare-associated infections

For over 10 years there has been dramatic success in improving the quality of patient care by focusing on the implementation of a group of evidenced-based preventive practices to achieve a better outcome than when implemented individually. Implementation science is therefore crucial for increasing the efficiency of hospital-wide programs, especially hand hygiene compliance among healthcare workers. Bacteria involved in HAIs are becoming increasingly resistant to antibiotics, making IPC actions even more important nowadays. This method has strongly contributed to the success of behavior change by tailoring IPC interventions to local practices and culture for better understanding, acceptance, and efficiency of healthcare staff. These strategies may therefore induce a subsequent decrease in HAIs and cross-transmission of multidrug-resistant

organisms or communicable nosocomial diseases worldwide. The public health response by IPC should be constrained by prevention and control actions, which must be a priority for limiting the consequences of antimicrobial resistance for all health systems of the world at all levels of care. As many HAIs are preventable, they may be considered an important indicator of the quality of patient care and represent an important patient safety issue in healthcare. Moreover, emerging and re-emerging infectious diseases, continue to challenge healthcare systems in Sub-Saharan Africa. Consequently, nurses, the keystones to IPC practice, need to have a better understanding of which, in what combination, and in what context implementation strategies should be best utilized to ensure their safety and that of their patients. In addition, IPC measures should be complementary with strategies to prevent and control the emergence and spread of antimicrobial resistance in hospitals, by implementing a whole-system approach.

Crucial role of environment in infection prevention control

The environment in the many components of a hospital plays an important role in the occurrence of HAIs. An IPC team member should also be involved in the planning of any new facility or renovation. The role of infection control in this process is to minimize HAIs. These include items such as ensuring appropriate hand washing facilities; a safe water supply, adequate isolation facilities for the hospital; adequate ventilation for isolation rooms and high-risk areas like surgery or devices procedures; cleaning of the hospital environment as surfaces of operating theatres, transplant units and intensive care units; recommending traffic flow to minimize exposure of high-risk patients and facilitate patient transport; preventing exposure of patients to fungal spores during renovations, and outlining precautions to be taken to control vectors responsible for transmission of infection. Cleanrooms and associated controlled environments provide for the control of contamination of air and, if appropriate, surfaces, to levels appropriate for accomplishing contamination-sensitive activities. The International Organization for Standardization (ISO) is a worldwide federation of national standards bodies. ISO has produced the document titled ISO Classification System 14644-1:2015 to describe standards for cleanrooms and associated controlled environments with part 1 for the classification of air cleanliness by particle concentration. Contamination control can be beneficial for the protection of product or process integrity in applications in industries such as pharmaceuticals, medical devices, healthcare and food.

Education and training of environmental services employees are essential in assuring effective disinfection practices. Monitoring disinfection practices and providing personnel with performance feedback using fluorescent markers, adenosine triphosphate assays, or less commonly cultures of surfaces, can help reduce multidrug-resistant organisms transmission and fight the spread of antimicrobial resistance. No-touch disinfection methods such as electrostatic spraying, hydrogen peroxide vapor, or ultraviolet light devices should be considered for terminal disinfection of multidrug-resistant organisms' patient rooms.

Hospital-acquired pneumonia

Hospital-acquired pneumonia (HAP) is one of the most serious HAIs, especially ventilator-associated pneumonia (VAP). They are the second most frequent HAI, representing the first HAI in terms of morbidity and mortality. The pathogenesis of HAP is multifactorial. Colonization of the respiratory tract with multi-resistant hospital bacteria is very common in patients on broad-spectrum antibiotics, receiving mechanical ventilation

or following surgery. This can occur within the first 24 hours in a critical care unit. Prevention of aspiration pneumonia in the hospital may be promoted in comatose patients, oral feeds if neurological or swallowing abnormalities, medications impairing consciousness (sedatives, narcotics), and general anesthesia, especially for chest and/or abdomen surgical procedures. Compromised host defenses such as critical illnesses, comorbidities, drugs, and surgical procedures can contribute to the development of HAP. To prevent HAP, oral feeds should be avoided in patients with neurological or swallowing abnormalities, and medications impairing consciousness must be limited.

In critically ill patients admitted intensive care unit, most of them required invasive ventilation with endotracheal intubation. However, risk factors of VAP include invasive ventilation, longer duration of intubation, and failure of extubation, by providing a source of colonization, leading to the migration of bacteria in the lower respiratory tract and the development of VAP. Reducing the duration of invasive ventilation by daily weaning strategy protocol compliance, especially with noninvasive ventilation in patients suffering from chronic obstructive pneumonia disease, may reduce the risk of VAP. Half-seated patient positioning could also reduce the risk of microaspirations around the tracheal-tube cuff and the formation of biofilm leading to progressive bacterial spread in the tracheobronchial tree, ultimately leading to VAP. In cases of severe acute respiratory distress syndrome (ARDS), the patient must be prone positioned to improve gas exchanges and limit the potential for aspiration. The administration of stress ulcer prophylaxis has been described to increase the risk of VAP. Moreover, a beneficial effect of oral antiseptic use, as Chlorhexidine mouthwash or gel, has been shown in the prevention of VAP according to several meta-analyses. Clinicians should take these findings into account when providing oral hygiene care to intubated patients. Subglottic secretion drainage may also reduce the duration of mechanical ventilation, length of stay, ventilator-associated events, mortality, or antibiotic usage. The implementation of an active, long-lasting program for preventing VAP may successfully increase compliance of healthcare workers with preventive measures. The critical impact of a multifaceted program of VAP prevention on its prevalence directly depends on healthcare workers' bedside performance. Otherwise, selective digestive decontamination with systemic antimicrobial therapy may reduce mortality and should be considered in critically ill patients at high risk for death. This controversial IPC measure should be discussed on a case-by-case basis, to avoid the spread of antimicrobial resistance. Otherwise, a recent multicenter, double-blind, randomized, controlled, superiority trial, showed that a subsequent 3-day course of inhaled amikacin reduced the burden of VAP among patients who had undergone mechanical ventilation for at least 3 days. This may decrease systemic antibiotic use and antimicrobial resistance spread.

The hospital water environment is a potential reservoir for Gram-negative bacteria, and it has been shown that contaminated sinks contribute to the spread of Gram-negative bacteria in outbreak and non-outbreak settings. Few studies, but no randomized controlled trials, have investigated the association of sinks in patient rooms with healthcare-associated acquisition of Gram-negative bacteria in non-outbreak settings but their heterogeneity in study design made it impossible to generalize the results.

The incidence of hospital-acquired respiratory viral infections correlates closely with respiratory viral transmission in the community. They may be complicated by pneumonia or even ARDS. The higher the incidence of viral infections in the community, the greater the chance that a healthcare worker, visitor, or patient will be infected and transmit infection to a patient. During the period of seasonal respiratory infections, regular and rigorous alcohol-based handrubs associated with the wear of facial masks for healthcare staff may protect immunosuppressed, neonates and aging patients admitted to the hospital to reduce the risk of communicable viral respiratory infections. One-fifth or more of cases of HAP may be caused by viruses rather than bacteria. Moreover, the morbidity associated with respiratory viruses extends beyond pneumonia. Viruses can also cause substantial harm by exacerbating patients' underlying conditions. Acute respiratory viral infections are well-established triggers for obstructive lung disease flares, heart failure exacerbations,

arrhythmias, ischemic events, neurologic events, and death. Literature is limited on the impact of patient vaccination on the risk of hospital-acquired influenza. A recent incident test-negative case-control study nested in a surveillance program has shown a reduced risk of hospital-acquired influenza by almost 60% in vaccinated patients admitted to a French teaching hospital, thus encouraging the use of vaccination against pneumotropic pathogenic viruses as a method of preventing HAP.

Protecting healthcare staff against pathogen respiratory virus is essential to ensure their own safety, maintain continuity and quality of care, and reduce nosocomial transmission of respiratory pathogens from healthcare staff to patients, especially those immunosuppressed and patients at extreme ages of life. Protection conferred by personal protective equipment was mainly studied for influenza, SARS-CoV, MERS-CoV, and SARS-CoV-2. Recent studies suggest that protection of staff caring for COVID-19 patients, should partial or complete immunization by vaccination, and wear a surgical face mask (apart from aerosols-generating procedures), eye protection, and a gown, but no evidence was confirmed for the protection conferred by gloving.

Surgical site infections

In the hospital theaters, bacteria and viruses are natural inhabitants of the environment, both in the community and in the hospital, and may expose patients to HAIs, especially surgical site infections (SSIs). Early deep SSIs occur within 30 days of the surgical procedure, or they become chronic above 30 days, especially if there is an implant or foreign body such as a prosthetic heart valve or joint prosthesis. Bacterial airborne contamination in the operating room during surgery indicates an increased risk for SSIs. SSIs prevention is complex and requires the integration of a range of measures before, during, and after surgery. There are existing evidence-based procedures and interventions undertaken pre- and peri-operatively to drastically reduce SSIs, e.g. pre-operative surgical prophylaxis and minimizing hypothermia. However, many rituals and behaviors take place in operating theatres that are derived from tradition and custom rather than from evidence. Given the burden of SSIs worldwide, the numerous gaps in evidence-based guidance, and the need for standardization and a global approach, WHO decided to prioritize the development of evidence-based recommendations for the prevention of SSIs.

The conventional surveillance method for bacteria in the air is by air sampling, plating, and counting colony-forming units (CFU). A strong correlation exists between air particle counts and microbial contamination but no evidence shows benefit for laminar airflow compared with conventional turbulent ventilation of the operating room in reducing the risk of SSIs in total hip and knee arthroplasties, and abdominal surgery. In the operating room environment, there is a need to fill research gaps in existing clinical, practical and technical knowledge, focusing on five topics including ventilation systems, thermal comfort, staff work practice and behavior, door operation and passage, air cleaning technology, and clothing systems.

Preoperative antibiotic prophylaxis (PAP) is an essential adjunct to many surgical procedures. In surgery, pathogenic bacteria are found in more than 90% of operative wounds during closure. This exists whatever the surgical technique and whatever the environment. These bacteria are few but can proliferate. They find in the operative wound a favorable environment (hematoma, ischemia, modification of oxido-reduction potential) and the surgery induces anomalies of the immune defenses. The objective of PAP is to prevent bacterial growth to reduce the risk of infection at the site of the intervention. The preoperative consultation represents a privileged moment to decide on the prescription of a PAP. It is possible to define the type of intervention planned, the associated risk of infection, and therefore the necessity or not of PAP, the time of prescription before surgery, and any allergic antecedents that may modify the choice of the selected

antibiotic molecule. For some operations, there is inevitable contamination of the surgical wound following the opening of a hollow viscus such as the gastrointestinal tract or the incisions through mucous membranes with a rich normal microbial flora such as the mouth, esophagus and vagina. In other operations, the use of implants as in cardiac valve prostheses or joint arthroplasties increases the risk of persistence of normal skin flora at the prosthetic site. In such procedures, PAP reduces the incidence of HAIs. PAP is to be given with induction of anesthesia before surgery incision and continued for not more than 24 hours. The choice, dosage, route and duration of PAP are important. Nasal decolonization with mupirocin ointment with or without chlorhexidine gluconate body wash in previous nasal carriers of *Staphylococcus aureus* undergoing cardiothoracic and orthopedic surgery can be proposed with evidence of cost-effectiveness in high-income countries.

Otherwise, after the ancient work of Semmelweis, advances in medical and scientific knowledge have led to the realization that the main risk factor for these invasive group B streptococcal disease in newborns is exposure to maternal rectovaginal group B streptococcal colonization during delivery. In high-income countries, pregnant women undergo screening for group B streptococcal colonization late in the third trimester, and intrapartum antibiotic prophylaxis is administered to those with positive results. Intrapartum antibiotic prophylaxis is more than 80% effective in the prevention of early-onset disease in infants but has not been effective against late-onset disease or prebirth sequelae associated with group B streptococcal infection. Consequently, a potential for maternally administered vaccine development was explored for the prevention of infant group B *Streptococcus* infections in an ongoing phase 2, placebo-controlled trial involving pregnant women, resulting in a reduction risk of invasive group B streptococcal disease correlated with the transfer of serotype-specific anti–capsular polysaccharide (CPS) IgG against group B *Streptococcus* in newborns.

Skin preparation solution is an important factor in the prevention of SSIs before surgery. No hair removal, or if hair removal was necessary, only use electric clippers. Use of alcohol-based antiseptic solutions for surgical site skin preparation. Concerning antisepsis, two studies have directly compared chlorhexidine gluconate in alcohol with iodine povacrylex in alcohol to reduce SSIs. The results of one randomized, controlled trial involving 788 patients who underwent elective colorectal surgery under clean-contaminated conditions (i.e., in which the surgical area is entered under controlled conditions with a low probability of contamination) were inconclusive. Conversely, a prospective study involving 3209 general surgery patients favored iodine povacrylex in alcohol for the prevention of SSI. Otherwise, approximately 178 million persons fracture a limb each year, including more than 1 million who are treated surgically in the United States. The high burden of traumatic injuries worldwide may induce a high incidence of SSIs, further exacerbating the health and socioeconomic situation of accident victims. Among patients with closed extremity fractures, a recent American multicenter pragmatic study showed skin antisepsis with iodine povacrylex in alcohol resulted in fewer SSIs than antisepsis with chlorhexidine gluconate in alcohol. However, there was no difference in the efficacy of using these two types of skin antisepsis in patients with open fractures. Nonetheless, these results suggest that the use of iodine povacrylexin alcohol as preoperative skin antisepsis could prevent SSIs in thousands of patients with closed fractures in North America, if not millions worldwide.

Other perioperative bundles must ensure the patient's normothermia with a target temperature >36 °C and use a protocol for intensive perioperative blood glucose control with intraoperative target blood glucose levels <200 mg/dL for adult patients undergoing surgical procedures.

Sterilization is the destruction of all micro-organisms including bacterial spores. Operationally, this is defined as a decrease in the microbial load by 10-6. This procedure is crucial before surgery to prevent surgical site infections by pathogens potentially transmissible by contaminated surgical instruments, but its quality may be insufficient in low-income countries. Sterilization can be achieved by either physical or chemical means, depending on local health systems resources. Moist heat sterilization: exposure to saturated steam at 121°C

for 30 minutes or 134°C for 4 minutes in an autoclave. Dry heat sterilization: exposure to 160°C for 120 minutes, or 170°C for 60 minutes, or 180°C for 30 minutes. Chemical sterilization by ethylene oxide and formaldehyde is being replaced in many countries because of safety concerns at the turn of the century. Low-temperature sterilization uses plasma systems using peracetic acid or hydrogen peroxide.

The surgical techniques may also influence the risk of SSIs. These can lead to greater morbidity, mortality, and healthcare costs. The identification of risk factors of SSIs remains an important point for preventive strategies to reduce their incidence. In the case of spine surgery, the Scoliosis Research Society identified potentially modifiable factors such as obesity, diabetes, smoking status and procedure-related parameters. Non-modifiable risk factors were also identified, including ASA score and age. These factors may prove useful for patient counseling as well as surgical planning. Procedure-related risk factors included revision status, operative time, use of osteotomy, fusion length and extension of fusion to the sacrum or pelvis. In gastrointestinal surgery, a recent meta-analysis of randomized controlled trials investigating the value of prophylactic drainage following colorectal anastomoses did not support the routine use of prophylactic drains. Otherwise, another recent meta-analysis showed that patients who underwent laparoscopic pancreaticoduodenectomy had a significantly lower incidence of surgical-site wound, superficial wound, and deep wound infections than those who received robotic pancreaticoduodenectomy. Meta-analyses intended to evaluate the effect of both robotic and open-cut operations on postoperative complications of stomach carcinoma revealed no statistically significantly different rates of postoperative abdominal abscesses among patients who had received robotic operations than in those who had received open surgical procedures. In urology, a meta-analysis comparing margin and perioperative complication rates for open retropubic, laparoscopic, and robot-assisted radical prostatectomies. Rates for readmission, reoperation, nerve, ureteral, and rectal injury, deep vein thrombosis, pneumonia, hematoma, lymphocele, anastomotic leak, fistula, and wound infection showed significant differences between groups, generally favoring robot-assisted radical prostatectomy. In gynecology, a meta-analysis showed that the rate of infectious complications associated with robotic-assisted hysterectomy was no different than that associated with conventional laparoscopic-assisted hysterectomy. In orthopedics, a meta-analysis assessing the risk of complications between manual and robotic-arm-assisted total knee arthroplasty, showed no difference in arthrofibrosis, superficial and deep infection, wound dehiscence, or overall complication rates.

In our recent context of limited resources for economic, human, and environmental reasons, a reduction in HAI levels ensures economic savings for hospital and social authorities, improved life expectancy, and disability-free life for patients admitted to hospital.

Urinary tract infections

Urinary tract infections (UTIs) are the most frequent HAIs. The great majority of these infections are associated with an indwelling urethral catheter. Urinary catheterization is a common procedure, with approximately 15% to 25% of all people admitted to the hospital receiving short-term (14 days or less) indwelling urethral catheterization at some point during their care. However, the use of urinary catheters is associated with an increased risk of developing UTIs. It is estimated that around 20% of hospital-acquired bacteremia arise from the urinary tract and are associated with mortality of around 10%. Most of the risk factors of UTIs are reversible and include invasive urological procedures, urinary catheter catheterization unless compelling, and duration of catheterization.

Consequently, WHO recommended that the urethral catheter insertion bundle should avoid the use of urinary catheters if not necessary and use a correct insertion technique to minimize contamination.

WHO also recommended that the urethral catheter maintenance bundle should take care of a closed drainage system to avoid catheter colonization, assess the daily need for indwelling urinary catheters, avoid routine antimicrobial prophylaxis in patients with a urinary catheter, use daily aseptic technique, and shorten the duration of catheterization to 72h or less, if possible, to not increase the risk of HAIs and mortality.
A recent meta-analysis explored the strategies for the removal of short-term indwelling urethral catheters in adults. There is some evidence to suggest the removal of indwelling urethral catheters late at night rather than early in the morning may reduce the number of people who require recatheterization. It appears that catheter removal after shorter compared to longer durations probably reduces the risk of symptomatic catheter-associated UTIs and may reduce the risk of dysuria. However, it may lead to more people requiring recatheterization. Few trials compared the use of prophylactic alpha blockers *versus* no intervention or placebo. They remained uncertain if prophylactic alpha blockers before catheter removal had any effect on the risk of requiring recatheterization or risk of symptomatic catheter related UTIs.

Catheter-related bloodstream infections

The management of many medical and surgical conditions often involves long-term infusion of intravenous fluids, broad-spectrum antibiotics, chemotherapeutic agents for cancer, critical care therapies, antibiotics administered at home, total parenteral nutrition, or hemodialysis. The insertion of intravenous catheters exposes patients to local skin and catheter-related bloodstream infections remain a significant issue despite advances in infection prevention, and a significant effect on morbidity, mortality, and health care costs. The American Centers for Diseases Control defines catheter-related bloodstream infections as a laboratory-confirmed bloodstream infection in a patient who has had a central venous catheter in place for more than 48 hours before the date on which blood was drawn for culture if no other source of bacteremia or fungemia is identified. Catheter-related infections are thought to arise by several different mechanisms: infection of the exit site, followed by migration of the pathogen along the external catheter surface; contamination of the catheter hub, leading to intraluminal catheter colonization; and hematogenous seeding of the catheter, even endocarditis. The risk of short-term catheter-related bloodstream infection is influenced mainly by extraluminal microbial colonization of the insertion site. Subclavian, jugular, and femoral central venous catheterization are associated with infectious, thrombotic, and mechanical complications but the localization of the insertion site may become less evident for infectious risk, probably due to continuous progress in healthcare. Strategies and devices for preventing central line-associated bloodstream infection should include checklists use, catheter-insertion cart or kit, hand hygiene, maximal sterile barrier precautions, alcoholic chlorhexidine skin antisepsis before central catheter insertion, selection of subclavian catheter-insertion site in patients in the intensive care unit, chlorhexidine dressings, chlorhexidine bathing, antibiotic- or antiseptic-impregnated catheters, and manual decontamination of catheter hubs and caps before catheter insertion, and antiseptic-containing hubs and caps.
Peripheral intravenous catheters are the most used invasive medical devices in healthcare. While they are often perceived as innocuous because they are common, this perception does not match their risk factors. Duration of peripheral intravenous catheter insertion is another topic that remains actively discussed. The results of a Swiss cohort study using a large, prospective surveillance database suggest that replacement of peripheral intravenous catheters only when clinically indicated may be associated with an increased risk of peripheral intravenous catheters-bloodstream infection compared with routine replacement every 96 hours. For skin antisepsis, chlorhexidine plus alcohol before intravenous catheter insertion may provide greater protection against peripheral venous catheter-related infectious complications than does povidone iodine plus

alcohol according to a recent single multicenter open-label, randomized controlled trial. The use of innovative devices may also extend the catheter complication-free dwell time.

Gastrointestinal infections

Clostridioides difficile is an anaerobic Gram-positive, spore-forming, toxin-producing bacillus that is transmitted among humans through the fecal-oral route. The relationship between the bacillus and humans was once thought to be commensal, but *C. difficile* has emerged as a major enteric pathogen with worldwide distribution. *C. difficile* spore mechanic detorsion could decrease the spread to the hospital environment and the colonization of other patients, this could induce infections of *C. difficile* in cases of additional infectious risk factors. Alcohol-based handrubs are efficacious against multidrug-resistant bacteria and viruses, except *C. difficile*, for which soap and water handwashing is indicated by its mechanic detorsion. Environmental hygiene measures to curtail multidrug-resistant organisms include disinfecting high-touch surfaces in rooms of patients with *C. difficile* infection (CDI) daily with a sporicidal agent such as sodium hypochlorite. Collective and institutional efforts to control CDI contributed to the decline in the estimated national burden of CDI and associated hospitalizations decreased from 2011 through 2017 in the United States of America, owing to a decline in HAIs.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 49

The role of multidisciplinarity in preventing healthcare-associated infections

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Introduction

Over the past 40 years, significant progress has been made in the knowledge of how to combat healthcare-associated infections (HAIs). Core components of effective prevention and control programs have been identified based on scientific evidence; research has discovered several effective care measures to reduce the risk of infection: HAI rates may be reduced by 35–55% with multifaceted interventions. However, effective programs and good clinical practices are not uniformly and systematically adopted, as recently underlined by the WHO global report on infection prevention and control.
Why is it so difficult to put into practice the principles of infection control? Several factors may halt or promote practice change, related to the organisational and economic context, to the social context, and to individual professionals. For infection prevention and control, the following issues should be carefully considered:

- Murray and Holmes, discussing the crucial role of organizational factors in infection control, reminded us that 'Infection Prevention and Control (IPC) can be considered as an indicator for managing complexity. In hospitals where IPC or other aspects of patient safety have not been well managed, subsequent reports have shown a failure to manage complex systems effectively and a failure to balance safety against performance'. An effective infection control program should address the multiple aspects that determine healthcare infections; **Figure 1** shows an example of the multiplicity of factors which may influence HAI.
- To be effective, infection control should become "everyone's responsibility". In the last decades a shift took place: previously, infection control was perceived as the task of a small, technically focused infection control group; now infection control is viewed as everyone's responsibility. Bottom-up strategies "promoting inter-group collaboration and participative processes encourage change at the grassroots level within an organization". We should 'get everybody on board so we can actually ensure that we then can implement the findings of research'.
- Improving practices implies modifying healthcare workers' behaviour, which is influenced by knowledge, attitudes, beliefs and personal traits. These factors, through multidisciplinary working teams, should be taken into account when implementing change at the local level.

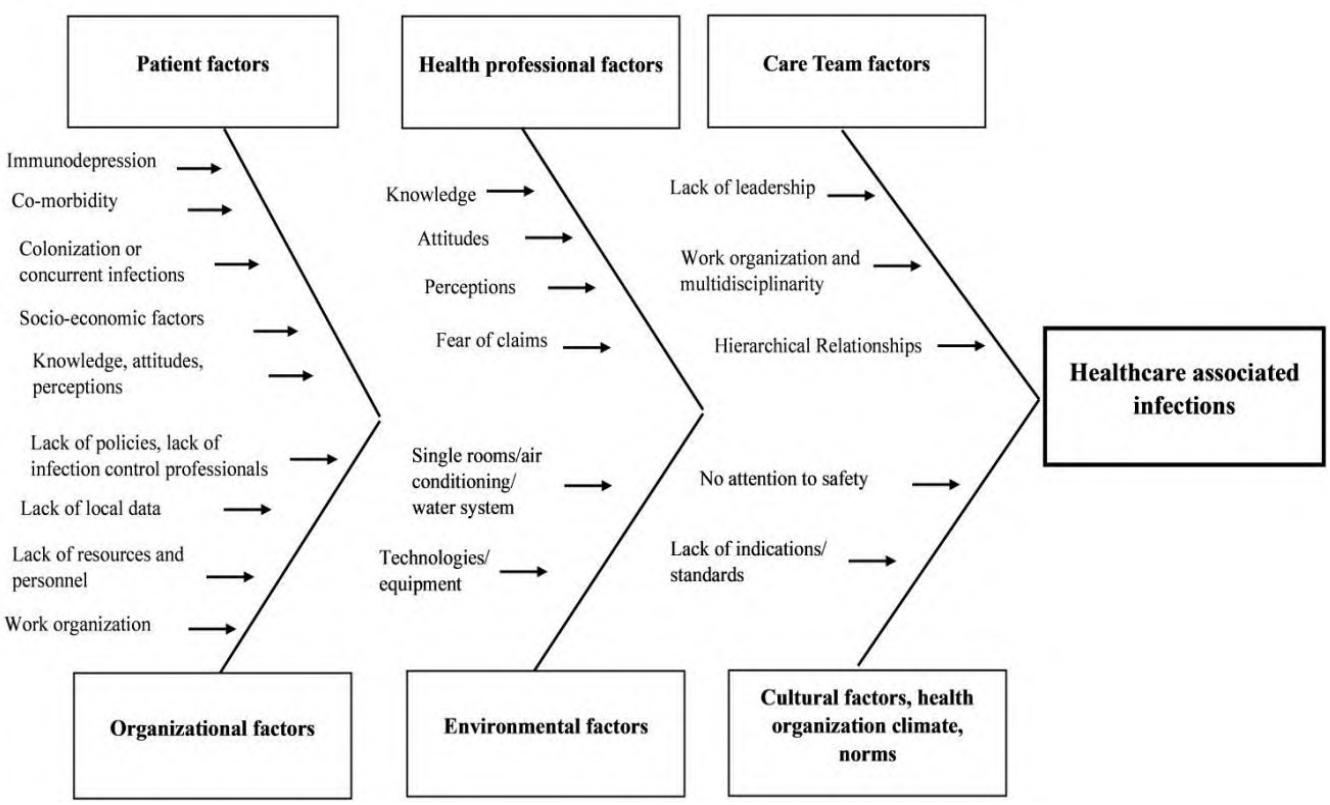

Figure 1. Barriers to effective infection prevention and control.

Multidisciplinarity in preventing healthcare-associated infections

The need for a multidisciplinary and multi-professional approach to infection prevention and control clearly emerges from what was briefly discussed in the introduction: the organization as a whole should be part of the process of change, the aim of providing safe care should be the responsibility of everyone working in healthcare; strategies aimed at promoting innovation, encouraging multidisciplinary participation and taking into account local barriers, are more effective. This means that both in the planning, delivering and evaluating infection control programs as well as in conducting specific implementation interventions, a multidisciplinary approach is crucial.

The role of management

Clear national and regional strategies as well as local structural capacity are indispensable conditions for IPC. The existence of political commitment and policies (the "favorable policies" mentioned in **Figure 2)** to scale up and enforce the core components of Infection Prevention and Control (IPC) are essential conditions for effective programs. At the local level, a multidisciplinary infrastructure is the heart of IPC programs.

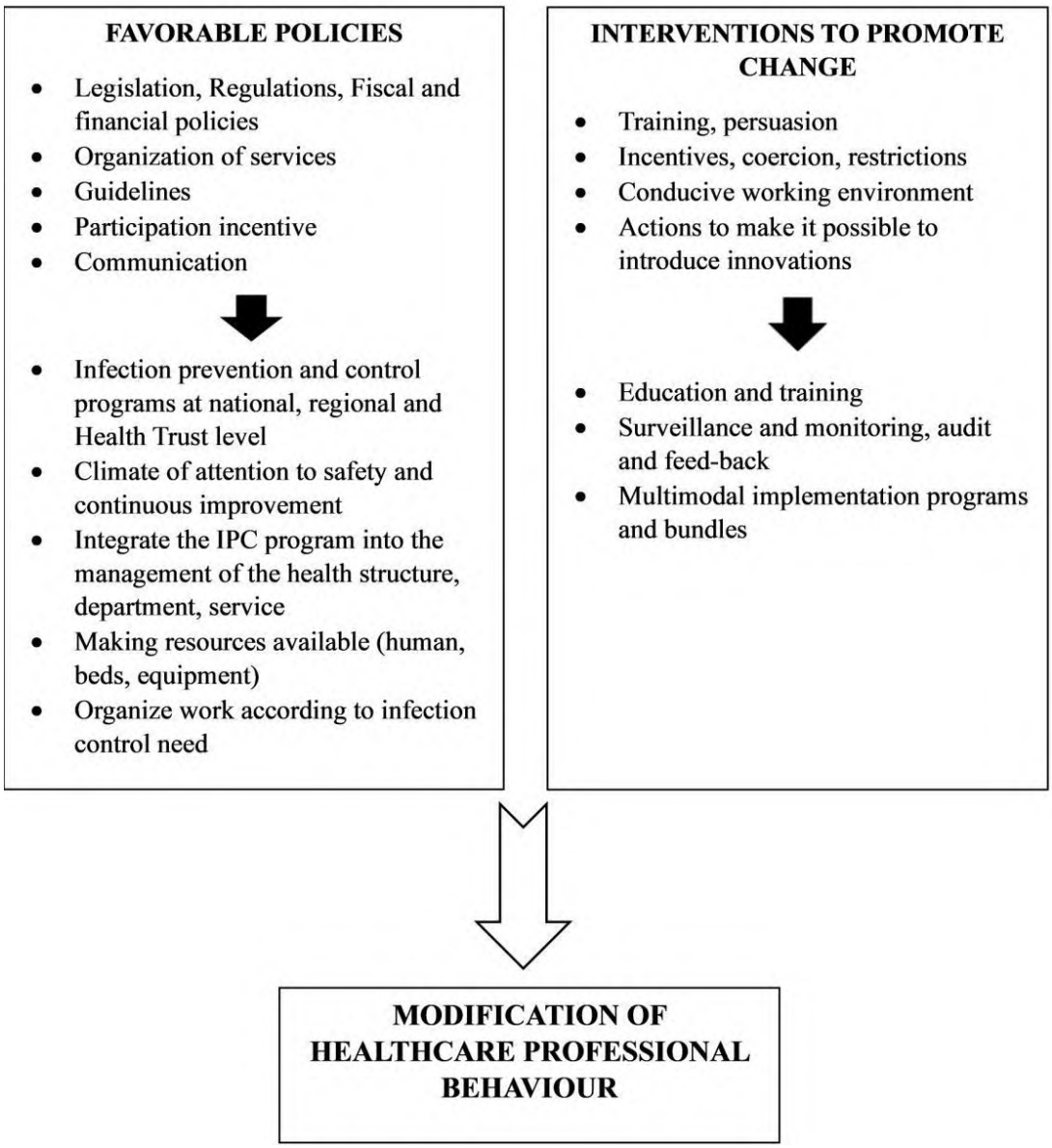

Figure 2. How to promote effective infection prevention and control programs.

The facility's top managers should fully endorse the IPC program, assuring the budget and allocating the necessary resources; the IPC program should be integrated into the complex and multiple interlinking systems within health facility management. Given the complexity of the IPC issue, the annual program should be developed by a facility multidisciplinary group of senior leaders from various disciplines, which succeed in raising the issue of IPC agendas in the organization. According to WHO, the IPC committee is a "A multidisciplinary group with interested stakeholders across the facility, which interacts with and advises the IPC team". In some countries, as in the Emilia-Romagna Region in Italy, the IPC program planning and evaluation is the responsibility of the Health Trust Board of Directors, which is also in charge of patient safety in general.
Multidisciplinarity is also crucial for the IPC team (IPC professionals supported by other fundamental professionals such as the microbiologist and the pharmacist), which should put into practice the objectives of the annual program defined by the IPC committee. To implement the program, the IPC team must work jointly with each ward, through the so-called IPC link persons, which are healthcare professionals (medical doctors, nurses or other healthcare professionals), with an expressed interest in a specialty and a formal link to

specialist team members. These professionals are seen as facilitators for the implementation of IPC measures in direct patient care, like introducing new guidelines or promoting compliance with specific surveillance or control activities. Several publications delineated the role of link professionals, and some studies reported on their effect in terms of patient outcomes or guideline adherence, showing positive short-term effects.
The IPC program, developed by the IPC committee and supported by the necessary budget and resources, then implemented by the IPC operational team with the support of the link professionals, should include all the elements shown in **Figure 2**, able to influence the health workers behaviour, with particular emphasis on education and training, surveillance and monitoring, audit and feedback, multimodal implementation programs and bundles.
The local IPC infrastructure is eminently multi-professional and multidisciplinary: the responsibility for defining and/or implementing the program is shared (with different tasks and charges) by the facility top manager, by the senior leaders part of the IPC committee, by the IPC professionals and essential professionals of other disciplines (e.g. microbiologist or pharmacist) part of the IPC operative team, by all the link professionals in hospital wards or community services, and finally by the healthcare workers at large.
Along with the need for a multidisciplinary approach, in recent years the fundamental role of leadership, at all levels of healthcare organization (high level, middle level, frontline), has been underlined. The success of IPC measures largely depends on the quality of leadership: "Hospital administration and heads of IPC units, need to demonstrate high self-efficacy, address barriers effectively, and champion a culture of clinical excellence"; the same applies to middle-level leaders and frontline staff.
A positive effect of training programs, aimed at improving the leadership capacity of hospital managers and IPC professionals, has been reported.

Engagement and empowerment of health professionals

As underlined before, infection control should become "everyone's responsibility". Thus, to disseminate good clinical practices for infection prevention and control, both senior physician and nurse leaders, as well as frontline staff should be fully engaged and empowered. Actually, both middle-level managers (physicians and nurses responsible for the management of clinical wards) and frontline staff have a crucial role in assuring patient safety: middle managers are instrumental in promoting a culture of safety and continuous quality improvement, while frontline staff engagement is essential for day-to-day prevention.
However, we know that poor infection control practices are still adopted in day-to-day practice, due to the existence of barriers at different levels. Healthcare professionals, in fact, work in social, organizational and structural settings, where change may be supported or impeded; they learn by observing others' actions and the results of those actions, as well as through role modelling; the availability of rules and policies, as well of the necessary resources may influence the success or failure of introducing change.
In the last 20 years, behavioural science has been increasingly used to understand behaviour in infection control. Several predictors as well as theories of human behaviour were studied, such as cognitive, adult learning, behavioural, social influence, marketing, and organisational theories.
We have also learned that innovations spread through an organization following some common rules. A small portion of people (~2.5%) may be called innovators because are those who introduce new ideas for change. Early adopters (~13.5%) are the next and are recruited through one-to-one conversations. Then, the majority of people (early and late majority, summing up to ~69% of the population) need to be recruited through small group discussions or meetings (early majority) or campaigns (late majority). Laggards (~16%) are the last to adopt change. Thus, to promote the participation of health professionals in the intended change is necessary to be aware of the appropriate methods to recruit them.

In every community there are certain individuals or groups who are able to find better solutions to problems than their peers while having access to the same resources and facing similar or worse challenges: they are called 'positive deviants'. Several recent publications suggest that positive deviance may be an effective implementation strategy for infection prevention and control.

At the same time, competing interests and shifting priorities within an organization may challenge safety implementation. Saint has highlighted how active resisters and organisational constipators affect healthcare-acquired infection prevention efforts. "Active resistors," are personnel who open and vigorously oppose changes in infection prevention, while organizational "constipators" are mid- to high-level executives who prevent or delay certain actions without active resistance, acting as insidious barriers to change. Multilevel interventions are required to overcome barriers posed by organizational resistors and constipators.

Human behaviour is influenced by several factors: the psychological or physical capability to perform a behaviour (knowledge and skills); the opportunity to change behaviour due to the physical and social environment around the individual; and the motivation to perform behaviour, affected by automatic habitual processes and reflective decision-making processes. Greene and Wilson reviewed the evidence on the application of behaviour change theories to interventions to improve IPC practice in healthcare settings. The theories of focus were the Theoretical Domains Framework (TDF), Capability, Opportunity, Motivation, Behaviour (COM-B) and Behaviour Change Wheel (BCW), which combine several theoretical components into a single framework. These authors identified 11 studies, respectively focused on hand hygiene (7 studies), antimicrobial stewardship (3 studies), and methicillin-resistant *Staphylococcus aureus* (MRSA) screening (1 study). Only three studies described an intervention targeting the behavioural determinants identified; three domains were identified across all three of these studies: beliefs about consequences, environmental context and resources, and social/professional role and identity.

A systematic review focused on specific healthcare-associated infections, makes clear how important is to identify local barriers and facilitators, to be able to find solutions, effective at overcoming those obstacles. For example, Atkins *et al.* reviewed the barriers and facilitators for catheter-associated urinary infections (CAUTIs) prevention. The following were identified: 1) environmental context and resources ("limited and inconsistent documentation and records relating to urinary catheter use", "transitions of care", "lack of time to perform alternatives to urinary catheterisation", "lack of available medical alternatives to urinary catheterisation" and "choice and availability of urinary catheters"); 2) knowledge (knowledge of "clinical guidelines", "duration of catheter insertion", "risks associated with catheter use", and "how to manage patients without catheterisation"); 3) beliefs about consequences ("convenience and ease of monitoring", "perceived severity of CAUTI" and "lack of perceived benefits to interventions targeting CAUTI"); 4) social influences ("requests from patients and their carers to have a catheter inserted", "lack of peer support and buy-in", "physicians dictating nurses" and "cultural norms regarding standard catheterisation practice for specific patient groups"). They are specific to CAUTIs but are illustrative of dimensions common to other infections.

Sreerampju reviewed the application of socio-adaptive approaches to reduce healthcare-associated infections in recent years. Some of the approaches which have been tried are listed below: 1) comprehensive unit-based safety programs, aimed at learning from defects through 'educating healthcare personnel on the science of safety, identifying defects, engaging executives, having multidisciplinary conversations on learning from defects, and implementing teamwork tools'. The effectiveness of this approach, as an addition to the technical bundle of strategies to reduce device-associated infections, has been demonstrated for both central catheter and urinary catheter infections; 2) the Positive Deviance approach explores social aspects of infection prevention practices among healthcare personnel (identifying barriers and potential solutions, identifying and deploying peer role models to generate positive peer pressure and mobilize change). Its adoption allowed to reduce MRSA infections, to promote a culture of safety, and to reduce the rate of several

healthcare-associated infections; 3) the Social Network Analysis aimed at analyzing social networks in healthcare settings to influence the results of intervention and monitor success; 4) Link Nurses and Local Liaisons, who, given their visibility in the unit or service, have a greater chance of being accepted by healthcare personnel and greater ability to influence local change in infection prevention practices; 5) Stop the Line Policies means a positive, nonpunitive culture for speaking up about errors or opportunities for improvement without fear of retaliation.
In conclusion, to engage the entire population of healthcare workers not only technical but also behavioural and social interventions are necessary, based on the knowledge of local and social context and choice of the appropriate approach.

Multidisciplinary teams and multimodal interventions

To be able to change, both a top-down approach and a bottom-up approach should be used. The bottom approach promotes the engagement of health professionals, working in each area where change is pursued, being part of the change process. To allow a locally driven and locally appropriate approach, multidisciplinary inter-group collaboration and participative processes are necessary. Inter-group collaboration and participation allow to achieve commitment and insights from staff with experience in the local system and to align changes with their motivations and concerns.
Several strategies have been investigated to promote behaviour change. Multifaceted interventions have been demonstrated to be more effective than single approaches, such as education, opinion leaders or audit and feedback, implemented as stand-alone interventions. A recent review of systematic reviews of strategies designed to implement research evidence into clinical practice has shown that multifaceted interventions (several elements or components implemented in an integrated way to improve an outcome and change behaviour), appear to be more likely to generate positive results than single interventions, even if a lot of nuances was highlighted. Multifaceted interventions have a positive effect, particularly for more complex healthcare areas: interventions that link local opinion leaders, audits and feedback, and reminders were the most effective strategies. Interventions where barriers to change were prospectively identified were more likely to be successful.
Multimodal interventions are considered by the WHO as one of the core components of effective infection prevention and control programmes. “A multimodal strategy consists of several elements or components (three or more - usually five) implemented in an integrated manner. It includes tools, such as bundles and checklists, developed by multidisciplinary teams that take into account local conditions. The five most common components include (i) system change (improving equipment availability and infrastructure at the point of care) to facilitate best practice; (ii) education and training of healthcare workers and key stakeholders (e.g. managers and hospital administrators); (iii) monitoring of practices, processes, and outcomes and providing timely feedback; (iv) improved communication (e.g. reminders in the workplace or videos); and (v) culture change by fostering a safety climate’.
An important feature of multimodal intervention is the encouragement of a multi-disciplinary approach, given the central role of different professional groups in collectively incorporating evidence-informed practice.
Ariyo, in a systematic review of implementation strategies to reduce surgical site infections, reported that 76 (63%) of the 125 reviewed studies described efforts to engage frontline staff as an implementation strategy, largely by forming multidisciplinary teams. Marche, in orthopaedics and traumatology, found that building a multidisciplinary team was among the successful implementation methods to prevent infections and improve compliance with good practices (it was considered in 8 out of 11 successful studies). The same applies to colorectal bundles for surgical site infection prevention, where a multidisciplinary collaborative team or

steering committee, led by a colorectal surgery champion, with members from surgery, anesthesia, quality improvement, infection control, infectious disease, pharmacy, hospital administrators, was among the most frequent implementation strategies used. A team of health different professionals who work collaboratively to provide care to the patients was included in 8 out of 15 multifaceted interventions for ventilator-associated pneumonia prevention.

People (the multidisciplinary team) must be engaged in the earliest phases of initiation and decision-making, implementation planning or implementation execution. In the WHO implementation manual to support the prevention of surgical site infections at the facility level, among the barriers which may contribute to failure, the following two are enlisted at the very beginning: lack of direct leadership involvement (for example, senior managers, heads of clinical services) to facilitate and profile local culture change and to directly support implementation; and not involving multiple levels of staff (for example, administration, clinicians, housekeeping) or disciplines (for example, doctors, nurses, specialist consultants).

The multidisciplinary team should contribute to planning and execution through all the phases of a multimodal improvement strategy, including formulating a concrete, attainable proposal, with clear targets; analysing what factors at the local level are stimulating or hampering the process of change; assessing the actual performance; developing and executing an implementation plan; selecting and developing a set of strategies for change; integrating the improvement within the normal practice routines; and evaluating and revising the plan.

Conclusion

The fight against healthcare-associated infection and antimicrobial resistance cannot be won by infection control practitioners by themselves or through the diffusion of guidelines only. In the last seventy years, the structure of infection control staff and methods for infection control have considerably evolved.

Only a multidisciplinary approach can allow to cope successfully with the challenges of modern infection control and hospital epidemiology. Healthcare delivery is undergoing radical changes, that influence effective infection prevention and control: low boundaries and high exchange between organization units and functions request more system integration and patient involvement; the expansion of care outside the hospital calls for breaking the IPC boundaries; the crucial issue of behaviour change and its implementation requires capability to use behaviour science and implementation science methodology to promote behaviour change; the progressive increase of automation and digitalization requires capability of data processing; technology innovations and scientific discovery ask for capability to evaluate and implement new technologies and innovations. To face all these challenges, a number of different skills and knowledge are necessary and a multidisciplinary approach only can arrange the necessary skills and guarantee multidisciplinary inter-group collaboration and participative process.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 50

Healthcare-associated infections as patient safety indicators

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Introduction

Healthcare-associated infections (HAIs or HCAIs) represent a very serious threat to the safety of hospitalized patients and a major challenge for healthcare systems worldwide. They are responsible for the leading cause of preventable morbidity and mortality associated with different clinical, diagnostic and therapeutic procedures. Healthcare-associated infections (HAIs) are infections that occur while receiving health care. Patients with medical devices (central lines, urinary catheters, ventilators) or who undergo surgical procedures are at risk of acquiring HAIs.

HAIs remain a major clinical problem in terms of morbidity, mortality, length of hospital stay and overall cost in all regions of the world. These infections increase the resistance to antimicrobials and produce unnecessary deaths. Their actual prevalence and incidence are unknown due to the difficulty in collecting and interpreting data on a global basis. The Global Alliance for Infections in Surgery, formed in 2017, considers it a priority to carry out HAI prevention to reduce their incidence at the hospital level worldwide.

HAIs are undoubtedly preventable adverse events within healthcare systems, where bacteria are acquiring significant resistance to antibiotics, so their prevention is essential to combat these resistances, which represent a serious healthcare problem and are an indicator of the quality of care and patient safety. The application of appropriate infection prevention and control by healthcare workers (HCWs) can reduce the risk of HAIs and many hospitals have made the prevention of these infections a major priority.

Healthcare-associated Infections as patient safety indicators

HAIs can be classified into several categories, including catheter-associated urinary tract infections (CAUTIs), central line-associated bloodstream infections (CLABSIs), surgical site infections (SSIs), ventilator-associated pneumonia (VAP), and hospital-acquired pneumonia not associated with mechanical ventilation (HAP). A further significant hospital-acquired infection is *Clostridioides difficile* infection (CDI).

Each of these types of HAIs will be addressed in a dedicated chapter of this book. This chapter will focus on surgical site infections, which are the most common HAIs in the surgical field.

HAIs are closely associated with the emergence of hospital-acquired bacterial resistance. Over the past few decades, there has been a notable increase in the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and carbapenem-resistant *Enterobacteriaceae* (CRE), particularly *Escherichia coli* and *Klebsiella pneumoniae. Acinetobacter* has also developed significant antibiotic resistance.

To prevent the development of these serious nosocomial infections, a range of interventions must be developed at the hospital level. The most significant of these are hand hygiene, hospital hygiene, surgical antibiotic prophylaxis and antibiotic stewardship (**Table 1**).

Table 1. Measures to prevent healthcare-associated infections (HAIs) in hospital settings and to improve patient´s safety.

Measures to prevent HAIs
• Hand hygiene
• Hospital hygiene
• Hospital implementation of multiple infection-control interventions
• Knowledge of hospital microbiology (MRSA, VRE, CRE, *Clostridium difficile* and *Candida*) and antimicrobial resistance (AMR)
• Use of checklist in the operating room
• Use of proper surgical antibiotic prophylaxis (SAP)
• Antibiotic stewardship programs (ASPs)
• Infection prevention control (IPC) team
• In surgical services: have a surgical expert or “champion” in surgical infections
• Recording, monitoring and interpretation of HAIs
• Surveillance of HAIs
• Education of healthcare workers (HCWs) about the prevention of nosocomial infections and improving their compliance with infection control measures
• Improving hospital design with single rooms
• Development of randomized controlled trials on infection-control interventions

Hand hygiene

Hand hygiene is an effective strategy for reducing infection and multi-resistant pathogen transmission, as well as the safeguarding of patients from HAIs.

The hands of HCWs can become colonized with pathogens such as MRSA, VRE, CRE, *Clostridioides difficile* and fungi such as *Candida*. The hands of HCWs have the potential to contaminate a range of items in the

patient's environment, including gowns, bed linen, bedside furniture and other objects. Contamination can occur through direct contact with the patient's skin or objects in the patient's room.
To prevent the transfer of pathogens, it is essential to clean the hands thoroughly. Alcohol-based formulations are more effective than soap and water in removing contaminants from the hands. However, it is important to note if exposure to spore-forming pathogens is strongly suspected, including *Clostridioides difficile*, hand washing with soap and water is the preferred means.
It is important to note that the use of gloves does not replace the need for hand washing.
The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have published guidelines on proper hand hygiene. The five moments of hand hygiene described by WHO are: before touching a patient; before clean and aseptic procedures; after exposure to body fluids; after contact with a patient; and after touching or coming into contact with the patient's environment. The best way to avoid increasing antimicrobial resistance in hospitals is to keep the hands of healthcare workers clean.

Hospital hygiene

To prevent the spread of nosocomial infections in hospitals, two basic principles must be adopted: separating the source of infection from the rest of the hospital and cutting off any routes of transmission.
Source separation includes isolation of the infected patient, but also all “aseptic techniques” or measures designed to act as a barrier between the infected patient and the environment, including other patients and staff. Hand hygiene of healthcare personnel is the main preventive measure.
The use of physical barriers is a key aspect of controlling infection. Interventions include geographic separation from the patient, the use of gloves, gowns and other protective equipment by staff, patients and visitors, including the use of masks.
Cleaning is essential. The main purpose of cleaning is to remove visible dirt. It is essentially a mechanical process. Water dissolves the dirt. Soaps and detergents act as solubilizing agents. The effectiveness of the cleaning process depends entirely on this mechanical action since neither soap nor detergents have antimicrobial activity. Thorough cleaning will remove more than 90% of microorganisms. Diluting and removing dirt also remove the culture medium for bacteria and fungi. Non-sporulating bacteria are unlikely to survive on clean surfaces.
Disinfection describes a process that eliminates many or all pathogenic microorganisms, except bacterial spores, on inanimate objects. Disinfection is not sporicidal. The main requirements for a good antiseptic are the absence of toxicity and rapid and adequate activity on the natural flora especially on pathogenic bacteria and other microorganisms after a very short exposure time.
Sterilization describes a process that destroys or eliminates all forms of microbial life and is carried out by physical or chemical methods. Once an item has been sterilized (e.g., a tool that penetrates intact skin and comes into contact with the vascular system) has been sterilized, all microorganisms have been removed. Hypothetically, nothing survives sterilization.
To prevent germs from infecting more people, we must break the chain of infection. There are six points at which the chain can be broken: the infectious agent, the reservoir, the portal of exit (open wounds, aerosols, body fluids including saliva, and sneezing), the mode of transmission (direct or indirect contact, ingestion or inhalation), the portal of entry (broken skin, respiratory tract, mucous membranes, catheters and probes) and the susceptible host. It is possible to break the chain by cleaning hands frequently, following standard isolation and contact rules, using personal protective equipment correctly, cleaning and disinfecting the environment, sterilizing medical instruments and equipment, and using antibiotics prudently to prevent antibiotic resistance.

In healthcare facilities, floors and shoes can be contaminated with several different species of healthcare-associated pathogens, including *Staphylococcus aureus*, *Enterococcus faecalis* and vancomycin-resistant enterococci, *Escherichia coli, Acinetobacter* spp., and *Clostridium difficile*. Because floors and shoes are low-touch surfaces, they were not considered to be critical surfaces for cleaning and disinfection, but the review by Limper *et al.* demonstrated that floors and shoe soles contribute to the spread of infectious pathogens, such as MRSA, VRE, and *Clostridioides difficile* in healthcare facilities, and are responsible for the occurrence of healthcare-associated infections. It is important to note that 13 of the 18 (72%) articles used for this review were published after 2015, showing increased consideration of pathogen transfer to high-touch surfaces from shoe soles or floors during patient care.

Surgical site infections

A surgical site infection (SSI) is an infection that occurs after surgery in the part of the body where the surgery took place. According to the CDC, surgical site infections are classified into incisional, superficial or deep SSIs, and organ/space, which affect the rest of the body apart from the wall layers.

In superficial SSI, the infection affects only the skin and subcutaneous tissue of the incision. In deep SSI, the infection affects the fascia and muscle layers; it also includes the superficial tissues of the incision. In organ/space SSI, the infection affects any part of the anatomy in organs and space other than the incision that was opened or manipulated during the operation.

SSIs are the most common HAIs among surgical patients. The prevention of SSIs is a global priority, as stated in the Global Alliance Against Surgical Infections. SSIs are a major clinical problem in terms of morbidity, mortality, length of hospital stay and overall cost (direct and indirect costs).

The prevention of SSIs is complex and requires the integration of a series of measures before, during and after surgery. The WHO, the CDC, the American College of Surgeons, the Surgical Infection Society (SIS) and the World Society for Emergency Surgery (WSES) have published guidelines for the prevention of SSIs. This fact highlights the enormous importance given in the surgical field to the fight against surgical infections, since in the opinion of many experts, SSIs are the main problem of surgery in the twenty-first century.

The Global Alliance for Infections in Surgery's proposal for a surgical site infection prevention package includes bathing/showering the patient preoperatively; prescribing appropriate surgical antibiotic prophylaxis (SAP); not removing hair or removing it immediately before surgery by clippers; using a correct surgical hand scrub preparation; and, using the correct antiseptic preparation.

Microbiology of SSI

Knowledge of the microbiology of surgical site infections is important for surgeons in all surgical specialties. All bacteria can cause surgical site infections, but it is usually the bacteria that are common in a particular anatomical area that will lead to their development.

This is mostly endogenous contamination during the operative procedure, which is caused by opening anatomical areas where bacterial flora is usually present. The small and large intestine are the best example of this microbiological process. The surgical team operating must make every effort to avoid contamination of the operative field, both the abdominal cavity and the soft tissues that make up the abdominal wall, thus avoiding organ/space and incisional SSIs.

Among nosocomial infections, those caused by multi-resistant germs, such as MRSA and VRE, are of particular concern in the surgical field, especially the latter because their incidence is increasingly high in patients with SSIs.

Enterococcus are Gram-positive, gut-borne, facultative anaerobic cocci. They are very versatile bacteria, capable of adapting very well to the hospital environment, with intrinsic resistance to common antibiotics, such

as cephalosporins and clindamycin, and with a high capacity to acquire resistance to other antibiotics, such as ampicillin and vancomycin. Most strains belong to two species: *Enterococcus faecalis* and *Enterococcus faecium*.

Initially, almost 90% of the isolates belonged to the *E. faecalis* species, but with the emergence of resistance to ampicillin and vancomycin, there has been a progressive increase in other species, mainly *E. faecium*.

The Clinical and Laboratory Standards Institute defines an *Enterococcus* strain as vancomycin-resistant when the minimum inhibitory concentration is equal to or greater than 32 mcg/mL.

In most US and European healthcare facilities, *Enterococcus* is the second or third most frequently isolated pathogen in patients with nosocomial infections. They can cause urinary tract infections associated with urethral catheters, infections associated with endovenous catheters, bacteraemias, endocarditis and surgical site infections, both incisional and organ/space infections.

Several factors increase the likelihood of colonization and subsequent infection by enterococci:

- Long-term antimicrobial pre-treatment (in particular with cephalosporins and vancomycin).
- Patient characteristics. These include hospitalization for more than 72 hours, the presence of severe underlying diseases (end-stage renal failure requiring dialysis, cancer, transplantation), admission to a critical care unit and the use of invasive devices.
- Exposure to contaminated surfaces. Includes furniture, gloves and gowns used by staff and devices used with the patient (stethoscopes, thermometers, blood pressure monitors, etc.).

Transmission can occur by direct contact, through the hands of HCW, or by indirect contact, through furniture or objects used in the healthcare process. It has been shown that there may be a causal relationship between the proportion of patients colonized and the more or less rapid occurrence of contamination on inanimate objects surrounding patients.

In critical care units, the proportion of colonized patients may exceed 50%.

VRE infection prevention and control strategies may vary between countries and even between facilities, but include a number of common principles within a multifactorial approach, such as optimal management of surgical wounds, vascular and urinary catheters, judicious use of antimicrobials, prevention of transmission and early diagnosis of infections, and effective treatment of infections:

- Hand hygiene. Since patient-to-patient transmission of VRE occurs primarily through the hands of healthcare workers, the most practical and important means of prevention is hand hygiene. Antimicrobial soaps, such as those containing chlorhexidine, are very useful.
- Contact precautions. The Healthcare Infection Control Practices Advisory Committee and the CDC recommend the use of contact precautions for patients infected or colonized with VRE. Contact precautions include the use of single-use gowns gloves and equipment only for affected patients, as well as isolation, either individually or by cohorts. However, some studies suggest that they are not very useful and, in many facilities, efforts are being redirected towards horizontal infection control strategies: hand hygiene, unclothed forearms, patient cleansing with chlorhexidine, disinfecting rooms and inanimate objects.
- Correct administration of antibiotics. Especially the judicious use of vancomycin, third and fourth-generation cephalosporins and anti-anaerobics is recommended. It is also important to reduce the duration of treatment as much as possible, as the longer the duration, the greater the risk of resistance.

Nosocomial MRSA infections are defined as infections occurring in hospitalized patients more than 48 hours after admission or occurring outside the hospital setting within 12 months of discharge. MRSA can cause severe skin and soft tissue infections, bacteraemia and pneumonia, and is one of the most frequent causes of surgical site infection. They are very capable of forming biofilms on the surface of catheters and prostheses

introduced into the body, which facilitates their survival and multiplication in the body. Worldwide, *Staphylococcus aureus* is estimated to cause 15% of infections, of which about one-third are caused by MRSA.
Risk factors for MRSA infection can be categorized into three groups:

- Patient-dependent: previous MRSA colonization or infection, recent contact with colonized or infected persons, injecting drug use, sex between men, HIV infection and antibiotic treatment in the previous 6 months (particularly cephalosporins and fluoroquinolones).
- Exposure to certain medical care in the previous 12 months: hospitalization, recent surgery, haemodialysis or residency in long-term care facilities.
- Exchange of needles or blades.

MRSA are most commonly transmitted through the contaminated hands of healthcare personnel, but can also be transmitted through contaminated surfaces of inanimate objects in the hospital environment and medical equipment. These germs can colonise the skin and nose of patients, healthcare workers and other healthy individuals. Colonization is an important risk factor for the development of subsequent infections.
The principles of MRSA infection prevention are proper hand hygiene with soap and water or alcohol solutions, cleanliness of the environment and equipment, prudent use of antibiotics and, in some facilities, contact precautions, particularly in critical care, dialysis and transplant units, and if outbreaks occur.

Antibiotic prophylaxis

Surgical antibiotic prophylaxis (SAP) is one of the most important components of a preoperative prevention strategy, and should be recommended for operative procedures that have a high rate of postoperative wound infection (clean-contaminated and contaminated surgery) or when foreign material is implanted (clean surgery). In dirty surgery, SAP is not used, because the patient needs to receive an antibiotic treatment.
Surgeons have to answer six questions when considering the use of SAP:

1. For which patients should SAP be administered?
2. Which antibiotics should be chosen for SAP?
3. When should SAP be administered?
4. How should the dose be chosen for SAP?
5. When should SAP be re-dosed intra-operatively?
6. Should SAP be prolonged after surgical intervention?

Therapeutic concentrations of antibiotics should be present in the tissues throughout the entire period the wound is open.
Prophylactic antibiotic agents have activity against the common bacteria – aerobic and anaerobic pathogens- that are most likely to contaminate the surgical site and cause postoperative wound infections after a specific surgical procedure. Stein-Thoeringer *et al.* of Klinikum Grosshadern in Munich, recommend piperacillin-tazobactam as appropriate antibiotic prophylaxis for preventing adverse outcomes after pancreatoduodenectomy, as in 101 patients (38 non-cancer and 63 cancer patients, 50 of whom had pancreatic ductal adenocarcinoma) they found a very high number of *Enterococcus* in bile specimens and upper gastrointestinal tract; these patients had severe SSIs in the postoperative period and elevated mortality rates up to 24 months.
Antibiotic prophylaxis should be administered within 30 to 60 minutes before surgical incision to ensure adequate serum and tissue concentrations during the period of potential contamination. It is valid for most antibiotic agents, and only a few antibiotics need to be administered before 60 or 120 minutes. The Temple Hospital of Philadelphia, recommends administering antibiotic prophylaxis at the time of the intraoperative "timeout" that occurs in the operating room just before draping the patient, with the surgeons,

anesthesiologist and nursing staff present, immediately before making the incision. This procedure can be considered part of the surgical checklist and leads to compliance. The antibiotic agent dose used is the conventional one, but is it important to take into account the weight of the patient because obese patients (>120 kg) require a higher dose of antibiotic agents. Re-dosing is necessary for operations lasting for more than three hours or when there is a significant blood loss of more than 1.5 L. (**Table 2**).

Table 2. Measures to prevent surgical site infections (SSIs).

Measures to prevent SSIs
Preoperative period
● Non-parenteral antibiotic prophylaxis. ● No hair removal or clipping immediately before surgery. ● Antiseptic prophylaxis: showering or bathing the patient. ● Applications of alcohol-based antiseptic agents. ● Plastic adhesive drapes. ● Administer antibiotic prophylaxis (SAP) at the appropriate time, i.e., 30 minutes before surgery or in the "time out", for most antibiotics. Some specific antibiotics need to be administered 120 or 60 minutes before surgery.
Perioperative period
● Use checklist. ● Maintain the patient's core body temperature. ● Control blood glucose <200 mg/dl. ● Correct oxygenation: inspired oxygen (FiO_2). ● Redosing antibiotic prophylaxis in operations of more than 3 hours duration. ● Redosing antibiotic prophylaxis in patients who have lost >1.5 L of blood. ● Transfusion of the necessary blood products. ● Use of coated sutures.
Postoperative period
● In patients with significant contamination during the surgical procedure, maintain antibiotic prophylaxis 24 hours postoperatively but never longer. ● Aseptic surgical wound dressings.

There is no evidence to support the use of postoperative SAP, although if there is significant contamination of the surgical site during the operation, it could be necessary to maintain antibiotic prophylaxis during the first 24 hours of the postoperative period. Prolonged SAP can be responsible for the development of *Clostridium difficile* infections.

The use of SAP contributes considerably to the total amount of antibiotics used in hospitals and may be associated with increased antibiotic resistance. For this reason, standardizing a shared protocol of antibiotic prophylaxis is an important part of Antimicrobial Stewardship Programs (ASPs) in hospitals. Each institution should develop guidelines for proper surgical prophylaxis according to the local microbiology of SSIs, antibiotic resistance in the hospital, and the recommendations of published guidelines.

Clostridioides difficile infection

Clostridium difficile is an anaerobic, spore-forming Gram-positive bacillus, which rarely forms part of the normal intestinal microbiota in the gut of healthy adults. *Clostridioides difficile* infection (CDI) may be of special concern in surgical patients, because surgery may predispose patients to this infection and surgery itself needs to treat severe cases of CDI.

These bacteria are spread via the oral-fecal route, and in hospitalized patients may be acquired through the ingestion of spores or vegetative bacteria spread to patients by HCW or from the environment. Risk factors for CDI are host factors (over 65 years of age, immune status, underlying comorbidities, inflammatory bowel diseases, malnutrition and low serum albumin level), exposure to *Clostridium difficile* spores (hospitalizations, and long-term care facilities) and factors that disrupt normal colonic microbiome (antibiotics, other medication and surgery). Antibiotics play a central role in the pathogenesis of CDI, presumably by disruption of the normal flora, providing a perfect setting for *Clostridium difficile* to proliferate and produce toxins. All antibiotics have been associated with CDI, but clindamycin, third and four-generation cephalosporins and fluoroquinolones have been considered at greatest risk. A controversial risk factor is exposure to gastric acid-suppressive medications such as histamine-2 blockers and proton pump inhibitors (PPIS).
This is particularly important in reducing environmental contamination as spores can survive for months in the environment and patients should be placed in an individual room with toilet facilities. Hand hygiene with soap and water and the use of contact precautions along with good cleaning and disinfection of the environment and patient equipment, should be used by all health-care workers.
A bundle proposal from the Global Alliance for Infections in Surgery for the prevention of *Clostridioides* infection includes: enhancing antimicrobial stewardship programs, activating surveillance of all cases, hand cleaning and the use of protective equipment, cleaning and disinfecting the environment and educating staff and patients/visitors. It is necessary to carefully comply with the guidelines for the treatment of CDI in surgical patients.

Antibiotic stewardship programs

Hospital-based programs dedicated to improving antibiotic use, referred to as Antimicrobial Stewardship Programs (ASPs), can optimize the management of infections and reduce adverse events associated with antibiotic use.
In 2017, a global declaration signed by an interdisciplinary task force of 234 experts from 83 different countries was published, which highlights the threat posed by antimicrobial resistance (AMR) that had emerged as one of the main public health problems of the 21st century, and the need for appropriate use of antibiotics and antifungal agents in hospitals worldwide, with a special focus on surgical infections. This declaration was promoted by the Global Alliance for Infections in Surgery and the WSES and it was endorsed by the Surgical Infection Society (SIS), the Surgical Infection Society of Europe (SIS-E) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).
The preferred means of improving antibiotic stewardship should involve a comprehensive program that incorporates collaboration between various specialties including surgeons, anesthesiologists, intensivists, infectious diseases specialists, hospital pharmacists, clinical pharmacologists, microbiologists, epidemiologists, infection prevention control (IPC) specialists, intensive care nurses, and administrators.
The mission of the ASP is to establish principles of appropriate antibiotic prophylaxis in surgical procedures and principles of appropriate antibiotic therapy in surgical procedures. The ASP policies should be based on both international and national guidelines and tailored to local microbiology and resistance patterns.
In clinical situations of high morbidity and mortality such as intra-abdominal infections, is very important to take into account the guidelines published at the international level by surgical Societies: the WSES published guidelines in 2017 and recently, the SIS updated their previous guidelines, including new antibiotics and established a number of clinical recommendations. Surgeons and clinicians need to follow the rules for optimal antibiotic use in their clinical practice in hospital settings.
We consider it important to identify a local opinion leader to serve as a “surgeon champion” because they may integrate best clinical practices and encourage their colleagues to change behaviors within their own

sphere of influence while maintaining a tight collaboration with antimicrobial stewardship and Infection Prevention Control (IPC) teams. The "champion" or surgeon who is an expert in surgical infections should have an extensive knowledge of surgical microbiology, as well as considerable expertise in the antibiotic management of surgical infections. Furthermore, they should increase the awareness of surgical infections in young staff surgeons and surgical residents.

Gardam *et al.*, from the University of Toronto Infection Prevention and Control Unit, consider that role modelling is important, particularly for key behaviors such as hand hygiene and compliance with precautions to prevent the transmission of HAIs, and that ensuring that change management strategies include staff physicians is an important element and that leadership from the top is necessary for ensuring coordination across the complex organization of a modern hospital. He recommends hospital implementation of multiple infection-control interventions and the development of randomized trials on infection-control interventions (**Table 1**).

The adequacy of prevention and management of infections in acute care facilities depends on the behavior of HCWs and on the organizational characteristics of acute health care facilities to support best practices and promote behavioral change. After a cross-sectional web-based survey organized with information from the Global Alliance for Infections in Surgery, contacting 1,432 HCWs, the authors developed 15 statements for several questions regarding the prevention and management of infections in surgery that may be the starting point for future evidence-based recommendations.

The recording, monitoring and interpretation of nosocomial infection data are indicators of the quality of care in any healthcare system worldwide and, therefore, of patient safety.

Conclusion

HAIs are currently a serious problem in hospitals and, in particular, in surgical services around the world, because they increase the morbidity and mortality of surgical patients and significantly increase the cost of surgery.

A major part of the severity is because various bacteria have acquired resistance to numerous antibiotics, resulting in the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus* (VRE) or carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae* (CRE). *Clostridioides difficile* is also resistant to a large number of antibiotics. Many of the patients currently undergoing surgery are 70 years of age or older and their immune systems do not function properly, so it is easy for them to develop nosocomial infections caused by these highly antibiotic-resistant microorganisms.

HAIs significantly reduce the quality of surgery and are a perfect indicator of the safety of hospitalized patients. Therefore, HCWs must do everything possible to prevent healthcare-associated infections. Fortunately, these infections are preventable and often with very simple measures. The most common measures to prevent these infections are hand hygiene, hospital hygiene, especially on floors and all surfaces, the use of appropriate antibiotic prophylaxis when indicated, the implementation of antibiotic stewardship measures, and hospital infection control practices.

The most appropriate way to prevent nosocomial infections is adequate training of hospital staff: surgeons, nurses and other hospital personnel. In surgical services, it is recommended that there should be a surgeon with expertise in surgical infections - the surgeon champion - who, in addition to knowledge of surgical technique, has knowledge of microbiology, pharmacology, and antibiotics and is a member of the hospital's infection committee. This champion surgeon should be the bridge between the surgical service and the healthcare infection control practice (IPC) team.

Currently, there are several claims in the literature for the prevention of nosocomial infections, but HAIs must be adequately monitored and surveilled to provide evidence-based recommendations in the near future.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 51

Infection prevention and control in critically ill patients

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Introduction

Infection prevention and control (IPC) is an important aspect of patient safety, more so when dealing with critically ill patients, particularly in the context of surgical infections. Primarily the role of IPC is prevention of infection to avoid adverse outcomes. Infection control is essential when prevention fails, or when the presenting problem is sepsis, to ensure reversal of the sepsis response and improve the time to survival, with timely source control and antimicrobial therapy. Sepsis remains a major cause of morbidity and mortality in the critically ill with multiple organ systems affected, with the consequences of sepsis heightened by the relative or actual immunosuppression of critical illness. In this chapter the authors will address the general principles and some specific aspects of the approach to and management of both prevention and treatment of sepsis in the critically ill patient group, firstly in the emergency department, but secondly with a specific focus on the intensive care (ICU) environment, given an almost 10% incidence of peri-operative sepsis.
This chapter must be seen as an overview since the specific sub-topics may be reviewed in much more detail in preceding or subsequent chapters. The aim here is to present the epidemiology and some specific ICU-related approaches.

Understanding the issue of IPC in the ICU requires an understanding of the epidemiology of ICU sepsis both in high-income and lower-and-middle-income countries (HIC and LMIC).
In the ICU, approximately 25% of cases of sepsis with organ dysfunction were ICU acquired with almost 50% having a hospital source. Mortality of ICU patients with HA sepsis with organ dysfunction was over 50%, however, this varies between 35 and 60% with higher values in children. While pathogens causing sepsis in LMICs are similar to those in high-income countries, resistance patterns can be very different. However, the causes of sepsis in LMICs often include tropical diseases or unusual organisms. ICU capacities differ majorly around the world; with the lowest capacities in LMICs with much heterogeneity within individual LMICs. Even where such capacity is reasonable, the outcomes in LMIC patients with surgical sepsis appear worse than in HICs. This aspect makes this chapter relevant to all providers of care to the critically-ill.
This chapter is presented in the form of short summarized sections each detailing one or more aspects of IPC in the ICU including some less-common infections.

IPC teams in the ICU – teamwork is the dreamwork!

Teamwork in the prevention of infection is essential with the basics of hand hygiene, microbial surveillance and selective empiric *versus* culture-guided directed therapy, preventing resistance as much as possible. Early identification of clinical changes by nursing staff, care of invasive lines and catheters, dressings on lines and wounds, regular airway toilet and other simple interventions, commonly described as care bundles reduce infection. External IPC teams that monitor the in-house staff identify weaknesses and education strategies to improve compliance with bundles. This includes monitoring the separation of waste correctly and the management of sharps. Teams consist of varying members depending on country and resources but are often led by IPC nurses, along with clinical pharmacists and microbiologists in addition to the treating unit clinical staff. Appropriate sterile technique with best-practice antisepsis when performing bedside procedures is another aspect of importance in the prevention of nosocomial infections.

Sepsis prevention strategies in the ICU patient

The approach to sepsis prevention in critically ill patient is more extensive than just addressing the issues around CLABSI, CAUTI, VAP and HAP and the consequent increase in the cost of hospitalization and length of stay, with resultant morbidity and increased mortality. Prevention starts with addressing aspects such as the compromised skin barrier, avoiding unnecessary immunocompromising medications, optimized chronic health conditions and prevention of malnutrition. It is well documented that glucose control and the use of insulin infusions via titrated doses reduce infection in surgical ICU populations.
Hand hygiene is important for both hospital personnel and patients alike, with clean short nails reducing nosocomial transmission. General handwashing or the use of alcohol-based hand lotions between patients and tasks remains essential. Even cleaning of rooms or ICU pods between patients may not effectively reduce transmission of resistant organisms, with up to two weeks required to clear certain organisms, a practical impossibility with the high turnover of ICU beds. Water and air filtration systems that are regularly cleaned reduce transmission, however, fresh-water systems may be a source for *Aeromonas* or *Pseudomonas* transmission.

Admission patient screening for colonization with resistant organisms is an important adjustment to avoiding outbreaks in the ICU, followed by patient decontamination with chlorhexidine baths, mupirocin nasal ointments and gut decolonization have all been tried for this purpose.
Other prevention strategies that can be applied to all patients include early head-up, use of sucralphate in preference to anti-acid medications for reflux prevention, central-line management teams and routine gown-and-glove for all invasive procedures.

Infection surveillance and quantification in critical illness

Sepsis screening should include a comprehensive clinical evaluation of any new onset fever in excess of 38.4°C with systemic signs of inflammation. Non-septic causes of fever must be excluded. Blood tests will include white cell count (which may lag behind other markers), platelets (an unexpected drop is often related to sepsis, but thrombocytosis may also occur), and the sending of blood, sputum, stool, urine, and wound specimens for culture to the relevant laboratory, along with the use of sepsis markers, of which procalcitonin (PCT) and beta-d-glucan appear the most clinically relevant. CRP may be useful for fungal sepsis but due to CRP and D-Dimers being almost universally abnormal in the acute post-surgical period, these tests may be considered for use in patients presenting to the Emergency Department in a critically ill state, but are largely useless in the ICU patient due to their increase with inflammation, thus making their value for sepsis far less robust. Higher PCT cut-offs have been associated with better diagnostic discrimination, especially in surgical patients where the surgical trauma itself raises the PCT somewhat, more so in children. Indiscriminate use of antimicrobials is not without adverse effects, including a risk for *Clostridioides* infection, so rational prescribing and different treatment strategies are important. Selective digestive tract decontamination does not appear to work in practice as well as in the various trials previously conducted and is not recommended presently.
Routine surface cultures and nasal and hand swabs may also assist in the prevention of nosocomial sepsis through appropriate use of treatment of staff who are carriers and decontamination of affected surfaces and beds.
Specific aspects of IPC in the ICU include hand hygiene protocols, indwelling catheter insertion and maintenance protocols; urinary catheter management protocols; ventilator-associated pneumonia prevention (e.g. sub-glottic suction on endotracheal tubes; head elevation and oral care), and advocating for early enteral feeding and pressure sore prevention. While often not considered as an infection prevention strategy optimal glucose control is associated with less septic complications. Control of pain and temperature ensures optimal patient comfort and reduces infection risk, allowing gradual weaning and extubation, also thereby reducing the risk of nosocomial infection.

Colonization *versus* infection, classification of risk (for wounds)

An important distinction in the patient in hospital is the decision around colonization that occurs within 48 hours in an ICU environment with hospital-acquired organisms and actual infection. Simply culturing an organism from a “wound-swab” or a surface in a patient with a new onset pyrexia does not equate with infection caused by that organism. Even endotracheal aspirates may simply reflect colonization rather than infection. Wounds must be classified according to the sepsis risk (clean, clean-contaminated, contaminated or

dirty) and for the most part offered topical treatments, unless there is evidence of deep tissue sepsis or organ space infection. Source control is important in surgical ICU patients, often enabling shorter antibiotic courses. This applies equally to the approach to selective antimicrobial use when infection is not yet proven, especially in patients who are not in septic shock.

ICU antibiotic stewardship, duration of therapies and exceptions to short-course therapy

Good antibiotic stewardship is known to reduce the development of resistance to antimicrobials and this is of particular concern in the ICU where patients are already immunocompromised due to their underlying disease, let alone the effect of blood transfusions, nutritional status and other challenges. Stewardship depends on good surveillance, which is a challenge for many LMIC nations, more so than HIC nations. For surgical site infection good stewardship of antimicrobials is linked to early appropriate source control.

Surveillance takes many forms, including routine area cultures, monitoring changing susceptibility patterns and following clinical responses to therapy. This is usually unit-specific and cannot be generalized across a facility, let alone geographic regions.

Good stewardship follows with the derivation of antibiotic protocols, limitation of prophylaxis duration and limitation for most antimicrobials to short directed courses. Additionally, it allows for best-choice empiric therapy in cases where one cannot await culture results.

Stewardship implies choosing antimicrobials based on the most likely organism, site penetration and an adjusted dose to ensure time above minimum inhibitory concentration for optimal killing power. Factors to consider in ICU when choosing an antimicrobial include route of administration (nebulized, intravenous or intrathecal, *versus* oral), infusion *versus* bolus dosing, and patient factors (volume of distribution, comorbidity, renal function etc.)

For the vast majority of ICU patients, a standard short-course (4-5 days appropriately dosed) antimicrobial will have a therapeutic effect. If not, one has to consider either an incorrect agent or a resistant organism. Having said that there are distinct infections that may require prolonged therapy that penetrates the infected tissues and this includes meningitis, ventriculitis, brain abscess, endocarditis, osteitis, fungal infections and *Clostridioides difficile* infection.

On the other hand, certain ICU complications do not require systemic therapy, e.g. superficial surgical site infections (topical therapy), pressure sores (debridement and dressing care) and when the cause of inflammation is a non-infective source (e.g. deep venous thrombosis).

Common and uncommon causes of ICU sepsis are listed in **Table 1.**

Table 1. Causes of infection in the critically ill ICU patient.

Common causes of ICU sepsis	Uncommon causes of ICU sepsis
Ventilator-associated infections	Sinusitis and otitis media
Catheter-related bloodstream infections	Infective enteric erosions (e.g., esophagitis)
Catheter-related urinary tract infections	Diarrheal infective diseases
Wound and surgical site sepsis	Meningitis and ventriculitis
Tracheitis and bronchitis	Endocarditis (and septic embolic syndrome)
Nosocomial bacteremia or fungemia	Pressure sore-related systemic sepsis
	Tropical diseases and unusual organisms

Abbreviation. ICU: Intensive Care Unit.

Common septic causes in ICU patients

Tracheitis and bronchitis - Tracheitis in the ventilated patient is not an uncommon occurrence but is confounded by the lack of definitive consensus diagnostic criteria, with an apparent role of both CRP and PCT, lack of a demonstrated therapy strategy and only an assumed association with progression to VAP, with the treatment option that showed the best results being the use of nebulized antimicrobials. Similarly, bronchitis is common but good airway management (bronchial toilet) is associated with shorter ventilator days. Early weaning and timely extubation are advocated and where possible non-invasive respiratory support options will be largely preventative.

Pneumonitis and pneumonia - Using updated criteria, the incidence of ventilator-associated events are far more common than actual pneumonitis or pneumonia (VAP), either classified as possible or probable VAPs. Aspiration pneumonitis and pneumonia are common in emergency admissions with a history of vomiting, traumatic brain injury or upper gastrointestinal haemorrhage, however, for the vast majority, this does not require antimicrobial cover but is best addressed with early bronchoscopic airway toilet and ventilatory support. For those who aspirate with an underlying distal bowel obstruction, however, the risk of bacterial overgrowth in the gut stasis content warrants Gram-negative and possibly even anaerobic cover.

Catheter related infection - refers to two groups of conditions, namely central catheter-related bloodstream infection (CLABSI) and catheter-related urinary tract infection (CAUTI). Both of these pathologies can be prevented by sterile technique when placing the devices, using full gown-and-glove strategies, with appropriate skin attachment to prevent undue movement, along with good dressing care. CLABSI is more of a risk with femoral and internal jugular devices than subclavian devices, while peripherally inserted central catheters (PICC-lines) have much lower infection rates. Routine central catheter changes were previously advocated along with antibiotic-impregnated devices. Neither of these strategies has proven to be useful in the prevention of CLABSI.

Blood-stream infection management includes the removal of the catheter after blood culture through the lumen, along with a peripheral blood culture. Most cases of early CLABSI do not require systemic therapy once the line is removed. If the symptoms do not settle or if there is evidence of systemic sepsis, then only should antimicrobials be added. A positive culture of the same organism in the line-specimen and the peripheral culture confirms the diagnosis.

In a similar vein, peripheral catheter changes are recommended, especially in cases where the catheter was placed in an emergency scenario. We use a 72-hour rule locally, however earlier removal is recommended if any phlebitis or exudate is noted at the insertion site.

Catheter-associated urinary tract infection - may be over-diagnosed since most ICU patients with prolonged urine catheter devices will develop asymptomatic bacteriuria, without actual infection – this is best addressed by using silastic catheters and changing catheters at regular intervals. Bacterial infection or fungal infection of urine in the critically ill is not an uncommon occurrence, especially in cases with inadequate urine output resulting in bladder stasis. Additionally, far more common and often inappropriately treated as infection is asymptomatic bacteriuria. The incidence of UTI is between 15 and 25% depending on the criteria used for diagnosis and whether asymptomatic positive urine cultures are considered as infection or not. Treatment, when indicated, can include systemic antimicrobials that are renally excreted, along with bladder washouts with saline, particularly in those with bladder stasis.

Wound and soft-tissue sepsis - includes inflammation and infection at the different levels of skin and soft tissue planes and the importance is the need for and timing of the surgical approach, particularly in the case of necrotizing soft-tissue sepsis. Commonly cellulitis may be noted in sites adjacent to drip-lines or in cases of immune-compromised diabetics with minor wounds. Deeper infections include abscess formation (including furunculitis and intra-muscular abscesses), peri-anal sepsis (often in excoriated wounds), and deeper non-necrotizing and necrotizing infections. The latter requires early identification and early surgical debridement, with repeated regular debridement every 12-36 hours, combined with adjusted dose antimicrobial therapy, with consideration of other adjuncts such as hyperbaric oxygen therapy and immunoglobin therapy.

Surgical site sepsis - is of particular importance in critically ill post-operative patients, many of whom will be post-surgery for cancer, trauma or other emergency surgical primary pathologies that have indicated the ICU admission and with relative immunosuppression. Mostly this is simple superficial surgical site sepsis, treated by suture/staple removal, saline irrigation and topical wound care. Systemic therapy is not warranted without systemic sepsis signs. Deeper tissue space infections, may, on the other hand, require operative intervention and drainage. These may be difficult to diagnose and the use of uncommon diagnostic modalities, such as PET-CT may have a role to play. The risk of these becoming necrotizing infections is high in trauma cases or in those with fresh or sea-water contamination. The organisms involved must be carefully reviewed to utilize appropriate antimicrobial cover, especially for cases of hospital-acquired soft tissue infections.

Signs and symptoms include erythema, fever, bulging suture lines, the increase in exudate from the previously clean wound and increased wound pain. In sedated and ventilated ICU patients it is even more important to clinically review all wounds regularly. If the wounds were clean elective surgical wounds, then at least 48 hours of coverage should be allowed prior to the first dressing change. For emergency and trauma patients the wounds should be evaluated within 24 hours of ICU admission. Effective local surveillance programs will ensure the correct choice of drugs to cover the most likely ICU infective organisms in these wound infections.

Less common causes of ICU sepsis

Sinusitis or otitis media is not uncommon (around 10% of patients with nasal tubes), but maybe a source of occult sepsis or recurrent sepsis is due to either nasal intubation or the presence of long-term naso-enteric tubes. For the most part, this is reversible by removing the naso-enteric tube and converting the patient to either an oral endotracheal tube or a tracheostomy tube if continued ventilation is required. Antimicrobials may not be required; however, the risk of *Pseudomonas* infections must be considered. This condition may lead to impaired sensory function and risk for delirium, a constant challenge in ICU with the inevitable polypharmacy in these patients. Progression to mastoiditis and subsequent brain abscess is also a possibility to be excluded.

Esophagitis, gastritis and similar unexpected inflammatory changes are found in around a third of ICU patients if upper-endoscopy is performed for research indications. Abnormalities include gastritis/erosions, nasogastric tube trauma, or esophagitis less commonly, while non-bleeding duodenal ulceration is much less common. The contribution of acid secretion to the observed pathology was suspected in about 50% of cases, however, remains unclear. The use of acid-suppressive therapy was not associated with a reduction or prevention of an endoscopic abnormality in the largest reported series. Hemoglobin concentrations, packed red cells transfused and mortality were not associated with mucosal abnormalities.

Diarrhea in the intensive care unit (ICU) is defined by the World Health Organization as >3 liquid bowel movements per day and/or a Bristol Stool Chart score of 7. Diarrhea occurs in 35 - 75% of all ICU patients and varies based on the definition applied. *Clostridioides difficile* associated diarrhea (CDAD) is surprisingly uncommon at around 2%. Risk factors include total use of more than prophylactic antibiotics, type of enteral nutrition, and the use of enemas and suppositories. The high osmolarity and high fiber composition of certain enteral nutrition formulations may contribute to diarrhea occurrence. Opiates decrease diarrhea incidence whereas probiotics have no effect on the prevention, incidence or duration of diarrhea. There is a resultant increased length of ICU stay and hospital stay, however, the impact on mortality is unclear. Stool cultures and screening for toxigenic *Clostridioides difficile* is required. Addressing the underlying cause is important and the treatment of most patients with an infective source is with fluoroquinolones, metronidazole and in cases of *C. difficile* the use of oral vancomycin or fidaxomicin for at least 10 days.

Meningitis, ventriculitis/brain abscess in the ICU patient are also less common infections but are more likely in patients with neurosurgical or maxilla-facial and otorhinolaryngological interventions with meningitis common in open head trauma, ventriculitis a risk when there have been indwelling intrathecal devices and brain abscess may complicate mastoiditis, frontal sinusitis and facial or skull base fractures. Patients in ICU mostly present with high fevers and may not portray the classic neck stiffness or pupillary signs. While in community-acquired cases, lumbar puncture is generally recommended, due to the underlying critical illness in this cohort, empiric treatment with antimicrobials that cross the blood-brain barrier is required and surgical drainage in selected cases may be required. Intrathecal antimicrobials prior to removal of devices such as external ventricular drains are associated with more rapid resolution, however in these patients longer antimicrobial courses are accepted to ensure clearance of the offending organisms.

Endocarditis as a nosocomial sepsis diagnosis in the ICU patient remains uncommon and challenges surround clinical suspicion, diagnosis and extrapolation of community-acquired endocarditis treatment to the ICU population. These are often late-onset infections after long ICU stays in “at risk” patients (with longstanding invasive lines or abnormal cardiac anatomy), however, these can result from other surgical wounds. Echocardiography is the diagnostic modality of choice in patients presenting with unexpected new cardiac failure, embolism to brain or distal tissues and new onset murmurs. Management remains complicated in these patients who may not be fit for major cardiac surgery (e.g. in case of valve failure). Echocardiography identified vegetations, myocardial abscesses, and valvular perforation: Long treatment durations with culture-directed antimicrobials are required (4 to 6 weeks and until 2 sets of cultures 48 hours apart are negative). The mortality remains high at over 65%.

Pressure sore-related systemic sepsis is generally of low incidence in ICU patients due to positive blood cultures being lower in those with higher CRP levels or in those whose injury occurred after trauma or surgery. When these bloodstream infections do occur, however, mortality was higher in those caused by pressure-sore-induced infections. The risk factors include low albumin levels, renal failure, and prolonged ICU stay during sepsis episodes. Pressure-injury-induced sepsis, when present, was associated with a higher risk of 28-day mortality.

Specific organisms that cause unexpected or important infectious consequences and complications (over and above resistance issues) in ICU patients include *Pseudomonas* and staphylococcal sepsis. Those harboring pseudomonal sepsis are at risk of disseminated micro-abscesses (e.g. renal and hepatic) and penetrating infections with full-thickness corneal ulcers being a less common, yet organ-threatening infection, with occult clinical signs. Early ophthalmological intervention is required. In the case of staphylococcal sepsis, there is always the risk of pleural seeding with serious lung complications, including necrotizing pleuritis/pneumonia leading to complications such as on-ventilator pneumothorax and empyema. The risk of tension pneumothorax is significant. Clinical identification may be confounded by the underlying pathology. Most cases will be MSSA, but increasingly MRSA is being identified.

Tropical and other less common causes of sepsis/wound infection are possible in both LMIC and travelers returning to HICs from LMICs such as malaria, Chaga's disease, Lyme disease, vibrio or other unusual organisms, which may only become apparent later in the course of the patient's progress after an unrelated incident that required the ICU admission.

When prophylaxis is required in the ICU surgical patient, what is different?

Generally speaking, antimicrobial prophylaxis should be with agents covering skin commensals and in most general populations this will require anti-Gram-positive cover (e.g. Cefazolin in high doses, for between 1 and maximally 3 doses). This is suitable for most community-related prophylaxis. Once a patient has been in the hospital and in particular in the ICU for more than 72 hours, they are mostly colonized with Gram-negatives and many of these will be resistant to baseline antimicrobials. For this reason, when patients from the ICU need to undergo surgical intervention, it is important to consider the options for prophylaxis and adjust these to the likely colonized organisms, which may require adaptation of drug choices to a wider spectrum than usually used in the patient fresh from the community.

This does not mean that the prophylaxis is prolonged, however, the drug choice is adapted to the organisms, and the drug is still administered for ideally one dose, 60-120 minutes prior to the procedure. A second dose may be advised for higher blood-loss surgery or prolonged cases (in excess of four hours).

Take-home messages

Critical illness complicates the management of infections and septic shock because the patient is immunocompromised, and has many potential sources for infection beyond that of the general ward patient or community patient. Prevention strategies are clearly documented along with the need for antibiotic stewardship guided by appropriate surveillance to ensure wise empiric choices for therapy. IPC teams and multidisciplinary cooperation is essential along with the application of hygiene practices. Infections may be caused by uncommon organisms and may involve more occult sites requiring either unique drug therapy, surgical source control, or the use of unusual diagnostic modalities to identify the cause of the infection. Prophylaxis for new surgical interventions may require the use of atypical drugs due to colonization from hospital-acquired organisms.

Conclusion

Infection prevention and control is an essential component of critical care management of the patient at risk for infection. This chapter has provided an introduction to the approaches and common septic scenarios in the ICU patient and also listed a differential diagnosis or sepsis mimics to consider when evaluating the critically ill patient.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 52

Healthcare-associated infection risk factors in the intensive care unit

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Introduction

The incidence and burden of healthcare-associated infections (HAIs) in intensive care units (ICU) were previously determined. HAIs are associated with extra cost, length of stay (LOS), mortality, and high antimicrobial resistance, which increases the risk of mortality. Each type of HAI has a specific set of risk factors. In this chapter, the author analyzed the studies on HAIs in ICUs regarding the incidence, clinical outcomes, burden, risk of mortality, and HAI.

One of the central premises of HAI prevention and control is that thorough surveillance knowledge of the occurrence of HAIs is essential to address this public health burden effectively. In low and middle-income countries (LMIC), such accurate knowledge is often underestimated, and HAI's actual, critical impact on the population of LMIC settings is difficult to assess. To determine which countries are referred to as “LMIC,” the World Bank categorizes countries worldwide into four economic strata based on 2015 gross national income (GNI) per capita: (1) low-income economies, $1,025 or less; (2) lower-middle-income economies, between $1,026 and $4,035; (3) upper-middle-income economies, $4,036 and $12,475; and (4) high-income economies, $12,476 or more. Within this categorization, 144 out of 209 (68%) are low-income and lower-middle-income economies, which can also be referred to as lower-income countries, resource countries, developing economies, or developing or emerging countries.

Patient populations vary substantially, so calculating and reporting risk-adjusted HAI rates has become standard. Device-associated HAI rates shall be reported adjusted to their most important known confounding factor: the number of device days. Risk adjustment consists of calculating rates per 1,000 device-days, which shall be central line-associated bloodstream infections (CLABSI) per 1,000 central lines (CL) days, peripheral intra venous catheters-related bloodstream infections (PIV-BSI) per 1,000 peripheral venous catheter days, ventilator-associated pneumonia (VAP) per 1,000 mechanical ventilators (MV) days, and catheter-associated urinary tract infections (CAUTI) per 1,000 urinary catheters (UC) days. Unfortunately, very few studies from LMICs report device-associated HAI per 1,000 device days, making it impossible to have a benchmark with device-associated HAI rates of other countries.

Studies on DA-HAI rates in LMICs had been minimal before 2002. In most instances, authors had reported percentages (cases over discharges or admissions) of DA-HAIs, or DA-HAI rates as number of infections per 1,000 patient-days, rather than DA-HAIs per 1,000 device-days. In such instances, the denominator of the number of device days was unknown; thus, it was impossible to have a basis for comparison between hospitals. On the one hand, since 2003, the International Nosocomial Infection Control Consortium (INICC) has published rates of HAIs per particular country as HAIs per 1,000 device days, such as from the following

countries: Argentina, Brazil, China, Colombia, Cuba, Ecuador, Egypt, El Salvador, India, Kuwait, Lebanon, Mexico, Mongolia, Morocco, Peru, Philippines, Poland, Saudi Arabia, Turkey, and Vietnam.

On the other hand, INICC has published rates of HAIs and nine studies pooling data from different LMICs from 2002 to 2024 since 2006. Recently, the INICC surveyed 2015 to 2020, covering 630 ICUs across 123 cities in 45 LMICs, including regions in Africa, Asia, Eastern Europe, Latin America, and the Middle East. The study collected prospective data through the INICC Surveillance Online System (ISOS), using the Centers for Disease Control and Prevention (CDC) / National Health Care Safety Network (NHSN) definitions to monitor device-associated (DA) HAIs. The data comprised 204,770 patients, with 1,480,620 patient days, 936,976 CL days, 637,850 MV days, and 1,005,589 UC days. The study reported 4,270 CLABSIs, 7,635 VAPs, and 3,005 CAUTIs. The overall DA-HAI rate was 7.28%, equating to 10.07 DA-HAIs per 1,000 patient days. Specifically, the rates were 4.55 CLABSIs per 1,000 CL days, 11.96 VAPs per 1,000 MV days, and 2.91 CAUTIs per 1,000 UC days. Alarmingly, bacterial resistance rates were also high, with *Pseudomonas aeruginosa* showing 50.73% resistance to imipenem and 44.99% to ceftazidime, while *Klebsiella* spp. exhibited resistance rates of 48.29% to imipenem and 72.03% to ceftazidime. Coagulase-negative Staphylococci and *Staphylococcus aureus* showed oxacillin resistance in 81.33% and 53.83% of cases, respectively. These findings underscore the critical need for ongoing efforts globally to reduce DA-HAI rates and bacterial resistance.

From the available literature, it is obvious that the adverse consequences of HAI in LMICs are attributable to mortality, prolonged LOS, and extra hospital costs. Among the most serious consequences attributable to HAI in LMICs, the mainstream literature has shown that mortality can range from 3 to 75.1%.

Regarding extra mortality, Rosenthal *et al.* have shown mortality due to CLABSI has rates that range from 4 to 75.1%. Cost, LOS, and mortality attributable to DA-HAI have been determined by INICC internationally through prospective, matched analyses. In a review to analyze the incidence of CLABSI in LMIC performed by Rosenthal in 2009, it was demonstrated that the CLABSI rate was associated with significant extra mortality, with an odds ratio ranging from 2.8 to 9.5. Similarly, mortality attributable to VAP is as high as 56.7%. Concerning mortality due to CAUTI, reports are scarce, and there is diversity in the interpretation of findings. Some publications stated that CAUTI was not associated with mortality, but other findings specified rates up to 21.3%. In several studies, researchers have highlighted the extreme vulnerability of neonates hospitalized in NICUs to mortality attributable to DA-HAI, with rates ranging from 24% in the pre-surfactant era to 11% in the post-surfactant era in developed countries.

Regarding the extra LOS, in a study performed in hospitals member of INICC in 10 LMICs to estimate extra LOS and mortality in an ICU due to a VAP, a cohort of 69,248 admissions were followed for 283,069 days in ICUs. Data were arranged according to a multi-state format. Extra LOS and increased risk of death were estimated independently in each country, and their results were combined using a random effects meta-analysis. The findings of the analysis showed that a VAP prolonged LOS by an average of 2.03 days (95% CI: 1.52, 2.54 days) and increased the risk of death by 14% (95% CI: 2, 27%). For measuring LOS and mortality attributable to DA-HAI, the INICC applied a new multi-state model, including specific censoring to ensure the estimation of the independent effect of each DA-HAI and not the combined effects of multiple DA-HAIs. To estimate the excess LOS and mortality in the ICU attributable to the CAUTI, a statistical model that accounted for the timing of infection was applied in 29 ICUs of hospital members of INICC from 10 countries: Argentina, Brazil, Colombia, Greece, India, Lebanon, Mexico, Morocco, Peru, and Turkey. In a cohort of 69,248 admissions followed for 371,452 days in 29 ICUs, a multi-state model was applied to estimate the extra LOS due to HAI. This model included specific censoring to ensure that estimations considered the independent effect of CAUTI and not the combined effects of multiple infections. The extra LOS and increased risk of death were independent for each country, and then the results used a random effects meta-analysis. The conclusions showed that a CAUTI prolonged LOS by an average of 1.59 days (95% CI: 0.58, 2.59 days) and increased the risk of death by 15% (95% CI: 3, 28%). A study to estimate the excess LOS in an ICU due to CLABSI was performed on hospital members of INICC in three Latin American countries (Argentina, Brazil, and Mexico). A

statistical model that accounted for the timing of HAI was used to analyze the data. A cohort of 3,560 patients hospitalized in 11 ICUs was followed for 36,806 days. The average excess LOS due to a CLABSI increased and varied between –1.23 and 4.69 days.

Regarding extra cost, to calculate the cost of CLABSI in ICUs, a 5-year prospective nested case-control study was undertaken in six adult ICUs from three hospitals in Argentina, members of INICC. One hundred and forty-two patients with CLABSI (cases) and 142 patients without CLABSI (controls) were matched for hospital, type of ICU, year of admission, LOS, gender, age, and average severity of illness score. The mean extra LOS for cases (compared to the controls) was 11.90 days, the mean extra antibiotic defined daily doses was 22.6, the mean extra antibiotic cost was $1,913, the mean extra cost was $4,888.42, and the excess mortality was 24.6%. To calculate the cost of CLABSIs in ICU, an 18-month prospective nested case-control study was undertaken at three hospitals in Mexico City, members of INICC, in four ICUs. Fifty-five patients with CLABSI (cases) and 55 patients without CLABSI (controls) were compared by analyzing the hospital, type of ICU, year of admission, LOS, gender, age, and average severity of illness score. The results indicated that the extra LOS of patients with CLABSI was 6.05 days. The mean extra cost of antibiotics amounted to $598, the mean extra cost of other drugs was $25.77, and the mean extra cost of hospitalization was $8,326. The mean extra cost for cases (compared to the controls) amounted to $11,591. Finally, the extra mortality attributable to BSI was 20%.

To calculate the cost of VAP in ICU, a 5-year matched cohort study was undertaken at six ICUs of three hospitals in Argentina as members of INICC. Three hundred and seven patients with VAP (exposed) and 307 patients without VAP (unexposed) were matched for hospital, ICU, period, LOS more than seven days, gender, age, and average severity of illness score (ASIS). The mean extra LOS for 307 cases (compared to the controls) was 8.95 days, the mean extra antibiotic defined daily doses (DDD) was 15, the mean extra antibiotic cost was $996, the mean extra total cost was $2,255, and the extra mortality was 30.3%. Another study from northern India, patients with VAP experienced significantly more extended LOS [21 (IQ=14-33) days *versus* 11 (IQ=6-18) days, $p<0.0001$)] and incurred more significant hospital costs [USD 6250.92 (IQ=3525.39-9667.57) *versus* $2598.84 (IQ=1644.33-4477.65), $p<0.0001$]. Multiple regression analysis revealed that the cost-driving factors in this study population were the occurrence of VAP infections ($p<0.0001$) and the duration of LOS ($p<0.0001$). The attributable cost of VAP infection was calculated to be USD 5200 (95% CI=3245-7152). Studies from Europe have shown that extra mortality caused by AMR exceeds $25,000 annually, and the extra healthcare costs and loss in productivity have been estimated to be €1.5 billion each year. Because the data available on the health and financial burden of AMR is scarce in many countries, it is difficult to estimate the actual magnitude of the problem accurately.

In the last INICC Report, which contains a data summary of the DA-HAIs of 45 countries for 2015- 2020, Bacterial resistance among pathogens isolated from patients with HAIs in adult and pediatric ICUs reveals alarmingly high resistance rates. Methicillin-resistant *Staphylococcus aureus* (MRSA) accounted for 53.83% of *Staphylococcus aureus* cases, *Enterococcus faecalis* exhibited 17.87% resistance to vancomycin, and *Klebsiella pneumoniae* showed 66.95% resistance to ceftriaxone and 48.29% to imipenem. *Enterobacter* species had a 40.76% resistance rate to ceftriaxone and 19.44% to imipenem, while *Pseudomonas aeruginosa* exhibited resistance rates of 44.99% to ceftazidime and 50.73% to imipenem. *Acinetobacter* species had the highest resistance rates, with 91.91% to piperacillin-tazobactam and 89.09% to imipenem. When comparing these findings with bacterial resistance data from U.S. CDC/NHSN ICUs, resistance rates in LMICs are significantly higher for many pathogens. For instance, the MRSA rate in LMICs was 53.83%, compared to 50.7% in CDC/NHSN data. Similarly, vancomycin resistance in *Enterococcus faecalis* was 17.87% in LMICs, compared to 9.8% in CDC/NHSN ICUs. *Klebsiella pneumoniae* in LMICs exhibited a resistance rate of 66.95% to ceftriaxone and 48.29% to imipenem, compared to 24.1% and 10.9% in CDC/NHSN data, respectively. *Enterobacter* species in LMICs had a ceftriaxone resistance of 40.76% and imipenem resistance of 19.44%, higher than CDC/NHSN rates of 36.1% and 6.6%. *Pseudomonas aeruginosa* resistance to ceftazidime and imipenem was

44.99% and 50.73% in LMICs, *versus* 24.2% and 18.4% in CDC/NHSN data. Finally, *Acinetobacter* species in LMICs showed a striking 89.09% resistance to imipenem, much higher than the CDC/NHSN rate of 46.6%. The unnecessary or inappropriate administration of antimicrobials influences antimicrobial resistance (AMR). The increase in antimicrobial treatments and generalized overuse of antimicrobials during the last decades has turned some once-common infections that were easy to treat into a severe and, many times, life-threatening illness. The evolving public health threat of AMR is driven by both appropriate and inappropriate use of anti-infective agents for human and animal health and food production, together with inadequate measures to control the spread of infections.

Antimicrobial resistance (AMR) is a growing global health challenge in the 21st century. A study estimated deaths and disability-adjusted life-years (DALYs) attributable to, and associated with bacterial AMR from 1990 to 2021, covering 22 pathogens and 11 infectious syndromes across 204 countries. Statistical modeling leveraged multiple data sources, including hospital records and mortality surveillance, to estimate the AMR burden for locations lacking direct data. In 2021, an estimated 4.71 million deaths were associated with AMR, including 1.14 million directly attributable to it. AMR-related deaths decreased by over 50% among children under 5 but rose by more than 80% among adults over 70. Projections indicate AMR-related deaths could reach 8.22 million globally by 2050, with the highest mortality rates forecasted in South Asia and Latin America. This study highlights the importance of infection prevention, antibiotic stewardship, and better healthcare access to combat the rising threat of AMR.

Risk factors for mortality in intensive care units

Regarding risk factors for mortality, research conducted in surgical ICUs analyzed risk factors and mortality of patients with CLABSI, finding with multivariable analyses that males (OR = 7.20, *p*=0.03) have shown the highest risk factors for mortality. A trial analyzing risk factors for mortality from VAPs concluded that older age (adjusted OR [aOR], 1.02), higher APACHE II score on ICU admission (aOR, 1.06), pneumonia (aOR, 1.49), blood transfusion (aOR 1.43), immunosuppressive drugs (aOR, 1.69), CL (aOR, 2.06), and >/=2 VAEs in the ICU (aOR, 1.99) were associated with higher risks for all-cause mortality in an ICU. A study about risk factors for mortality of critically ill patients admitted to an ICU found In-hospital mortality was independently associated with MV (subdistribution hazard ratio (SHR) 2.74), vasopressors (SHR 2.56), neurological disease (SHR 1.77), and Mortality Prediction Model II score (SHR 1.01) regardless of age and with malignancy (SHR, hematological 3.65, nonhematological 3.4) and prior renal replacement therapy (RRT, SHR 2.21) only in the elderly. Long-term mortality was associated with low hemoglobin concentration (SHR 0.94), airway disease (SHR 2.23), and malignancy (SHR hematological 1.11, nonhematological 2.31) regardless of age and with comorbidities, especially among the nonelderly. An additional study analyzing risk factors for the mortality of trauma victims in the ICU revealed in a logistic regression analysis that one point on the NISS and SAPS II scores increased the risk of death by 6% and 7%, respectively.

A study conducted by Saydain found that severe pulmonary hypertension, lower mean arterial pressure, cardiac index, need for MV, vasopressors, higher SOFA, APACHE II, and pulmonary vascular resistance index were associated with increased mortality. In addition, research analyzing HAI in adult ICUs identified diabetes mellitus and MV as predictors for increased mortality in patients with HAI. In an analysis of risk factors and associated mortality in a Turkish university hospital, with logistic regression analyses, age (>60 years), APACHE II score >15, MV, and CL were found to be significant risk factors for mortality.

Rosenthal *et al.* conducted a comprehensive multinational, multicenter prospective cohort study investigating the impact of HAIs on mortality in ICUs across a diverse range of countries, including those in Asia, Africa, Eastern Europe, Latin America, and the Middle East. The study, carried out by the INICC, spanned from July

1, 1998, to February 12, 2022, and involved 300,827 patients across 786 ICUs in 312 hospitals in 147 cities across 37 countries. These patients were followed over 2,167,397 patient days, during which 21,371 HAIs were acquired. The study identified several significant mortality risk factors using multiple logistic regression analysis. CLABSIs increased the risk of mortality with an adjusted odds ratio (aOR) of 1.84 (p<0.0001), VAP with an aOR of 1.48 (p<0.0001), and CAUTI with an aOR of 1.18 (p<0.0001). Additional risk factors included medical hospitalization (aOR: 1.81; p<0.0001), LOS, with a 1% risk increase per day (aOR: 1.01; p<0.0001), female gender (aOR: 1.09; p<0.0001), age (aOR: 1.012; p<0.0001), CL days, with a 2% risk increase per day (aOR: 1.02; p<0.0001), and MV-device utilization (DU) ratio (aOR: 10.46; p<0.0001). Interestingly, the study also found that coronary ICUs had the lowest mortality risk (aOR: 0.34; p<0.0001). While some risk factors, such as income level, facility ownership, hospitalization type, gender, and age, are immutable, others, including CLABSI, VAP, CAUTI, LOS, and MV-DU ratio, are adjustable. To reduce ICU mortality, the authors recommend shortening LOS, minimizing MV use, and implementing evidence-based practices to prevent HAIs.

In a comprehensive prospective cohort study conducted over 18 years, Rosenthal *et al.* examined the risk factors for mortality in 317 ICUs across 96 hospitals in 44 cities within 9 Asian countries, including China, India, Malaysia, Mongolia, Nepal, Pakistan, the Philippines, Sri Lanka, Thailand, and Vietnam. The study followed 157,667 patients over 957,517 patient days, during which 8,157 HAIs were recorded. Multiple logistic regression analysis identified several key risk factors for increased mortality. CLABSI posed a significant risk, with an adjusted odds ratio (aOR) of 2.36 (p<0.0001), followed by VAP) (aOR, 1.51; p<0.0001) and CAUTI (aOR, 1.04; p<0.0001). Additionally, female sex (aOR, 1.06; p<0.0001) and older age, which increased mortality risk by 1% per year (aOR, 1.01; p<0.0001), were significant factors. Mortality risk also rose by 1% for each additional bed day (aOR, 1.01; p<0.0001) and by 2% for each CL day (aOR, 1.02; p<0.0001). UC days they increased the risk by 4% per day (aOR, 1.04; p<0.0001). The highest mortality risks were observed in patients requiring MV, with an aOR of 12.48 (p<0.0001), and those in upper-middle-income countries (aOR, 1.09; p=0.033), surgical hospitalizations (aOR, 2.17; p<0.0001), pediatric oncology ICUs (aOR, 9.90; p<0.0001), and adult oncology ICUs (aOR, 4.52; p<0.0001). In contrast, patients treated in university hospitals experienced the lowest mortality risk (aOR, 0.61; p<0.0001). While some factors, such as age, sex, national economy, and ICU or hospitalization type, are unchangeable, others, including LOS, use of CLs, UCs, MV, and the prevention of CLABSI, VAE, and CAUTI, are adjustable. The authors recommend focusing on strategies to reduce LOS, minimize the use of invasive devices, and implement infection prevention measures to mitigate mortality risk in ICUs.

Rosenthal *et al.* conducted a multinational prospective cohort study over 24 years to identify mortality risk factors in 198 ICUs across 96 hospitals in 46 cities in 12 Latin American countries. The study, part of the INICC, followed 71,685 patients over 652,167 patient days, during which 4,700 HAIs were acquired and 10,890 patients died. The study identified 11 independent risk factors associated with increased mortality in ICU patients using multiple logistic regression. These included the acquisition of VAP, with an adjusted odds ratio (aOR) of 1.17 (95% CI: 1.06-1.30; p<0.0001), and ry tract infections (CAUTI) (aOR = 1.34; 95% CI: 1.15-1.56; p<0.0001). Older age increased the risk of mortality by 2% per year (aOR = 1.02; 95% CI: 1.01-1.02; p<0.0001), while each additional CL day raised the risk by 3% (aOR = 1.03; 95% CI: 1.02-1.03; p<0.0001). Similarly, UC days increased the risk by 1% daily (aOR = 1.01; 95% CI: 1.01-1.26; p<0.0001). The highest mortality risk was associated with MV (aOR = 6.47; 95% CI: 5.96-7.03; p<0.0001) and UC-DU ratio (aOR = 1.19; 95% CI: 1.11-1.27; p<0.0001). Mortality was also more likely in lower-middle-income countries (aOR = 2.94; 95% CI: 2.10-4.12; p<0.0001) and in private (aOR = 1.50; 95% CI: 1.27-1.77; p<0.0001) and public hospitals (aOR = 1.47; 95% CI: 1.24-1.74; p< 0.0001) compared to university hospitals. Medical hospitalizations (aOR = 1.67; 95% CI: 1.59-1.75; p<0.0001), neurologic ICUs (aOR = 4.48; 95% CI: 2.68-7.50; p<0.0001), and adult oncology ICUs (aOR = 3.48; 95% CI: 2.14-5.65; p<0.0001) were also associated with increased mortality risk. The authors concluded that while factors such as age, income level, and facility ownership are immutable, efforts should

focus on reducing modifiable factors, including CL and UC days, MV-DU ratio, and the rates of VAP and CAUTI, on decreasing ICU mortality rates.

Rosenthal *et al.* conducted a prospective cohort study from August 1, 2003, to February 12, 2022, to identify mortality risk factors in ICUs across 10 Middle Eastern countries. The study, part of the INICC, involved 66,440 hospitalized over 652,167 patient days in 236 ICUs within 77 hospitals in 44 cities. A total of 13,974 patients died during the study period. Using multiple logistic regression, the study identified several independent mortality risk factors. Age increased the risk of mortality by 2% per year (adjusted odds ratio [aOR]: 1.02; p<0.0001), and LOS increased the risk by 2% per day (aOR: 1.02; p<0.0001). Each additional day of CL use raised the risk by 1% (aOR: 1.01; p<0.0001), while the MV-DU ratio had a significant impact on mortality risk (aOR: 14.51; p<0.0001). Acquisition of CLABSI (aOR: 1.49; p<0.0001) and VAP (aOR: 1.50; p<0.0001) were also associated with increased mortality. Female gender (odds ratio [OR]: 1.14; p< 0.0001), public hospital admissions (OR: 1.31; p<0.0001), and medical hospitalizations (aOR: 1.64; p<0.0001) further elevated the risk. In contrast, patients from high-income countries experienced the lowest mortality risk (aOR: 0.59; p<0.0001). While certain factors such as income level, facility ownership, hospitalization type, gender, and age are unlikely to change, others, including LOS, CL, and MV use, and the rates of CLABSI and VAP, can be modified. The authors recommend strategies to shorten LOS, reduce the use of CL and MV, and implement evidence-based guidelines to prevent CLABSI and VAP to lower mortality rates in ICUs.

In conclusion, these studies conducted by Rosenthal *et al.* provide crucial insights into the global mortality risk factors associated with HAIs in ICUs across various regions, including Asia, Latin America, the Middle East, and beyond. The research highlights both preventable and non-preventable risk factors for mortality. Preventable factors include CLABSI, VAP, CAUTI, MV-DU ratio, LOS, CL and UC days, hospitalization type (medical *vs.* surgical), public hospital admissions, the use of invasive devices, and lower- and middle-income country status. These modifiable factors present opportunities for intervention through infection prevention measures, reducing the use of invasive devices, and minimizing LOS, which could substantially lower ICU mortality rates. Conversely, non-preventable factors such as age, female gender, national income level, ICU type (e.g., oncology, pediatric, neurologic), and facility ownership (public or private *vs.* university hospitals) remain immutable but require tailored management strategies. By addressing the modifiable risks while adapting to non-modifiable challenges, healthcare providers can implement evidence-based practices that improve patient outcomes in ICUs worldwide, ultimately mitigating the global impact of HAIs on mortality.

Risk factors for central line-associated bloodstream infection in intensive care units

Studies found the following variables as CLABSI risk factors (RFs): body mass index >40, multiple CLs, multilumen catheters, femoral site, guidewire exchange, heavy microbial colonization at the insertion site or catheter hub, indwelling time, prolonged LOS before catheterization, neutropenia, total parenteral nutrition, patient cared for by a float nurse, transfusion of blood products, prematurity, reduced ICU nurse-to-patient ratio, substandard CL-care, and few others.

In a 24-year multinational prospective cohort study, Rosenthal *et al.* investigated the incidence and risk factors for CLABSI in LMICs. The study, conducted between July 1, 1998, and February 12, 2022, included 728 ICUs from 286 hospitals in 147 cities across 41 countries in Africa, Asia, Eastern Europe, Latin America, and the Middle East. The study followed 278,241 patients for 1,815,043 patient days, during which 3,537 CLABSIs were recorded. The pooled CLABSI rate was 4.82 infections per 1,000 CL days, significantly higher than the CDC's NHSN reported. Multiple logistic regression identified several independent risk factors for CLABSI, including LOS, with the risk increasing by 3% per day (adjusted odds ratio [aOR], 1.03; 95% CI, 1.03-1.04;

p<0.0001), and the number of CL days, with a 4% increased risk per day (aOR, 1.04; 95% CI, 1.03-1.04; *p*<0.0001). Other significant factors included surgical hospitalizations (aOR, 1.12; 95% CI, 1.03-1.21; *p*<0.0001), tracheostomy use (aOR, 1.52; 95% CI, 1.23-1.88; *p*<0.0001), and hospitalization at publicly owned facilities (aOR, 3.04; 95% CI, 2.31-4.01; *p*<0.0001) or teaching hospitals (aOR, 2.91; 95% CI, 2.22-3.83; *p*<0.0001). The highest CLABSI risks were found in adult oncology ICUs (aOR, 4.35; 95% CI, 3.11-6.09; *p*<0.0001), pediatric oncology ICUs (aOR, 2.51; 95% CI, 1.57-3.99; *p*<0.0001), and pediatric ICUs (aOR, 2.34; 95% CI, 1.81-3.01; *p*<0.0001). Among the types of CLs, the internal jugular catheter posed the highest risk (aOR, 3.01; 95% CI, 2.71-3.33; *p*<0.0001), followed by the femoral catheter (aOR, 2.29; 95% CI, 1.96-2.68; *p*<0.0001), while peripherally inserted central catheters (PICC) had the lowest CLABSI risk (aOR, 1.48; 95% CI, 1.02-2.18; *p*=0.04). The authors concluded that although certain risk factors like country income level, facility ownership, hospitalization type, and ICU type are unlikely to change, efforts should focus on reducing LOS, minimizing CL days and tracheostomy use, favoring PICC over internal-jugular or femoral CLs, and implementing evidence-based CLABSI prevention strategies.

In a multinational prospective cohort study conducted from March 27, 2004, to February 11, 2022, Rosenthal *et al.* investigated the incidence and risk factors for CLABSI across 281 ICUs in 95 hospitals located in 44 cities across 9 Asian countries, including China, India, Malaysia, Mongolia, Nepal, Pakistan, the Philippines, Sri Lanka, Thailand, and Vietnam. A total of 150,142 patients were hospitalized for 853,604 patient days, and 1,514 CLABSIs were acquired. The overall pooled CLABSI rate was 5.08 per 1,000 CL days, with the highest rates seen in femoral (6.23), temporary hemodialysis (4.08), and jugular (4.01) catheters, and the lowest rates observed with PICC (2.47) and subclavian lines (2.02). Multiple logistic regression analysis revealed several significant risk factors for CLABSI, including the LOS before CLABSI acquisition, with the risk rising by 4% per day (adjusted odds ratio [aOR] = 1.04; 95% CI = 1.03-1.04; *p*<0.0001), and the number of CL days before CLABSI acquisition, which increased the risk by 5% per day (aOR = 1.05; 95% CI = 1.05-1.06; *p*<0.0001). Additional factors associated with increased CLABSI risk included medical hospitalization (aOR = 1.21; 95% CI = 1.04-1.39; *p*=0.01), tracheostomy use (aOR = 2.02; 95% CI = 1.43-2.86; *p*<0.0001), and admission to publicly owned facilities (aOR = 3.63; 95% CI = 2.54-5.18; *p*<0.0001). Lower-middle-income countries also had higher CLABSI risk (aOR = 1.87; 95% CI = 1.41-2.47; *p*<0.0001). Among ICU types, pediatric ICUs had the highest risk (aOR = 2.86; 95% CI = 1.71-4.82; *p*<0.0001), followed by medical-surgical ICUs (aOR = 2.46; 95% CI = 1.62-3.75; *p*<0.0001). The highest CLABSI risks were associated with internal-jugular (aOR = 3.32; 95% CI = 2.84-3.88; *p*<0.0001) and femoral lines (aOR = 3.13; 95% CI = 2.48-3.95; *p*<0.0001), while subclavian lines had the lowest risk (aOR = 1.78; 95% CI = 1.47-2.15; *p*<0.0001). The authors concluded that certain risk factors, such as country income level, facility ownership, hospitalization type, and ICU type, are unlikely to change. However, efforts should focus on reducing LOS, minimizing CL days and tracheostomy use, and favoring subclavian or PICC lines over internal-jugular or femoral lines while implementing evidence-based CLABSI prevention strategies.

In a multinational prospective cohort study conducted between January 1, 2014, and February 10, 2022, Rosenthal *et al.* examined the incidence and risk factors for CLABSI in 58 ICUs across 34 hospitals located in 21 cities in 8 Latin American countries, including Argentina, Brazil, Colombia, Costa Rica, the Dominican Republic, Ecuador, Mexico, and Panama. The study followed 29,385 patients for 92,956 patient days, during which 400 CLABSIs were recorded. The pooled CLABSI rate was 4.30 per 1,000 CL days. The study identified several significant risk factors for CLABSI using multiple logistic regression. LOS before CLABSI acquisition increased the risk by 3% per day (adjusted odds ratio [aOR] = 1.03; 95% CI = 1.02-1.04; *p*<0.0001), and the number of CL days before CLABSI acquisition increased the risk by 4% per day (aOR = 1.04; 95% CI = 1.03-1.05; *p*<0.0001). Publicly owned facilities were associated with a higher risk of CLABSI (aOR = 2.33; 95% CI = 1.79-3.02; *p*<0.0001). Among ICU types, medical-surgical ICUs had the highest risk (aOR = 2.61; 95% CI = 1.41-4.81; *p*<0.0001). Regarding CL types, femoral lines had the highest risk (aOR = 2.71; 95% CI = 1.61-4.55; *p*<0.0001), followed by internal-jugular lines (aOR = 2.62; 95% CI = 1.82-3.79; *p*<0.0001). In contrast, PICC

were not significantly associated with CLABSI risk (aOR = 1.25; 95% CI = 0.63-2.51; *p*=0.52). Based on these findings, the authors suggest focusing on strategies to reduce LOS and CL days, using PICC instead of femoral or internal-jugular lines, and implementing evidence-based CLABSI prevention recommendations to mitigate infection risk in Latin American ICUs.

In this series of several multinational prospective cohort studies, Rosenthal *et al.* examined the incidence and risk factors for CLABSI across LMICs, including regions in Africa, Asia, Eastern Europe, Latin America, and the Middle East. Across all areas, the pooled CLABSI rate was found to be significantly higher than that reported by the CDC's NHSN, with specific rates of 4.82 CLABSIs per 1,000 CL days globally, 5.08 in Asia, and 4.30 in Latin America. Common risk factors for CLABSI included increased LOS, with a 3-4% risk increase per day, and the number of CL days, with a 4-5% increase in risk per day. Other significant factors included surgical hospitalizations, tracheostomy use, and admissions to publicly owned facilities or teaching hospitals. Specific ICU types such as oncology and pediatric ICUs and using internal jugular and femoral catheters were associated with higher CLABSI risks. In contrast, PICC and subclavian lines were linked to lower infection risks. The studies also highlighted that while non-modifiable factors such as country income level, facility ownership, and ICU type remain unchanged, modifiable factors like reducing LOS, minimizing CL days, and favoring PICC or subclavian lines over internal jugular or femoral lines can help mitigate CLABSI risk. The authors emphasize the importance of implementing evidence-based CLABSI prevention strategies, particularly in LMICs, to reduce infection rates and improve patient outcomes in ICUs worldwide. Incorporating this evidence, the INICC implemented a multidimensional approach in 30 countries, including a bundle with 11 components, effectively reducing CLABSI rates.

Risk factors for ventilator-associated pneumonia in intensive care units

Several authors identified the following as VAP risk factors (RF): tracheostomy, LOS, older age, trauma patients, post-surgical patients, burns patients, longer duration of surgery, history of smoking, low serum albumin concentration], high score on the American Society of Anesthesiologists Physical Status Classification System, APACHE II score >20, acute respiratory distress syndrome, lung injury, chronic obstructive pulmonary disease, upper respiratory tract colonization, sinusitis, PaO_2/FiO_2 ratio <200 mmHg, oropharyngeal colonization, biofilm on the surface and within the lumen of the endotracheal tube, duration of MV, frequent change in ventilator circuit, lack of use of heat and moist exchange humidifiers, supine position, frequent reintubation, enteral feeding, multiple CLs insertions, presence of CLABSI, paralytic agents, previous use of broad-spectrum antibiotics, and patients transported out of ICU.

Almuneef *et al.* conducted a prospective surveillance study of VAP among all patients receiving MV for 48 hours or more and who were admitted to a pediatric intensive care unit (PICU) in Saudi Arabia. On multiple logistic regression analysis, only prior antibiotic therapy, continuous enteral feeding, and bronchoscopy were independent predictors of VAP. Petdachai conducted a prospective observational study in a neonatal intensive care unit (NICU) of 170 infants who required MV for longer than 48 hours. Stepwise logistic regression analysis identified 3 RFs independently associated with VAP: umbilical catheterization, respiratory distress syndrome, and insertion of an orogastric tube.

Pawar *et al.* performed a prospective study in a cardiac surgical ICU at Escorts Heart Institute and Research Centre, New Delhi, India. Potential RFs were analyzed. On multivariate analysis, intermittent positive-pressure ventilation hours and steroids were independent of VAP RFs. Apisarnthanarak *et al.* conducted a prospective cohort study. By multivariate analysis, CLABSI before VAP was an independent VAP RF after adjustment for the duration of endotracheal intubation.

Bochicchio *et al.* conducted a prospective observational cohort study of 766 trauma patients admitted to the ICU, who received MV for >or= 48 h, and who did not have pneumonia on admission. Logistic regression analyses were performed on all variables related significantly to VAP. A substantially greater proportion of male patients developed VAP. Also, Patients with VAP had a longer duration of MV. On the other hand transfusion of blood products was an independent risk factor for VAP, and the risk increased with more units transfused. Rocha *et al.* conducted a case study *vs.* patients controlled under MV and hospitalized in clinical-surgical adults ICU from March/2005 to March/2006. Patients under MV for over 48 h were included in the study, including 84 with a diagnosis of VAP and 191 without VAP (control group). By multivariate analysis, the RFs predisposing for VAP were MV time and MV > seven days, tracheostomy, and use of > or = three antibiotics,

Joseph *et al.* performed a prospective study over 15 months to determine the incidence and the RFs for the development of VAP in critically ill adult patients admitted in different ICUs of Jawaharlal Institute of Post-graduate Medical Education and Research (JIPMER), a tertiary care hospital in Pondicherry, India. Univariate analysis indicated that the following were significantly associated with VAP: impaired consciousness, tracheostomy, re-intubation, emergency intubation, and nasogastric tube. Emergency intubation and intravenous sedatives were the specific RFs for early-onset VAP. At the same time, tracheostomy and re-intubation were the independent predictors of late-onset VAP by multivariate logistic regression analysis. A study by Markowicz *et al.* indicated that VAP was considerably caused by an increase in the amount of time spent on mechanical ventilation (MV), and the use of sucralfate is included in the list of risk factors (RF) for VAP.

Large volume aspiration, sedation, intubation due to respiratory/cardiac arrest or a drop in level of consciousness, emergency procedure, cardiopulmonary resuscitation (CPR), and Glasgow coma score (GCS) 9 were significantly found to be risk factors for pneumonia in a study by Rello *et al.* Continuous sedation (OR = 4.40, 95% CI = 1.83 - 10.59) and CPR were determined by multivariate analysis as significant risk factors for pneumonia (OR = 5.13, 95% CI = 2.14 - 12.26). Holzapfel *et al.* conducted a prospective, randomized clinical experiment in a general adult ICU at a non-teaching hospital. They found that sinusitis was a time-dependent factor that markedly enhanced the probability of nosocomial pneumonia by 3.8 D. R. Park demonstrates that VAP-causing bacteria are substantially more prevalent when other risk factors are present, such as in acute respiratory distress syndrome (ARDS) or after tracheostomy, traumatic injuries, or burns. These risk variables include prior antibiotic therapy, prolonged hospitalization, or MV. These variations seem to be brought on by the length of MV in these patients and the degree of prior antibiotic exposure.

Rosenthal *et al.* conducted a multinational prospective cohort study over 24 years to investigate VAP rates and risk factors in ICUs across 42 countries in Asia, Africa, Eastern Europe, Latin America, and the Middle East. The study was part of the INICC and included 289,643 patients admitted to 743 ICUs in 282 hospitals in 144 cities. These patients were followed for 1,951,405 patient days, during which 8,236 VAP cases were recorded. The pooled VAP rate in LMICs was significantly higher than in high-income countries. Multiple logistic regression identified several independent risk factors for VAP, including male sex (adjusted odds ratio [aOR], 1.22; 95% CI, 1.16-1.28; p<0.0001) and longer LOS, which increased the risk by 7% per day (aOR, 1.07; 95% CI, 1.07-1.08; p<0.0001). MV-DU ratio also contributed to increased risk (aOR, 1.27; 95% CI, 1.23-1.31; p<0.0001), with continuous positive airway pressure (CPAP) posing the highest risk (aOR, 13.38; 95% CI, 11.57-15.48; p<0.0001), followed by tracheostomy connected to an MV (aOR, 8.31; 95% CI, 7.21-9.58; p<0.0001) and endotracheal tube connected to an MV (aOR, 6.76; 95% CI, 6.34-7.21; p<0.0001). Other risk factors included surgical hospitalization (aOR, 1.23; 95% CI, 1.17-1.29; p<0.0001), admission to a public hospital (aOR, 1.59; 95% CI, 1.35-1.86; p<0.0001), and middle-income country status (aOR, 1.22; 95% CI, 1.15-1.29; p<0.0001). ICU type also influenced risk, with adult oncology ICUs showing the highest risk (aOR, 4.05; 95% CI, 3.22-5.09; p<0.0001), followed by neurologic ICUs (aOR, 2.48; 95% CI, 1.78-3.45; p<0.0001) and respiratory ICUs (aOR, 2.35; 95% CI, 1.79-3.07; p<0.0001). Conversely, coronary ICUs had the lowest risk (aOR, 0.63; 95% CI, 0.51-0.77; p<0.0001). The authors concluded that while some risk factors, such as sex,

hospitalization type, ICU type, facility ownership, and country income level, are unlikely to change, efforts should focus on reducing LOS, minimizing MV use, limiting CPAP usage, and implementing evidence-based VAP prevention strategies to reduce the incidence of VAP in ICUs.

Rosenthal *et al.* conducted an 18-year multinational prospective cohort study to identify the risk factors for VAP in nine Asian countries, including China, India, Malaysia, Mongolia, Nepal, Pakistan, the Philippines, Sri Lanka, Thailand, and Vietnam. Between March 27, 2004, and November 2, 2022, the study followed 153,717 patients over 892,996 patient days across 279 ICUs in 95 hospitals in 44 cities. During this period, 3,369 VAP cases were recorded. The study identified several independent risk factors for VAP using multiple logistic regression. These included age, with VAP risk increasing by 1% per year (adjusted odds ratio [aOR] = 1.01; 95% CI = 1.00-1.01; p<0.0001), and male gender (odds ratio [OR] = 1.17; 95% CI = 1.08-1.26; p<0.0001). LOS increased the VAP risk by 7% per day (aOR = 1.07; 95% CI = 1.06-1.07; p<0.0001), while MV-DU ratio significantly elevated the risk (OR = 1.43; 95% CI = 1.36-1.51; p<0.0001). Tracheostomy connected to an MV had the highest risk (OR = 11.17; 95% CI = 9.55-14.27; p<0.0001). Additionally, patients in public (OR = 1.84; 95% CI = 1.49-2.26; p<0.0001) and private (OR = 1.57; 95% CI = 1.29-1.91; p<0.0001) hospitals faced a higher VAP risk compared to those in teaching hospitals. Patients in upper-middle-income countries also showed increased risk (OR = 1.86; 95% CI = 1.63-2.14; p<0.0001). Among ICU types, medical-surgical ICUs had the highest VAP risk (OR = 4.61; 95% CI = 3.43-6.17; p<0.0001), followed by neurologic ICUs (OR = 3.76; 95% CI = 2.43-5.82; p<0.0001), medical ICUs (OR = 2.78; 95% CI = 2.04-3.79; p<0.0001), and neuro-surgical ICUs (OR = 2.33; 95% CI = 1.61-3.92; p<0.0001). The study concluded that certain VAP risk factors, such as age, gender, ICU type, facility ownership, and country income level, are unlikely to change. However, the authors recommend reducing LOS, decreasing the MV/DU ratio, and implementing evidence-based VAP prevention strategies to reduce the incidence of VAP in these regions.

Rosenthal *et al.* conducted a 24-year multinational prospective cohort study to identify risk factors for VAP in 187 ICUs across 95 hospitals in 45 cities in 12 Latin American countries, including Argentina, Brazil, Colombia, Costa Rica, Cuba, the Dominican Republic, Ecuador, El Salvador, Mexico, Panama, Peru, and Venezuela. The study followed 67,437 patients over 456,575 patient days, during which 1,800 patients acquired VAP between July 1, 1998, and February 10, 2022. Multiple logistic regression identified several variables as independent risk factors for VAP. Age increased VAP risk by 1% per year (adjusted odds ratio [aOR] = 1.01; 95% CI = 1.00-1.01; p<0.0001), and male gender was also associated with a higher risk (aOR = 1.39; 95% CI = 1.26-1.56; p<0.0001). LOS increased VAP risk by 11% per day (aOR = 1.11; 95% CI = 1.11-1.12; p<0.0001), and MV-DU ratio was another significant factor (aOR = 1.17; 95% CI = 1.13-1.21; p<0.0001). The use of an endotracheal tube posed a significantly higher risk compared to tracheostomy (aOR = 9.96; 95% CI = 8.57-11.57; p<0.0001), and surgical hospitalizations also contributed to increased risk (aOR = 1.44; 95% CI = 1.29-1.61; p<0.0001). Public hospitals showed a higher risk of VAP (aOR = 1.45; 95% CI = 1.07-1.96; p=0.02). Among ICU types, adult-oncology ICUs had the highest VAP risk (aOR = 12.17; 95% CI = 5.05-29.36), followed by medical-surgical (aOR = 3.47; 95% CI = 2.14-5.64; p<0.0001) and surgical ICUs (aOR = 2.48; 95% CI = 1.41-4.38; p<0.0001). The authors concluded that while some VAP risk factors, such as age, gender, ICU type, and facility ownership, are unlikely to change, efforts should focus on reducing LOS, lowering the MV/DU ratio, and implementing evidence-based VAP prevention strategies.

In this series of multinational prospective cohort studies, Rosenthal *et al.* examined the rates and risk factors for VAP across ICUs in various global regions, including Asia, Latin America, Africa, Eastern Europe, and the Middle East. The pooled VAP rates were significantly higher in LMICs compared to high-income countries. Across all studies, several key risk factors were identified using multiple logistic regression. Preventable factors include the LOS, with the risk increasing by 7-11% per day, and the MV DU ratio, all of which significantly elevated VAP risk. Admission to public hospitals, surgical hospitalizations, and male gender also contributed to the increased risk. Non-preventable factors included age, with a 1% risk increase per year, and ICU type, with adult oncology, neurologic, and medical-surgical ICUs showing the highest risk, while coronary ICUs had

the lowest risk. Despite immutable factors such as age, gender, facility ownership, and ICU type, the studies recommend reducing modifiable risks by limiting MV use, decreasing LOS, and implementing evidence-based VAP prevention strategies, particularly in LMICs, to mitigate infection rates and improve patient outcomes. Incorporating this evidence, the INICC implemented a multidimensional approach in 32 countries, including a bundle with 8 components, effectively reducing VAP rates.

Risk factors for catheter-associated urinary tract infection in intensive care units

Studies identified the following variables as risk factors (RFs) for CAUTI: female sex; age over 50 years, age > 60; increased days of catheterization; duration of catheterization longer than six days; increased LOS in ICU, after a urological surgical procedure, mobility issues, diabetes, hypertension, spinal cord lesions, cerebrovascular disease, outpatient setting, non-O blood type, improper use of antibiotics, poor hygiene, systemic prophylaxis instead of when clinically indicated, and poor hygiene.

During a cross-sectional study at Bugando Medical Centre, Ndomba *et al.* conducted a survey that showed outpatient settings as a higher risk factor for CAUTI than inpatient settings. Individual risk factors for those outpatients included older age, education level, and catheter duration. Sulaiman *et al.* found type-O blood type to be a protective factor for CAUTI and non-O blood type as a risk factor.

According to a systematic review, the duration of catheterization is the main contributing risk factor for CAUTI incidence. A cross-sectional study was conducted on patients with long-term and short-term indwelling urinary catheterization. CAUTI was significantly higher among out-patients than in-patients. Older age, level of education, and catheter duration of ≥6 weeks independently predicted CAUTI among outpatients. While the female gender and catheter bags are not freely hanging among in-patients. In a study conducted in a pediatric ICU, using a multivariate logistic regression analysis, the significant associated variables for CAUTI were duration of catheter drainage and LOS. A study was conducted among patients with cesarean delivery; longer operative time and pregnancies complicated by sexually transmitted infections were associated with higher rates of CAUTI. Rosenthal *et al.* conducted a multinational prospective cohort study to examine the incidence and risk factors for CAUTIs across 623 ICUs in 224 hospitals located in 114 cities across 37 countries in Asia, Africa, Eastern Europe, Latin America, and the Middle East. The study included 169,036 patients hospitalized for a total of 1,166,593 patient days between January 1, 2014, and February 12, 2022. 2,010 CAUTIs were recorded, resulting in a pooled CAUTI rate of 2.83 per 1,000 UC days. The highest CAUTI rates were associated with the use of suprapubic catheters (3.93 per 1,000 UC days), patients hospitalized in Eastern Europe (14.03) and Asia (6.28), trauma ICUs (7.97), neurologic ICUs (6.28), and neurosurgical ICUs (4.95). Additionally, higher rates were observed in lower-middle-income countries (3.05 per 1,000 UC days) and in public hospitals (5.89). Multiple logistic regression analysis identified several independent risk factors for CAUTI, including age (adjusted odds ratio [aOR], 1.01; $p<0.0001$), female sex (aOR, 1.39; $p<0.0001$), LOS before CAUTI acquisition (aOR, 1.05; $p<0.0001$), UC-DU ratio (aOR, 1.09; $p<0.0001$), public facilities (aOR, 2.24; $p<0.0001$), and neurologic ICUs (aOR, 11.49; $p<0.0001$). The study concluded that CAUTI rates are highest in patients with suprapubic catheters, those in middle-income countries, public hospitals, trauma and neurologic ICUs, and facilities in Eastern Europe and Asia. To reduce CAUTI rates, the authors recommend focusing on strategies to shorten LOS, minimize UC use, and implement evidence-based CAUTI prevention practices.

In a multinational prospective cohort study conducted from January 1, 2014, to February 12, 2022, Rosenthal *et al.* investigated the incidence and risk factors for CAUTIs in 235 ICUs across eight Asian countries, including India, Malaysia, Mongolia, Nepal, Pakistan, the Philippines, Thailand, and Vietnam. The study followed 84,920 patients over 499,272 patient days, during which 869 CAUTIs were recorded. The pooled CAUTI rate was 3.08 per 1,000 UC days. Higher CAUTI rates were associated with suprapubic catheters (4.11), trauma ICUs (10.55),

neurologic ICUs (7.17), and neurosurgical ICUs (5.28). Rates were also higher in lower-middle-income countries (3.05), public hospitals (5.98), and private hospitals (3.09), with teaching hospitals having the lowest rate (2.04). Multiple logistic regression identified several independent risk factors for CAUTI, including older age (adjusted odds ratio [aOR] = 1.01; 95% CI = 1.01-1.02; *p*<0.0001), female sex (aOR = 1.39; 95% CI = 1.21-1.59; *p*<0.0001), use of suprapubic catheters (aOR = 4.72; 95% CI = 1.69-13.21; *p*<0.0001), longer LOS before CAUTI acquisition (aOR = 1.04; 95% CI = 1.04-1.05; *p*<0.0001), UC-DU ratio (aOR = 1.07; 95% CI = 1.01-1.13; *p*=0.02), and hospitalization in trauma (aOR = 14.12; 95% CI = 4.68-42.67; *p*<0.0001), neurologic (aOR = 14.13; 95% CI = 6.63-30.11; *p*<0.0001), and neurosurgical ICUs (aOR = 13.79; 95% CI = 6.88-27.64; *p*<0.0001). Public facilities also showed a higher risk for CAUTI (aOR = 3.23; 95% CI = 2.34-4.46; *p*<0.0001). The study concludes that CAUTI rates are higher for older patients, women, and those hospitalized in trauma, neurologic, or neurosurgical ICUs, as well as public facilities. To reduce CAUTI risk, the authors recommend focusing on strategies to reduce the LOS, decrease the UC-DU ratio, avoid suprapubic catheters, and implement evidence-based CAUTI prevention practices.

Yin *et al.* conducted a prospective cohort study between January 1, 2014, and February 10, 2022, to investigate the incidence and risk factors for CAUTIs in 145 ICUs across nine Latin American countries: Argentina, Brazil, Colombia, Costa Rica, the Dominican Republic, Ecuador, Mexico, Panama, and Peru. The study involved 31,631 patients hospitalized for 214,669 patient days, during which 305 CAUTIs were recorded. The pooled CAUTI rate was 2.58 per 1,000 UC days, with suprapubic catheters showing a rate of 2.99 and indwelling catheters a rate of 2.21. Multiple logistic regression analysis identified several independent risk factors for CAUTI, including age, with risk increasing by 1% per year (adjusted odds ratio [aOR] = 1.01; 95% CI = 1.01-1.02; *p*<0.0001), and female gender (aOR = 1.28; 95% CI = 1.01-1.61; *p*=0.04). LOS before CAUTI acquisition increased the risk by 7% per day (aOR = 1.07; 95% CI = 1.06-1.08; *p*<0.0001), while the UC-DU ratio also elevated the risk (aOR = 1.14; 95% CI = 1.08-1.21; *p*<0.0001). Public facilities showed a significantly higher CAUTI risk (aOR = 2.89; 95% CI = 1.75-4.49; *p*<0.0001). The study also found that 2014 to 2016 and 2017 to 2019 had significantly higher CAUTI risks than 2020 to 2022. There was no notable difference in CAUTI risk between suprapubic and indwelling catheters. The authors concluded that while certain CAUTI risk factors, such as age, gender, hospitalization type, and facility ownership, are unlikely to change, efforts should focus on reducing LOS, lowering the UC/DU ratio, and implementing evidence-based CAUTI prevention strategies to mitigate infection rates in Latin American ICUs.

Jin *et al.* conducted a prospective cohort study between January 1, 2014, and December 2, 2022, to investigate the incidence and risk factors for CAUTIs in 212 ICUs across nine Middle Eastern countries, including Bahrain, Egypt, Jordan, Kuwait, Lebanon, Morocco, Saudi Arabia, Turkey, and the UAE. The study involved 50,637 patients hospitalized for 434,523 days, during which 580 CAUTIs were recorded. The pooled CAUTI rate was 1.84 per 1,000 UC days. Multiple logistic regression analysis identified several independent risk factors for CAUTI, including age, with the risk increasing by 1% per year (adjusted odds ratio [aOR] = 1.01; 95% CI = 1.01-1.02; *p*<0.0001), and female sex (aOR = 1.31; 95% CI = 1.09-1.56; *p*<0.0001). LOS before CAUTI acquisition was another significant factor, with the risk rising by 6% per day (aOR = 1.06; 95% CI = 1.05-1.06; *p*<0.0001), as was the UC-DU ratio (aOR = 1.11; 95% CI = 1.06-1.14; *p*<0.0001). Patients in lower-middle-income countries (aOR = 4.11; 95% CI = 2.49-6.76; *p*<0.0001) and upper-middle-income countries (aOR = 3.75; 95% CI = 1.83-7.68; *p*<0.0001) had similarly elevated CAUTI risks. Among ICU types, neurologic ICUs had the highest risk (aOR = 27.35; 95% CI = 23.03-33.12; *p*<0.0001), followed by medical ICUs (aOR = 6.18; 95% CI = 2.07-18.53; *p*<0.0001) when compared to cardiothoracic ICUs. Additionally, the study found that the periods from 2014-2016 (aOR = 7.36; 95% CI = 5.48-23.96; *p*<0.001) and 2017-2019 (aOR = 1.15; 95% CI = 3.46-15.61; *p*<0.001) had similar risks, both of which were higher than the period from 2020-2022. The authors concluded that certain CAUTI risk factors, such as age, sex, ICU type, and country income level, are unlikely to change. To reduce CAUTI risk, the study suggests focusing on strategies to reduce LOS, lower the UC/DU ratio, and implement evidence-based CAUTI prevention recommendations.

In this series of multinational prospective cohort studies, Rosenthal *et al.* and others investigated the incidence and risk factors for CAUTIs across ICUs in various global regions, including Asia, Latin America, the Middle East, and other low- and middle-income countries. The pooled CAUTI rates ranged from 1.84 to 3.08 infections per 1,000 UC days, with the highest rates observed in regions such as Eastern Europe and Asia, in trauma, neurologic, and neurosurgical ICUs, and in public hospitals. Several common risk factors for CAUTI were identified through multiple logistic regression analysis. Preventable factors include longer LOS, with risk increasing by 5-7% per day, UC-DU ratio, the use of suprapubic catheters, and admissions to public facilities, particularly in lower- and middle-income countries. Non-preventable factors include older age, female sex, and ICU type, with neurologic, trauma, and medical ICUs showing significantly higher CAUTI risk. While immutable factors like age, sex, ICU type, and facility ownership are unlikely to change, the studies consistently emphasize that efforts should reduce modifiable risks. These include shortening LOS, lowering the UC-DU ratio, avoiding the use of suprapubic catheters, and implementing evidence-based CAUTI prevention strategies across regions to mitigate infection rates and improve patient outcomes. Incorporating this evidence, the INICC implemented a multidimensional approach in 37 countries, including a bundle with 9 components, effectively reducing CAUTI rates.

Conclusion

HAIs, particularly CLABSI, VAP, and CAUTI, pose a serious threat to patient safety in adult, pediatric, and neonatal ICUs. These infections and the rise in antibiotic-resistant pathogens significantly complicate patient care and increase the risk of severe complications. High resistance rates in pathogens like *Staphylococcus aureus, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Acinetobacter* species make treating these infections increasingly difficult. The prevalence of antimicrobial resistance in common ICU infections such as CLABSI, VAP, and CAUTI leads to longer LOS, higher healthcare costs, and an increased risk of mortality. This issue is especially critical in LMICs, where resistance rates are often significantly higher than in high-income settings, highlighting gaps in infection prevention, control, and antibiotic stewardship. The burden of CLABSI, VAP, and CAUTI, compounded by drug-resistant pathogens, emphasizes the urgent need for global initiatives focused on reducing infection rates, improving infection control measures, and advancing the development of new antimicrobial therapies. Without concerted action, HAIs will continue to contribute to significant morbidity and mortality worldwide.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 53

Risk factors and diagnosis of *Clostridioides difficile* infection

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Introduction

Clostridioides (*Clostridium*) *difficile* is a Gram-positive, spore-forming anaerobic bacterium, a major cause of healthcare-associated diarrhoea and colitis in hospitalised patients and long-term care residents. However, recent studies have shown a notable increase in the incidence of *C. difficile* infection (CDI) in the community. This shift suggests that CDI is becoming a significant concern in the general population.
C. difficile transmits directly or indirectly by the faecal-oral route *via* spores, though vegetative cells are sensitive to oxygen. Spores can be present outside and within the hospital environment, and humans and animals can be a reservoir for *C. difficile*. After digestion of *C. difficile* spores, the patient can be asymptomatically colonised or under specific conditions, spores germinate and *C. difficile* vegetative cells multiply and produce toxins. Two toxins, toxin A (TcdA) and toxin B (TcdB) are crucial in the disease's pathophysiology.

Certain *C. difficile* strains also produce a binary toxin (*C. difficile* transferase, CDT) that enhances virulence by facilitating bacterial adherence and colonisation.
Risk factors for CDI include those associated with changes in the composition of gut microbiota and immune system suppression e.g. antibiotic treatment, advanced age, use of proton pump inhibitors and chemotherapy. Risk factors for recurrent CDI also include previous CDI, especially with healthcare-associated origin and prior hospitalisation. Importantly, 25-30% of CDI patients with no risk factors were reported from the community, thus laboratory testing should not be restricted only to high-risk populations.
Appropriate and early laboratory detection of CDI is crucial to initiate timely CDI-specific antibiotic treatment in true CDI cases and prevent over-treatment in patients only colonised by *C. difficile*. The rapid identification of CDI cases allows the initiation of epidemic measures that reduce the risk of *C. difficile* spread. Because no single test is suitable for accurate CDI laboratory confirmation, a combination of laboratory tests should be used. After the first step, a sensitive test which detects the presence of *C. difficile*, in positive samples a more specific test for CDI should be used to detect the presence of toxins, as CDI is a toxin-mediated disease.

Risk factors for *Clostridioides difficile* infection

C. difficile is an opportunistic pathogen, and its pathogenicity is highly dependent on the ability of *C. difficile* to form spores, the host's condition and the presence of specific triggers that create an opportunity for *C. difficile* to cause disease.

C. difficile spore exposure

C. difficile can exist in two forms, the vegetative form which does not tolerate oxygen and the dormant spore form which allows *C. difficile* to survive outside the host. Although transmission of *C. difficile* is thought to be primarily healthcare-associated by direct patient-to-patient transmission or indirect transmission *via* contaminated surfaces and medical devices, *C. difficile* reservoirs were also identified outside the hospitals (**Figure 1**). Humans and food animals can be considered as amplification hosts for *C. difficile*. *C. difficile* spores shed by humans suffering from CDI or colonised with *C. difficile* can survive the sewage treatment process and can be released into surface water. *C. difficile* spores from livestock can be disseminated through contaminated meat, the air and manure which can either be composted or used directly as fertiliser. A contaminated farming environment further contributes to the spread of *C difficile* spores to vegetables and also to surface water. Wild animals and seafood can be exposed to spores from contaminated water. Consumption of contaminated food by humans and companion animals closes the circle of *C. difficile* circulation. After digestion of spores, the patient can be asymptomatically colonised and under specific conditions, *C. difficile* spores germinate, and *C. difficile* vegetative cells multiply and produce toxins, mediating clinical disease (**Figure 1**).

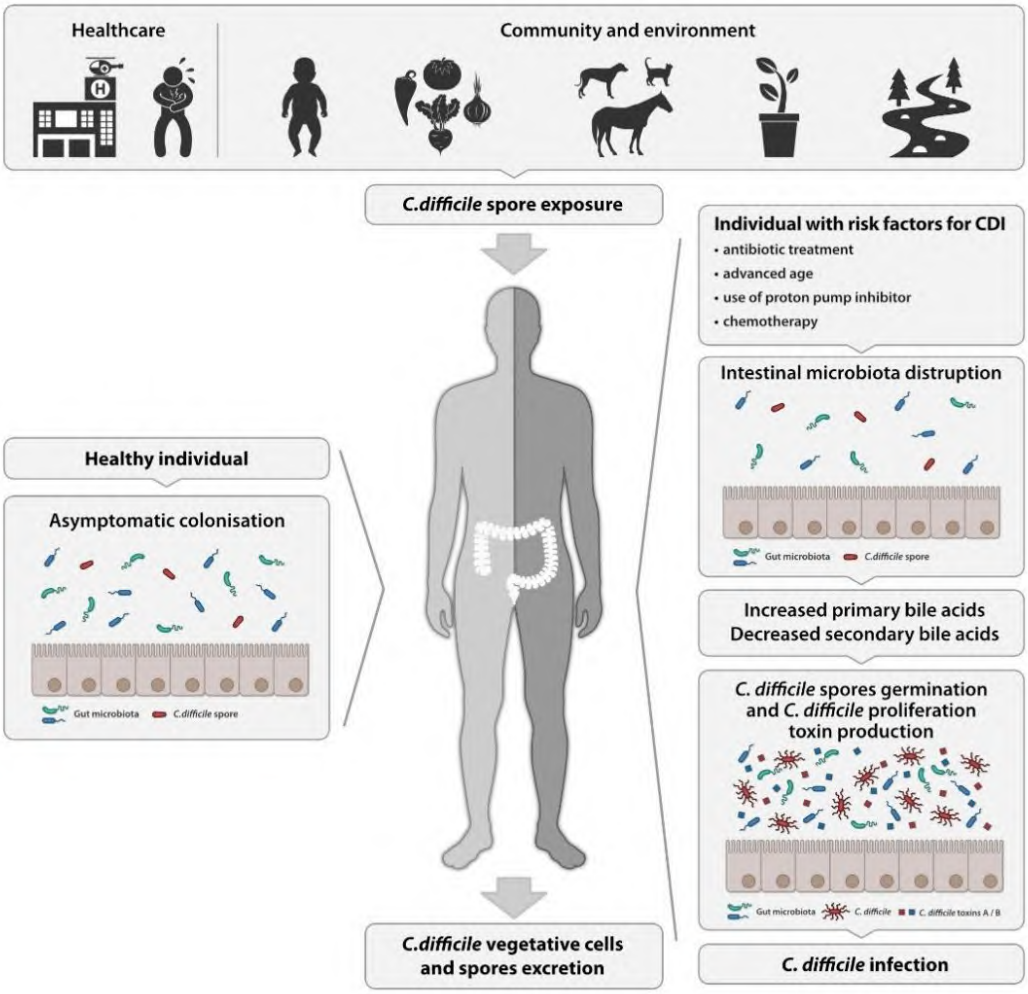

Figure 1. *Clostridiodes difficile* life cycle in humans.

Loss of gut microbiota colonisation resistance

C. difficile infection primarily affects individuals whose gut microbiome is disrupted. Changes in microbiota involve a significant reduction in microbial diversity and the depletion of beneficial bacterial groups such as Firmicutes (particularly *Clostridium* clusters IV and XIVa), Bacteroidetes, Bifidobacterium, and Lactobacillus that normally inhibit the growth of *C. difficile*.

The gut microbiota changes alter the balance of bile salt metabolism, often leading to a reduction in secondary bile salts and an accumulation of primary bile salts. Bile salt metabolism plays a crucial role in CDI by influencing the germination and growth of *C. difficile* in the gut. Primary bile salts, such as cholic acid and chenodeoxycholic acid, are produced by the liver and released into the intestines, where these are converted into secondary bile salts by the gut microbiota through 7α-dehydroxylation produced by commensal bacteria and a series of other biochemical transformations. Primary bile salts like taurocholate can promote the germination of *C. difficile* spores into their vegetative, toxin-producing form, while secondary bile salts (like deoxycholic acid and lithocholic acid) generally inhibit the growth of *C. difficile*.

The changes in the gut microbiota can be caused by various factors, including age, antibiotics, chemotherapy, and proton pump inhibitors (PPIs). The composition of gut microbiota differs significantly between young and older patients due to age-related physiological changes, dietary habits, immune function, and medication use. In young individuals, the gut microbiota is typically more diverse and richer in beneficial bacterial species,

such as *Bifidobacterium* and *Faecalibacterium*, associated with anti-inflammatory effects, enhanced metabolism, and robust gut barrier function. In contrast, older adults generally exhibit a reduction in microbial diversity, with an increase in pro-inflammatory bacteria like Proteobacteria and a decrease in beneficial species. Additionally, the gut microbiota in older adults often shows a reduced capacity for producing short-chain fatty acids (SCFAs), like butyrate, essential for maintaining gut health and immune regulation.

Antibiotics significantly influence gut microbiota composition by disrupting the balance of microbial communities, often leading to a reduction in microbial diversity. Worldwide, the burden of CDI is strongly dependent on antibiotic consumption. Antibiotics associated with an increased risk of CDI include clindamycin, fluoroquinolones (especially ciprofloxacin), cephalosporins, carbapenems and broad-spectrum penicillin's with and without b-lactamase inhibitors. The highest risk for CDI was found during therapy and in the first month after antibiotic use and the increased risk for CDI lasted in 3 months after cessation of antibiotic therapy.

Chemotherapy can also significantly impact the gut microbiota. Chemotherapy drugs target rapidly dividing cells, which include not only cancer cells but also the rapidly proliferating cells of the gut lining and certain gut microbes. Additionally, chemotherapy-induced mucositis (inflammation and ulceration of the gut lining) can further disrupt the gut barrier, allowing the translocation of bacteria and their products into the bloodstream, increasing the risk of infections and systemic inflammation. Moreover, chemotherapeutic drugs can alter the metabolic activities of the microbiota, affecting nutrient absorption, immune modulation, and the synthesis of SCFAs, which regulate epithelial barrier function as well as mucosal and systemic immunity.

Other factors disturbing colonisation resistance include PPIs that increase the pH of the stomach, reducing its natural barrier against ingested pathogens and leading to the overgrowth of bacteria that would typically not survive in a more acidic environment. This can result in decreased microbial diversity.

Compromised immune system

The immune system reacts to CDI by producing antibodies against *C. difficile* cell wall components, toxins A and B, as well as cytokines and chemokines that recruit immune cells to the site of infection. The production of systemic and local anti-toxin antibodies, such as IgA and IgG, neutralizes the toxins and prevents tissue damage. However, the effectiveness of the immune response varies significantly among individuals: patients with weakened or dysregulated immune systems, such as the elderly or immunocompromised, often have lower levels of these protective antibodies, which increases their susceptibility to CDI and its recurrences. Immunological factors, such as genetic variations in immune receptors or previous exposure to *C. difficile*, also impact the effectiveness of the immune response.

Patients with immunosuppression are at risk for CDI due to their altered immune responses, e.g. those with cancer, particularly those undergoing chemotherapy. Patients with autoimmune diseases, or inflammatory bowel disease (IBD), are also at higher risk when immunosuppressive medications are prescribed, like corticosteroids, methotrexate, and biologicals. Further, organ transplant recipients on immunosuppressive drugs to prevent organ rejection are particularly vulnerable to CDI due to their critically suppressed immune systems and frequent antibiotic exposure. Individuals with HIV/AIDS, especially those with low CD4 counts, and patients with hematologic conditions, such as leukaemia or lymphoma, are similarly at risk because of the disease and the treatments or chronic conditions requiring immunosuppressive therapy, such as chronic kidney disease (CKD) or liver cirrhosis.

Risk factors for recurrent *C. difficile* infection

The paradox of CDI treatment, at least with the traditional antimicrobial agents, metronidazole and vancomycin, is that CDI treatment in itself affects the gut microbiota constitution and colonisation resistance. Thereby, patients are at risk of entering a cycle of treatment and recurrent infection (rCDI). With each subsequent CDI episode, it becomes harder to achieve a sustained cure defined as clinical resolution of

symptoms without recurrence. Recurrence rates of a first CDI episode are up to 25%, while recurrence rates of second and third episodes may be as high as 45% and 65%. So, a previous CDI episode is an important risk factor for recurrence.

The risk factors mentioned above for primary CDI remain valid also for patients with rCDI. In addition, risk factors that predispose to rCDI are greater age, kidney disease, healthcare-associated CDI, severe CDI and prior hospitalisation. These risk factors may very well reflect the comorbidities present in this population with implications for immune function and microbiota constitution, which are important factors as discussed above.

For example, the MODIFYI/II (phase-3) trials included prespecified risk factors for recurrence, which were: age ≥65 years, history of CDI, compromised immunity, severe CDI, and infection with hypervirulent ribotypes 027/078/244. Indeed, in a post-hoc analysis, the CDI recurrence rate in the placebo group exceeded 30% for each risk factor compared with 21% among those without a risk factor. Also, recurrence rates increased with the number of risk factors (1 risk factor: 31%; ≥3 risk factors: 46%).

Laboratory diagnostics of *Clostridioides difficile* infection

Laboratory diagnosis is essential to confirm CDI cases which will facilitate timely CDI-specific antibiotic treatment in true CDI cases and prevent overtreatment in patients only colonised by *C. difficile*.

Patients' selection and sampling

A significant limitation for effective diagnosis of CDI is stool testing only at the physician's request. As was shown in a large multicentric study including 482 European hospitals, 23% of CDI-positive stool samples were not diagnosed due to a lack of clinical suspicions. The higher rates of CDI underdiagnosis were identified in general practice as in 12714 unformed stool samples, only 40% of CDI cases were detected based on physician request. The CDI patients from the community were not recently using antibiotics, were young and had no comorbidity. Both studies support testing all unformed stool samples for CDI submitted to the laboratory. The exception to this rule are children ≤2 years of age, where the colonisation of toxigenic *C. difficile* is commonly found, without having CDI. CDI testing of infants and younger children should be performed on a case-by-case basis in consultation with a paediatrician and clinical microbiologist. If CDI laboratory testing is indicated in children, a co-infection should be excluded since this is frequently found in children. A pooled prevalence of other gastrointestinal pathogens co-infection was 20.7% in 1718 paediatric patients with a positive *C. difficile* test.

For laboratory confirmation of CDI, unformed stool samples, i.e. taking the shape of the container should be accepted. Rectal swabs or formed stool samples are only examined in patients with ileus when peristalsis is stopped. It's important to note, that stool sample collection for CDI testing should be done before starting the CDI-antibiotic treatment as 14%, 35%, and 45% of positive CDI tests converted to negative after 1, 2, and 3 days of treatment, respectively.

CDI laboratory diagnostics algorithm

No single commercial assay is suitable for accurate CDI laboratory confirmation due to inadequate predictive values; therefore, a combination of laboratory tests is recommended. In the first step, a sensitive screening test, e.g. nucleic acid amplification test (NAAT) for *C. difficile* toxin gene(s) detection or *C. difficile* glutamate dehydrogenase (GDH) identifies samples with *C. difficile*. For positive samples by the screening test, the second step differentiates colonisation from infection by detecting toxins using a highly specific enzyme

immunoassay. As the sensitivity of tests for toxin A/B detection varies, the patients with positive screening tests and negative *C. difficile* toxin detection need clinical evaluation through false negative test results due to lower assay sensitivity or *C. difficile* carriage is possible (**Figure 2**).

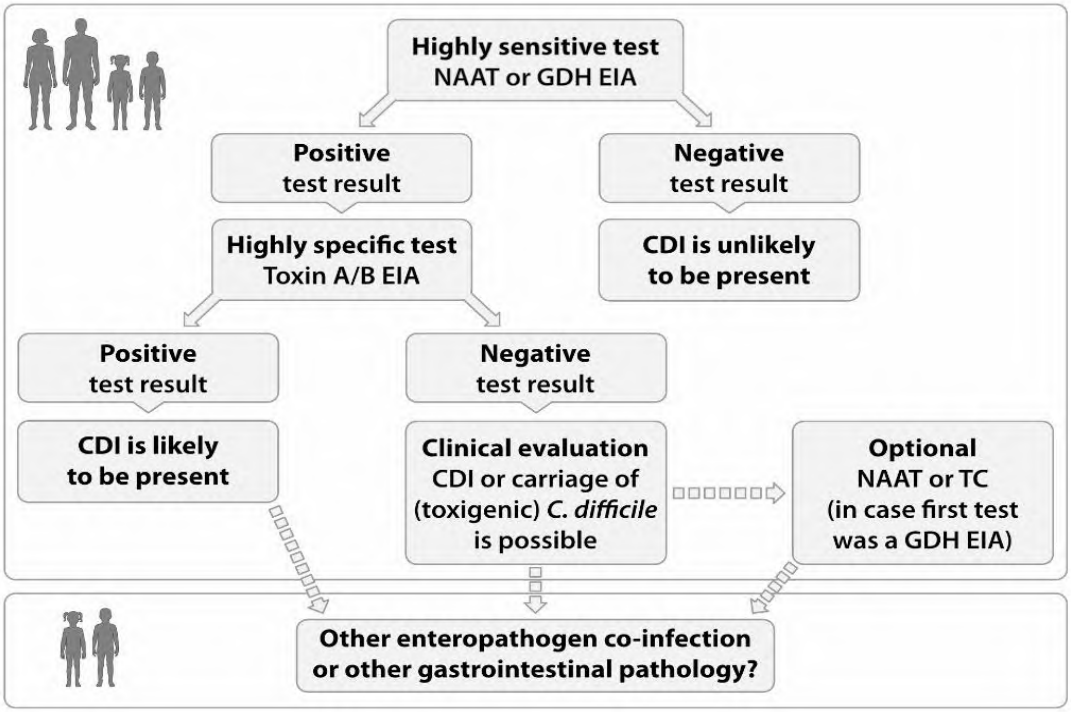

Figure 2. *Clostridioides difficile* infection diagnostic scheme (Adapted from: Crobach MJ, *et al.* 2016). CDI: *Clostridioides difficile* infection, GDH: glutamate dehydrogenase, EIA: enzyme immunoassay, NAAT: nucleic acid amplification test, TC: toxigenic culture.

Repeated testing and test of cure testing

Repeat testing is generally discouraged as in endemic situations the negative predictive value of commonly used initial tests (GDH and or PCR) is high and the additional diagnostic yield of repeat sampling is low. However, in epidemic situations, with persistent suspicion of CDI and no alternative cause of diarrhoea, or initial discrepancy between PCR or GDH test and toxin test, repeated testing is justified. Test of cure is not recommended since patients with completed CDI treatment can still be colonized with *C. difficile* and test positive. Improvement of clinical symptoms is crucial to determine the effectiveness of CDI treatment.

Antimicrobial resistance in *C. difficile*

In vitro antimicrobial susceptibility testing (AST) should be performed in *C. difficile* isolates for drugs of choice fidaxomicin and vancomycin. As *C. difficile* culture with AST is not routinely performed in all microbiological laboratories, *C. difficile* isolates from patients with CDI treatment failure should be sent to the reference laboratory for testing and typing. In Europe, resistance to vancomycin has not been reported, while phenotypic resistance to vancomycin has recently been reported in high frequency in 3 distinct geographic regions outside Europe. Fidaxomicin resistance is so far rare but has recently been reported in individual isolates. However, fidaxomicin susceptibility testing in routine microbiology is limited through the absence of commercial E-tests. Although metronidazole is not recommended for CDI treatment when one of the above treatment options is available, it is still commonly used for CDI treatment. Several mechanisms can mediate the

metronidazole resistance, but detection in regular clinical microbiology laboratories is challenging, as some of them require testing on media supplemented by hemin.

Conclusion

C. difficile infection (CDI) can affect patients in hospitals, long-term care facilities, and individuals in the community without previous contact with healthcare. CDI can also be diagnosed in children but coinfection with other gastrointestinal pathogens is common in this population. There are many potential sources of *C. difficile* spores including healthcare facilities, livestock, contaminated food and the environment. The risk factors for CDI development are those associated with disruption of gut microbiota and compromised immune system including advanced age, antibiotics, chemotherapy, PPIs, and immunosuppressants. Patients with previous episodes of CDI are at risk of recurrence of the disease. Optimally, all unformed stool samples should be tested for general enteropathogenic microorganisms and *C. difficile*. Children ≤2 years of age should be tested on a case-by-case basis after consultation with a clinical microbiologist. As *C. difficile* is a toxin-mediated disease, toxin detection by a specific immunoassay should be a part of the CDI diagnostic algorithm to distinguish between *C. difficile* colonisation and active infection. *C. difficile* isolates from patients with CDI treatment failure should be investigated in reference laboratories as antimicrobial susceptibility testing is not routinely performed in all microbiological laboratories and new emerging mechanisms of resistance and specific media requirements have recently been described in *C. difficile*.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 54

Clostridioides difficile infection. Principles of prevention and management

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Introduction

Clostridioides difficile (*C. difficile*) is a Gram-positive, anaerobic, spore-forming bacterium causing hospital-acquired diarrhea worldwide. The *C. difficile* infection (CDI) frequently occurs in patients with disrupted gut microbiota due to the administration of antibiotics. Transmission occurs via the faecal-oral route through spores, which can germinate, multiply and release toxins, leading to a range of conditions from mild colitis to death. The elderly and frail patients are most affected, with a high rate of recurrence and a mortality rate of up to 13.5%.

By 2011, *C. difficile* was the most reported hospital-acquired pathogen, responsible for 12% of healthcare-associated infections. Recent data suggest a slight reduction in healthcare-associated CDI and an increase in community-acquired CDI. A current issue is the ongoing evidence of suboptimal adherence to diagnostic testing guidelines, infection control measures and CDI treatment guidelines.

Historically, metronidazole and vancomycin constituted the main treatments for CDI. In 2013, a trial reported the efficacy of fecal microbiota transplantation (FMT) for recurrent CDI. In 2017, fidaxomicin and vancomycin were recommended as first-line therapies for initial CDI episodes.

The following section reviews the current evidence on CDI, focusing on epidemiology, pathogenesis, prevention, clinical manifestations, and treatment options.

Epidemiology

Despite the inherent challenges in comparing CDI epidemiology across countries due to varying diagnostic methods, definitions and data reporting, it is evident that the epidemiology of CDI has undergone a significant transformation. In 2004, a novel strain, NAP1/027, was identified in the United States and subsequently disseminated globally, resulting in an increase in the prevalence, recurrence, and severity of cases.

A systematic review conducted between 2009 and 2019 reported that the incidence rates of healthcare-associated CDI (HA-CDI) and community-associated CDI (CA-CDI) in the United States were 8.00 and 2.00 per 10,000 patient days, respectively.

In Canada, the HA-CDI reported incidence was 4.3 per 10,000 patient days. In Europe, HA-CDI ranged between 6.18-and 1.99 per 10,000 patient days, and CA-CDI between 1.4 and 0.56 per 10,000 patient days. In Australia, HA-CDI and CA-CDI rates were 3.19 and 1.19 per 10,000 patient days, respectively.

Between 2006 and 2017 in Japan, a HA-CDI incidence of 0.8–4.71 episodes per 10,000 patient days. Recent data show a moderate reduction in the rates of healthcare-associated CDI, likely due to reduced fluoroquinolone use and decreased NAP1/027 strain prevalence.

Concurrently, a rise in community-acquired CDI has been observed in Europe, underscoring the necessity for a comprehensive understanding of both hospital and community transmission for the development of effective interventions.

Finally, the studies that have been conducted thus far indicate that there has been no significant increase in the incidence of CDI during the COVID-19 pandemic.

Pathogenesis

C. difficile mainly spreads via the fecal-oral route, in the form of spores. The gut microbiota disruption, typically resulting from the administration of broad-spectrum antibiotics, facilitates the colonization and proliferation of vegetative *C. difficile* cells.

From a physiological standpoint, bile acid metabolism in the small intestine plays a role in host resistance against *C. difficile*. When the microbiota is disrupted, there is a reduction in the relative abundance of *Clostridioides scindens*. The imbalance between the intestinal colonization of *C. difficile* and *C. scindens* results in an increase in the ratio of primary to secondary bile acids. This, in turn, facilitates the germination and overgrowth of *C. difficile*. Despite the administration of an appropriate antibiotic regimen, recurrent cases of CDI are often observed, indicating that the remaining spores of *C. difficile* may germinate and proliferate, particularly in the presence of an increase in primary bile acids.

Vegetative *C. difficile* cells possess genes encoding up to three different toxins, which are responsible for the onset of clinical symptoms. Toxin A and toxin B are glucosyltransferases that bind to host cell receptors and upon endocytosis inactivate the Rho family GTPases. This inactivation results in the destruction of the host cytoskeleton and the breakdown of epithelial barrier function. A third toxin, called binary toxin, catalyzes the depolymerization of actin upon endocytosis. Collectively, the *C. difficile* toxins disrupt the colonic epithelium, causing fluid secretion, inflammation, and tissue damage.

Prevention and infection control

CDI is closely associated with the disruption of the microbiota resulting from the administration of broad-spectrum antibiotics. A meta-analysis conducted in 2014 reported that restrictive antibiotic stewardship programmes were associated with a significant reduction in the incidence of CDI, with a risk reduction of up to 52%. The surveillance of CDI, giving timely feedback on infection rates, is a recommended strategy for incidence reduction. It is crucial to implement rigorous hand hygiene policies in order to prevent cross-infections in clinical settings. Mechanical washing with soap and water is recommended over alcohol-based hand rubs, as the *C. difficile* spores are highly resistant to alcohol.

Patients may contract CDI through direct contact with infected individuals or contaminated environments. The environmental persistence of the spores contributes to the challenge of CDI control policies. Hospitals should implement isolation measures for patients with suspected or confirmed CDI, enforce rigorous hand hygiene protocols, and maintain contact precautions to prevent the spread of infection. These measures should be maintained for at least 48 hours after the resolution of diarrhoea in CDI patients. However, compliance among healthcare workers varies widely, and low compliance with infection control measures for suspected CDI continued to be reported.

Clinical manifestation, diagnosis and treatment - adult & pediatric

Clinical manifestation

CDI present distinct clinical manifestations in both adult and paediatric populations, reflecting variations in host immune response, gut microbiota composition, and underlying health conditions.

In adults, beyond the cases of asymptomatic carriage, CDI typically manifests as a spectrum of gastrointestinal symptoms ranging from mild diarrhoea to severe or even fulminant colitis. Mild cases often present with watery diarrhoea, abdominal cramping, and low-grade fever. Patients may show more intense symptoms such as profuse diarrhoea (10-15 times per day) and intense abdominal pain. Although the definition of severe disease varies, the combination of the following findings is usually accepted to identify of severe case: leucocytosis (over 15,000 cells/mL), rise in serum creatinine levels (at least 1.5 mg/dL or at least 1.5 times higher than premorbid values), fever (>38.3°C), hypoalbuminemia (<2.5 mg/dl). Pseudomembranous colitis, characterized by the presence of yellowish plaques on the colon mucosa, is another hallmark of severe CDI and can be detected through colonoscopy. Complications of severe CDI include toxic megacolon, bowel perforation, septic shock, and multi-organ failure, which necessitate urgent medical intervention. Recurrent infections are also common, posing significant treatment challenges and increasing morbidity.

In paediatric patients, CDI manifestations can differ similarly. Asymptomatic carriage is very frequent in the early age of life, whereas symptomatic cases may experience from mild malaise up to potentially fatal colitis. When symptomatic, paediatric patients may experience similar gastrointestinal symptoms to adults, including diarrhoea, abdominal pain, and fever, though the severity and frequency may vary. The disease in children is often cecocolonic or colonic. Severe manifestations such as pseudomembranous colitis and related complications (toxic megacolon, pneumatosis intestinalis, perforation, peritonitis, and shock with multisystem failure) are less common but can occur, particularly in children with underlying health issues or prolonged antibiotic exposure.

Diagnosis

The diagnosis of CID involves primarily a combination of clinical evaluation and laboratory testing. Sometimes endoscopy to visualize pseudomembranous colitis and colonic histopathology (even post-mortem) can have a role. The main difficulty lies in avoiding overdiagnosis, which in turn leads to overtreatment, by correctly identifying episodes of active infection and discarding cases of mere colonization.

An episode of CDI is defined by combining consistent clinical and microbiological findings. Among the former, not otherwise explained diarrhoea stands out, characterized by at least 3 unformed bowel movements, corresponding to Bristol stool scale 6-7. Among the latter, the gold standard is represented by the detection of free toxins by *C. difficile* in the stools, but other tools can be used as explained below.

Clinical examination is key, but no pathognomonic signs or symptoms can be identified, therefore it is crucial to rule out other causes of diarrhoea (laxatives, chemotherapy) before screening for CDI.

Only a high index of suspicion should prompt physicians to resort to one (or more) of the available tests. They can be classified into three categories according to the target: in **Table 1** the pros and cons of each test are described. In **Figure 1** some of the potential algorithms combining the available tests described are depicted.

Table 1. An overview of the main available test to diagnose *Clostridioides difficile* infection.

Target	Interpretation	Type of test	Strengths	Limitations
Free toxins in stool	Infection by CDI	EIA for toxins A and B	• High specificity • Quite inexpensive • Rapid	• Low sensitivity (50-80%)
		CCNA	• High sensitivity • High specificity	• Long turnaround time • Lack of standardization • Technically complex to perform • Used mostly as a reference for validation or in research settings
Presence of *C. difficile* in stools	Toxigenic strain or not?	EIA for GDH	• High NPV • Quite inexpensive • Rapid	• Low specificity
		Culture	• High sensitivity • It allows antimicrobial susceptibility testing	• Low specificity • Used mostly in reference laboratories or in research settings
Presence of a toxigenic *C. difficile* in stools	True infection or simple carriage of a toxigenic strain?	NAAT	• High sensitivity • Rapid	• Low PPV • Suboptimal specificity • Cost
		Toxigenic culture	• High sensitivity • It allows antimicrobial susceptibility testing	• Low specificity • Used mostly as a reference for validation or in research settings • Long turnaround time • Technically complex to perform

Abbreviations. CCNA: cell culture cytotoxicity neutralization assay; CDI: *Clostridioides difficile* infection; EIA: enzyme immunoassay; GDH: glutamate dehydrogenase; NAAT: nucleic acid amplification test; NPV: negative predictive value; PPV: positive predictive value.

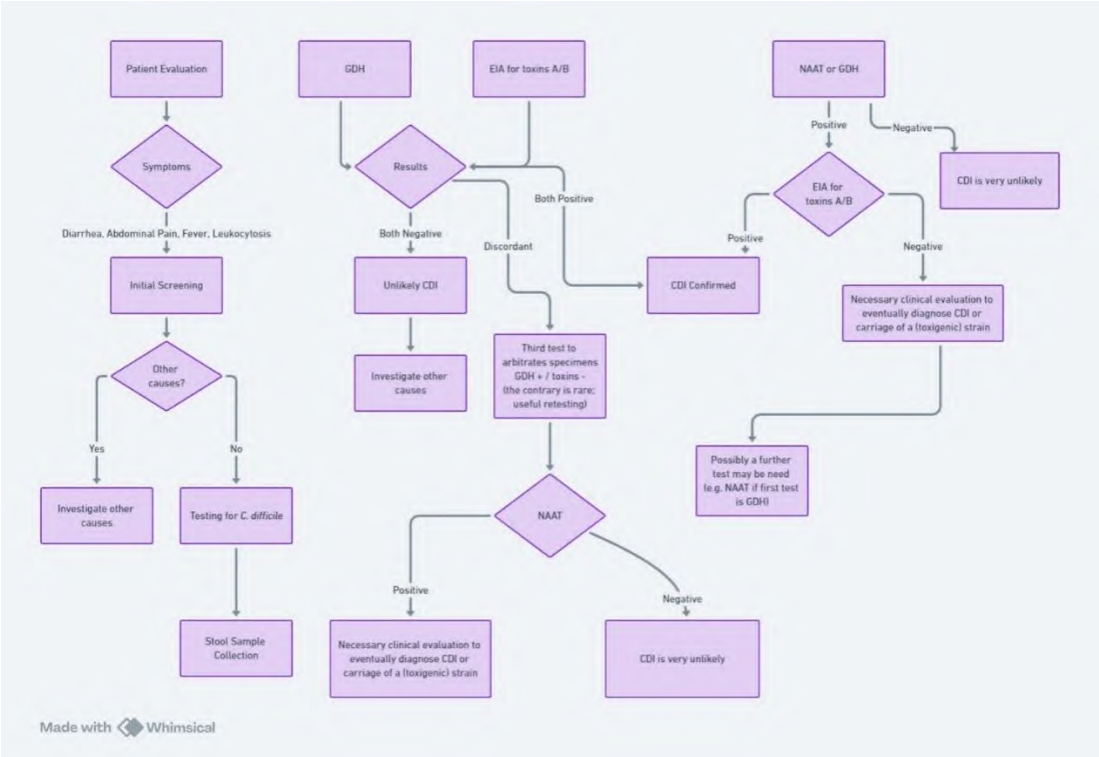

Figure 1. Suggested algorithm for the diagnosis of *Clostridioides difficile* infection. *Abbreviations*. CCNA: cell culture cytotoxicity neutralization assay; CDI: *Clostridioides difficile* infection; EIA: enzyme immunoassay; GDH: glutamate dehydrogenase; NAAT: nucleic acid amplification test; NPV: negative predictive value; PPV: positive predictive value.

In paediatric patients, the diagnostic process is the same as in adults. Nevertheless, diagnosis of CDI is even more challenging due to the high likelihood of *C. difficile* colonisation and coinfection with other intestinal pathogens. The frequency of asymptomatic carriage decreases with age, being at its peak within the first year: in this timeframe, testing is warranted just in specific instances: Hirschsprung disease or other severe motility disorders; pseudomembranous colitis; toxic megacolon or clinically significant diarrhoea without any alternative plausible cause. Anyway, also in subjects under 2 years old, CDI testing should be performed only on a case-by-case basis after consultation with a paediatrician and clinical.

In summary, accurate diagnosis of CDI requires a combination of clinical judgment, against the backdrop of an astute clinical global impression, and appropriate laboratory testing with careful interpretation of the ensuing results.

Treatment of non-severe infection (primary episode)

The goal of the anti-CDI treatment is two-fold: the clinical resolution of the ongoing episode, usually represented by a return to normal stool, and the prevention of recurrence, which is very frequent. Meeting these two criteria is defined as a sustained clinical response. Unfortunately, very few therapeutic agents are available for CDI treatment. Over the last decades, only three oral options have been approved: metronidazole, vancomycin and fidaxomicin.

Each of them has distinct targets (DNA synthesis, peptidoglycan biosynthesis, RNA polymerase, respectively) and presents with peculiar pharmacological features when it comes to systemic absorption, stool concentration, effect on the diversity of microbiota, potential activity against spores and sporulation. In brief, metronidazole shows the worst and fidaxomicin the best profile regarding the above-mentioned aspects: as a

matter of fact, fidaxomicin has the narrowest spectrum of antimicrobial activity and can inhibit sporulation and be still active on spores *in vitro*.
The main drivers of unsuccessful treatment in CDI are the inability to mount a valid immune response, explaining the vulnerability of immunosuppressed people, and the failure to restore a healthy microbiota combined with bacterial spores' persistence. In this respect, based on its features fidaxomicin has emerged as the best option to curb recurrence rates as confirmed by clinical trials informing the most recent guidelines for adult patients that highlight the preference of fidaxomicin over vancomycin due to better sustained clinical cure in the light of fewer recurrences. Similar evidence has been mounting also in younger subjects.
In **Table 2** the current therapeutic protocols for the treatment of the first (non-severe) CDI episode in adult and paediatric patients are reported. It is not recommended the so-called "test of cure" since toxins and/or spores can persist for several weeks despite symptoms' resolution.
In conclusion, effective CDI management requires a comprehensive approach, including appropriate therapeutic choice inspired by the principle of "treatment as prevention" (therefore preferring regimens linked with fewer recurrences), discontinuation of potential inciting factors (such as systemic antibiotics, if feasible, and proton pump inhibitors, allowing normal gut flora to recover), adoption of infection control measures to prevent the spread of infections in healthcare settings.

Treatment of recurrence

Treating recurrent CDI presents significant challenges, requiring a nuanced approach that combines antibiotic therapy with innovative treatments such as the monoclonal antibody bezlotoxumab, faecal microbiota transplantation (FMT) or its derivatives, namely the live biotherapeutic products (LBPs). Of note, among the newer options, only FMT has been assessed in children.
Bezlotoxumab is a monoclonal antibody against the *C. difficile* toxin B administered intravenously as a single shot: it has not a curative function, but as adjunctive therapy to the standard of care reduces the risk of recurrence. From clinical trials, patients with risk factors such as age older than 65 years, previous CDI in the last 6 months, immunocompromised status, or severe CDI showed the highest benefit in terms of recurrence reduction. Therefore, the drug should not be used when none of these risk factors is present and caution is needed in those who have already experienced congestive heart failure due to an increased risk of heart failure aggravation. Of note, bezlotoxumab can be considered a preventative drug also in the case of the first CDI episode, as long as some risk factors for recurrence are present.
The best antimicrobial backbone to which bezlotoxumab can be added in the event of a first CDI recurrence remains an unresolved matter. Current evidence seems to suggest that fidaxomicin might be preferable to vancomycin also in this scenario. The implementation of FMT, which is still a non-standardized practice, presents numerous logistical difficulties, including donor screening, stool processing, administration, and monitoring for unfavourable occurrences for the recipients. Nevertheless, it is considered standard of care for patients experiencing at least their third episode of CDI.

Table 2. Therapeutic choices for primary and recurrent non-severe *Clostridiodes difficile* infection in both adult and paediatric subjects.

	First episode	Second episode (first recurrence)	Third episode (second recurrence)	Notes
Subjects aged 18 years and older	*Preferred choice*: Fidaxomicin 200 bid for 10 days or in extended-pulsed fashion. *Alternative choice*: Vancomycin 125 qid for 10 days Bezlotoxumab may be added if risk factors for recurrence are present.	*Preferred choice*: Fidaxomicin 200 bid for 10 days or in extended-pulsed fashion plus bezlotoxumab. *Alternative choice*: Vancomycin 125 qid for 10 days plus bezlotoxumab or fidaxomicin alone 200 bid for 10 days or in extended-pulsed fashion.	*Preferred choice*: FMT or LBP. *Alternative choice*: Fidaxomicin 200 bid for 10 days or in extended-pulsed fashion plus bezlotoxumab.	Metronidazole (500 mg tid for 10 days) for the first episode should be reserved in cases of unavailability of fidaxomicin or vancomycin. The extended-pulsed regimen of fidaxomicin consists in its prolonged administration (allowing persistence of the drug at above inhibitory concentrations, thus prolonging suppression of *C. difficile*, and concurrently facilitating microbiota restoration): 200 mg bid on days 1-5, and 200 mg once daily on alternate days on days 7-25. When preferred/alternative regimens for recurrent episodes are not available, a vancomycin tapering and pulse scheme can be used (e.g., 2 weeks at 125 mg qid, followed by 1 week 125 mg bid, then 1 week 125 mg daily, then 1 week 125 mg every second day, and finally 125 mg orally every third day for 1 week). There are two LBPs approved in the United States but none has been approved.
Subjects aged under 18 years	*Preferred choice*: Fidaxomicin for 10 days according to body weight. *Alternative choice*: Vancomycin 10 mg/kg per dose (max 125 mg) qid or metronidazole 7.5 mg/kg per dose tid (max 500 mg) for 10 days.	*Preferred choice*: Fidaxomicin 200 bid for 10 days (or in extended-pulsed mode) according to body weight. *Alternative choice*: Vancomycin prolonged tapered and pulsed or vancomycin followed by a rifaximin chaser.	*Preferred choice*: FMT. *Alternative choice*: Fidaxomicin 200 bid for 10 days (or in extended-pulsed mode) according to body weight or vancomycin prolonged tapered and pulsed or vancomycin followed by a rifaximin chaser.	The dose of fidaxomicin increases with body weight: 40 mg bid < 4 kg, 80 mg bid 4-6.9 Kg, 120 mg bid 7-8.9 Kg, 160 mg bid 9-12.4 Kg, 200 mg bid ≥ 12.5 Kg. Extended-pulsed fidaxomicin has not been studied in subjects younger than 18 years old. Rifaximin is not approved for use under 12 years of age (suggested dosage 200 mg bid).

Abbreviations. BID: bis in die. LBP: live biotherapeutic product. FMT: fecal microbiota transplantation. QID: quarter in die. TID: ter in die.

The problem is that FMT stool preparations are not completely characterized.
More than 50% of the genes found in faeces and more than 80% of faecal metabolites have unknown functions, even using the most advanced multi-omics technology. Recently, two LBPs, both stool-derived preparations, have been developed and approved in the United States: RBX2660 and SER-109. Further, microbiota-based therapies are under development or evaluation to fulfil the unmet need to deliver a standardized microbiota-based therapy. Notably, FMT and LPBs can be administered orally or via enema.
In **Table 2** the current therapeutic protocols for recurrent CDI infections in adult and paediatric patients are described.

Fulminant or severe-complicated forms

Diagnosis

Fulminant forms represent the most severe forms of CDI, accounting for 3-8% of all CDI, with a high mortality rate, ranging between 15% to 80% according to literature data. In recent years, most of the international society updated their diagnostic and therapeutic recommendations on CDI; they used different definitions for severe-complicated (or fulminant) forms. Both guidelines defined a fulminant form a patient with CDI and megacolon, ileus or shock, but ESCMID guidelines extended the definition also in case of a rapid clinical deterioration or bowel perforation or increased serum lactate. In a recent study by Perry DA *et al.,* authors sought to compare the most used scores in literature, using a composite outcome of ICU admission, colectomy, or death. Sensitivity and specificity weren't so high, ranging between 40% to 62% for sensitivity and between 64% to 99% for specificity.
Sadly, they didn't use the last ESCMID fulminant criteria because the observation period was between 2010 and 2016 (before the 2021 guidelines update). The authors concluded that none of the used risk scores had good predictive ability for adverse outcomes. The lower sensitivity of all the risk scores, and consequently the higher number of false negatives, it's the main problem in diagnosis and it could increase mortality. So, we could speculate that ESCMID criteria for fulminant CDI in the last guidelines update, by extending the criteria to other variables, could reduce the number of false negatives and thus increase sensitivity. On the other hand, these differences in diagnostic criteria among all the main international CDI guidelines pose a first issue for inclusion criteria in a possible randomized clinical trial on fulminant forms.

Radiological features

Fulminant forms are often associated with "toxic megacolon", an acute complication observed in inflammatory bowel diseases (ulcerative colitis, Crohn's disease) and, less commonly, in infectious colitis (particularly from *C. difficile*) or other causes. In fulminant forms of CDI, there can be a loss of neurogenic tone of the colon, resulting in severe dilation (megacolon) and an increased risk of perforation. Recognising a megacolon early allows physicians to pose an early diagnosis of fulminant forms, and consequently a rapid management. Abdominal X-ray, computed tomography and ultrasound have pros and cons.

Abdominal x-ray

Conventional radiography is usually diagnostic, although Computed Tomography (CT) scans are often obtained to exclude acute complications such as perforation. The transverse colon is typically dilated to at least 6 cm, in case of toxic megacolon. The "3-6-9 rule" can be referred to as a simple reminder that describes normal bowel thickness: small intestine < 3 cm, large intestine < 6 cm, appendix < 6 mm, cecum < 9 cm. Above these dimensions, the bowel is generally considered dilated and obstruction or adynamic/paralytic ileus may

be suspected. Radiography can be useful in monitoring the progression of toxic megacolon, even with bi-daily examinations. In the supine position, the transverse colon is normally the most anterior loop and therefore appears more evidently dilated. On the radiograph, thickened and irregular contours due to submucosal infiltration can sometimes be appreciated. Signs of pneumoperitoneum may be present if the dilation has progressed to perforation. In this case, it is necessary to perform the radiographic exam in an upright projection, or if clinically impossible, to perform a cross-table lateral or lateral decubitus view. A barium enema and colonoscopy should not be performed due to the high risk of perforation.

Computed tomography of the abdomen

During toxic megacolon, the CT scan will show dilation of the affected segment with a thin intestinal wall and loss of haustral markings. Other signs may include pericolic fat infiltration and venous occlusions. The accordion sign may indicate the presence of CDI colitis/pseudomembranous colitis, not necessarily toxic megacolon. CT plays a crucial role in more accurately detecting colon dilation, wall thickness, any effusion, and complications such as colonic wall perforations and septic thromboses of the portal system.

Abdominal ultrasound

This method is less accurate in the diagnosis of megacolon, compared to CT or Magnetic resonance imaging. However, due to its practicality. Furthermore, it can be useful as a non-invasive, easy and rapid bedside patient monitoring to detect bowel structural alterations. In literature, some authors describe typical findings that may be observed in case of toxic megacolon such as marked distension (noticed as a loss of haustrations for >5 cm) and a thin wall (< 2mm) in the transverse colon and an increase in wall thickness (>7 mm) in the descending colon, fluid between loops, and signs of pneumoperitoneum. It could therefore help clinicians in daily and bedside monitoring of the patient, but it may require a bit of the physician's expertise in bowel ultrasound.

Medical treatment

Medical treatment varies between international guidelines. Until 2020, the recommended treatment was oral vancomycin (high dose) 500 mg q6h with the addiction of intravenous metronidazole 500 mg q8h for 10 days. In 2021 ESCMID panelists in their CDI guidelines update discourage the routinary use of i.v. metronidazole and they suggest as best available therapy oral vancomycin 125 mg q6h or fidaxomicin 200 mg q12h for 10 days. Based on 3 retrospective studies, not all the scientists agreed with this choice as discussed recently and confirmed by the same author's metanalysis. Randomized clinical trials are needed, but meanwhile, we should be careful approaching a patient with fulminant CDI due to the high mortality rate and the very low quality of evidence; secondly, in fulminant CDI patient has reduced intestinal movement, and an oral drug may not reach therapeutic levels in the bowel. So, intravenous drugs may be added to the oral ones. Finally, some authors established the efficacy of FMT also in the case of fulminant CDI: a less invasive procedure than surgical procedures, with fewer complications, a higher success rate (88%) and lower mortality (7% *vs.* 30%).

Surgical treatment

Surgical management is considered a cornerstone treatment for the fulminant CDI. A meta-analysis showed not only that a surgery approach may reduce mortality but also that an early surgery may reduce mortality compared to a late surgery. Historically, two are considered the main kind of surgical intervention: firstly, diverting loop ileostomy (DLI) in which the surgeon creates a diverting loop ileostomy, then performs a colonic lavage with 8 liters of polyethylene glycol 3350 or balanced electrolyte solution, and finally performs

enemas with vancomycin 500 mg q6h for 10 days through the ileostomy; secondly, colectomy, divided in (TAC) total abdominal colectomy (if the entire colon is resected, except for the rectum) and subtotal colectomy (if the entire colon is resected, except for the rectum and sigmoid colon) or partial colectomy (if only a part of the colon is resected). A meta-analysis by Ferrada and colleagues showed a similar morality rate among total or partial colectomy. Recent literature data in 2020 showed a lower mortality rate among patients undergoing DLI was lower compared to TAC with an OR of 0.73 in favor of DLI. The authors analyzed 5 retrospective observational studies published until 2020, the metanalysis didn't reach statistical significance but showed a mild reduction in mortality among patients undergoing DLI. However, given the high mortality rate of the surgical approach on one hand and, on the other hand, given the promising results (with lower mortality) of FMT in patients with fulminant CDI, maybe FMT should be considered as the future treatment of fulminant CDI forms.

Conclusion

The prevalence of *C. difficile* infection will be higher in the future. The worldwide aging, the increasing rate of multidrug-resistant microorganisms and the consequently increase in the use of antibiotics, could increase the rate of CDI. The higher rate of CDI will increase the rate of fulminant forms and the mortality too. So, a prompt diagnosis and adequate therapy will help clinicians to reduce mortality.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 55

Hospital-acquired and ventilator-associated pneumonia. Principles of prevention and management

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Introduction

Hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) continue to be associated with significant patient morbidity, mortality, prolonged length of hospital stay and increased healthcare costs. are important causes of morbidity and mortality in hospitalised patients. This treatment challenge persists despite significant research on diagnosis, supportive and preventative care and antimicrobial therapies. HAP is defined as an infection of the pulmonary parenchyma that develops 48 hours or more after hospital admission which is thought not to have been incubating at the time of hospital admission. It is the second most common nosocomial infection and the leading cause of death from nosocomial infections in critically ill patients. VAP is a subset of HAP that occurs in patients who are more than 48-72 hours after endotracheal intubation. It is estimated that approximately 10% of patients on invasive mechanical ventilation will develop VAP, with an estimated mortality rate of 13% in this group.

The pathogenesis of HAP and VAP involves the complex interplay between patient factors, namely underlying patient conditions, the healthcare environment itself, and microbial factors. Within the critically ill population, there is increased complexity due to impaired host defences, exposure to invasive procedures and an increased prevalence of multidrug-resistant organisms within this population.

Efficacious prevention and management of HAP and VAP require a multifaceted and multidisciplinary approach including prompt recognition, infection prevention and control measures and evidence-based therapy and clinical practice. Understanding and applying these measures are imperative for improving patient outcomes and reducing the burden of these infections in the healthcare setting.

Within this chapter, we describe the diagnosis, management, and prevention of these diseases based on current guidelines and evidence.

Diagnosis of HAP and VAP

Clinical criteria and scoring systems

HAP and VAP can be challenging to diagnose promptly, given the broad differential diagnosis for respiratory deterioration in patients in the critical care setting and the variability of definitions within clinical practice guidelines, particularly between European and US guidelines. The IDSA/ATS guidelines propose that diagnosis of HAP and VAP require all of the following:

- New infiltrates on chest imaging: chest X-ray or CT.
- Respiratory deterioration: Hypoxaemia, increased ventilatory support.
- Fever or hypothermia.
- Productive cough/increased respiratory secretions.

In particular, the absence of a new infiltrate on imaging significantly lowers the probability of HAP/VAP and should prompt a further diagnostic workup for alternative causes of respiratory deterioration.

Clinical scoring systems incorporating the above diagnostic criteria have been proposed to support the diagnosis of VAP, most notably the Clinical Pulmonary Infection Score (CPIS), first proposed by Pugin *et al.* in 1991. A score of greater than 6 was associated with a sensitivity of 93% and a specificity of 100% for VAP in the initial study. The most notable limitation is that this scoring system is dependent on the results of tracheal aspirate culture, thus delaying utility and therefore management by up to 48 hours.

Respiratory sampling

Respiratory culture is imperative in the diagnosis and therefore targeted antimicrobial treatment of patients with HAP and VAP. In those patients who are not intubated, it should be possible to obtain a sputum sample of adequate quality through expectoration or assisted expectoration.

In patients who are not capable of expectorating sputum, diagnostic options include semiquantitative sputum samples (non-invasive e.g. endotracheal aspiration), quantitative samples (non-invasive or invasive methods such as bronchoscopy or mini-bronchoalveolar lavage).

The International ERS/ESICM/ESCMID/ALAT guidelines explored these diagnostic modalities in their evidence-based guidelines for the management of HAP and VAP: Literature review demonstrated that non-invasive diagnostic methods were more likely to over-identify bacteria, with important implications for antibiotic-free days and overall antibiotic exposure.

Serum laboratory testing

Blood cultures are recommended for all patients with HAP or VAP: 15% of patients with VAP are bacteraemic, and up to 25% of blood cultures from patients with VAP may demonstrate a secondary non-pulmonary source of infection.

Procalcitonin levels are not without their limitations, however, they may provide a useful adjunct to clinical assessment in the diagnosis of HAP or VAP. Cytokines, associated with bacterial infections, enhance procalcitonin release, however, procalcitonin levels are not elevated in up to 20% of typical bacterial infections. Furthermore, the utility of PCT is particularly questionable in cases of renal impairment, haemodialysis or haemofiltration or after resuscitated cardiac arrest. DSA/ATS guidelines state that procalcitonin should not replace clinical judgment in deciding on antibiotic initiation for patients with a diagnosis of HAP or VAP. The International ERS/ESICM/ESCMID/ALAT guidelines do not support the use of routine measurement of serial serum PCT levels to reduce the duration of the antibiotic course in patients with HAP or VAP when the

anticipated duration is 7–8 days, however, it may be useful in conjunction with clinical examination to aim to reduce the duration of antimicrobial treatment.
CRP is more prone to persistent elevation because of non-infectious inflammatory disorders, which are prevalent in the critically ill population.

Molecular diagnostics

Molecular testing such as polymerase chain reaction (PCR) panels and next-generation sequencing (NGS) are being increasingly utilised in the diagnostic armamentarium of HAP and VAP. Precise pathogen identification through these techniques, and therefore targeted treatment in HAP/VAP are increasingly important given ongoing concerns regarding MDR organisms (**Figure 1a** and **Figure 1b**).
Polymerase chain reaction (PCR) techniques allow rapid detection of bacterial DNA directly from respiratory samples, including BAL samples and endotracheal aspirates. There are a variety of potential techniques. Real-time PCR can target specific genes of common respiratory pathogens, multiplex PCR can allow simultaneous identification of multiple respiratory pathogens; commercially available examples include BioFire Film Array. Multicentre studies have shown excellent correlation when compared with conventional culture methods. Utilising these techniques has also shown the importance of consideration of viral co-infection: One study showed that viral infection and/or co-infection contributes to up to 20% of cases of VAP and HAP
Next-generation sequencing techniques have also been increasingly utilised in the diagnosis of HAP and VAP. 16S rRNA gene sequencing targets the bacterial 16S ribosomal RNA, which is highly conserved across bacterial species. This method can identify multiple bacteria in a single sample. 16S rRNA gene sequencing targets the 16S ribosomal RNA gene, which is highly conserved across bacterial species. This method can identify a broad range of bacteria in a sample, including rare and difficult-to-culture organisms. It is particularly useful in polymicrobial infections. Metagenomic and transcriptomic techniques allow simultaneous testing of large numbers of specific pathogen and resistance genes in clinical samples. These techniques have also been utilised in the research setting to evaluate the alterations in immune response in critically ill patients with VAP, showing depressed expression of culprit genes involved in the cellular immune response including interaction between antigen-presenting cells and lymphocytes.

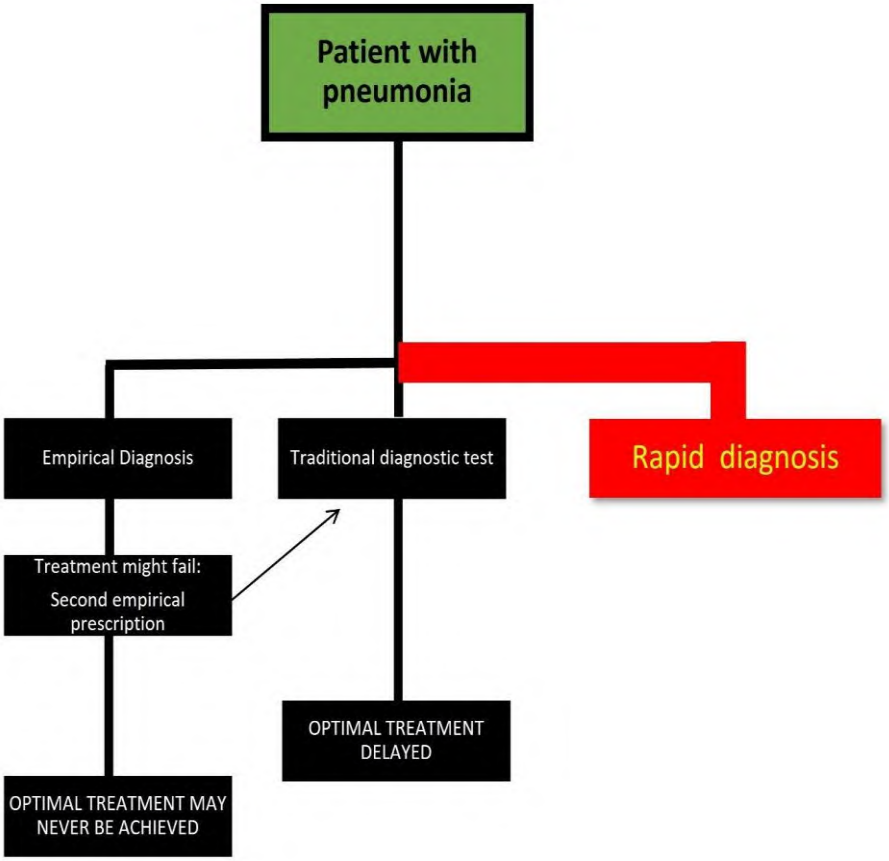

Figure 1a. Diagnostic approach.

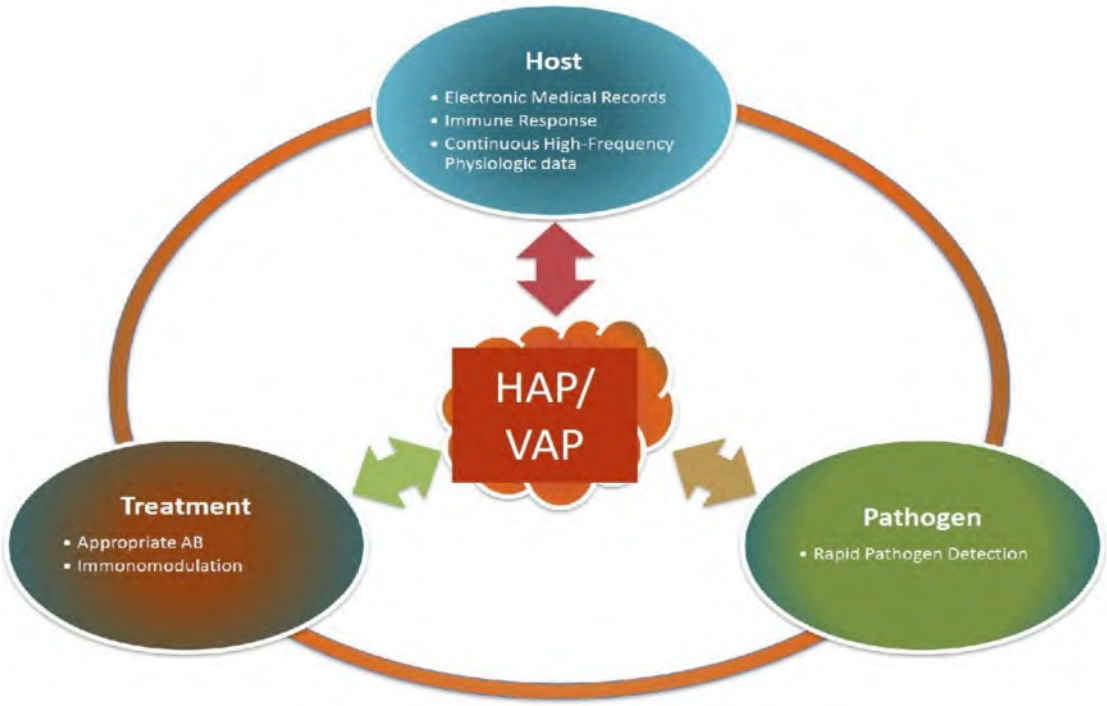

Figure 1b. Diagnostic approach.

Management

The management of HAP and VAP requires a comprehensive and multimodal approach, including appropriate antimicrobial therapy, supportive care and prevention and prompt recognition of complications. The goals of instituting a comprehensive approach are to reduce morbidity and mortality, minimise the duration of mechanical ventilation and prevent the emergence of multidrug-resistant organisms.

Antimicrobial treatment

Initial treatment strategies and evidence-based guidelines for HAP and VAP emphasise the importance of prompt and appropriate antimicrobial therapy. There is an implicit risk within this strategy however: prompt initiation without follow-up rationalisation of antimicrobials may result in inappropriate use of broad-spectrum antimicrobials which then propagates the emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant bacteria (PDR).

A more nuanced approach is therefore required. It is imperative that an institution-specific and therefore region-specific antibiogram should guide the selection of an appropriate empiric antimicrobial regimen. Additional key considerations are patient-specific specific risk-factors such as immunosuppression and severity of illness. In the absence of a hospital-specific antibiogram, empiric coverage of methicillin-susceptible *Staphylococcus aureus* and Gram-negative bacilli such as *Pseudomonas aeruginosa* should be selected. In the absence of septic shock, risk factors for MDR pathogens or high background rate or resistant pathogens within the specific hospital environment, it may be appropriate to utilise narrow-spectrum antibiotics (ertapenem, ceftriaxone, cefotaxime, moxifloxacin or levofloxacin).

Risk factors for multidrug-resistant organisms include hospital settings with high rates of MDR pathogens, recent antibiotic use, hospitalisation of > 5 days duration, presence of septic shock and/or acute respiratory distress syndrome, underlying cystic fibrosis or bronchiectasis and previous colonisation with MDR pathogens. The use of antimicrobials within 90 days preceding new pneumonia is consistently correlated with MRSA and multidrug-resistant *P. aeruginosa* HAP and VAP.

Vancomycin or linezolid should be initiated only in those who received intravenous antibiotics in the last 90 days, are hospitalized in a unit where at least 20% of *S. aureus* isolates are methicillin-resistant or where the prevalence of MRSA is unknown, or are at high mortality risk.

Initial empiric therapy for the high-risk or septic shock patient should be with a dual-pseudomonal regimen plus MRSA coverage (if the ICU in question has > 25% of respiratory *S. aureus* isolates as MRSA). Consideration in the dual-pseudomonal regimen should also be given for *Acinetobacter* spp. and ESBL-producing *Enterobacteriaceae* depending on local prevalence. The antipseudomonal β-lactams include imipenem, meropenem, cefepime, piperacillin/tazobactam, ceftazidime and aztreonam.

Appropriate targeted therapy should be instituted following the availability and sensitivities of culture results to target the specific pathogens identified, reducing the risk of antibiotic resistance and toxicity.

The duration of antimicrobial treatment for uncomplicated HAP and VAP is 7 days of therapy

Longer courses have not been demonstrated to reduce the risk of recurrent infection, treatment failure, duration of mechanical ventilation, mortality or hospital length of stay. Patients with pulmonary or extrapulmonary complications including empyema, bloodstream infection, abscess or septic emboli may warrant a more protracted treatment course. Patients with underlying lung disease or immunocompromise may also require a longer treatment duration. Treatment should be individualised to clinical response, specific microbiological cultures and monitoring of biomarkers.

Clinical evaluation

Clinical evaluation is imperative in the appropriate management of patients with HAP or VAP. This involves frequent assessment of temperature, tracheobronchial secretion volume, culture and purulence assessment of tracheobronchial secretions, interval chest radiograph resolution, white blood cell count, PaO_2 /FIO_2, and calculation of clinical scores where appropriate e.g. SOFA (Sequential Organ Failure Assessment).

Adjunctive treatment considerations

In addition to the aforementioned, it is important to recognise the importance of optimisation of patient factors within the critical care setting, including pursuing lung protective ventilation strategies, monitoring and optimisation of fluid balance, appropriate attention to sedation and analgesia with a view to minimising duration of mechanical ventilation and expediting extubation where appropriate.

Prevention of HAP and VAP

Preventative strategies for HAP and VAP are of paramount importance in mitigating adverse patient outcomes and involve a multi-modal proactive approach.

Reducing aspiration risk

Oral care aims to reduce microbial burden in the oropharynx, reduce the risk of aspiration and the risk of HAP and VAP. A systematic review and meta-analysis including 2 studies of critically ill, non-ventilated patients reported a significant reduction in the risk of HAP through the use of chlorhexidine oral cleansing and oral hygiene instruction. There have been several recent systematic reviews and meta-analyses that compared the use of oral chlorhexidine with usual care, however, the ERS/ESICM/ESCMID/ALAT guidelines did not make a recommendation on the use of chlorhexidine to perform selective oral decontamination (SOD) in patients requiring mechanical ventilation due to incomplete and conflicting data.

Patient position is an important intervention in the reduction of the rates of HAP and VAP. The recommendation is a semi-recumbent position with elevation of the head of the bed to 30 or 45° with a view to improving ventilation and perfusion and enhanced clearance of secretions with the aid of gravity.

Other strategies to reduce aspiration risk include monitoring and maintenance of adequate cuff pressure, avoidance of nonessential tracheal suctioning, appropriate use of stress ulcer prophylaxis and avoidance of gastric overdistension.

Nursing care bundles encompassing many of the above recommendations have been instituted globally with a view to addressing the persistently high incidence of HAP and VAP. There have been some successful studies regarding the institution of these bundles, including the Zero-VAP project in Spain. The results overall however have been heterogeneous: in part, this may be attributable to varying components of these bundles and varying definitions of HAP and VAP within these study populations.

Early extubation

The presence of an endotracheal tube is the major risk factor for HAP in the critically ill and for VAP. This is due to interference with the physiologic protective upper airway secretions, increased mucus generation, irritation of the respiratory mucosa and the risk of microaspiration of contaminated oropharyngeal secretions. Frequent assessments for readiness for extubation are therefore a key preventative strategy for reducing VAP.

Refined antimicrobial use

Refined antimicrobial use through antimicrobial stewardship is a key component in the prevention of HAP and VAP. Ensuring the judicious use of antibiotics can reduce the incidence of these infections, prevent the emergence of resistant organisms, and improve patient outcomes.

General prevention strategies

General prevention strategies for HAP and VAP in the critical care setting include adherence to infection control precautions, optimal nutritional support, early mobilisation and physical therapy. From an infection control perspective, single-patient stethoscopes and universal glove-gown contact precautions, although near ubiquitous, are not supported by a firm evidence base. Daily review and minimisation of invasive devices such be instituted as standard. as central lines and urinary catheters. Early diagnosis and treatment of dysphagia, particularly in the elderly population, is advised to reduce the incidence of aspiration events. On a population health level, the importance of appropriate vaccination should be emphasised to patients to reduce transmission of influenza, *Haemophilus influenzae*, and *Streptococcus pneumoniae*

Conclusion

As HAP and VAP continue to be a challenge within our hospital settings, particularly within the critically ill population, ongoing efforts will be required to improve diagnosis, management and prevention. These strategies remain open to ongoing research and clinical refinement. The effective management of HAP and VAP requires timely initiation of appropriate empiric antibiotics, tailored therapy based on culture results, and a focus on prevention and supportive care. The use of standardised care bundles, coupled with vigilant monitoring, can significantly improve outcomes for patients affected by these serious infections.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 56

Catheter-associated bloodstream infections. Principles of prevention and management

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Introduction

Vascular access devices are crucial in the management of many medical conditions for both hospitalized and home-based patients. These devices facilitate the safe intravenous administration of medications, enable the monitoring of hemodynamic parameters, provide parenteral nutrition, support hemodialysis, and assist in fluid resuscitation. Despite their vital role in patient care, these devices are associated with a risk of infection, which can be minimized through proper prevention strategies. The risk factors are often related to the device itself but can be effectively mitigated. Thus, education and training of healthcare workers, along with continuous unit-based improvement programs, are essential. Such adverse events contribute significantly to morbidity and mortality, resulting in prolonged hospital stays and increased healthcare costs.

Infectious complications can be classified as either local or systemic. Local infections include those at the exit site of non-implantable catheters, pocket infections for totally implantable devices like ports, tunnel infections, and phlebitis or thrombophlebitis for catheters inserted into superficial arm veins. These conditions can escalate to severe cellulitis and fasciitis, posing serious problems for patients.

Systemic infections include bloodstream infections, which can be further classified into catheter-related bloodstream infections (CR-BSI) and catheter-associated bloodstream infections (CA-BSI). CR-BSI occurs when the catheter is confirmed to be the direct cause of the bloodstream infection, while CA-BSI is diagnosed when the catheter is suspected as the likely source, though definitive proof is lacking. These infections can lead to severe complications, such as septic shock and endocarditis. Additionally, bloodstream infections may be associated with local infections, compounding the risks to the patient.

Epidemiology

According to recent data, the incidence of CR-BSI varies significantly, depending not only on the country but also on the specific hospitals or wards being studied. The rate can range from 0 to 30 episodes per 1,000 catheter days. The cost of a single CR-BSI episode can reach 25-30 thousand euros, and the estimated mortality rate is around 25%. In a recent European study, 42.6% of bloodstream infections were associated with the presence of a central venous catheter (CVC), with CR-BSI levels still as high as 1 to 6.2 per 1,000 catheter days.

Diagnostic method

The suspicion of catheter-related infection is initially based on clinical criteria and then is confirmed by microbiological findings.
An infection at the exit site, characterized by erythema, swelling, warmth, exudate, and tenderness to palpation, warrants a local culture. When these symptoms are particularly severe, especially if accompanied by systemic signs such as fever, leukocytosis, tachycardia, and tachypnea without other identifiable sources of infection, the suspicion of bacteremia is high, and both CVC and peripheral blood cultures are indicated.
Isolation of the same microorganism (identical species and antibiogram) from both cultures, with a differential time to positivity (DTP) of two or more hours earlier in the CVC culture, is indicative of a CR-BSI. Alternatively, CR-BSI can be diagnosed when simultaneous quantitative blood cultures show a ratio greater than 3:1 colony-forming units per milliliter (CFU/mL) in the catheter compared to peripheral blood. However, this method is rarely used. As CR-BSIs can originate from any lumen of a CVC, it is recommended to examine each CVC limb if clinically feasible. However, CR-BSIs often originate from the CVC lumen used for the administration of parenteral nutrition or blood products; this lumen should therefore be prioritised for investigation. The microbiological samples must be brought to laboratories for further processing as quickly as possible (<8 h storage time) for valid results. The collection of 3 blood culture sets (1 set consisting of 1 aerobic and 1 anaerobic blood culture bottle) with a total blood volume of 60 ml (10 ml blood per blood culture bottle) results in a higher detection rate of bacteraemia/fungaemia compared to 2 blood culture sets. It is not necessary to divide the blood culture sets into different collection times. The culture of a removed catheter without clinical suspicion of CR-BSI is not recommended.

Principles of prevention

Catheter colonization can occur through two main routes: extraluminal (from the outside) and intraluminal (from the inside). For short-term catheters, infection from the skin's surface is the primary pathway. This can occur due to healthcare workers' hands or non-sterile medical devices used during insertion, most commonly within the first 7 days after catheter placement. It is believed to occur at the time of insertion.
In contrast, intraluminal colonization, caused by a contaminated hub or the infusion of contaminated solutions, is more common in long-term catheters. Pathogens can access the catheter's intraluminal surface, where they adhere and form biofilm—a layer of microorganisms embedded in a protective matrix. This biofilm supports ongoing infection and the spread of pathogens into the bloodstream. Infection typically occurs more than 7 days after catheter insertion and is linked to how the catheter is cared for and maintained, and the frequency of its use or handling. Contaminated infusate, which can taint the catheter, is a rare event but

can occur during its preparation or administration. Less commonly, catheters become contaminated from a secondary bloodstream infection originating from another focus of infection.
The occurrence of bacteremia caused by common skin organisms (e.g., coagulase-negative staphylococci [CoNS] or *Staphylococcus aureus*) is a major criterion for the diagnosis of CR-BSI, although Gram-negative microorganisms have been increasingly observed in recent years, particularly in cases where the femoral site is used for insertion.
Understanding the mechanisms of these infections is crucial for identifying, treating, and preventing them. Patients with weakened immune systems, such as those in intensive care units (ICUs) or hematology wards, dialysis patients, obese individuals, and especially premature infants, are at higher risk. Factors such as prolonged hospital stays, extended catheter use, multi-lumen catheters, and parenteral nutrition can all increase the risk of CR-BSI.
The use of care bundles has proven particularly effective in preventing bloodstream infections. Compliance checklists ensure that procedures are performed safely. Bundles standardize procedures for every step of vascular access management, from selecting the best vein and device to post-placement care. This includes maintaining a strict aseptic technique during the procedure and proper device management. The infection monitoring and auditing systems allow for the evaluation of implemented measures and the identification of areas for improvement. Additionally, ongoing education for healthcare professionals is essential.
The implementation of such bundles has been shown to reduce the median incidence of CR-BSI from 6.4 per 1,000 catheter days to 2.5 per 1,000 catheter days.
In the ICU, a high-risk environment, it is crucial to ensure an adequate nurse-to-patient ratio and limit the use of inadequately trained staff. Specialized vascular teams dedicated to managing these devices are key to significantly reducing infections. To optimize prevention, it is necessary to act on three levels: during the planning of catheter placement, during the insertion procedure, and the ongoing management of the devices. The best way to prevent infections is to avoid the insertion of unnecessary devices.

Before insertion

The correct choice of vascular access device (peripheral or central) is crucial for preventing CR-BSI. The decision depends on several factors: the type of therapy (its compatibility with peripheral veins), the method of administration (continuous or intermittent), and the expected duration. For short-term therapies with non-irritating medications, short peripheral cannulas may be sufficient. For longer therapies, midline or central venous catheters, depending on the type of therapy, are more suitable. Tunneled and totally implantable catheters, though effective in reducing infections, should only be used when strictly necessary, considering the costs and benefits.
Additional factors influencing device selection include the vascular pathway, patient's age, and comorbidities. Patient preference for both the exit site and the vascular device should be considered when feasible. Proper evaluation of the exit site is important: flexion sites should be avoided for peripheral catheters. For CVCs, the mid-arm, supraclavicular, and subclavian regions are preferred. Highly contaminated skin areas, such as the neck and groin, or areas near stomas, should generally be avoided except in emergencies. The use of ultrasound has enabled the puncture of the superficial femoral vein in the middle third of the thigh, away from potentially contaminated areas. Tunneling is indicated for CVCs in cases where optimizing the exit site is necessary.
Peripheral vascular devices have a lower infection risk because they inhibit bacterial attachment and biofilm formation; however, recent guidelines suggest avoiding the insertion of a peripheral catheter as a CR-BSI prevention strategy when a central catheter is indicated. Current evidence supports the use of CVCs coated with chlorhexidine/silver sulfadiazine and minocycline/rifampin in high-risk patients to prevent CR-BSI. While other antimicrobial coatings have been investigated, none have demonstrated significant clinical efficacy.

Antibiotic prophylaxis is not recommended to reduce the incidence of infections and may contribute to antimicrobial resistance.

During insertion

The risk of infection begins at the time of catheter placement. Strict adherence to aseptic techniques is essential. Hand hygiene, performed using an alcohol-based hand rub or antiseptic solution, is of primary importance and should be carried out as thoroughly as before a surgical intervention. The use of maximal sterile barrier precautions—including sterile gloves, a long-sleeved sterile gown, a procedure mask, a cap, and a large sterile drape—has been associated with a reduced incidence of CR-BSI.

Prior to catheter insertion, cutaneous antisepsis should be performed using alcoholic chlorhexidine gluconate at a concentration of at least 2% in 70% isopropyl alcohol. This combination exhibits superior bactericidal activity, likely due to its rapid action and quicker drying time compared to other antiseptics. If contraindicated, an iodophor (e.g., povidone-iodine) or 70% alcohol may be used. The available evidence supports the use of an alcoholic preparation of chlorhexidine rather than its aqueous competitors, which may be considered if skin reactions or anaphylaxis occur.

Allow the antiseptic to dry completely naturally without manual intervention. Applying antiseptic with applicators or sterile gauze minimizes contamination risk and may enhance skin penetration. Single-use antiseptic vials reduce contamination compared to multi-use bottles, although they come at a higher cost. To facilitate the application of dressings, it is advisable to remove excess hair from the skin with single-use scissors or disposable-head surgical clippers.

If aseptic techniques cannot be assured, it is recommended to remove the device within the next 24-48 hours.

Ultrasound guidance should always be employed, as it allows for the assessment of the most suitable vein, promotes a higher success rate of implantation and, reduces the number of puncture attempts. These advantages indirectly reduce the risk of infectious complications by decreasing procedure time. To maintain asepsis, a sterile probe cover should be used when employing ultrasound.

The risk of infection is reduced when sutures are avoided; instead, the device should be stabilized using an appropriate sutureless system. The catheter exit site should be protected with cyanoacrylate glue and covered with a semi-permeable transparent dressing.

The use of all-inclusive catheter insertion kits or carts has been shown to decrease the incidence of CR-BSI by providing all necessary components in a single, sterile package.

After insertion

To prevent medical adhesive-related skin injury (MARSI) and catheter infections, it is essential to protect the exit site with a semi-permeable transparent dressing. These dressings should be replaced every 7 days or immediately if they become damp, loosened, or soiled. During dressing changes, the exit site should be disinfected with 2% alcoholic chlorhexidine. The catheter securement device, except for those used with subcutaneous catheters, should be replaced with each dressing change. Starting from the second week after catheter insertion, it is recommended to use chlorhexidine-impregnated dressings to protect the exit site, except for tunneled catheters.

Excessive catheter manipulation increases the risk of CR-BSI by facilitating bacterial entry. The catheter hub should be disinfected with alcoholic chlorhexidine gluconate prior to use. Mechanical friction for at least 30 seconds during disinfection is recommended. Novel antiseptic barrier caps offer continuous passive disinfection of the hub, reducing CR-BSI rates.

Immediate removal of unnecessary central and peripheral catheters is crucial for the prevention of CR-BSI.

Principles of treatment

Immediate removal of the CVC is not routinely recommended when CRBSI is suspected in hemodynamically stable patients, without immunosuppressive therapy, intravascular foreign bodies or organ transplantation, and no suppuration at the insertion site.

Although CVC removal and reinsertion may be burdensome for cancer patients, early CVC removal is particularly encouraged in patients with deteriorating clinical state, sepsis, or septic shock and in case of severe complications such as endocarditis, septic thrombosis, abscess formations, or osteomyelitis.

In addition, in patients with tunnel or pocket infection, CVC removal is usually required.

As CVC retention may result in treatment failure or recurrence of infection despite antibiotic therapy, removal is encouraged whenever possible.

Systemic antibiotic treatment should be initiated immediately after sampling of blood cultures and chosen depending on the severity of the infection, patient's comorbidities, and potential colonization with multidrug-resistant (MDR) pathogens as well as local resistance patterns.

Once CR-BSI is suspected, empiric antimicrobial therapy should be administered after appropriate cultures are obtained. It should be based on an assessment of the risk factors for infection, the severity of the clinical picture and the likely pathogens based on local ecology and the catheter site of insertion. Empiric antibiotics should always cover Gram-positive organisms; based on the high frequency of *Staphylococcus* in this type of infections and its potential associated clinical severity. Coverage for other pathogens, Gram-negative bacilli or fungi, should be considered especially in septic shock. It is worth noting that these pathogens are more frequently involved when a femoral catheter is the source of infection.

The management of CR-BSI involves making decisions related to: 1) whether the CVC should be removed or retained with antibiotic catheter lock therapy; 2) the type of antimicrobial therapy, based on the type of organism and its resistance pattern; and 3) the duration of antimicrobial therapy (**Figure 1**).

Routine replacement of a CVC by guidewire exchange is not recommended because this is associated with a higher risk of infectious complications. If catheter removal is indicated for CR-BSI, it should not be replaced over a guidewire; instead, a new catheter must be placed at a different site. Guidewire exchange should be restricted to patients with very difficult venous access (i.e., extensive burns, morbid obesity, or severe coagulopathy) and without documented CR-BSI. In this case, a meticulous aseptic technique and culture of the catheter tip are mandatory.

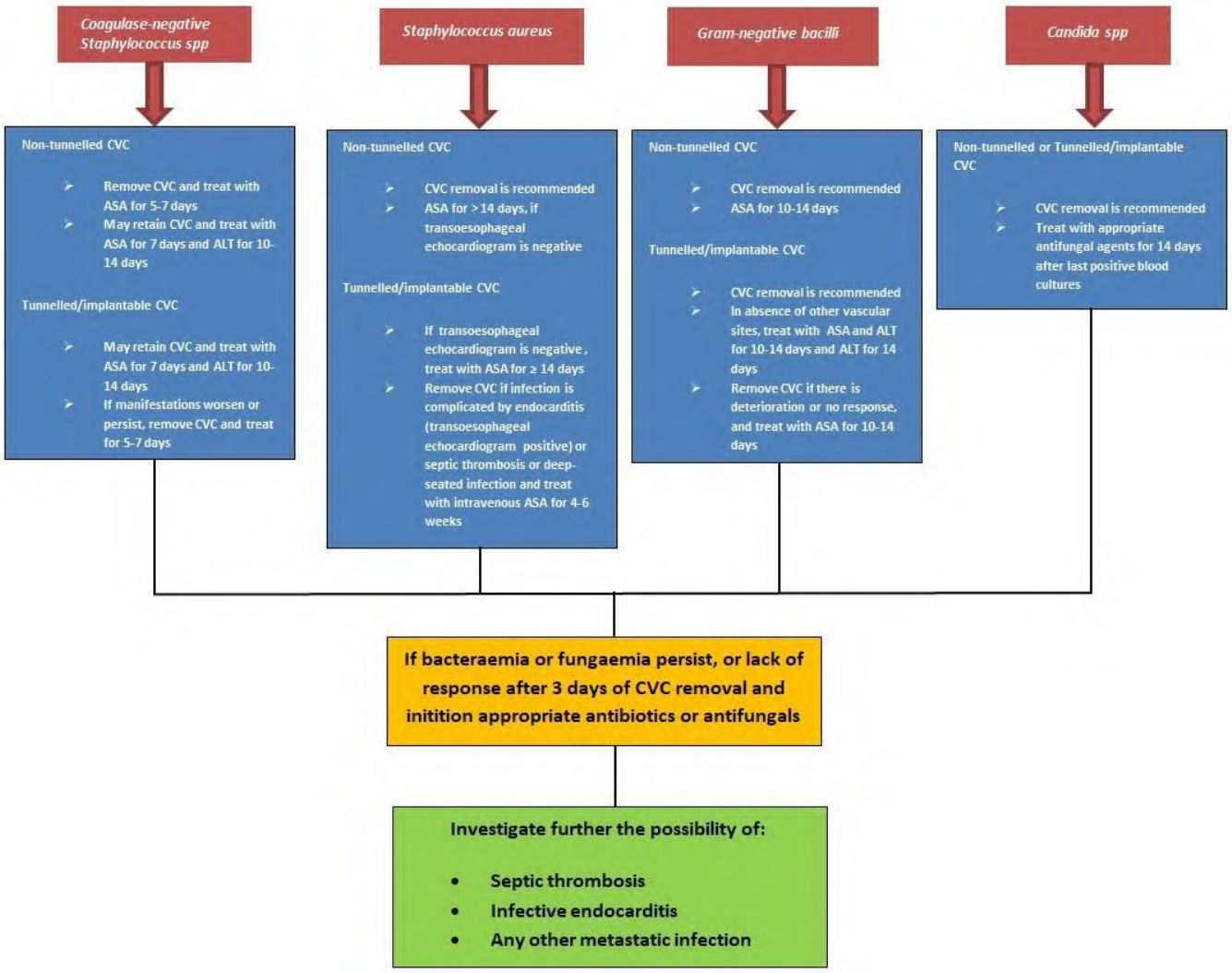

Figure 1. Management of catheter-related bloodstream infections (adapted from Raad I, *et al.* 2007)
Abbreviations: CRBSI=catheter-related bloodstream infection. CVC=central venous catheter. ASA=appropriate systemic antibiotic. ALT=antibiotic lock therapy.

Antibiotic treatment

Systemic antibiotic treatment is the second mainstay of treatment of CR-BSI and should be started immediately after sampling of blood cultures. Antimicrobial therapy should be started as soon as possible with a bactericidal agent active against *Staphylococcus aureus* and CoNS, especially if associated with sepsis or septic shock. Vancomycin is recommended for empirical therapy in patients with suspected CR-BSI. Teicoplanin is not recommended as empirical therapy, given the existence of CoNS with reduced susceptibility. Daptomycin can be administered for cases of CR-BSI with septic shock, acute kidney injury and to patients with recent exposure to vancomycin.

Patients with suspected CR-BSI should receive empirical antibiotic therapy (in addition to coverage for Gram-positive pathogens) to cover Gram-negative bacilli under any of the following circumstances: hemodynamic instability (septic shock), neutropenia or hematologic malignancy, solid organ or bone marrow transplant, femoral catheter in place, or prolonged ICU admission. Antimicrobial therapy should include an antipseudomonal agent (i.e., piperacillin-tazobactam, carbapenems, a fourth-generation cephalosporin, aztreonam, quinolones or aminoglycosides). Aztreonam and cephalosporins should be avoided in patients with colonization or at risk for extended-spectrum beta-lactamase infections. The need for empirical antifungal therapy in

a patient with suspected catheter-related candidemia should be evaluated along with the possibility of catheter removal. Empirical therapy for suspected candidemia should be considered in patients who are hemodynamically unstable with one or more of the following conditions: total parenteral nutrition, prolonged use of broad-spectrum antibiotics, malignancy, femoral catheterization, colonization due to *Candida* spp. at multiple sites or intense previous anti-anaerobic therapy.

Among *Candida* CR-BSI, echinocandins have the advantage of their fungicidal activity and their activity against yeasts in biofilm. Fluconazole is an alternative for patients who are stable, have had no prior azole exposure, and whose catheter is removed. Lipid formulation of amphotericin B and voriconazole are alternatives that may be considered, especially if *Candida krusei* is identified. The recommended minimal duration of therapy for candidemia without metastatic complications is 14 days after documented clearance of *Candida* from the bloodstream.

Empiric treatment should be modified according to microbiological results of susceptibility testing. Duration of the therapy depends on the pathogen detected, the resolution of symptoms, the absence or emergence of complications such as endocarditis or osteomyelitis, and clinical, microbiological, and laboratory evidence of response to antimicrobial treatment.

Depending on the causative pathogen and for uncomplicated CR-BSI, the antibiotic should be continued for at least 7 days, counting the day of the first sterile blood culture as day one of treatment and catheter removal. Longer therapy duration may be indicated in case of complications such as endocarditis and for treatment of specific pathogens such as *Staphylococcus aureus*, *Candida* spp. and other fungi, *Stenotrophomonas* spp., and others (**Table 1**).

Table 1. Antimicrobial therapy of catheter-related bloodstream infections.

Pathogen	Therapy	Duration
Staphylococcus aureus (methicillin-sensitive)	Isoxazolyl penicillin (anti-staphylococcal penicillin)	≥ 2 weeks
Staphylococcus aureus (methicillin-resistant)	Glycopeptide, linezolid, daptomycin	≥ 2 weeks 4-6 weeks (in complicated infection)
Coagulase-negative staphylococci	According to susceptibility pattern; glycopeptides only in case of methicillin resistance	5-7 days after defervescence (in neutropenic patients)
Enterococci	Aminopenicillin; glycopeptide and aminoglycoside in case of ampicillin resistance; linezolid in case of vancomycin resistance	5-7 days after defervescence (in neutropenic patients)
Stenotrophomonas spp.	Co-trimoxazole According to susceptibility pattern in case of allergy (e.g. levofloxacin)	≥ 2 weeks
Pseudomonas spp.	According to susceptibility pattern	≥ 2 weeks
Candida albicans	Echinocandin according to susceptibility pattern or amphotericin B lipid-based formulations after stabilization step down to fluconazole	≥ 2 weeks
Non-*albicans Candida* spp.	Echinocandin; step down to azole according to susceptibility pattern or amphotericin B lipid-based	≥ 2 weeks (after first sterile blood culture)
All other pathogens	According to susceptibility pattern	Not defined

Whenever a conservative treatment is chosen, antibiotic lock therapy (ALT) should be combined with a systemic antimicrobial. Lock solutions can be used as an additive therapy for tunneled or totally implanted CVCs, although they are not effective on the extraluminal surface and recurrences of CRBSIs are common. The patient should also be in a stable condition and the causative microorganism considered of low virulence

(i.e., CoNS), metastasis or local septic complications should be excluded before initiating conservative treatment. Lock therapy involves filling the catheter lumen with a mixture of an anticoagulant and a highly concentrated antibiotic or antiseptic, and temporarily stopping the catheter from flushing. There is no complete agreement at present about the choice of drugs, the duration of each lock period or local treatment.
Vancomycin is probably the most widely used antibiotic for ALT, it has been shown to cure 77-93% of infections caused by CoNS and it can be combined with heparin at 20-100 IU/ml and 4% sodium citrate, as well as with other antibiotics such as ciprofloxacin, gentamicin, amikacin and ceftazidime, which facilitates the treatment of polymicrobial infections.
Most studies use the volume of the lock solution between 2 and 3 ml in tunneled catheters and 3-5 ml in totally implantable ports. However, considering the great variability of catheters used, the exact catheter volume specified in the instructions provided by the manufacturer should be instilled. Before using the catheter or replacing the ALT solution, the previous mixture should be removed to prevent the risk of adverse events associated with the rapid infusion of antibiotics at high concentrations. The optimal duration of ALT is not known. In most recent studies, ALT was given for 10-14 days, although a shorter treatment duration may be efficacious, especially for Gram-negative infections. The frequency of ALT replacement has not been established. It is usually performed every 24-72 hours and adapted to the use and needs of the infected line. In hemodialysis patients, ALT is replaced after each hemodialysis session. If more frequent use of the catheter is needed, the lock is replaced every 24 hours. Ideally, the catheter should not be used while the ALT solution is in place. However, for patients receiving parenteral nutrition or those with few or no other venous access options, ALT and catheter may be alternated. In such cases, a minimum of 8-12 hours a day is recommended. All lumens should be treated.
Other non-antibiotic substances have been used for lock therapy. Solutions such as taurolidine, citrate, EDTA and ethanol only have an intraluminal effect and can be altered in their intraluminal concentration by 'lock spillage' (leakage of lock solution or blood leakage into the CVC lumen). When ethanol is used to maintain the patency of intravascular catheters, protein precipitation with consecutive carry-over into the pulmonary circulation can occur. Lock solutions with hypertonic citrate also interact with plasma proteins and have weak (*E. coli*) or no (*Staphylococcus aureus*) antimicrobial efficacy.
Taurolidine, like 70% ethanol, has been evaluated in several large, randomized studies of the prevention of CRBSI. It, mostly compared with heparin, was associated with significant reductions in the rate of bloodstream infections.
EDTA and citrate can disrupt biofilm, thus increasing antimicrobial activity. Several *in vitro* studies have demonstrated the proven anti-biofilm effect of EDTA alone or in combination with gentamicin or minocycline plus 25% ethanol.

Management of local infections catheter-related

Short-term catheters (peripheral venous, non-tunneled CVCs and arterial catheters) with erythema, pain, warmth, induration and/or purulent drainage within 2 cm of the catheter exit site should be removed despite the absence of concomitant bacteremia. In immunocompromised patients, any exudate at the exit site should be submitted for Gram staining, routine and fungal culture. In uncomplicated infections involving long-term catheters (defined as the absence of fever, positive blood cultures or purulence), cultures from the exit site should be obtained. Topical application of an antibiotic ointment at the insertion site may be considered, based on culture results. If the infection does not resolve or purulent exudate develops, systemic antibiotics should be administered. If clinical signs of infection persist after 48-72 hours of appropriate antimicrobial therapy, the catheter should be removed. For tunnelitis without fever in hemodialysis catheters, systemic antibiotic therapy may be attempted first. In tunnel infection with fever, catheter removal is the first therapeutic option together with systemic antimicrobial therapy.

Management of a port reservoir infection requires removal of the port, drainage of affected tissues and administration of antibiotic therapy for 7-10 days in the absence of concomitant bacteremia or fungemia.

Conclusion

CR-BSI remains a leading cause of healthcare-associated infections, particularly in ICUs. It is the most frequent cause of bacteremia and it is mostly accessible to prevention if rigorous policies are implemented. These include strong practices, such as strict adherence to aseptic techniques in particular hand hygiene and the use of maximal sterile barrier precautions.

The use of care bundles, infection monitoring, the ongoing education for healthcare professionals have proven particularly effective in preventing bloodstream infections.

The management of CR-BSI requires catheter removal in most critically ill patients. In noncomplicated intravascular catheter infections, a short course of antimicrobial treatment is usually appropriate.

In conclusion, addressing CR-BSI requires a comprehensive strategy that incorporates technological advancements, consistent adherence to preventive practices, and a focus on building a resilient healthcare system.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 57

Catheter-associated urinary tract infections. Principles of prevention and management

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Introduction

Catheter-associated urinary tract infections (CAUTIs) are urinary tract infections occurring in individuals with indwelling catheters inserted in the bladder within 48 hours.
Between 15% and 25% of hospitalized patients receive short-term indwelling urinary catheters. In many cases, catheters are inserted for inappropriate indications.
CAUTIs are the most common healthcare-associated infections accounting for more than 30% of infections reported by acute care hospitals, CAUTIs may be a causative agent of secondary bloodstream infections, that can lead to sepsis.
Age, female gender, diabetes and prolonged catheterization are considered risk factors for CAUTIs. The duration of catheterization is associated with increased risks of CAUTIs and is the most important factor for the development of bacteriuria, with a risk of 3–7% daily. In recent years, CAUTIs have received significantly less attention than other HAIs, probably because CAUTIs present generally lower morbidity and mortality compared with the other HAIs, as well as have a lower financial impact. However, because they are very common, it should be important to consider their large cumulative impact.

Pathogenesis of catheter-associated urinary tract infections

Microorganisms causing CAUTIs can be either endogenous, via meatal, rectal, or vaginal colonization, or exogenous, via contaminated hands of healthcare workers or equipment. Urinary pathogens can enter the urinary tract either by the extraluminal route, migrating along the outside of the catheter, or by the intraluminal route, migrating along the internal lumen of the catheter because of a contaminated collection bag or a contaminated catheter-drainage tube junction.
In addition, urinary catheters may also traumatize the uroepithelium, disrupting the physiologic mucopolysaccharide coating, and rendering it susceptible to bacterial adhesion and entry. in the context of a urinary catheter, whether it be a urethral catheter or suprapubic tube, CAUTIs may be initiated upon bacterial adherence to the catheter, with subsequent biofilm formation. Formation of biofilm by urinary pathogens on the surface of the catheter occurs universally with prolonged duration of catheterization.
Biofilm consists of scaffolds that are made from extracellular DNA, exopolysaccharides and microbial surface structures, concretely pili and flagella. Biofilm serves as a reservoir for microbial seeding of the urinary tract

and is central to the pathogenesis of CAUTIs. According to studies, the biofilm formation begins within minutes of catheterization and it progresses as a function of indwelling time.

Criteria for diagnosing CAUTIs and challenges

Uropathogenic *Escherichia coli* (UPEC) is the most common pathogen for both non-complicated and complicated UTIs, making up 75% and 65% of infections, respectively. In complicated UTIs, where CAUTIs make up the majority of cases, the overall most common causative organisms after UPEC include *Enterococcus* spp. (11%), *Klebsiella pneumoniae* (8%), *Candida* spp. (7%), *Staphylococcus aureus* (3%), *Proteus mirabilis* (2%), *Pseudomonas aeruginosa* (2%), and Group B *Streptococcus* (2%).

Signs and symptoms of UTI include increased bladder sensation, urgency, frequency, dysuria and pain during urination., suprapubic tenderness, fever, rigours, altered mental status, malaise, lethargy with no identified cause, flank pain and costovertebral angle tenderness. But, these signs and symptoms, in the context of CAUTIs may be subtle and cannot relied upon. Especially the classic trio of symptoms including urgency, frequency and dysuria cannot be relied upon because of the lack of the volitional voiding and because of subpopulations that might present with neurogenic bladder.

Urine culture is an important component of diagnostics in CAUTIs, but represents also a challenge because of the controversial diagnostic cutoff. The IDSA states that a CAUTI is defined by symptoms associated with a urine culture with growth of ≥103 colony-forming units (CFU)/mL of ≥1 bacterial species in a single catheter urine specimen, taken in midstream voided specimen in an individual whose catheter was removed in the preceding 48 hours. Importantly, the IDSA notes that in the absence of symptoms, >103 CFU/mL may also be compatible with asymptomatic bacteriuria, and outside the context of symptoms, generally does not warrant treatment.

The Centers for Disease Control (CDC)/National Healthcare Safety Network (NHSN) use a cut-off of 105 CFU/mL. The IDSA states that the 103 CFU/mL cutoff represents a compromise between the sensitivity of detecting CAUTI and the feasibility of laboratory quantitation of organisms.

Pyuria, or the presence of white blood cells in the urine, is indicative of inflammation of the urinary tract presenting with CAUTI as well as asymptomatic bacteriuria. In a study of over 700 recently catheterized patients, the presence of pyuria for bacteriuria (105 CFU/mL) was 47% and specificity was 90%, with a positive predictive value of 32%. In a study assessing 177 urinalyses with urine cultures performed in a cohort of 14 long-term catheterized patients, both bacteriuria and pyuria were common in asymptomatic episodes, and levels did not change considerably in the context of symptoms.

The presence of cloudy and malodourous urine should not be used to differentiate CAUTI and asymptomatic bacteria.

The techniques of obtaining urine specimens from CAUTI patients should meet some criteria and most importantly, the sample must be obtained before the initiation of antibiotics. One of the techniques suggested by IDSA to obtain urine specimens is by syringe in the tube of a catheter. In patients with indwelling catheters for a longer time, it is preferable to remove the catheter and obtain the urine specimen from the new catheter inserted. In the case of patients with symptoms suggestive of CAUTI, catheter removal should be done immediately before starting antibiotics. Culture specimens should not be obtained from the urine drainage bag due to the high risk of contamination, although the CDC notes that large-volume urine specimens may be obtained through this way for special analyses other than culture.

Urine culture stewardship, as a method to prevent and reduce CAUTI, the example of the WakeMed Urine Culture Stewardship Program (WMUCSP)

Wake Med Health Hospitals, located in North Carolina, USA, conducted a prospective, 2-year quality improvement program for evidence-based urine culture stewardship, from October the 1st 2018 to September the 30th 2020.

The design of the urine culture stewardship program consisted of these three core elements:

- criteria for allowing or restricting urine cultures from catheterized patients,
- a best practice advisory integrated into the ordering system of an electronic medical record and
- a systematic provider education and feedback program to ensure compliance.

A team for CAUTIs were formed, consisting of experts in the matter to implement the three core elements of UCS, especially monitoring the insertion of catheters, the duration of catheters and de-escalation/removing the catheter when to obtain the urine culture as well as the treatment options. The guidelines and a monitoring program designed and approved by the CDC were integrated to assess adherence to the guidelines presented.

After the implementation of WMUCSP, the rate of CAUTIs before and after the implementation of the program decreased significantly from 2.09 to 0.90 (p<0.001), and the rate of CAUTIs trended downward after the implementation of the program.

Principles of prevention and management and innovations

Multiple fundamental principles of intervention prevent and reduce the risk of CAUTI.

Best practices for catheter insertion and management may prevent the acquisition of CAUTIs and decrease the risks of symptomatic infections. Best practices should include correct insertion techniques to minimize contamination and maintaining a closed drainage system to avoid catheter colonization.

The duration of the catheterization is one of the most important factors that increases the rate of CAUTIs. Thus, the intervention of minimizing the use of indwelling catheters, shortening the duration of catheterization and removing them according to the medical condition of the patient, as soon as possible, is fundamental. The assessment daily of the catheter and considering removing it accordingly is very important. Also, alternative strategies for bladder drainage by intermittent cleaning of catheterization should be considered. External catheters are an alternative to indwelling catheters and are recommended by the CDC, including for men the condom catheters and for women viable external strategies.

To minimize catheter use, the infrastructure and stewardship programs at the hospital level should be in place. Sufficient staffing and staff education, with access to necessary equipment, should be ensured. Guidelines- and Electronic medical records (EMR) documentation of catheter insertion and removal dates as well as indications and reminders for removal are important. Also, the EMR should be a measurement of compliance and adherence to guidelines.

Insertion technique and drainage considerations

The major route of infection in CAUTI is ascending (i) at the time of insertion of a catheter through the urethra, (ii) via the mucosal layer between the catheter and urethra and (iii) through the catheter lumen. The risk of acquiring CAUTI depends mainly on the method and duration of catheterization.

The aseptic catheter insertion technique is an important element of catheter management to reduce CAUTI rates. Hand hygiene should be performed before and after the catheter insertion. The Infectious Diseases Society of America (IDSA) provides guidelines designed to reduce CAUTIs following catheter insertion. Firstly, a closed drainage system should be employed. If breaks or leaks occur in the aseptic technique, the closed drainage system, the catheter and the drainage bag should be replaced using the aseptic technique and new equipment. The drainage bag should be kept below the level of the bladder and connection tubing. Positioning the tubing above the bladder or below the drainage bag level is associated with an increased risk of bacteriuria.
Precautions should be taken to minimize urethral trauma during insertion Catheter insertion should only be performed by trained personnel, with adequate lubricant, and with the smallest calibre catheter necessary for its purpose. Catheter securement should be performed to minimize urethral traction and trauma.

Catheter exchange timing
The timing of catheter exchange is still debated and integrates several factors. In clinical practice, catheters are generally removed and replaced at least every 4 weeks. A frequent catheter change does not stop the formation of the biofilms. Due to the lack of conclusive clinical trials, the IDSA guidelines do not recommend changing urinary catheters at set time intervals, but rather in cases of suspected or confirmed infection, obstruction, or breaks in the closed drainage system.

Catheter materials and coatings
Catheter selection is an additional consideration in CAUTI rate reduction. The two most commonly used catheters are latex *versus* silicone. The studies on these two catheters have not shown a significant difference in the rate of reduction of CAUTIs, rather the selection of the material is related to the compliance of the patient's organism with the material (latex allergy).
In the last few years, it has been reported that biofilm formation on the urinary catheter may play a key role in the pathogenesis of CAUTI and the resistance of CAUTIs to management. Renewed interest has therefore arisen in altering the catheter surface to inhibit biofilm formation. A recent approach to solve some of the problems associated with CAUTIs has been the application of a range of different coatings to the surface of the catheter. The results have been varied.
Nitrofurazone-impregnated catheters are innovative catheters now commercially available. Nitrofurazone inhibits the replication of DNA, thus reducing bacterial growth and biofilm formation. Clinical results, however, have been variable and some side effects have been shown to surface.

Antibiotic prophylaxis
There is sparse evidence regarding antibiotic prophylaxis in the context of a long-term indwelling catheter.
A Cochrane review in 2013, demonstrated that in surgical patients undergoing catheterization from 24 hours to two weeks, there was a lower rate of febrile mortality associated with prophylactic antibiotics. The same review also concluded that in non-surgical patients, there was limited evidence that prophylactic antibiotics reduced bacteriuria. Again, whether this translated to symptomatic UTIs was not assessed.
The utility of prophylaxis at the time of catheter removal remains controversial. A meta-analysis in 2013 indicated an overall benefit of antibiotic prophylaxis at the time of removal of a catheter to prevent urinary tract infections. However, the authors concluded that the increasing burden of antimicrobial resistance (AMR), healthcare costs for antibiotics, and the potential for side effects of antibiotic administration were disadvantages that needed careful review and suggested being careful not to encourage antibiotic use when

it might not be necessary. Therefore, antibiotic prophylaxis might be administered before catheter removal, after taking into account the individual risk factors.

CDC guidelines on management of CAUTIs do not recommend the use of routine prophylaxis with systemic antibiotics for prevention of CAUTIs in patients requiring short- or long-term urinary catheterization, unless clinical indications exist (e.g., in patients with bacteriuria upon catheter removal post urologic surgery).

Catheter irrigation/washout

A Cochrane review analyzed the available evidence regarding catheter irrigation/washout in the prevention of blockage and infection in those with indwelling catheters. Seven trials included were limited and generally of poor quality, and the evidence was not substantial enough to make recommendations regarding the benefits and/or risks of washout.

A subsequent randomized controlled clinical trial of 60 comatose patients in intensive care units demonstrated that daily bladder irrigation with normal saline was effective in reducing CAUTI risk. Another study demonstrated that daily intravesical povidone-iodine bladder irrigation was associated with a significant reduction in symptomatic UTIs. However, more randomized clinical trials are needed to confirm these results and determine whether they are generalizable.

Innovations

Innovations in the prevention of biofilms in catheters are being carried on. The studies on the progression of biofilms have indicated the necessity to produce catheters with a coating that can reduce or prevent the formation of biofilms. One innovation system is the use of nanoparticles due to bioavailability to reduce the biofilms. Nanoparticles have been used to deliver silver, gold, zinc and copper. Catheters coated with silver have shown different results in clinical data, however, the nanoparticles remain still an innovation to be evaluated further.

Another innovative strategy that is seen as a preventable method of CAUTI is antimicrobial peptides (AMP), which are a group of host defence peptides with broad antimicrobial activity against Gram-negative and Gram-positive bacteria. AMPs exhibit great potential, but challenges persist and include inadequate AMP surface density, suboptimal coating, altered AMP orientation, and pH sensitivity. Moreover, resistance to AMPs has been described. AMPs require additional study *in vivo* and clinical trials.

Finally, bacteriophages are also seen as an innovative way of preventing biofilms and treating CAUTI.

Management

Bacteriuria in the absence of symptoms is very common among catheterised patients. Antibiotic therapy for asymptomatic bacteriuria should not be administered because it does not affect patient outcomes, and can increase the emergence of AMR. Thus, with few exceptions such as immunocompromised patients, antibiotic therapy for catheterised patients with asymptomatic bacteriuria is not suggested. Removal of the catheter allows the resolution of bacteriuria in most cases.

Empiric antibiotic therapy for patients with CAUTIs depends on patients' clinical conditions and whether the infection has proceeded beyond the bladder (which generally can distinguish acute complicated UTIs from acute uncomplicated UTIs).

Moreover, empirical antibiotic selection for CAUTIs should take into account risk factors for resistant infections (past urine cultures, previous antibiotic therapy, healthcare exposures and healthcare setting resistance patterns). Once culture and antimicrobial susceptibility testing results are available, the antibiotic regimen should be tailored to the specific bacteria isolated.

The repetitive inappropriate administration of antibiotics can lead to the development of antimicrobial resistance. The optimal duration of antibiotic therapy is uncertain. Seven days is the recommended duration of antibiotic treatment for patients with CAUTI who have a prompt resolution of symptoms. Oral therapy can be used for antibiotic treatment if the patient is susceptible and the patient is well enough to take the oral medication with adequate absorption.

Conclusion

CAUTIs are the most common healthcare-associated infections. Multifaceted interventions including evidence-based best practices, engagement of both the medical and nursing staff and education are more effective than single intervention. Designing stewardship programs directed towards the control of CAUTIs is quite important in reducing their rate, thus including observing and deciding when a catheter should be inserted or removed, as well as when a urine culture should be obtained or not.
The education of the staff that are responsible for catheter insertion is of high importance. Techniques of catheter insertion should be observed, evaluated and improved repeatedly.
The two most important strategies to prevent CAUTI are not to use a urinary catheter and, if a catheter is necessary, to remove it promptly, when no longer needed. Catheters should be inserted only when they are truly needed and removed as soon as they are no longer indicated

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 58

Biofilm and medical device-associated infections

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Introduction

In modern-day medical practice, the insertion of biocompatible indwelling or implanted foreign materials in the form of bioinert, bioactive or bioresorbable medical devices has become an integral component of patient management. These devices are made of biomaterials designed to take forms that can direct, through interactions with living systems, the course of therapeutic, diagnostic or rehabilitation activities, either as temporary applications or as permanent implants. It is not an exaggeration to state that the use of biomaterials has saved the lives of millions of patients globally.

It is estimated that every person during their lifetime will need to use at least one indwelling medical device. However, with the increase in the use of such devices, the number of cases of device-associated infections (DAIs) is also increasing, which carries significant clinical and economic implications. DAIs include infections associated with catheters, contact lenses, fracture fixation devices, dental implants, joint prostheses, vascular grafts, cardiac pacemakers, mammary implants, mechanical heart valves, and heart-assisted devices among others. DAIs are the result of microbes adhering to the devices and forming extracellular polymeric substances (EPS) to produce communities called biofilms. Within biofilms, the microbes are protected from mechanical, chemical, and environmental stresses. Microbial adherence to the surface of medical devices depends on microbial characteristics (e.g., binding appendages, load, microbial hydrophobicity), device surface properties (e.g., surface chemistry, topography, roughness), and the environmental conditions (e.g., immune cells, pH, flow rate) of the tissue or organ where the device is deployed. DAIs predominantly originate from implant contamination, from the patient's own or healthcare workers' resident normal microbiota, or other external environmental sources during the implantation phase.

Biofilms: an overview

In general terms, microbial biofilms are defined as organized multidimensional communities of mono- or poly-microbial populations that reside within a self-generated matrix of sticky EPS composed mainly of polysaccharides, proteins, extracellular nucleic acids (eDNA and eRNA), and lipids. Biofilms are conventionally described as aggregates made of individual cells in sessile and planktonic stages of their life cycle. However, the physiology of biofilm cells has been compared to that of eukaryotic models where different cells play different roles, ultimately providing a collective function as if they were structural and functional units of an organism rather than a collection of individual organisms. Biofilms can be described as diversity incubators, which emphasize the generation of diverse cells because of mutations driven by different stimuli. The mature biofilm might consist of bacteria in different conditions which include viable but non-culturable cells (VBNC), resistant cells, tolerant cells, and planktonic cells.

Biofilm formation on medical devices

As shown in **Figure 1**, both tissue and device-associated infections are associated with biofilms. These biofilms are associated with at least 80% of multidrug-resistant infections which might require surgery. Once the medical devices are colonized by microbes, particularly as biofilms, complete removal of the device is often the only therapeutic option. Leaving such contaminated devices in place can be life-threatening to the patients, while at the same time, removal from the body site can also pose life-threatening risks depending on the nature and location of the device.

Different microbes are responsible for the colonization and biofilm formation on medical devices including a wide spectrum of bacteria as well as fungi, such as the emerging yeast *Candida auris*. In many cases, device-associated biofilms consist of mixed species or mixed kingdom of microbes providing synergistic or competitive polymicrobial interactions.

Initial microbial attachment to the surface of a device

Biofilm formation encompasses multiple sequential steps commencing with initial reversible attachment of microorganisms and culminating in the establishment of irreversible attachment and robust biofilms. Typically, the understanding of the pathobiology of biofilm-associated infections is limited to the context of microbial EPS. However, additional consideration should be given to biomolecules from the host or surrounding environment contributing to biofilm formation which may intercalate with the microbial EPS. This diverse array of biomolecules from the host, pathogen and environments, is collectively termed the matrixome.

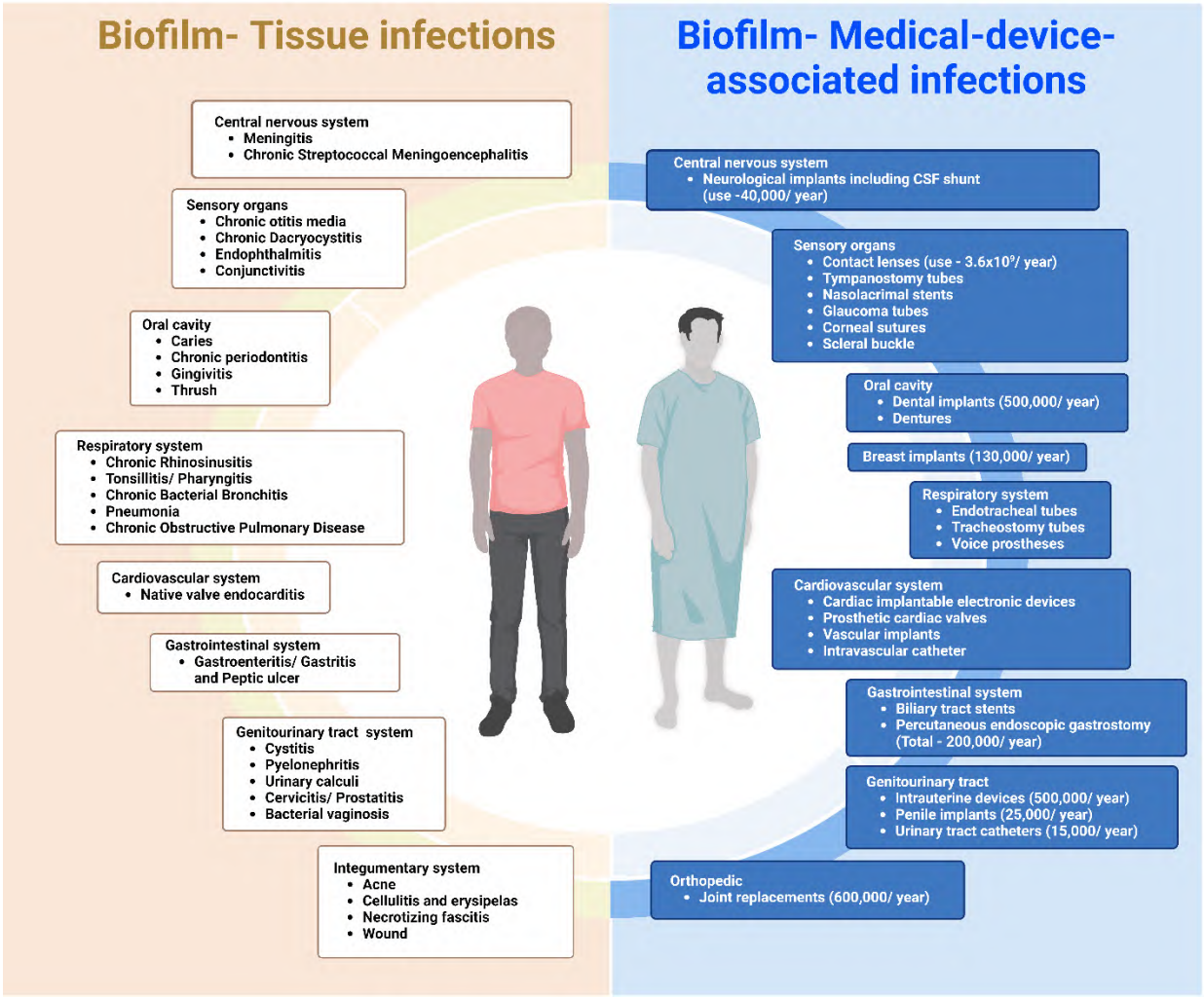

Figure 1. Tissue and device-associated infections are associated with biofilms (Created in BioRender. Mishra, S. (2024) BioRender.com/x75o804)

Surface parameters influencing adherence of microbes

Different surface properties of medical devices influence the attachment of bacteria. These include surface charge density, wettability, roughness, topography, and stiffness. The cell surface of bacteria is anionic due to the presence of carboxyl, amino, or phosphate groups on their cell walls or outer membranes, thus favoring their adhesion on cationic surfaces. Likewise, high surface energy on surfaces and low surface tension in liquids generally enhance wettability. Similarly, rough surfaces increase the available area for microbial attachment and provide a basis for their adhesion. Further, these surfaces offer a protectant for microbes against shear forces.

Microbial characteristics governing biofilm formation

To find their substratum for attachment, bacteria can utilize their motility, either swimming or swarming and Brownian motion or twitching motility in the case of non-motile bacteria. Initially, the microbes are loosely adhered to the surface. These cells undergo a shift towards a firmer and flatter attachment to the surface developing into “surface sentient” states with increased levels of cyclic-di-adenosine monophosphate (c-di-AMP) which upregulates the production of biofilm matrix. Microbes can then begin the multiplication and

production of biofilm EPS constituents, resulting in the formation of microcolonies, which subsequently expand to form large cellular aggregates encased within the EPS. In flagellated Gram-negative bacteria, cyclic-diguanylate monophosphate (c-di-GMP) signals an increase in the biofilm which reduces the swimming motility of bacteria while increasing matrix formation. Type IV pili-associated twitching motility is required for microcolony formation. In biofilms, bacteria produce low molecular weight signaling molecules which enable them to sense their density and also allow them to exhibit intercellular cross-talk; a phenomenon called quorum sensing (QS). These QS molecules are generally N-acyl-L-homoserine lactones (AHLs) and 4-quinolines in Gram-negative bacteria, while they are post-translationally modified peptides (e.g. pheromones) in Gram-positive bacteria. QS influences both biofilm formation and dispersal. The motility of bacteria has been further identified as a factor determining the shape of biofilm. In biofilms, non-motile cells of *P. aeruginosa* form the "stalks" of mushroom-shaped biofilm by forming microcolonies while the motile population remain as top colonisers forming the "cap" of "mushroom" biofilm arrangements.

In contrast to the initial phase of attachment, biofilm dispersal occurs due to phenomena such as QS, upregulation of motility, reduced c-di-GMP signals, and activation of lysogenic bacteriophages, along with other environmental and nutritional factors. In the inner areas of biofilms, there is a reduced concentration of oxygen which induces the generation of nitric oxide. This in turn activates phosphodiesterases which trigger a reduction in cellular c-di-GMP levels, initiating planktonic modes of growth with an increase in bacterial motility and dissemination of cells from the biofilm. These microbes differ from their planktonic counterparts in terms of metabolic activities, growth, gene transcription, and susceptibility to antimicrobial agents.

Environmental factors influencing biofilms

Environmental conditions such as temperature, pH, nutrients and oxygen concentration are major factors influencing the physiology of organisms. Hydrodynamics and osmolarity are other factors that influence homeostasis. Flow-induced shear stress increases the c-di-GMP levels and induces the formation of a biofilm matrix in the form of EPS. This can be correlated with respect to the flow of body fluid and the development of biofilm in indwelling medical devices. In the case *of Staphylococcus aureus*, flow-induced flexible filamentous biofilm structures called streamers are formed in curvy channels of medical devices clogging the interior in the presence of blood plasma. Such an event is associated with the viscoelastic properties of the biofilm. Examples of medical devices/implants, their frequency of associated infections, and causative organisms, are summarized in **Table 1**.

Table 1. Overview of device-associated infections related to biofilm formation

Medical device/Implant	Overview	Infection frequency	Causative organisms
Breast implants	● These implants are used in procedures such as postmastectomy breast reconstruction or cosmetic surgery. ● Treatment of breast-implant-associated infection may require removal of the implant besides systemic antimicrobial therapy. ● The T-cell stimulation from chronic bacterial biofilm infection of breast implants can result in breast implant-associated anaplastic large-cell lymphoma.	● Incidence of breast implant-associated infection is around 3%.	*Staphylococcus* spp., *Cutibacterium acnes*, streptococci, *Bacillus* spp., *Escherichia coli*, *P. aeruginosa*, *Mycobacterium* spp., *Actinomyces* spp., *Corynebacterium* spp., lactobacilli, *Ralstonia* spp., *Curvularia* spp.
Cardiovascular implants (CVIs)	● The major CVIs include cardiac implantable electronic devices (pacemakers, implantable cardioverter-defibrillators, cardiac resynchronization therapy devices), prosthetic heart valves, and vascular implants. ● These implants are used in cardiac patients to prevent heart failure. ● It is challenging to remove infected vascular implants; thus, infections result in high mortality and morbidity. Even with prolonged antimicrobial treatment, the two-year mortality for infected endografts, left in situ, can be almost 100%. ● Around 1-6% of vascular graft placements are complicated by prosthetic vascular graft infections.	● The rate of infected CVIs is around 1.2-2.4% of the total implanted devices which can increase to 10-times post-device upgrade or replacement.	*Staphylococcus* spp., streptococci, enterococci, *Corynebacterium* spp., *C. acnes*, HACEK (*Haemophilus* spp., *Aggregatibacter* spp., *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*), *P. aeruginosa*, *Mycobacterium chimaera*, *Enterobacterales*, *C. albicans*
Contact lenses	● Contact lenses are often used to correct myopia, hyperopia, astigmatism and other forms of refractive error. ● There are more than 140 million contact lens wearers globally. They would use at least 26 pairs of lenses a year (with biweekly replacements), resulting in approximately $3.6x10^9$ lenses used worldwide, making contact lenses probably the most common medical device used. ● The infecting microorganisms also colonise the contact lenses cases as biofilms. ● Contact lens related corneal infections (microbial keratitis) requires intensive antibiotic therapy and can lead to scar formation and blindness.	● Annually, approximately 2 out of every 10,000 individuals who wear contact lenses on a daily disposable or daily wear basis experience ocular infections.	*P. aeruginosa*, *S. aureus, Streptococcus* spp., *Moraxella* spp., *Acinetobacter* spp., *Enterobacterales, Stenotrophomonas maltophilia, Acanthamoeba* spp.

(cont.)

Table 1. Overview of device-associated infections related to biofilm formation *(cont.)*

Medical device/Implant	Overview	Infection frequency	Causative organisms
Intravascular catheters	● Peripheral intravascular (IV) and central venous catheters (CVCs) are used for the delivery of fluids, medications, parental nutrition and administration of hemodialysis. ● These devices are in direct contact with blood, making them susceptible to biofouling as blood proteins and platelets adhere to their surfaces. Biofilms on their surfaces can trigger immune responses, leading to the formation of fibrin matrix that can eventually clog the lumen. ● The mortality rate for patients with central line-associated bloodstream infections (CLABSIs) ranges from 12-25%. ● These infections depend on catheter type and material, anatomic location, insertion duration, as well as insertion site care.	● In the United States, the annual frequency of approximately 30,000 CLABSIs have been reported from ICUs and wards.	*S. aureus*, *S. epidermidis*, *Enterococcus faecalis*, *P. aeruginosa*, *Enterobacterales, S. maltophilia*, *Burkholderia cepacia* complex, *C. albicans*
Cochlear implants	● These implants are often used in the acquisition or improvement of hearing through electrical stimulation of the auditory nerve. ● Infections due to the formation of biofilm in the implant can necessitate its removal and, in severe cases, can be fatal.	● The incidence of cochlear implant-associated infections falls between 1.7 and 4.1%.	*S. aureus*, *S. pneumoniae*, *P. aeruginosa*, *S. pyogenes*, *S. epidermidis*, *C. albicans*
Dental implants	● These implants are placed in the maxillary and/or mandibular areas to treat tooth loss and aid in reconstructing orofacial structures. ● Microorganisms associated with dental plaque, which are biofilms on teeth, are not only responsible for dental caries and periodontitis, but also for peri-implantitis. ● Further, the biofilm on dental implants is similar to the polymicrobial biofilm on hydroxyapatite, a material that commonly constitutes tooth surfaces. ● It is difficult to treat infection in these implants, often requiring their removal.	● The prevalence of peri-implantitis has been estimated to be 22%.	*Porphyromonas gingivalis*, *Prevotella intermedia*, *Veillonella* spp., *Treponema denticola*, *Streptococcus* spp., *Fusobacterium* spp. *Candida* spp.

(cont.)

Table 1. Overview of device-associated infections related to biofilm formation *(cont.)*

Medical device/ Implant	Overview	Infection frequency	Causative organisms
Endotracheal tubes (ETTs)	● In critically ill patients, ETTs are used for mechanical ventilation. However, these tubes can increase the risk of VAP by promoting the accumulation of respiratory secretions. ● The prevalence of biofilm production in ETTs has been found to range from 20-100% (median prevalence 72%). ● Polymicrobial species are found in 8-58% of the cases. ● Mortality rate associated with these infections ranges from 16.2% to 74.2%.	● The incidence of VAP ranges from 2.13/1000 ventilator days to 116/1000 ventilator days.	*Pseudomonas* spp., *Acinetobacter* spp., *Staphylococcus* spp., *K. pneumoniae*
Gastrointestinal (GI) implants	● Percutaneous endoscopic gastrostomy (PEG) tubes, intraabdominal mesh and biliary stents are the common GI implants. ● In long-term care facilities, percutaneous gastrostomy endoscopes, which is used for enteral nutrition, can be colonized by bacteria and yeast in biofilms. Similarly, biliary stents used in post-hepatic jaundice patients can get colonized by duodenal microbiota with the formation of biofilms.	● Recent data on overall GI implant infections are not available. However, mesh-associated infection has been estimated from 5-20% in different studies.	*Bacillus* spp. *Enterococcus* spp., *Staphylococcus* spp., Enterobacteriaceae, *Candida* spp.
Genitourinary implants	● Implants including urinary catheters, ureteral stents, nephrostomy tubes, intrauterine devices, penile implants are employed to manage urinary tract obstruction, leaks, stricture formation prevention, and reproductive conditions. ● These implants are often colonized by microbes in biofilms. ● The likelihood of developing catheter-associated urinary tract infection (CAUTI) due to biofilm formation in its either intraluminal or extraluminal surfaces increases by more than 5% each day that they are used.	● In patients with indwelling bladder catheters and bacteriuria, around 25% develop symptomatic CAUTI. ● Microbial colonisation has been found to be 100% and 70% in permanent and temporary ureteric stents respectively.	*Enterobacterales*, *P. aeruginosa*, *Staphylococcus* spp., *Enterococcus* spp. *Candida* spp.

(cont.)

Table 1. Overview of device-associated infections related to biofilm formation *(cont.)*

Medical device/ Implant	Overview	Infection frequency	Causative organisms
Neurological/ Neurosurgical implants	● These implants include cerebrospinal fluid (CSF) shunts, neurostimulators, and external ventricular and external lumbar CSF drainage devices. ● The infections associated with neurological implants often lead to serious complications with high mortality. ● The incidence of these infections is higher in patients with craniectomies and external ventricular CSF drainages	● Their infection ranges from 3-15%	*Staphylococcus* spp., *C. acnes*, streptococci, *Enterobacter* spp., *P. aeruginosa*, *Candida* spp.
Orthopedic implants	● The use of orthopedic implants, including spinal instrumentation and joint replacements, helps improve the quality of life for patients dealing with bone and joint ailments. However, prosthetic joint infection is a common postoperative complication due to biofilm-forming bacteria, which can lead to osteomyelitis. ● In recalcitrant prosthetic joint infections, resection arthroplasty or even amputation might be warranted. ● Similarly, in cases of spinal implant-associated infections with epidural abscesses and spinal cord involvement, immediate medical intervention is warranted.	● The incidence of periprosthetic joint infection (PJI) is approximately 2% for hip and knee primary arthroplasty surgeries. ● In revision surgeries, the incidence of postoperative spinal implant infections can reach to 27%.	*S. aureus*, *S. epidermidis*, *S. lugdunensis*, *P. aeruginosa, Mycoplasma* spp*., Mycobacterium* spp*., Candida* spp*.*
Suture, dressings and surgical meshes	● Contaminated sutures with biofilms are one of the major factors causing surgical site infection (SSI). ● Moreover, wound dressings, which are used to halt further microbial colonization from the external environment, have also been regarded as a "static biofilm reactor" that promotes biofilm on the underside of the dressing.	● SSIs constitute 15.7% of healthcare-associated infections.	*S. aureus*, *P. aeruginosa*, *E. coli*, *Candida* spp.

The impact of biofilms

A niche for chronic and persistent infections tolerant or resistant to antibiotics

Biofilms act as niduses of persistent and chronic infections despite antibiotic therapies and are associated with at least 80% of microbial infections and at least 60% of hospital-acquired infections. Tolerance as well as resistance are responsible for the recalcitrance of biofilm bacteria towards antibiotics. Physical, physiological and genetic phenomena are involved in the tolerance of biofilms to antibiotics, whereas antibiotic resistance in biofilm cells is due to mutations. The antibiotic-resistant cells differ from tolerant cells in that the former possess resistance factors which enable them to resist antibiotics while the latter survive antibiotic

treatment for the duration which would otherwise kill other susceptible bacteria, without developing resistance, by generally reducing metabolic activities. Within biofilms, there can be a small subset of a clonal bacterial population that exhibits dormancy and survives for a prolonged time even with exposure to bactericidal concentrations of antibiotics. These bacteria are termed “persisters”. Bacterial persistence can be triggered due to stress (e.g., starvation), or spontaneously, even occurring when bacteria are in steady-state exponential growth. To treat biofilm infections caused by such tolerant cells, antibiotic concentrations upwards of 1000 times higher than those effective against planktonic cells may be necessary. Reaching such a high concentration through systemic administration in living beings without causing toxicity is not generally feasible. The general mechanisms of biofilm tolerance and resistance are as follows:

- Physical tolerance – The matrixome restricts the penetration of antimicrobial agents (including reactive oxygen species from phagocytic cells), preventing them from effectively reaching and destroying sessile cells.
- Physiological tolerance – In biofilms, persister cells, that are often metabolically inactive, are resilient to antimicrobial agents. The microenvironment inside a biofilm is different than its surroundings, with alterations in pH, nutrient depletion, and an increase in the anaerobic environment inside the biofilm reducing antimicrobial efficacy. The SOS stress response activated by oxidative stress and nutrient starvation, can also confer bacterial survival in biofilms.
- Adaptive tolerance – In biofilms, microorganisms can have altered gene expression. For example, *P. aeruginosa* exhibits induced AmpC β-lactamase-production, lipopolysaccharide alteration and increased efflux pump activity when in a biofilm environment, all of which confer further protection against antibiotics.
- Secreted outer membrane vesicles (OMVs) of biofilms can inactivate antimicrobials.
- Genetic exchange occurs at a higher frequency in biofilms, which may help disseminate antibiotic resistance genes.
- In biofilms, often due to their low oxygen, several efflux pump-encoding genes are more expressed, thereby facilitating pumping out of antibiotics, as well as biofilm formation, stimulating factors like siderophores, which are designed to capture iron for bacterial survival.

Bacteria in biofilms can evade and modulate the immune system, thereby preventing their destruction by host defenses. Antibodies are also not effective in clearing bacteria in biofilms. The antibodies produced against sessile bacteria can however form immune complexes on the surface of biofilms and damage the tissue.

Economic impact due of biofilm device-associated infections

In 2018, the medical device market in the United States (US) surged to approximately 90 billon USD. Projections of the size of the medical device market for 2030 are USD 300 billion for the US, and USD 200 billion for China. Catheter-associated infections are the most common manifestations of biofilm formation. It has been estimated that the annual cost associated with infections of CVCs is USD 11.5 billion, and CAUTIs cost USD 1 billion, globally. Similarly, biofilm-associated ocular infections cost around USD 760 million per year, while the global cost of treating/removing biofilm-associated infections in pacemakers and defibrillators has been estimated to be USD 220 million and for VAPs USD 920 million annually.

Strategies to prevent and manage DAIs due to biofilm formation

The infections associated with biofilms do not normally respond to antibiotics, and progress into chronicity. Though planktonic cells can be killed, the sessile cells encased within biofilms are protected. Therefore,

different strategies have been employed for the prevention or management of DAIs. Surgical intervention or removal of devices are warranted to treat recurring infections attributed to biofilms in tissues or devices, but these procedures can bring further complications. Removing implants such as prosthetic joints and pacemakers can result in further undesirable consequences due to inherent surgical risks as well as disruption of biofilms leading to seeding of pathogens into the bloodstream.

Photodynamic therapy and water jets are some of the physical means of antibiofilm measures. Similarly, the use of low-intensity ultrasound waves can also help to break up and destroy biofilms. However, patient safety is always a crucial consideration to be taken while adopting any strategy, and these physical means of biofilm destruction may not always be appropriate or indicated.

Different biomaterials have been developed with surface modification strategies by physical means (gel coating, nano-coating, metal ion deposition, graft polymer brushing) or by chemical methods (polymerization of surface atomic radicals) which can act either by killing microbes, preventing their colonization, or in combination, encompassing both antimicrobial and anti-biofouling properties. Ideally, any compound that is being used for the antibiofilm activity should have rapid action with multiple mechanisms, be active in different environmental conditions, act on both metabolically active as well as inactive cells, should be immobilizable on a surface, inhibit matrix synthesis, and interfere with biofilm regulatory pathways.

Antimicrobial coatings can function in a myriad of different ways: a) release sterilization, in which there is sustained release of antimicrobials which kill bacteria before colonization and biofilm formation; b) contact killing, which involves immobilization of antibacterial agents on the surface by covalent bonds without allowing them to leach out, ensuring a persistent presence on the surface; c) self-cleaning coatings, in which superhydrophobic surfaces have “lotus leaf” effects, whereby microbes are carried away by water droplets rolled down on such surfaces, preventing their contamination.

Coatings based on titanium- and titanium dioxide, iron and iron oxide, silver, magnesium hydroxide, 2D-nanomaterials such as graphene oxide, black phosphorus, molybdenum disulfide, boron nitride, gold nanocomposites, have been found to be effective for their antibiofilm activity; however, International Agency for Research on Cancer (IARC) has classified titanium dioxide nanoparticles as a possible carcinogen. Studies on nanomaterial-based antimicrobial coating for biomedical implants are mainly limited by the lack of sufficient *in vivo* studies, particularly their long-term effects in animal models.

Antimicrobial peptides (AMPs) are a diverse class of evolutionally conserved molecules that are components of the innate immunity of all organisms. These AMPs exhibit potent antimicrobial activity and have been found to disrupt pre-formed mature biofilms, as well as inhibit microbial adhesion on surfaces. Different antibiofilm mechanisms have been described for AMPs which include motility inhibition, quorum quenching, disruption or degradation of the membrane potential of sessile cells, degradation of the matrixome, inhibition of the alarmone system to avoid the bacterial stringent response, and repression of genes responsible for biofilm. They have shown antibiofilm activity either as monotherapy or in combination with conventional antibiotics or antifungals, or with other AMPs.

Antimicrobial polymeric nanoparticles are promising antimicrobials to combat biofilm infections. Their multivalency allows for enhanced microbial cell recognition and binding. Currently, smart coatings are being developed to deliver antimicrobials specifically when bacteria are present. When these coatings are triggered by changes in the chemical environment, they are referred to as chemo coatings. Nano, micro and millimeter scale robots, which are controlled remotely by chemical fuel catalysis, or magnetic, light, and ultrasound fields, are the recent technologies employed for biofilm disruption, with their diverse capabilities to maneuver through narrow spaces and perform precise tasks. Though biocompatibility and scalability of production can be the existing hurdles for the implementation in practice, carbon dots are another unique substrate to

disrupt the biofilm. Antibiotic lock therapy is another method in which catheter lumens are filled with pharmacologically concentrated antibiotics for an extended period, allowing them to exhibit an antibiofilm role.
Bacteriophage treatment is an emerging strategy due to its host-specific bacteriolytic activity and anti-EPS properties. However, eliminating mature biofilms through phage therapy is sometimes limited due to the complexity of the biofilm matrix, phage tolerance due to bacteria with reduced metabolism, and host tropism. The matrixome and tolerance properties can confer insusceptibility in microbes by other strategies too. Phage receptor presentation can be downregulated by the QS phenomenon in bacteria as another underlying mechanism for the insusceptibility of bacterial pathogens in biofilm. Nonetheless, the use of phage cocktails, phage engineering and phage-AMP combinations are emerging strategies to overcome the limitations of phage therapy for biofilm.
Different natural products such as honey and essential oils have also been studied as antibiofilm agents. Phytochemicals are plant-derived natural products which have been found to possess antibiofilm properties. They are active against different essential stages of biofilm formation, e.g., adhesion, motility, QS and EPS production. However, further investigations are required to develop their specific therapeutic and clinical applications, ensure their safety, and confirm their *in vivo* effectiveness, without allowing the development of resistance against them.
Inhibition or eradication of biofilms poses a problem not only in single-use medical devices but also in reusable medical devices. Multiple sequential procedures are undertaken to ensure appropriate reprocessing of reusable devices for clinical use. Precleaning and cleaning are some of the crucial steps involved. However, these steps are frequently overlooked, consequently, there is a high chance of further development of biofilms from previous runs on such devices over various cycles of use. To get rid of such biofilm, effective device cleaning and proper reprocessing, including high-level disinfection or sterilization followed by thorough drying, is recommended.

Conclusion

Biofilms on medical devices present a complex microenvironment allowing microbes to survive as antibiotic and immune-tolerant cells. Multiple approaches have been devised to mitigate the menace of biofilms. Therapeutic strategies should encompass not only matrixome degradation but also the elimination of embedded microorganisms with minimal adverse effects on tissues or the implants themselves. Future research should focus on multidisciplinary specialties including microbiology, biotechnology, medicinal chemistry, material science, chemical engineering, and clinical science. Antimicrobial coatings on biomaterials have played important roles in preventing microbial adhesion and hence biofilm formation on medical devices. Antimicrobial peptides or their mimics as coatings, as well as the synergistic activity of antimicrobial peptides with conventional antibiotics, are promising avenues in the prevention of biofilm-associated infections. All interventions, if successful, will help minimize the risk of patient mortality or morbidity, and reduce the high economic burden of biofilms. To date, most of the antibiofilm studies are based on *in vitro* studies which need to be replicated *in vivo* in animal models and clinical trials in the future.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 59

Healthcare-associated infections surveillance. Why and how

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Introduction

Recently, there has been an increased focus and attention on healthcare-acquired infections (HCAIs) which have devastating human and economic costs. These potentially avoidable infections increase hospital length of stays, morbidity and mortality and can worsen the economy of any country through unsustainable budget allocations or reallocations to cover excessive costs attributable to such infections. For this reason, everyone working in healthcare settings, patients and/or consumers of healthcare must work together to minimise avoidable infections to help ease human suffering and associated economic burden. This work must focus on establishing and sustaining robust clinical governance structures which support the implementation of evidence-based recommendations to get it right the first time for every patient who has access to healthcare. Furthermore, these structures must support or make provision for methods or systems that enable healthcare settings to collect robust data on key clinical quality metrics including data on HCAI.

First things first – Humans err, but do we ever learn from our mistakes?

In his influential book, Black Box Thinking, Matthew Syed discusses pertinent issues around the devastating impacts of cognitive dissonance which is the inner tension people feel when their beliefs are challenged by evidence. He reiterates the fact that 'the human mind is wired up to closing its eyes to inconvenient truths', with a tendency to deny errors or mistakes or simply become dismissive and therefore resistant to learn and change from the things they don't always get right. Within healthcare, this may suggest that people may feel less confident or intimidated to open up about their mistakes or challenge those in authority when mistakes happen simply because they as individuals or those in senior positions are working hard to protect their egos and the reputations of their organisations at the expense of exposing errors which may help save lives of current and future patients. Healthcare settings then end up operating in a closed-loop mechanism where those who attempt to challenge authority are shut down and those making mistakes are less likely to speak up due to fear of consequences for themselves as professionals or an organisation's reputation. This results in lost opportunities to potentially improve patient safety and consequently make the world better. It is however acknowledged that healthcare professionals will put defences when their professionalism is challenged because they don't want to think of themselves as inept, meaning that opening up about mistakes becomes traumatic and may resort to blaming others instead as a self-defence mechanism. These kinds of behaviours may in part explain why little progress is being made around the world today in reducing avoidable errors in

most healthcare settings where the reporting isn't good enough, with most organisations concealing data that has the potential to damage their reputations. Sadly, as Syed put it, "Intelligence and seniority when allied to cognitive dissonance and ego is one of the most formidable barriers to progress today." A different approach is therefore required to improve psychological safety in healthcare organisations through the creation of open and transparent cultures where people feel able to honestly report and address mistakes in supportive environments. This should help to address some of the costs attributable to avoidable infections and associated litigation costs due to medical negligence claims in healthcare. Openness and honesty coupled with a readiness to give full explanations of circumstances surrounding errors and offering an apology when applicable will not only promote learning organisations to continually improve patient experience and outcomes but will potentially reduce medical negligence claims. There is therefore a need for better systematic and independent processes to help organisations create psychologically safe workplace environments which liberate staff from becoming intimidated by hierarchical structures and where mistakes are not stigmatised. These safe workplace environments will support especially those staff with fixed mindsets to shift towards growth mindsets which should improve overall communication and team relationships and dynamics, consequently impacting their performance and patient outcomes. The following two questions are worth exploring when all this is applied to HCAI prevention and surveillance. Could stigmatisation of errors which is linked to cognitive dissonance be one of the reasons why many healthcare organisations around the globe don't have robust HCAI surveillance programmes today? Is there potential to improve HCAI surveillance by embracing human factors or ergonomics and psychological safety with what is already working to achieve optimum outcomes for patients? Some of the answers to these questions are beyond the scope of this chapter but are worth pondering upon.

HCAI surveillance: a historical perspective or background

Traditionally, organisations like the United Kingdom (UK) Health Security Agency (UKHSA), the Centres for Disease Control (CDC) in the United States, and the European Centre for Disease Prevention and Control (ECDC) in Europe have and continue to lead on coordination of HCAI surveillance programmes in their respective countries or regions. Additionally, point prevalence surveys are sometimes used to gain insight into healthcare settings' HCAI burden periodically. It is acknowledged that some of the HCAI surveillance programs are not as robust as they can be, thus there is still room for improvement. The latest point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals in 2022-2023 highlights increased HCAI burden stratified by different infections. Like previous PPS results, SSI is the 3rd most common HCAI after healthcare-acquired pneumonia (HAP) lower respiratory tract infections and urinary tract infections (UTI).

These results are echoed by the World Health Organisation (WHO) and many other experts in infection prevention and control who highlight SSI as one of the most frequently occurring adverse events with more than one in three deaths among SSI patients being attributed to the SSIs. This calls for urgent revolutionary strategies to tackle the growing threat to humanity by preventing these avoidable infections because with the present lack of open and transparent reporting of HCAI and other latent errors within healthcare, currently reported rates are likely to be gross underestimates of the true HCAI and associated collateral damage burden. What is not clear from the data on all HCAIs is the interconnectedness among the different HCAIs. For example, it is unclear from the ECDC PPS report how many of the patients with other infections such as UTI and HAP were a direct or indirect result of collateral damage linked with avoidable surgical infections, harm or SSIs. This presents a window of opportunity for healthcare settings to consider different perspectives that

potentially uncover reasons why so many patients are still incurring avoidable HCAI or harm in healthcare despite years of hard work trying to improve the surveillance of healthcare-acquired infections and their prevention thereof.

What is surveillance in the healthcare-acquired infection realm?

Surveillance can be used to monitor behaviour and gather information for informing decisions for which an exercise was set up to achieve or to fulfil the intended purpose. Sadly, surveillance has the potential to violate people's privacy and may provide evidence that challenges people's beliefs potentially rendering individuals to error denial or blaming others for their own mistakes to protect their own egos. This fear of being unfairly blamed or punished through available evidence means that rationales for undertaking surveillance must be justified, with consent being sought where necessary to dispel the potential fear of the unknown. It is acknowledged that in situations where surveillance is used to protect citizens or the public from crime, harm or safeguard vulnerable individuals, the need for consent can be waived. HCAI surveillance entails close monitoring of any infections that patients or consumers of healthcare acquire whilst receiving care or when in contact with healthcare facilities. According to the Department of Health, surveillance may be used to inform health protection, health improvement and health service delivery. It must be acknowledged that improvements are only possible where healthcare settings set up and sustain robust HCAI surveillance programs which provide a mechanism for tracking HCAI trends and benchmarking against other centres in psychologically safe workplace environments and communities. In Lord Kelvin's own words:
"To measure is to know, if you cannot measure it, you cannot improve it".
In those psychologically safe environments, robust data collection and active feedback mechanisms that are coupled with thorough root cause analysis or detailed investigation information on HCAI help to reveal potential areas for improvement. Staff are more likely to readily take corrective action or institute measures to prevent recurrence or other patients incurring the same avoidable HCAI or harm when they feel supported. There is no doubt that undertaking robust HCAI surveillance can help alleviate suffering and costs attributable to avoidable harm and yet surveillance has generally been thought to be resource-intensive and in some cases intrusive to people's or organisations' rights to privacy. Even though the former generic hypothesis regarding resource constraints features in many HCAI surveillance discussions, it is acknowledged that HCAI, specifically, surgical site infections (SSI) are costly. Yet, simple non-costly interventions can save healthcare organisations money whilst improving outcomes for patients, meaning that there must be a shift in attitudes and perceptions around the subject to persuade organisations to support more robust HCAI surveillance programmes.

How to undertake HCAI surveillance?

Different paper or digital data collection methods can be used to gather HCAI data which can be reviewed and actioned via different infection prevention teams, committees or multidisciplinary teams within healthcare settings or via formal and informal HCAI surveillance networks. Interrater reliability which is the degree of agreement between independent observers who assess the same phenomenon, in this case, HCAI that fit certain criteria or published definitions, is reported to be poor with manual or paper HCAI surveillance records, meaning that a shift towards digital technologies which harness the use of semi- or fully automated

surveillance systems is preferable. Objective data collection tools must be used to reduce the subjectivity that may be linked to the manual recording of HCAI criteria or data. From a global SSI prevention and surveillance champion's perspective which derives from her experiences of setting up a successful SSI surveillance service at a large acute organisation in central London, surgical wound documentation is thought to not always reflect the true clinical picture, hence not robust enough on paper records or digitally. For example, she often saw 'wound is oozy' being recorded on available healthcare records, which alone is not good enough objective criteria to inform clinical decision-making. A wound oozing pus or persistently oozing serous discharge depending on the holistic clinical picture may require urgent attention. Conversely, a wound oozing serous fluid within 3 days after a surgical procedure may not necessarily need a treatment intervention depending on the full clinical picture. Furthermore, a wound oozing serous fluid, and breaking down, coupled with fever, redness, and swelling, is likely to trigger a swift response. Standardised objective wound assessment documentation therefore makes a huge impact on subsequent wound management and is needed in SSI surveillance and prevention to improve the accuracy and timeliness of clinical decision-making processes that impact patient outcomes. Standardising surgical wound documentation can be done in healthcare settings whether paper or electronic healthcare records are used, with digital transformation being the preferred option given the myriad benefits it provides.

Digital transformation and automation in HCAI surveillance

Digital transformation improves the way healthcare organisations operate, releasing time to care thus helping to make care more personalised. It also helps in the efficient collection of important quality metrics, saving money and improving patient safety or outcomes in the process. There is no doubt that digital transformation joins up services, thereby improving interoperability. When data is available in real-time via dashboards or electronic records, it aids in timely interventions and better use of clinical and professional care information in key clinical decision-making. Frontline-driven prospective digital data collection methods are preferable as they allow healthcare professionals to review wounds in real time and validate symptoms before commencing treatment or corrective action. Trend data can be used to measure the efficacy of any antibiotic treatments, whilst other patient safety or quality improvement data can be easily retrieved during detailed investigations, for audit or assurance purposes. Organisations without HCAI surveillance programs are urged to design objective tools that capture a surgical wound status or potential infection or inflammatory markers in real-time from where HCAI or SSI criteria or other signs can be derived. This helps to expedite preventative and treatment interventions which in turn improve overall patient outcomes.

Digital surveillance is a fast-growing area with many HCAI including SSI surveillance and prevention technologies now available. In Germany, the well-established Krankenhaus Infections Surveillance System (KISS) network uses semi-automated methods to monitor and identify HCAI trends. Aghdassi and colleagues highlight in their publication in 2023 that participation is variable despite benefits being widely acknowledged. The Netherlands uses the PREventie van ZIEkenhuisinfecties door Surveillance (PREZIES) which employs automated HCAI tracking tools. The PRAISE network (Providing a Roadmap for Automated Infection Surveillance in Europe) comprising experts from ten European countries coordinates the development and implementation of automated HCAI surveillance systems in Europe. The CDC has also made advances through integrating automated surveillance into their National Healthcare Safety Network (NHSN) which takes advantage of existing electronic health records (EHRs). The picture is similar in the United Kingdom where the UKHSA coordinates HCAI surveillance in England. An HCAI Data Capture System (DCS) web-based application collects patient-level mandatory surveillance data on infections such as *Staphylococcus aureus* (methicillin-resistant

Staphylococcus aureus (MRSA), meticillin-sensitive *Staphylococcus aureus* (MSSA), and Gram-negative bacteraemia (*Escherichia coli, Klebsiella* spp., *Pseudomonas aeruginosa*) and *Clostridioides difficile* infections, thus providing an integrated platform for HCAI data analysis and reporting. The current degree of digital automation of surveillance of HCAIs varies, with the most frequently targeted types of HAI for automated surveillance being *C. difficile* infections, bloodstream infections (hospital-onset and/or central line-associated) and surgical site infections according to the ECDC PPS 2022-2023 report.

Interestingly, participation in SSI surveillance networks included in the last ECDC PPS 2022-2023 report, revealed that 37.1% of hospitals from 24 EU/EEA countries were engaged, an 18% decrease from the ECDC PPS 2016–2017 data. This was largely attributed to the United Kingdom no longer being included, where their participation in SSI surveillance had been high in 2016–2017. Some countries like Iceland, Montenegro and Serbia did not participate in SSI surveillance networks whereas up to 75% or more participation was reported in Austria and Spain. This highlights discrepancies that can exist in HCAI surveillance uptake between countries in the same continent or region and between different hospitals in one country.

A closer focus on SSI surveillance in the United Kingdom

The United Kingdom has made significant progress in SSI surveillance and prevention work in various specialties, acknowledgement to the UK Health Security Agency's SSI Surveillance Service which has been running for many years. Although this program has its limitations due to varying participation from various healthcare settings, it does highlight the powerful impacts of well-coordinated SSI surveillance services. For example, SSI incidences have declined within orthopaedics since mandating data collection for at least one quarter annually. More reductions within other specialties, notably cardiac surgery have been reported, attributed to relentless champions who have fiercely campaigned through cardiac SSI networks and own hospital HCAI surveillance programmes or settings. In a landmark report by Professor Mike Reed: *Time to Act: A State of the Nation Report on Surgical Site Infections in the UK,* the status of SSI surveillance and prevention services in the UK as of 2020 was presented. In the report, Reed reports how he has seen first-hand the devastating consequences of SSIs for patients and the challenges of implementing robust surgical patient safety programmes. There is an acknowledgement from Mike Reed's report that there is still more work to be done among the four UK nations (England, Wales, Scotland and Northern Ireland) to raise the profile of surgical site infections, considering how complex it is to reduce these infections depending on the location of surgery, age of the patient and comorbidities. Furthermore, there is variable participation by various health boards in Wales – some not reporting SSI surveillance data at all, whereas in Northern Ireland SSI surveillance data is limited as it's mostly reliant on 5-year ECDC prevalence surveys according to Reed. The progress in Scotland where SSI surveillance is mandated for caesarean section, hip arthroplasty and elective large bowel surgery is commendable, however about £183 million per year is attributable to HCAI, meaning that there is still work to do to reduce incidences of avoidable harm and associated costs.

More work is required to reduce SSI surveillance and prevention inequalities in the UK and globally to allow healthcare settings to be more open and transparent with their challenges and opportunities that when shared with others can help to make a significant difference to outcomes for all patients wherever they may receive care globally. The following clinical scenario is presented to help us better understand the devastating human, economic and climate impacts of HCAI in settings without robust or credible HCAI surveillance programmes.

A clinical scenario

Imagine an acutely unwell post-cardiac surgery SSI patient in an intensive or critical care unit who develops sepsis and ends up having open gastrointestinal surgery for a perforated bowel. This patient has a high Body Mass Index (BMI), type 2 diabetes and Chronic Obstructive Pulmonary Disease (COPD). The patient has a wound class of contaminated/infected and had already been commenced on antibiotics to manage the sepsis and gastrointestinal infection before surgery. Additionally, the patient receives surgical antibiotic prophylaxis and continuing antibiotic treatment due to persistent sepsis. The patient develops an organ/space infection after their second surgical procedure as an inpatient and requires negative pressure therapy dressings to manage their infection. Furthermore, they have invasive lines or devices to administer fluids, feeds and medications as well as manage excrements etc. This patient is likely to suffer significantly from their infection, requiring multiple surgical and medical interventions. They also become prone to deconditioning and pressure sores which may ultimately become chronic wounds due to prolonged hospital stay. They are at an increased risk of developing Hospital Acquired Pneumonia (HAP) due to prolonged ventilation and may require a surgical tracheostomy for prolonged oxygen requirements. They may also develop a urinary tract infection, *Clostridium difficile* and other HCAIs which all may subsequently increase the risk of antimicrobial resistance. Worst case scenario this patient may die from their infection.

The above infections and associated collateral damage may lead to huge economic and human costs for the patient, healthcare settings and respective countries/global economic prospects. Without robust HCAI surveillance and active data feedback to relevant clinicians, other patients may continue to suffer from avoidable harm. Furthermore, the risks presented by the patient's comorbidities cannot be ignored, meaning that health promotion and SSI prevention aspects must be combined to give the patient the best chance of survival from this hospital episode. HCAI surveillance must therefore encompass the whole health economy, embracing initiatives that aim to enhance populations' health through engagement in healthy living in their respective communities.

The above clinical scenario highlights that SSI also present collateral damage due to other HCAIs that may develop because of extended treatments and length of hospitalization, however, the collateral damage links do not appear to be presented in most published HCAI data. For example, in the PPS 2022-2023 report, 23% of patients were receiving antibiotics for treatment of infections at the time the survey was undertaken. With this acknowledgement, there is a need for healthcare professionals to review HCAI data from a different perspective to not only address antimicrobial resistance threats but to also explore the overall HCAI burden in surgical patients that is linked to avoidable surgical site infections. As already alluded to above, there is an urgent need to scale up SSI Prevention interventions in the UK and globally to achieve consistency in getting those tangible outcomes for all surgical patients. In the theme of scaling up interventions, the global SSI Prevention group has introduced the Prevent One SSI, Prevent Collateral Damage (P1PCoDAM®) strategy coupled with a strong emphasis on establishing multistakeholder collaboratives that promote learning from each other. As part of this new SSI Prevention movement, there is a heightened need to convince various stakeholders (patients, public or consumers of healthcare, healthcare leadership, politicians, industry and policymakers) to work together to reduce unwarranted variation in surgical services. Dismantling silo working mentalities not just within HCAI surveillance for different alert microorganisms or across the whole health economy, patient groups and public figures as well as among other patient safety and quality improvement groups is a top priority for the new global group. This will help to establish and maintain effective communication channels that enable all to share HCAI and associated collateral damage data. It is hoped that adopting the P1PCoDaM® mantra will enable surgical teams to consider interventions and collaborative working partnerships that they would not perhaps have previously considered. This should also help organisations to

challenge their status quo by extending collaboration beyond their immediate teams which in turn helps to break those silos that may inhibit productive working partnerships. A clinical scenario presented above therefore clearly demonstrates why this approach should become the new normal in surgical patient safety and other HCAI surveillance, which presents a window of opportunity for HCAI surveillance ACTION!

A window of opportunity: proposals for new look healthcare-acquired infection surveillance programmes

The new Prevent One SSI, Prevent Collateral Damage (P1PCoDAM®) approach facilitates a holistic approach to surgical patient safety, with a strong focus on generic HCAI prevention coupled with scope to cover aspects of health promotion, HCAI surveillance and prevention strategies or initiatives that improve population health outcomes from a very young age. Considering cognitive dissonance links to mistakes that happen in healthcare and the historical poor uptake of robust HCAI surveillance programmes or poor progress to date in alleviating human suffering caused by avoidable infections, there is a need to do things differently. With due consideration for Henry Ford's own words "If you always do what you've always done, you'll always get what you've always got," the newly formed SSI prevention group has identified a window of opportunity to make lasting changes within HCAI surveillance in the UK and globally. This interesting novel concept of preventing one surgical site infection, and preventing collateral damage presents healthcare professionals with proposals for a different approach to embracing holism in healthcare-acquired infection prevention and surveillance. The rest of the SSIP® group proposals that are being presented alongside the P1PCoDAM® approach or mantra promise to be a very welcome game-changer potentially changing the way HCAI surveillance is viewed for good.

Whereas previously HCAI surveillance has been managed in silos such as separately reporting and analysing *C. Difficile* surveillance, Gram-negative bacteraemia surveillance, and UTI surveillance data without an apparent direct link being established in HCAI surveillance reported data, the new proposals recommend data is managed holistically with collateral damage links being highlighted for surgical patients. The new SSIP® Strategy embraces a multistakeholder, multi-faceted approach to SSI prevention, encompassing, health protection aspects at the population level, preoperative, intraoperative, and postoperative interventions, as well as ongoing quality improvement efforts and staff education. The key proposals of this novel surgical patient safety initiative which are available from a British Journal of Nursing publication that was written by Chiwera aim to increase visibility and activism around SSI prevention (SSIP), improving the uptake of evidence-based SSI prevention recommendations in all healthcare and community settings through championing dedicated and delegated responsibility for SSIP implementation science via an SSI prevention champion model in all healthcare and community settings. This should help to reduce avoidable surgery-related harm in all patients/animals via a 'one health approach', which supports robust SSI surveillance and prevention strategies in all settings. Refer to SSIP.com and Chiwera for detailed SSIP summary proposals and key SSIP objectives. The P1PCoDAM® approach is then added as the unique novel aspect of the new look HCAI surveillance program. With this new approach, healthcare professionals are prompted to look beyond the avoidable surgical site infection and consider more fully any associated collateral damage and anything else that could have been addressed at the population level. This refers to any health promotion or management interventions that could have been used to prevent or mitigate patient risk factors that increase SSI risks. In the above clinical scenario, modifiable and potentially non – modifiable risk factors at the population level, such as high Body Mass Index (BMI), type 2 diabetes and Chronic Obstructive Pulmonary Disease (COPD) must be carefully

considered or reviewed to establish if they could potentially have been addressed to minimise SSI risk and associated collateral damage.

Why embracing SSIP recommendations has the potential to significantly improve the uptake of robust HCAI surveillance programmes

Different, more effective ways of feeding back that data to respective community healthcare providers, as well as voluntary and non-voluntary organisations and patient groups, must be considered, aiming to engender more targeted preventative or corrective action for future patients or generations. In line with global alignment with the 17 United Nations global sustainable development goals, SSIP aims to address the following among other goals.

a) **Goal 4. Quality education** by ensuring SSI prevention education is part of the education curriculum from a very young age to post-graduate education programmes. This means that addressing preventable high BMI and type 2 diabetes due to unhealthy lifestyles can be effectively promoted and managed through encouraging healthy lifestyles such as exercising, healthy eating and stress reduction through various well-being initiatives and education curricula at various stages spanning primary education to academia or university level education. Examples of devastating consequences of SSIs from available HCAI data can therefore be embedded within health promotion education from various well-being initiatives to demonstrate the implications of not managing one's health not just for immediate health outcomes but for outcomes following surgery, where said risk factors will have a huge bearing on patient outcomes. SSI data should therefore be readily available to holistically inform the health of the nation and proposed interventions to address SSI prevention at the population and healthcare setting level.

b) **Goal 10. Reduced inequalities** by helping to reduce inequalities in surgical patient outcomes between hospitals in a single country to different regions and countries around the world. This will be achieved through supporting the WHO calls for universal health coverage, and/or health for all and One Health agendas. As already mentioned above, improving health outcomes for all surgical can only be possible where organisations are transparent and accountable for their respective surgical services provision and patient outcomes coupled by a willingness to share SSI and associated collateral damage data. When these data elements are embedded with educational curricular and global patient safety agendas, they're likely to positively impact overall patient and population health.

c) **Goal 13. Climate action** by reducing avoidable SSIs using the P1PCoDAM approach, together with wider initiatives to reduce health inequalities and promote quality education across the education spectrum, SSIP® is contributing to global agendas on promoting a healthy sustainable future for all. Climate implications are clear from the above scenario, where prolonged hospitalisations and multiple returns to the operating rooms as well as the various medications and equipment used to manage the patient are likely to contribute to climate deterioration. All this work requires various stakeholders to work together with a common goal of making a difference for all patients wherever they may receive care, hence SSIP's desire to work with the different multistakeholder collaboratives that are directly or indirectly involved with surgical care provision and assurance of the best standards thus supporting the United Nations's

d) **Goal 17. Partnerships for the goals** by collaborating with various stakeholders to further our surgical patient safety initiatives agenda.

To achieve all the above, i.e., SSIP®'s strategic goals whilst embracing the UN's global sustainable goals and the novel P1PCoDAM ® approach, it is proposed that various work streams responsible for developing the required resources and subsequent dissemination thereof are commissioned to support wider HCAI surveillance agendas. SSIP® workstreams encompassing SSIP's 'Prevent one SSI, prevent collateral damage' mantra. All healthcare settings must ideally have identified leads for the following healthcare-acquired infections (HCAI) in surgery:

a) Sepsis.
b) Intravenous access device-related bacteraemia.
c) Catheter-associated urinary tract infection (CAUTI) related complications.
d) Hospital-acquired pneumonia (HAP)
e) *Clostridium difficile* infection (CDI).
f) Antimicrobial resistance / Antimicrobial stewardship.

Note that the application of the 'Prevent one SSI prevent collateral damage' mantra will differ from country to country depending on SSI surveillance and prevention journey status.

By establishing firm multistakeholder partnership goals where open communication and transparency are promoted across the whole health economy to not only help to reduce unwarranted variations but also to avoid re-inventing the wheel, the new SSIP® group hopes to open much-needed dialogue and data sharing among the various stakeholders across the whole health economy, helping to create the new look HCAI surveillance programs globally. Proposed SSIP® champions will act as catalysts for initiating and sustaining the new look HCAI surveillance programs which is guaranteed to transform surgical care provision, health promotion, SSI surveillance and prevention globally. This requires support from various multi-stakeholder collaboratives, healthcare leaders, politicians, patients and other consumers of healthcare or the public.

Conclusion

Various organisations have traditionally been responsible for collating country and regional HCAI data. The uptake of HCAI surveillance has been variable between hospitals in the same country and between different countries, with other countries lacking robust HCAI surveillance data due to the perceived resource intensiveness of the whole data-gathering exercise. Yet, it is widely acknowledged that HCAIs have devastating consequences for patients, healthcare settings and global economic prospects. Furthermore, inequalities still exist between surgical care or generic healthcare provision between hospitals in one country and between different countries globally which appear to have remained unchallenged despite various humanitarian campaigns and interventions. This may in part be attributed to cognitive dissonance and error denial issues that span humanity and the healthcare spectrum, preventing people from willingly acknowledging, reporting and challenging errors that occur in their settings for fear of damaging their or organisations' reputations or simply protecting their own egos. To help combat deteriorating climate deterioration, which is also impacted by HCAI among other causes, the new SSIP® group proposes a novel approach that encompasses multistakeholder collaboration coupled with strong SSIP® proposals which embrace the P1PCoDAM® approach aimed at dismantling the current silo working mentalities that still exist across the whole health economy as well as within infection prevention and control in general. By adopting the new look HCAI surveillance recommendations, working collaboratively with the World Health Organization, the United Nations, and various public Health Agencies, healthcare settings and other stakeholders together with proposed SSI prevention champions in different countries, it is hoped that a new revolutionised approach to HCAI surveillance that captures

a more holistic picture of not just SSIs but associated collateral damage, as well as modifiable and non-modifiable SSI risk factors, is adopted in all healthcare settings globally. This will help to facilitate more targeted SSI prevention and health promotion interventions at local hospitals or healthcare settings as well as at the population level, helping to improve overall surgical patient outcomes. This approach will no doubt be easily transferrable to other generic HCAI surveillance and other patient safety and quality improvement approaches. The time is now for multistakeholder collaboratives to come together, learn together and adopt novel HCAI surveillance and other available patient safety and quality improvement initiatives aimed at minimising avoidable infections to help ease human suffering and associated economic burden. Digitised HCAI surveillance has transformational potential to improve operational efficiency and must be embraced where available.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 60

Innovative techniques for infection control and surveillance in hospital settings

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Introduction

Hospital-acquired infections (HAIs) constitute a significant challenge in the field of healthcare, contributing to a considerable burden of morbidity, mortality, and increased healthcare costs on a global scale. It is estimated that approximately 7 out of 100 patients in high-income countries and 15 out of 100 in low- and middle-income countries are affected by at least one HAI during their hospitalization. This highlights the importance of infection control measures for improving patient safety and clinical outcomes. The conventional approach to infection surveillance relies on manual data collection and monitoring. While this method has proven effective, it is resource-intensive, time-consuming, and susceptible to delays in outbreak detection. Consequently, there is a growing interest in utilizing innovative digital tools to support or replace conventional surveillance techniques in healthcare settings. The recent advancements in artificial intelligence (AI) and machine learning (ML) have opened new perspectives for enhancing infection surveillance and control strategies. These technologies offer the ability to analyze vast amounts of healthcare data, enabling faster

and more accurate detection of infection trends, early outbreak identification, and tailored interventions. The transition from manual to automated systems has demonstrated the potential to improve accuracy, reduce healthcare professionals' workload, and enhance resource allocation in healthcare institutions.
Integrating AI-driven technologies into hospital settings also poses challenges, including the need for interdisciplinary collaboration, data security, and the adaptation of healthcare professionals to new tools. Nevertheless, the potential of these innovations, particularly in addressing healthcare-associated infections such as surgical site infections (SSIs), catheter-associated urinary tract infections (CAUTIs), and ventilator-associated pneumonia (VAP), is undeniable.
This chapter explores the most recent infection control and surveillance techniques in hospitals, focusing on the application of innovative digital technologies, and offers insights into the evolving landscape of hospital infection management.

Traditional methods for infection prevention and control in hospital settings

Traditional infection prevention and control methods in hospitals have relied heavily on manual surveillance techniques. This approach entails collecting and reviewing data by healthcare professionals, primarily infection control teams, who are responsible for monitoring trends (mainly troughs point prevalence study) and conducting audits to identify potential risks of infection outbreaks. These teams routinely review patient records, laboratory results, and other relevant clinical data to assess infection rates within the hospital. In addition to real-time monitoring, retrospective data analyses are frequently conducted to identify patterns that might not be immediately apparent.
Manual surveillance is frequently a labor-intensive process, requiring the dedicated input of personnel to manually gather, review, and interpret large volumes of data. Infection control practitioners must examine individual cases to determine whether an HAI has occurred, which involves sifting through comprehensive clinical and laboratory data. These audits are essential for ensuring compliance with infection prevention policies; however, they are also time-consuming and, in many cases, susceptible to delays in reporting. As a result, the identification of outbreaks or clusters of infections can be significantly delayed, compromising interventions' timeliness.
A significant drawback of conventional surveillance techniques is their dependency on passive data aggregation. This typically involves healthcare professionals reporting infections after they have occurred, which means that detecting an infection or outbreak is inherently retrospective. Consequently, these methods are reactive rather than proactive, with infection control teams responding to events after they have unfolded. This system can lead to delays in recognizing infection clusters, allowing them to spread more widely before control measures can be implemented.
Furthermore, manual surveillance is susceptible to human error, with inconsistencies in data collection, reporting, and interpretation all posing significant challenges. Given the complexity and volume of data, healthcare professionals conducting these reviews may overlook critical details, leading to underreporting or misclassifying infections. Additionally, because these systems rely on healthcare workers' vigilance and willingness to report, the process can be inconsistent, especially in high-pressure clinical environments where infection control may not be the immediate priority.
In conclusion, traditional methods of infection surveillance in hospitals, while foundational to infection prevention, are fraught with limitations. The reliance on manual data collection and passive surveillance, coupled with the time-consuming nature of audits, results in delayed responses to infection outbreaks and increases the risk of errors. Despite these drawbacks, these techniques have remained essential in infection

control practices, although they are increasingly being supplemented and even replaced by more modern, semi-automated systems.

The emergence of digital and innovative technologies in surveillance, prevention, and control of infectious diseases

Advances in digital and innovative technologies have fundamentally changed how healthcare systems monitor, prevent, and control infectious diseases. Traditional methods, often based on manual data collection and analysis, have proven to be resource-intensive and time-consuming. In contrast, digital technologies provide real-time data analysis and rapid response capabilities essential to effectively managing infectious disease outbreaks. These innovations improve early detection of infections and enable proactive interventions, ultimately strengthening public health responses to emerging threats. **Table 1** reports the digital technologies and the high-level technology groups illustrated by the European Centre for Disease Prevention and Control (ECDC).

Table 1. ECDC mapping of digital technologies into high-level technology groups (Adapted from ECDC, 2021).

High-level technology group	Digital technology classification
Advanced manufacturing technologies	3D-printing
Autonomous devices and systems	Drones. Robotics
Blockchain/distributed ledger technology	Blockchain/distributed ledger technology
Cloud computing/cloud-based networks	Cloud computing/cloud-based networks
Cognitive technologies	Artificial Intelligence (AI). Expert systems. Machine learning. Natural language processing. (Artificial) neural networks
Crowdsourcing platforms	Crowdsourcing
Data analytics (including big data)	Big data analytics (incl. data mining). Health informatics. Parallel computing. Social media and mobile data analysis
e-health	Digital health/e-health/m-Health. Electronic Health Records (EHRs). Telemedicine
Imaging and sensing technologies (including GIS)	Geographic Information Systems (GIS). Health informatics, Image processing, Satellite communication/imaging (incl. earth observation and remote sensing)
Immersive technologies	Virtual/augmented reality
Integrated, ubiquitous fixed and mobile networks	Cellular networks. Smartphones, and tablet computing devices
Internet of Things (IoT)	Biosensors. Internet of Things (IoT). Wireless sensor networks
Nanotechnology and microsystems	Biosensors. Digital DNA/RNA/protein analysis. Lab-on-Chip (LOC). Nanotechnology
Simulation	Mathematical models/simulations
Wearables (including ingestibles)	Wearables (incl. smart fabrics, ingestible)

E-health technologies, especially Electronic Health Records (EHRs), are among the most impactful innovations. EHRs collect and share data in one place, making it easier to share information across healthcare systems. This helps public health workers to keep track of patients and to stop outbreaks more quickly. During public health crises, EHRs help healthcare workers to make decisions based on the latest information.
Cloud computing and cloud-based networks further extend the reach and efficiency of these systems, enabling real-time data sharing across regions and health facilities. This allows a more cohesive response to outbreaks, as data can be shared and analyzed quickly and on a larger scale. In addition, telemedicine platforms

supported by cloud networks enable remote monitoring of patients, reducing the need for face-to-face consultations and limiting the spread of infections within healthcare settings.
Cognitive technologies such as artificial intelligence (AI), machine learning (ML), and natural language processing (NLP) have also been integrated into healthcare systems to improve data processing capabilities. These tools can quickly and accurately analyze vast amounts of data to identify trends, detect anomalies, and predict outbreaks before they escalate. In addition, AI can process information from social media and mobile data to provide insights into public behavior, providing a broader context for tailoring interventions during infectious disease crises.
Imaging and sensor technologies, particularly Geographic Information Systems (GIS), significantly contribute to understanding the geographical spread of disease. These technologies, combined with satellite communications, provide real-time insight into the environmental factors influencing outbreaks, enabling more accurate epidemiological mapping. This allows public health officials to target interventions, allocate resources more efficiently, and control the spread of disease with greater precision.
Immersive technologies such as virtual and augmented reality (VR/AR) are also becoming valuable tools in the healthcare sector. These technologies provide healthcare professionals with simulated environments where they can practice infection control measures without real-world risks. By providing hands-on training in a controlled environment, VR/AR technologies ensure that healthcare workers are better prepared to deal with disease outbreaks, reducing the risk of error in critical situations.
The Internet of Things (IoT) and wearable technologies have added another layer of innovation to infectious disease surveillance and prevention. IoT devices, such as biosensors and wireless sensor networks, enable continuous monitoring of patients' vital signs, providing real-time data that can be used to detect early signs of infection. Wearable devices, including smart fabrics and ingestible devices, can track physiological changes and provide early warnings that facilitate timely intervention, reducing infection severity and transmission risk.
Integrating these technologies significantly improves the surveillance, prevention, and control of infectious diseases. By improving real-time data collection, increasing detection accuracy, and promoting better coordination across sectors, these digital tools are strengthening the ability of public health systems to respond to emerging infectious threats. As the application of these technologies expands, artificial intelligence and machine learning are expected to play an increasingly important role, providing more accurate and efficient tools for infection surveillance and further supporting effective public health responses.

Artificial intelligence and machine learning in infection surveillance

Artificial intelligence (AI), especially machine learning (ML), has become one of the most promising and widely used technologies for hospital infection surveillance. AI includes a broad spectrum of computational methods that allow systems to carry out tasks typically requiring human intelligence, such as learning from data, reasoning, and decision-making. Machine learning, a specific branch of AI, employs algorithms to identify patterns in data, enabling the automation of tasks like detecting infections and predicting outbreaks. ML techniques are generally categorized into supervised and unsupervised learning, with supervised learning being the most commonly applied in infection surveillance. This approach relies on labeled datasets with predefined outcomes (e.g., infection status). The model learns from this data and is tested on new, unseen data to predict outcomes.
On the other hand, unsupervised learning does not use labeled data and instead identifies hidden patterns or groupings, although this is less commonly used in infection surveillance. Training ML models typically involves splitting the data into two sets: a training set for learning and a test set for evaluating the model's

accuracy. However, advanced preprocessing techniques are essential given the complexity of real-world health data, which often contains inconsistencies or missing information. Methods such as undersampling and oversampling help to balance datasets and prevent the model from over-representing specific categories. These techniques, including the Synthetic Minority Over-sampling Technique (SMOTE), are particularly important when working with highly imbalanced datasets, which are common in infectious disease surveillance.

In addition, cross-validation is often used to improve model performance. This method divides the dataset into multiple subsets or folds, allowing the model to be trained and validated on different data combinations. This process reduces bias, increases the model's reliability, and ensures that it performs well across various data sets.

Machine learning can be a valuable tool in infection surveillance, working alongside infection control teams to support their efforts. While ML automates the analysis of large datasets, human oversight remains essential. This human-in-the-loop approach ensures that healthcare professionals can interpret results, validate findings, and make informed decisions. By integrating ML with expert judgment, infection surveillance systems can become more efficient and effective in managing outbreaks and improving patient safety.

Innovative techniques for the surveillance of HAIs

Integrating the technological innovations outlined above into the surveillance of healthcare-associated infections represents a significant opportunity to improve both the efficiency of surveillance systems and the quality of care delivered while reducing healthcare costs and the workload of healthcare professionals - an issue exacerbated by the current shortage of healthcare workers. In the following paragraphs, we discuss some of the most common healthcare-associated infections, accompanied by examples of studies specifically designed to optimize their surveillance, monitoring, and treatment.

Surgical site infections (SSIs)

Surgical site infections (SSIs) occur after surgery at the procedure site, ranging from superficial skin infections to more severe complications involving deeper tissues. They represent a significant proportion of healthcare-associated infections and contribute to increased morbidity, mortality, and healthcare costs. Several studies have evaluated the positive impact of technological advances on the surveillance and management of SSIs. Machine learning (ML) models, as demonstrated by Chen *et al*. in their study of patients undergoing lumbar spine surgery, have proven effective in predicting SSIs by analyzing perioperative factors such as sebum thickness, hemoglobin, and glucose levels, with excellent predictive results. Years earlier, Branch-Elliman *et al*. developed an algorithm based on clinical variables such as wound culture and imaging orders, which proved to be a reliable method for detecting SSIs. Such approaches can save resources and allow for closer monitoring of patients with identified risk factors. Additionally, as highlighted by Dalcól *et al.*, digital tools for post-discharge surveillance contribute to improved monitoring. Indeed, tools such as mobile health apps and web platforms allow patients to report symptoms and upload wound images, facilitating early detection of SSIs and reducing unnecessary healthcare visits, thereby improving patient satisfaction and cost-effectiveness.

Catheter-associated urinary tract infections (CAUTIs)

Catheter-associated urinary tract infections (CAUTIs) occur when pathogens enter the urinary tract through a catheter and contribute to a significant proportion of healthcare-associated infections. These infections can increase morbidity, extended hospital stays, and higher healthcare costs. Traditional methods of CAUTI

surveillance are labor-intensive, often error-prone, and complicated by asymptomatic cases. Still, promising results have been published on the positive impact of new technologies on surveillance accuracy and efficiency. For example, Sanger *et al.* developed a natural language processing (NLP) algorithm that scans electronic health records (EHRs) to identify CAUTI symptoms from clinical notes, achieving high sensitivity (97.1%) and specificity (94.5%). This approach reduces manual workload while maintaining diagnostic accuracy. Similarly, van der Werff *et al.* validated a fully automated algorithm integrating microbiological data and NLP for detecting CAUTIs. Their method performed well, particularly when considering specific symptoms and excluding irrelevant cases, providing a robust alternative to manual review.

Central line-associated bloodstream infections (CLABSIs)

Central line-associated bloodstream infections (CLABSIs) occur when pathogens enter the bloodstream through a central venous catheter (CVC), increasing morbidity, mortality, and healthcare costs. To improve CLABSI management, Parreco *et al.* compared machine learning models, such as logistic regression and deep learning, to predict CLABSIs and mortality. Their results demonstrated the potential of deep learning to predict outcomes with a high degree of accuracy, supporting early detection, which is critical for timely intervention. Similarly, Noaman *et al.* investigated data mining techniques and showed that the algorithm they used (AdaBoost) could predict CLABSIs with 89.7% accuracy, providing a robust tool for clinical surveillance programs These techniques complement other automated surveillance systems used in infection surveillance.

Ventilator-associated pneumonia and events (VAPs and VAEs)

Ventilator-associated pneumonia (VAPs) are hospital-acquired infections that occur in patients who have been mechanically ventilated for more than 48 hours and are associated with increased morbidity, mortality, and healthcare costs. Ventilator-associated events (VAEs) refer to a broader category of respiratory complications in ventilated patients and are often used for surveillance purposes to track deterioration in respiratory status. As mentioned above, automated surveillance systems have also been used to improve the monitoring and detection of VAP and VAEs. In a study conducted in an academic medical setting, Hebert and colleagues validated a computerized algorithm for the surveillance of VAEs, achieving 100% sensitivity and 100% specificity compared with manual surveillance for possible and probable VAP. Implementing their automated system streamlined the workflow of infection prevention teams, resulting in reported time savings and demonstrating the potential of electronic surveillance systems to improve VAP detection while reducing the burden on healthcare workers.

Multi-drug-resistant organisms (MDROs)

Multi-drug-resistant organisms (MDROs) are micro-organisms, mainly bacteria, that have developed resistance to multiple classes of antibiotics. Common examples include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *enterococci* (VRE), and certain *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* strains. These microorganisms pose a significant threat in healthcare settings because their resistance to multiple classes of antibiotics complicates treatment and contributes to higher mortality rates and prolonged hospital stays. Early detection and control are essential for effective management of these infections.

Technological innovations, such as artificial intelligence (AI) and machine learning (ML), have proven to be valuable allies in improving the management of MDROs. Li *et al*. recently developed a machine learning model to predict MDRO colonization in ICU patients at admission, identifying key predictors such as biochemical markers and pre-ICU hospital stay, thus facilitating earlier interventions. Previously, Mora-Jiménez and

colleagues had begun to explore the potential role of AI in improving early risk assessment, focusing on predicting the risk of MDRO development within 48 hours of ICU admission, with promising results derived from the integrated use of AI and electronic health records. It is important to note that laboratory testing typically requires approximately 48 hours to confirm MDRO colonization. Early identification of patients as potential MDRO carriers through AI analysis of risk factors for colonization could significantly reduce the time required for patient isolation, thereby minimizing the risk of MDRO spread within the hospital environment.
New technologies can also assist in selecting the most appropriate treatment for the patient and monitoring the proper antibiotic use to control antibiotic resistance. The study by Ali and colleagues used artificial neural networks (ANN) to predict inappropriate empirical antimicrobial therapy (EAMT) in sepsis patients. The ANN model outperformed traditional logistic regression, showing MDRO infections as a significant predictor of inadequate therapy, reinforcing the importance of accurate, data-driven treatment strategies.

Sepsis

Sepsis, a severe and life-threatening condition resulting from the body's overwhelming response to infection, is a condition that requires effective management due to its high mortality rate and potential for serious complications. Technological innovations have become integral to improving sepsis care, improving both early detection and treatment. The advances discussed in the previous section, such as AI algorithms and wearable devices, continue to play a critical role in sepsis management.
For example, AI-driven tools and machine learning techniques are now being used to refine sepsis diagnostics. Komorowski *et al.* highlight that machine learning approaches, including biomarker panels and predictive models, improve the accuracy and timeliness of sepsis diagnosis, thereby improving overall patient outcomes. Similarly, Yang *et al.* highlight how AI is already being used for early detection, subtyping, and precise treatment of sepsis, contributing to more targeted and effective care. In addition, digital alerting systems have shown promise in improving clinical outcomes by reducing the length of stay in hospitals and intensive care units. However, their impact on mortality remains inconclusive.

Challenges in implementing innovative technologies for surveillance in hospital settings

Implementing innovative technologies for infection surveillance in hospitals presents several challenges that must be addressed to ensure effectiveness and compliance. These challenges range from data security and ethical considerations to the combined efforts of interdisciplinary collaboration and the training and adaptation of healthcare staff.
One of the most critical concerns is data security and privacy. Healthcare data in infection surveillance are highly sensitive and must comply with strict regulations, such as the General Data Protection Regulation (GDPR) in Europe and the Health Insurance Portability and Accountability Act (HIPAA) in the United States. Ensuring compliance with these frameworks requires robust encryption and access control mechanisms to prevent unauthorized access to patient information. Hospitals need to invest in secure data storage and transmission technologies, especially as the use of artificial intelligence (AI) and machine learning (ML) for surveillance requires the collection and analysis of large amounts of health data. Maintaining patient anonymity and ensuring data is used ethically and responsibly is paramount.
In this context, federated learning offers a valuable solution. It allows AI models to be trained on decentralized devices or servers that hold local data, eliminating the need to transfer data between entities. This

approach significantly reduces the risk of privacy breaches while enabling effective AI-driven infection monitoring. In addition, differential privacy provides another layer of protection by using mathematical techniques to ensure that individuals within a dataset cannot be re-identified, even when their data is used to train AI. By adding controlled noise to data, differential privacy allows healthcare organizations to share valuable insights from datasets without compromising individual privacy.

Ethical concerns also arise, particularly around the balance between improving public health outcomes and upholding individual rights. AI-driven systems can automate decision-making in ways that may exclude or misrepresent certain patient groups if biases are inherent in the data or algorithms. Ethical oversight is needed to ensure these technologies do not reinforce existing health inequalities. In addition, maintaining the transparency of AI decisions is critical, mainly when these systems influence clinical outcomes. Explainable AI (XAI) includes tools and frameworks that help understand and interpret predictions made by machine learning models. This is particularly important in the context of regulations such as the European Union's AI Act, which emphasizes transparency and accountability in AI applications to prevent potential harm to individuals and ensure responsible use.

Another major challenge is the integration of interdisciplinary collaboration with the training and adaptation of healthcare workers. Infection surveillance and control requires merging healthcare expertise with advanced technological skills. However, there are often gaps between healthcare professionals and IT experts, who may not share the same language, goals, or understanding of hospital workflows. In addition, many healthcare professionals may need more digital literacy skills, which are essential for the effective use of AI and other advanced tools in infection surveillance. This divide can lead to resistance to adopting new technologies due to unfamiliarity, fear of job displacement, or perceived complexity.

Bridging this gap requires ongoing communication and joint training to promote mutual understanding between clinical and technical teams. Effective collaboration is essential to ensure that technologies are designed to meet the practical needs of infection control teams. Dedicated training programs can equip staff with the necessary skills to interact with AI tools while emphasizing the role of these technologies as supporting rather than replacing tools. Involving infection control teams from the outset and maintaining a 'human-in-the-loop' approach ensures that healthcare professionals remain at the heart of decision-making, with AI acting as an adjunct rather than a replacement. By fostering interdisciplinary collaboration alongside staff training and adaptation, hospitals can create a cohesive environment where technological innovation is effectively integrated into clinical practice. Hygiene and preventive medicine specialists can play an important role in bridging the gap between technological advancements and practical implementation in infectious diseases surveillance. Their expertise is crucial in ensuring that new technologies are aligned with public health goals and integrated effectively into healthcare practices.

Conclusion

Hospital-acquired infections (HAIs) continue to pose a significant healthcare challenge, requiring the advancement of surveillance and control strategies to mitigate their impact on patient morbidity, mortality, and healthcare costs. This chapter has explored integrating innovative digital technologies into hospital infection surveillance, particularly artificial intelligence (AI) and machine learning (ML). The shift from traditional manual methods to these advanced technologies represents a crucial step towards more efficient, accurate, and proactive approaches to HAI management.

The adoption of electronic health records (EHRs), cloud computing, and telemedicine has streamlined data collection and sharing, facilitating real-time surveillance and coordinated public health responses. AI and ML

algorithms have improved the ability to analyze complex healthcare datasets, enabling early detection of infection patterns and prediction of outbreaks. Automating data analysis processes has also reduced the workload of healthcare professionals, allowing for more focused patient care.

Despite these significant benefits, adopting these technologies presents challenges that must be carefully addressed. Data security and patient privacy are paramount, requiring strict compliance with regulations like the General Data Protection Regulation (GDPR). Techniques such as federated learning and differential privacy offer promising solutions by enabling data analysis without compromising individual patient information. Ethical considerations, including the need to prevent algorithmic bias and ensure equitable healthcare, highlight the importance of transparency and the use of explainable AI models.

However, many healthcare professionals may need more digital literacy skills, which are essential for the effective use of AI and other advanced tools in infection surveillance. This digital divide can lead to resistance to adopting new technologies due to unfamiliarity, fear of job displacement, or perceived complexity. Overcoming these challenges requires targeted training and capacity-building initiatives to ensure healthcare professionals can engage with and benefit from these tools.

These issues underscore the need for a well-rounded, interdisciplinary approach to ensure that technological advancements contribute to safer, more effective infection surveillance without undermining ethical and legal standards.

Competing interests

The authors have no financial and non-financial competing interests to declare.

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT and Grammarly for English grammar checks. After using this tool/service, the authors reviewed and edited the content as needed and took full responsibility for the content of the publication.

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Chapter 61

Countdown to the global goals, 2030 – what infection prevention and control has to offer

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Introduction

At the time of writing this chapter, there are less than six years to go until 2030 - the endpoint of the global goals. The 17 global goals, perhaps better known as the sustainable development goals (SDGs) were adopted by all United Nations (UN) Member States in 2015 and triggered a shared commitment by all countries to address many issues affecting the sustainability of the planet, including improving health. Goal 3 of the SDGs focuses on good health and well-being and it is within this goal that universal health coverage (UHC) is addressed. At first glance, it is challenging to articulate the precise role that infection prevention and control (IPC) plays in such an ambitious global health agenda. In 2016, we attempted to provide an answer to this; we reviewed the relationship between IPC and the then newly launched SDGs. We drew attention to how IPC contributes to the overall quality and safety of health care and that expansion of access, which is the ethos behind UHC, should be accompanied by efforts to ensure that when people access care it is safe and of high quality. Additionally, Goal 6 of the SDGs is to ensure the availability and sustainable management of water and sanitation for all – this is also relevant to IPC.

Healthcare-associated infections (HAI) are a cause of harm and active IPC programmes are designed to contribute to a reduction of HAI. For every infection averted there is less need for treatment which therefore links IPC with the antimicrobial resistance (AMR) agenda. Prevention of HAI also leads to a reduction in complications from surgery and other life-saving interventions commonly used in healthcare. If surgery has a vital role in achieving UHC, as noted by Seyi-Oladjde *et al.*, then IPC is also a critical part of the surgery agenda given its role in the prevention of surgical site infections.

As the clock ticks ever closer to 2030, we look back on the progress that has been made in IPC in the last decade and summarise some of the key milestones and activities that act as an important foundation for the work to be done by all of us in the coming years. We believe that IPC is important, not only to those affected by HAI but also to the achievement of the SDGs. In this chapter, we explore how this might be realized, drawing on some recent calls to action and consider what this means to those working in healthcare across the globe going forward.

UHC, quality and IPC – drilling deeper

UHC is a hugely ambitious global goal and has been described by the World Health Organization (WHO) as all people having "access to the full range of quality health services they need, when and where they need them, without financial hardship. It covers the full continuum of essential health services, from health promotion to prevention, treatment, rehabilitation and palliative care". The realisation of UHC remains a challenge and insufficient progress has been made overall in achieving SDG3 (within which UHC sits), with the COVID-19 pandemic and other ongoing crises cited as key factors impeding progress.

Quality of care has been described as the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge. Quality per se has many dimensions and three of those could be said to have a direct relationship with IPC: effectiveness, safety and people-centeredness. In fact, Chiponda *et al*. describe quality care as people-centred, responsive to users' expectations including fulfilling their right to health. IPC programmes and their implementation could therefore be seen to be one of the essential foundations upon which quality health care is built.

IPC is a practical evidence-based approach that lies at the intersection of clinical practice and public health, and hence also contributes to broader public health issues such as the prevention and control of epidemics and pandemics and AMR (**Box 1**).

> "Increased support for more effective and sustainable IPC programmes is crucial to reduce risks posed by outbreaks to global health security and to ensure patient and health worker safety".

Box 1. Infection prevention and control in health-care facilities (World Health Organization, 2022).

Effective care is realised through the provision of care which is based on the best available knowledge through the development of evidence-based IPC guidelines. Safe care is realised if practitioners adhere to IPC guidelines, protocols and practices and this is predicated on successful implementation approaches. People-centred care is realised by respecting and responding to the preferences, needs and values of users when applying IPC measures.

IPC policy, practice and research – the journey so far

In Storr *et al.*'s paper, three broad areas for action were recommended related to policy, practice and research, to stimulate the global IPC agenda. Here we take a brief look at the advancements made across these three areas in the subsequent years.

Policy

International guidelines for effective IPC

WHO's evidence-based guidelines on the core components of IPC programmes were issued in 2016. These describe eight components that need to be in place at the national and health facility level for IPC to be

effective. They are; 1) IPC programmes, 2) IPC guidelines, 3) education and training, 4) surveillance of HAI, 5) multimodal strategies, 6) monitoring, evaluation and feedback, 7) workload, staffing and bed occupancy at the facility level, 8) built environment, materials and equipment at the facility level. Based on these core components a set of minimum requirements for IPC programmes were then issued in 2019 to support countries and facilities in a journey towards building strong IPC programmes. The effectiveness of the core component guidelines in high-income and upper-middle-income countries was the subject of a systematic review in 2023. This review highlighted, among other things, the need for further research on national IPC interventions. It also appears that multi-stakeholder collaboration aligned with the development of policy briefs, to address the contribution of the IPC core components to UHC and the SDGs would still be welcomed, building on the 2016 call to action (*Storr et al*).

Social marketing, campaigns and civil society

Campaigns and advocacy play an important role in global health. Advocating for IPC has increased in recent years, including action by civil society groups. Civil society refers to a wide range of entities that are neither governmental nor commercial and includes for example non-profit organisations and non-governmental entities that support many countries in their IPC efforts.

There is now a plethora of campaigns directly or indirectly related to IPC including a recently launched global day entitled World Patient Safety Day, marked every year on 17 September. It has featured calls to action for IPC. This is one example of how a campaign that targets a healthcare community beyond IPC has the power to integrate and amplify messages across health programmes. On this latter point, Storr *et al.* called for advocacy efforts to be combined, noting that the current plethora of global campaigns could result in competition for attention rather than complementary campaign messages. A civil society group, The AMR Narrative, has also been promoting IPC in their stories. The mainstay of global campaigning related to IPC, however, continues to be driven by the established, WHO-led World Hand Hygiene Day (WHHD) that started in 2009. It is interesting to note that in 2019 the call to action from WHO centred on the global movement to achieve quality UHC with the slogan 'Clean care for all: it's in your hands' and this was cobranded with the WHO generic #healthforall, the hashtag related to UHC.

There are many publications on the role of civil society in health but little in the way of their role in IPC. Learning from other programmes, such as HIV, collaboration and co-development with civil society can be a powerful key to success and the COVID-19 situation appeared to have accelerated some of this collaboration. In 2023, civil society groups were actively engaged in WHHD, for example, and a group called Hand Hygiene for All (HH4A) was established in 2020, which includes a number of civil society organizations. HH4A is a call to action for a whole of society approach to accelerate progress towards universal hand hygiene by 2030. WaterAid, as part of HH4A, for example, is playing a role in how IPC can be advocated for and strengthened across countries, including its linkages with necessary water, sanitation and hygiene actions.

Global strategy on IPC

The benefit of international agencies, such as WHO, is in their convening power; bringing the world together and catalysing action around important issues. In 2022, this happened in relation to IPC, when the first Global Strategy on IPC (GSIPC) was endorsed by all countries. The subsequent GSIPC was launched and is country- and stakeholder-driven, with a focus on IPC in any setting where health care is delivered across the continuum of the health system. The strategy highlights how IPC contributes to improving other critical health outcomes addressed by the SDGs and with potentially huge benefits in reducing health costs and providing safer health care. The vision of this global strategy is that by 2030, everyone accessing or providing health care is

safe from associated infections. The vision is deliberately stated as being in alignment with the agenda and timeline of the SDGs (particularly goals 3.1–3.3, 3.8, 3d, 3.d.2, and 6.1-6.2 (UN, 2015) – see **Box 2**).

SDG target 3: ensure healthy lives and promote well-being for all at all ages.

- 3.1: By 2030, reduce the global mortality ratio to less than 70 per 100,000 live births.
- 3.2: By 2030, end preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1000 live births and under-5 mortality to at least as low as 25 per 1000 live births.
- 3.3: By 2030, end the epidemics of acquired immunodeficiency syndrome (AIDS), tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases.
- 3.8: Achieve universal health coverage, including financial risk protection, access to quality essential health care services and access to safe, effective, quality and affordable essential medicines and vaccines for all.
- 3.d: Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks.
- 3.d.2: Percentage of bloodstream infections due to selected antimicrobial-resistant organisms.

SDG target 6: ensure the availability and sustainable management of water and sanitation for all.

- 6.1: By 2030, achieve access to safely managed drinking water services for all.
- 6.2: By 2030, achieve access to adequate and equitable sanitation and hygiene for all and end open defecation, paying special attention to the needs of women and girls and those in vulnerable situations.
- The WHO/UNICEF Joint Monitoring Programme has defined global indicators for water, sanitation, hand hygiene, cleaning and healthcare waste for which global reports and databases are updated every 2 years.

Box 2. Sustainable Development Goals (SDGs) and targets (Adapted from World Health Organization, 2023).

This GSIPC outlines eight solutions (termed strategic directions) to the problem of HAI and AMR. One solution is that all countries should have an active IPC programme at the national and healthcare facility levels in both the public and private sectors and that these programmes have annual plans and dedicated IPC-trained professionals and budgets. This concurs with the existing WHO core components for IPC programmes, on which global progress has been surveyed. Data from 2023 tell us that globally 1 in 10 countries did not have an IPC programme or an operational plan and only 39% had nationwide implementation of IPC programmes. Only 3.8% of countries worldwide met all WHO minimum requirements for IPC in 2021. Importantly, gaps in IPC facility implementation of the core components across income levels also hinder IPC progress. The presence of a global strategy is therefore clearly important but will only have any impact if it is acted upon. Currently, countries are expected to develop a national action plan on IPC to demonstrate what will happen in order to meet recommended targets and indicators, in line with a recently published global action plan and monitoring framework. All countries should report on their progress through 2030.

Strategic advances in AMR, in support of IPC

AMR continues to be described as one of the biggest threats facing the planet ever. For many years, all countries of the world have been tasked with developing AMR national action plans, and IPC forms a central feature of these action plans. The United Nations General Assembly (UNGA) in 2024 deemed the AMR crisis so critical that it made the decision to bring together global leaders on this topic. For UNGA, the UHC Movement Political Panel called on Member States to use the opportunity to leverage UHC to take a systems approach to addressing AMR, with individuals, families and communities at the centre. Collaboration, partnerships and

integration could be game changers for AMR IPC, and the SDGs overall. Allegranzi *et al.* noted that synergies and interconnections are particularly effective when IPC supports strategies aimed at reducing AMR.
To emphasise the connections between AMR and IPC, WHO Europe issued an advocacy brief aimed at decision-makers at the national level.
It makes no sense at any level of the health system for IPC to be considered in a vacuum. IPC integration and coordination is another one of the solutions outlined in the GSIPC.

Practice

Technical and implementation support for all levels of the health systems
Policies and guidelines require innovative and locally adapted implementation strategies and locally produced practical tools to ultimately catalyse behaviour change. There is a plethora of global technical support in the form of operational guidance and implementation resources available to countries, to stimulate local adoption and adaption and build institutional capacity (see some examples in **Table 1**).
However, as called for by Storr *et al.*, further reflection remains necessary in order to better understand how IPC guidance and strategies fit within the UHC agenda, for example, and how they take account of health system constraints to be as realistic and effective as possible in the real world.

Research
A research agenda obviously helps us to understand the drivers of IPC behaviour and practice, the prevailing gaps and challenges, and it shapes future interventions.
Research is yet another one of the WHO solutions, with a global research agenda set to be developed and a target to be achieved with regard to published national research agendas and research publications.
A WHO hand hygiene research agenda was published in 2023. A global AMR research agenda has also been published. An IPC research agenda, whether at the global or national level, could still lend itself to addressing the relationship between IPC and other health programmes including AMR and surgery. A worldwide approach to prevention alongside the acceleration of research could be beneficial to the global surgery agenda, for example. While during the height of the COVID-19 pandemic, there were many publications around social determinants of health and people's risk of infection, IPC-specific research remains as a gap and could continue to add value in terms of access, quality and equity in terms of avoidable infections and these social determinants of health in support of achieving the SDGs.

Table 1. Examples of globally targeted operational guidance and implementation resources.

Organization	Year	Resource
WHO	2017	Interim practical manual supporting national implementation of the WHO Guidelines on core components for infection prevention and control programmes
	2018	Improving infection prevention and control and the health facility level - Interim practical manual supporting implementation of the WHO Guidelines on Core components for infection prevention and control programmes
	2018	Global guidelines for the prevention of surgical site infection and implementation resources
	2017 and 2019	Guidelines for the prevention and control of carbapenem-resistant *Enterobacteriaceae*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in healthcare facilities and implementation manual
	2021	Resource considerations for investing in hand hygiene improvement in healthcare facilities
	2021	Strengthening infection prevention and control in primary care - a collection of existing standards, measurement and implementation resources
WHO IPC as a specialty	2020	Core competencies for infection prevention and control professionals
	2024	Infection prevention and control in-service education and training curriculum
WHO water, sanitation and hygiene focus	2019	WASH in health care facilities: Practical steps to achieve universal access to quality care
CDC and **ICAN**	2019	Best Practices for Environmental Cleaning in Healthcare Facilities in Resource-Limited Settings
CDC	2022	Environmental Cleaning Program Improvement Toolkit: A Practical Guide for Implementing the Best Practices for Environmental Cleaning in Healthcare Facilities in Resource-Limited Settings
SHEA/IDSA/APIC	2022	Strategies to prevent surgical site infections in acute-care hospitals: 2022 Update
	2023	Practice Recommendation: Strategies to prevent healthcare-associated infections through hand hygiene: 2022 Update
ISID	2019	Hand hygiene in low-and middle-income countries
	2020	Implementation of surgical site infection surveillance in low- and middle-income countries: A position statement for the International Society for Infectious Diseases 3

Abbreviations. APIC: Association for Professionals in Infection Control and Epidemiology, CDC: Centers for Disease Control and Prevention, ICAN: Infection Control Africa Network, IDSA: Infectious Diseases Society of America, ISID: International Society for Infectious Diseases, SHEA: The Society for Healthcare Epidemiology of America.

In summary, advances in these three areas of policy, practice and research go some way to ensuring all countries, wherever they are, whatever their income level are supported in their approaches to IPC. Securing global commitment to progressing safe, quality care through IPC has been a critical achievement. However, there remain significant and persistent gaps across all countries. The pandemic likely hindered progress with both IPC and the SDGs as previously noted, however, much can still be achieved in the coming years to meet their respective visions.

Looking forward

To help those committed to IPC, we present here a summary of some of the solutions that can be worked on in the coming years at the health facility level (**Box 3**), as well as building upon all that has already been outlined in this chapter. In particular, we translate some of the dry language within international edicts into some practical text. The full version of this information alongside the global, national and health facility actions, target and indicators can be found.

Storr *et al.* presented a theory of change that also remains relevant today since it suggested that the ultimate impact of IPC was the achievement of people-centred, quality UHC. Acting upon the GSIPC solutions for political commitment and policies, integration and coordination and advocacy and communication, in particular, would still help to achieve the outlined short and long-term outcomes in the theory of change. These outcomes should improve efficiency, and mean more resilient health services and increased quality of care as noted.

- Solution #1 - Political commitment and policies - Facility senior managers fund IPC programmes.
- Solution #2 - Active IPC Programmes - These programmes are in place for tertiary and secondary care facilities, and in primary care, at the very least there is an IPC link person.
- Solution #3 - IPC integration and coordination – As part of these programmes, IPC committees are representative and collaborative with other complementary programmes.
- Solution #4 - Knowledge about IPC among health and care workers and career pathways for IPC professionals – Fundamental to these programmes are implementation plans and resources for IPC training and education.
- Solution #5 - Data for action – Also fundamental are implementation plans and resources for HAI surveillance monitoring and feedback.
- Solution #6 - Advocacy and communications – A critical element of IPC programmes is communication and campaign activities on IPC priority topics.
- Solution #7 - Research and development – IPC programmes should also address research according to the facility's priorities.
- Solution #8 - Collaboration and stakeholders' support – IPC programmes should be collaborative with other healthcare facilities and national IPC societies.

Box 3. Summary of some of the solutions that can be worked on in the coming years at health facility level (Adapted from World Health Organization, 2023).

Conclusion

As Storr *et al.* stated, there are and can continue to be common goals across those working in IPC and on other agendas such as UHC and AMR. This remains true for the goals and targets which are set for 2030. Political commitment, integration and communications are paramount to success. IPC provides a small part of the much-needed big solutions to get the health-related SDGs back on track. There is still a need for a strong narrative that describes IPC as a trusted and evidence-based speciality and method to future-proof health systems to meet whatever challenges lie ahead, even beyond 2030, whether they be epidemic and pandemic-related, linked to AMR or as yet unknown. An increasingly globalised world is anticipated to present new threats from infectious diseases and challenge access to water, sanitation and hygiene for healthcare. Together we can achieve safe health systems through a range of actions. However, it will be necessary to consider a number of influencing factors alongside these actions, including the impact of climate

change, advances in technology, the changing workforce, consumer demands and geopolitics, all of which should also be aligned with the SDGs.

Competing interests

The authors are contracted to WHO to provide consultancy services.

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Chapter 62

Overcoming infection prevention and control challenges for surgical site infections in conflict-ridden settings

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Introduction

In conflict-ridden regions, hospitals face a dual challenge: providing urgent medical care to those wounded by violence while also dealing with the increased risk of surgical site infections (SSIs) of war wounds. SSIs not only extend hospital stays and elevate healthcare costs but also contribute to increased morbidity and mortality rates, particularly in resource-constrained settings. Weapon-inflicted injuries in conflict environments amplify the risk of infection, influenced by various factors. These include the nature of the injury, fracture presence and stabilization, foreign object embedding, patient physiology, wound location and size, and the adequacy of initial emergency surgical measures.

Moreover, within conflict-affected settings, where healthcare infrastructure may be compromised, additional factors such as delayed hospital presentation, limited access to clean water for peri-operative care, and inadequate postoperative monitoring can exacerbate the risk of SSIs. In war scenarios, the interval between injury and hospital admission correlates with heightened mortality and infection rates, as evidenced by studies spanning civilian trauma and limited war data. Furthermore, delays in administering antimicrobials and surgical interventions post-injury contribute to increased infection rates, as indicated by animal studies and civilian trauma research. The distinct challenges encountered in conflict zones necessitate tailored approaches to infection prevention and control (IPC) and SSIs, addressing issues like damaged infrastructure, resource limitations, disrupted supply chains, and heightened patient susceptibility.

This article seeks to describe these challenges to prevent SSIs and propose strategies for overcoming them, drawing insights from scientific evidence and practical field experiences.

Limited resources

One of the primary challenges in infection control in conflict-ridden settings is the scarcity of resources. Conflict zones, especially in low- and middle-income countries (LMIC), often lack adequate healthcare infrastructure, including sterile equipment, proper sanitation facilities, clean water, and trained personnel, essential for preventing SSIs. Scarce resources hinder the ability to maintain a hygienic environment. Additionally, frequent power outages and disruptions to water supplies further complicate efforts to uphold infection control

protocols. Moreover, the constant influx of patients, including those with traumatic injuries, presents a continuous challenge in preventing SSIs.

Research conducted by Allegranzi *et al.* highlights the burden of healthcare-associated infections (HAIs) in developing countries, where resource constraints are particularly pronounced. In conflict settings, the situation is further exacerbated by the diversion of resources to emergency medical care and security needs. As a result, healthcare facilities struggle to maintain basic infection prevention and control (IPC) measures, such as hand hygiene and environmental hygiene.

Addressing the challenge of limited resources requires innovative solutions tailored to the context of conflict zones. For example, organizations like the World Health Organization (WHO) have developed trauma kits equipped with essential instruments and supplies for major trauma, optimizing the equipment. Muhrbeck *et al.* in a retrospective study in ICRC hospitals, compared different trauma scores to predict surgical resource consumption and in-hospital mortality in resource-scarce conflict settings. WHO also provides community guidance on evidence-based alternative hand hygiene strategies in the absence of clean running water, soap or alcohol-based hand rub such as the use of sand or ash and even self-produced hand sanitiser. Furthermore, training local healthcare workers in improvised sterilization techniques and waste management practices can help mitigate the impact on SSIs of resource constraints.

Disrupted supply chains

Ongoing conflict disrupts supply chains, leading to shortages of essential medical supplies such as antibiotics, disinfectants, and surgical instruments. The instability and insecurity in conflict zones impede the timely delivery of supplies, exacerbating the risk of SSIs and complicating their management. A study by Nguyen *et al.* examined the incidence and aetiology of SSIs in Vietnam, highlighting the impact of disrupted supply chains on infection control efforts. The authors identified delays in the procurement of surgical supplies and medications as contributing factors to the high prevalence of SSIs in conflict-affected areas. In addition to shortages, the quality of available supplies may also be compromised due to substandard manufacturing, improper storage conditions or forced purchases on the local market. To address supply chain disruptions, collaboration between healthcare providers, humanitarian organizations, and local authorities is essential. Coordination efforts should focus on ensuring timely access to essential medical supplies, establishing contingency plans for emergencies, and strengthening local procurement and distribution networks. Innovative approaches, such as 3D printing of surgical instruments and decentralized production of essential medications, can also help mitigate the impact of supply chain disruptions on infection control.

Increased patient vulnerability

Conflict-affected populations are inherently more vulnerable to SSIs due to a combination of factors, including malnutrition, overcrowded living conditions, and limited access to healthcare. Displacement and migration further exacerbate the spread of infectious diseases, including SSIs, within and across borders. A review by Matzopoulos *et al.* examined the impact of violence on health in low- to middle-income countries, highlighting the complex interplay between conflict, displacement, and infectious diseases. The authors emphasized the need for targeted interventions to address the unique health needs of conflict-affected populations, including IPC measures.

Community engagement plays a crucial role in mitigating the risk of SSIs among vulnerable populations. Health education programs focusing on hygiene practices, wound care, nutrition support and early detection of infections can empower communities to take proactive measures to protect their health and facilitate timely interventions to prevent SSIs.

The direct impact of conflict on surgical site infections

The shift in warfare tactics from World War II to Vietnam and onwards, marked by smaller unit engagements and increased use of explosive devices like improvised explosive devices (IED), introduced new wound patterns and complexities. In conflicts like Operation Iraqi and Enduring Freedom (OIF/OEF), injuries from IEDs often result in severe tissue damage and perineal injuries, posing challenges in balancing infection risk with functional preservation during aggressive debridement procedures. Research by Lowe *et al.* sheds light on the challenges faced by hospitals in conflict-affected settings in controlling SSIs. In their qualitative study, inadequate hospital infrastructure, resource and workforce shortages, limited education of staff, and disrupted supply chains were identified as barriers to IPC measures, contributing to the increased incidence of SSIs. Furthermore, the study highlighted the impact of conflict-induced mass casualties and overcrowding on SSIs, underscoring the urgency of addressing these challenges in conflict zones. Coupled with inadequate isolation capacity in many of the hospitals studied and high infection rates due to the nature of war wounds, participants in the Lowe *et al.* study worried about the safety of the healthcare environment for patients, visitors and healthcare workers.

Understanding war wound bacteriology is crucial due to its association with sepsis, a common cause of post-24-hour mortality in Vietnam. Blyth *et al.* revealed shifts in wound microbial composition over time and with environmental factors. Initial Gram-positive dominance transitions to Gram-negative predominance, with *Pseudomonas aeruginosa* becoming prominent, influenced by antimicrobial use and climate. Despite the rise in Gram-negative infections, late complications often involve Gram-positive organisms like *Staphylococcus aureus*, highlighting the complexity of combat wound infections and the importance of tailored treatment strategies.

Eardley *et al.* underlined, already in 2011, that the importance of sanitation, hygiene, and nursing care, evident since the Crimea, remains critical in military hospitals. Compliance with essential protocols, such as proper hand hygiene and patient isolation, varies greatly among US military hospitals. Moreover, there is inconsistency in adhering to national and theatre-specific guidelines, as well as in implementing antimicrobial control measures. This situation is exacerbated in deployed settings where high turnover rates and less-than-optimal conditions make maintaining effective IPC even more difficult. Key areas identified to reduce infection risks include informed facility design, adequate resources, resupply management, enhanced microbiological support to assess MDR in SSIs, comprehensive education, leadership involvement, and trained infection control personnel. This capability is vital for effective patient care in military settings and is reflected in lower infection rates in British military hospitals compared to US medical facilities. Strategies to improve IPC practices, such as the establishment of IPC committees, regular in-service training, and the appointment of IPC champions, are essential for mitigating the risk of HAIs including SSIs. Additionally, collaboration (such as humanitarian clusters) between healthcare providers, humanitarian organizations, and local authorities is instrumental in ensuring timely access to essential medical supplies, coordinating efforts or programs and strengthening local healthcare systems to cope with the influx of patients during conflict situations.

Another perfect example of how to overcome IPC challenges is given by the WHO with a technical note tailored to Infection prevention and control and water, sanitation and hygiene measures in healthcare settings

and shelters/congregate settings in Gaza. Those guidelines serve as a prime illustration of how infection control, as well as water and sanitation measures, can and should be adjusted to suit wartime conditions.

"Migration" of multidrug-resistant organisms (MDRO)

In conflict-affected healthcare settings, antibiotic therapy plays a crucial role in managing wounds due to the elevated risk of infection, both for perioperative prophylaxis and treating established infections. In a cohort study involving Syrian patients treated in Jordan for injuries stemming from conflict, multidrug-resistant (MDR) strains were identified in 73% of patients with wound infections. Similarly, within a Reconstructive Surgery Project conducted by Doctors without Borders in Amman, 55% of 107 Iraqi civilians diagnosed with osteomyelitis upon admission were found to harbor MDR organisms. During conflicts such as the Vietnam War and Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF), antimicrobial therapy played a crucial role alongside surgical interventions in treating war wound infections. However, the rise of antibiotic resistance, particularly in Gram-negative infections, has presented significant challenges and led to poor outcomes. Multidrug-resistant organisms like methicillin-resistant *Staphylococcus aureus* (MRSA) and *Acinetobacter baumannii* complex (ABC) have emerged as serious threats to military personnel. In response to infection outbreaks during OIF, aggressive infection control measures and antimicrobial stewardship protocols were introduced, resulting in notable reductions in ventilator-associated pneumonia rates and improvements in antibiotic susceptibility patterns for ABC. Despite these strides, colonization rates of multidrug-resistant Gram-negative bacteria continued to climb, prompting the establishment of clinical practice guidelines in 2008 to advocate for more prudent antimicrobial use.

In conflict zones like Syria or Ukraine, the destruction of healthcare infrastructure has compelled injured individuals to seek treatment in neighboring countries, straining public health resources. Civilian medical facilities bear the burden of caring for patients due to the absence of well-equipped military hospitals. The movement of injured individuals facilitates the spread of multidrug-resistant (MDR) pathogens across borders. In such contexts, effective infection control practices are imperative to prevent further emergence and nosocomial transmission of MDR pathogens. For instance, in areas like Syria, where antibiotic resistance is prevalent due to widespread over-the-counter antibiotic use, neighboring hospitals receiving patients are implementing additional precautions. They conduct routine microbiological screenings upon admission, utilize specific trauma rooms for immediate care, and introduce isolation units within their wards to bolster infection control practices. Managing war-related injuries necessitates a multidisciplinary approach, drawing insights from the American military's experiences avoiding unnecessary surgical interventions and antibiotic overuse that can negatively impact wound infections and patient outcomes.

Despite ongoing conflicts, there is a dearth of comprehensive microbiological studies and clinical management guidelines in the Middle East, underscoring the need for further research and regional expertise development. In their retrospective investigation, Yaacoub *et al.* delved into the microbiological profiles and antibiotic resistance patterns of isolates (samples taken from skin, soft tissues and bones) collected from civilians injured by weapons. They found that *S. aureus* was the most commonly encountered bacterium, followed by *Enterobacterales* (44.6%), MRSA (44.6%), *P. aeruginosa* (7.6%), *Enterococci* species, and *A. baumannii*. The study also explored factors associated with multi-drug resistant (MDR) isolates, revealing heightened odds and rates of MDR among *Enterobacterales*, particularly among patients from Iraq. The prevalence of MRSA in the research corresponds with established literature on conflict-affected regions. Additionally, the prevalence of MDR *Enterobacterales* in this study reflects the endemic presence of carbapenemase-producing strains in the Middle East. Conversely, *A. baumannii* isolates were less common, with only a small subset

exhibiting MDR characteristics, consistent with previous findings on war-related injuries. The multivariable analysis revealed also that Iraqi patients exhibit elevated odds of MDR isolates in comparison to Syrian patients, and *Enterobacterales* isolates demonstrate higher odds of MDR compared to *S. aureus* isolates. Nosocomial transmission stands out as the foremost determinant of the extent of spread within hospitals. Additional contributing factors encompass the injury environment, injury site, and initial antibiotic selection. As the prevalence of these organisms in war-related wound infections continues to rise, it becomes crucial to widely disseminate and enforce infection control measures like isolation, standard and contact precautions, screening procedures and limitation of movements to curb their further emergence and transmission.
Managing war wound infections remains a multifaceted challenge, necessitating a comprehensive approach involving surgical intervention, antimicrobial therapy, and rigorous infection control measures.

Beyond trauma to address essential needs

In conflict zones, surgical care is frequently associated with addressing injuries sustained from violence, yet the majority of surgical requirements originate from causes such as infection, malnutrition, and obstetric emergencies. However, surgical initiatives in conflict areas often fail to address non-trauma surgical needs adequately, such as obstetric emergencies, general surgery and infectious diseases. The absence of reliable data on the surgical burden of disease in conflict settings results in incomplete needs assessments and insufficient planning. Despite the pressing demand for essential surgical care in conflict-affected regions, research tends to exhibit a bias towards trauma-related surgery. Additionally, humanitarian practice guidelines tend to narrowly focus on trauma and obstetric care, disregarding other surgical necessities. Limited surgical capacity, particularly in the poorest countries, contributes to the deficiency of general surgical services in conflict zones.
The psychological impact of conflict on SSIs could bring additional challenges faced by healthcare providers and patients. For example, prolonged exposure to stress and trauma in conflict settings can weaken the immune system, making individuals more susceptible to infections. Additionally, high-stress levels among healthcare workers may lead to decreased adherence to infection control protocols, further exacerbating the risk of SSIs. By acknowledging the psychological dimensions of the problem, healthcare systems/organizations can implement targeted interventions to support the mental health and well-being of both patients and providers in conflict settings.

Conclusion

Facing the intricate landscape of IPC within conflict zones demands a multifaceted and multidisciplinary approach. Despite the existence of consolidated guidelines to prevent and monitor SSIs by international organizations such as WHO and ECDC, effective collaboration among healthcare providers, humanitarian organizations, and local authorities is essential for addressing the challenges posed by limited resources, disrupted supply chains, and the heightened vulnerability of patients in these settings. By orchestrating targeted interventions and fortifying IPC practices, healthcare facilities operating amidst conflict can proactively mitigate the pervasive threat of SSIs, including those caused by MDROs, and substantially enhance patient outcomes. However, such efforts must extend beyond mere mitigation; they should embrace a proactive attitude at preventing infectious SSI outbreaks before they take root, particularly given the propensity for MDROs to

increase in conflict environments. Moreover, recognizing the crucial importance of addressing non-trauma surgical needs, such as obstetric emergencies and infectious diseases, cannot be overstated.

Addressing the role of policy and governance structures in shaping infection control practices in conflict settings is crucial for effective mitigation strategies. However, challenges such as limited resources, political instability, and bureaucratic barriers may hinder the effective implementation of these policies. By advocating for robust policy frameworks and strengthening governance structures, healthcare systems can better address the challenges of conflict settings and improve both immediate and long-term outcomes for patients affected by SSIs. It is through the fusion of concerted efforts and innovative strategies, that healthcare systems can successfully cope with the complexities of SSIs in conflict settings.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 63

Leveraging the synergy between infection prevention and control and antimicrobial stewardship to tackle antimicrobial resistance in hospital settings

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Introduction

Antimicrobial resistance (AMR) is a significant and urgent worldwide health issue in the 21st century. The World Health Organisation (WHO) has recognised AMR as a substantial menace to worldwide health, food security, and development. They have estimated that, if adequate measures are not taken, AMR might result in 10 million deaths per year by 2050. Hospitals, as crucial centres for patient care, have a significant impact on both the development and control of antimicrobial resistance (AMR). Hospitals are a breeding ground for the emergence and transmission of antibiotic-resistant bacteria due to the heavy use of antimicrobials and the susceptibility of hospitalised patients to infections. This emphasises the need for using various methods to develop a holistic strategy for containing AMR.

The complexity of addressing AMR in hospitals is demonstrated by the interdependent relationship between infection prevention and control (IPC) and antimicrobial stewardship (AMS). IPC primarily aims to prevent and control the spread of infections, while AMS focuses on maximising the effectiveness of antimicrobial drugs in treating infections and minimising the development of resistance. Understandably, these two interventions when combined can better support the efforts towards mitigating AMR.

The synergy between IPC and AMS is derived from their mutually reinforcing objectives. Implementing efficient (IPC strategies leads to a decrease in healthcare-associated infections (HAIs), thereby reducing antimicrobial use. AMS ensures that antimicrobials are provided in a suitable manner, thus preserving their effectiveness and reducing the selective pressure that leads to the development of resistance. IPC and AMS together form a strong defence against the transmission of drug-resistant pathogens in hospital environments. This chapter examines the crucial need for harnessing the collaboration between IPC and AMS to address AMR in hospitals. It examines the obstacles and hindrances to successful implementation and proposes creative solutions and future prospects for increasing this collaboration. As the healthcare community faces the challenges of AMR, it is crucial for infection prevention and antimicrobial stewardship to work together to preserve the effectiveness of antimicrobials and ensure the well-being of patients.

The role of infection prevention and control on antimicrobial resistance

IPC is a fundamental aspect of ensuring patient safety in healthcare environments, especially in hospitals, where the likelihood of HAIs is notably higher. Implementing IPC strategies is crucial for limiting the spread of infectious agents and decreasing the occurrence of HAIs. Implementing efficient IPC measures is essential in the fight against AMR as it effectively lowers the occurrence of healthcare-associated infections (HAIs) and therefore reduces the need for antibiotics. The decrease in antibiotic utilisation is crucial for impeding the progression of antimicrobial resistance. IPC plays a significant role in this process.

Reduction in healthcare-associated Infections

Direct impact. IPC measures, including hand hygiene, environmental cleaning, and isolation protocols, aim to prevent the transmission of infectious pathogens within healthcare facilities. By minimising the incidence of HAIs, these policies decrease the overall load of infections that necessitate medical intervention.

Reduced incidence of HAIs leads to a decreased need for antibiotic treatment in patients. This results in a decrease in the amount of antibiotics being prescribed and given in hospitals, which reduces the selective pressure that leads to the emergence of resistance strains.

Preventing the spread of resistant organisms

Implementing infection IPC strategies is crucial for effectively managing the transmission of multidrug-resistant organisms (MDROs) like methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant *Enterobacteriaceae* (CRE). Implementing isolation protocols, enforcing contact precautions, and utilising specific equipment for infected patients effectively restrict the spread of these drug-resistant infections, hence preventing their transmission to other patients.

Impact on antibiotic use. IPC by impeding the transmission of MDROs diminishes the necessity for the utilisation of last-resort antibiotics, which are frequently more effective and may carry a greater likelihood of promoting resistance. Efficient containment measures guarantee the continued availability and efficacy of these potent antibiotics for situations where they are genuinely necessary.

Breaking the chain of transmission

Interrupting infection cycles. IPC strategies disrupt the process by which infectious agents are transmitted in healthcare environments. For instance, strict adherence to hand hygiene protocols by healthcare personnel effectively inhibits the transmission of disease-causing microorganisms from one patient to another. Similarly,

thorough environmental sanitation effectively eliminates potential reservoirs of infection from various surfaces and equipment.

IPC interventions have a long-term impact on AMR by regularly interrupting the spread of infections in healthcare settings. This ultimately results in a decrease in the total number of illnesses, which in turn reduces the chances for pathogens to come into contact with antibiotics. Reducing this level of exposure is essential to minimise the emergence of resistant strains in the long run.

Preserving antibiotic efficacy

Slowing the development of resistance. The utilisation of antibiotics has the potential for bacteria to acquire mechanisms of resistance. By implementing efficient IPC measures, the reliance on antibiotics can be reduced, hence mitigating the rate at which antibiotic resistance emerges. This contributes to the preservation of the effectiveness of current antibiotics, guaranteeing their continued efficacy in the treatment of illnesses.

Impact on antibiotic stewardship. IPC enhances AMS initiatives by establishing conditions that reduce the need for antibiotics. The alignment between IPC and AMS enhances the overarching strategy to address AMR, as both approaches collaborate to reduce needless antibiotic utilisation and decelerate the development of resistance.

Protecting vulnerable populations

Infection prevention in patients at high risk. Individuals receiving medical care, especially those in intensive care units (ICUs) or with weakened immune systems, have an elevated susceptibility to infections. Implementing efficient IPC measures is crucial in safeguarding these susceptible populations from acquiring infections that would require antibiotic intervention.

Minimising AMR risks. Safeguarding vulnerable patients against infection decreases the necessity of subjecting them to broad-spectrum antibiotics, which are frequently necessary for serious or life-threatening illnesses. Additionally, this decreases the likelihood of acquiring resistance.

These elaborated roles clearly indicate that IPC plays a crucial role in combating AMR. IPC policies effectively lower the occurrence of HAIs, which in turn reduces the necessity for antibiotics. This reduction in antibiotic use helps to diminish the selective pressure that contributes to the emergence of resistant strains. IPC, when combined with antimicrobial stewardship, plays a crucial role in a holistic approach to slowing down the advancement of AMR and safeguarding the effectiveness of current medications. By strictly implementing IPC strategies, healthcare settings can make substantial progress in managing the transmission of drug-resistant organisms and safeguarding the effectiveness of antimicrobial treatments for the future.

The role of antimicrobial stewardship in mitigating antimicrobial resistance

AMS is a systematic approach that aims to optimise the utilisation of antimicrobial drugs in order to improve patient outcomes, minimise AMR, and reduce the transmission of infections caused by MDROs. AMS encompasses the careful selection, dosage, administration method, and duration of antimicrobial treatment to ensure that patients receive the most efficient therapy while minimising any negative side effects. Thus, effective antimicrobial stewardship treatments play a crucial role in maximising the use of antimicrobials and addressing resistance in hospital environments.

A range of AMS interventions have been used globally all of which may have the following objectives:

1. To verify the suitability of the antibiotic based on the patient's condition and the available diagnostic information

2. To mitigate the excessive and inappropriate utilisation of vital antimicrobial agents.
3. To ensure that the utilisation of antibiotics is in accordance with institutional norms and optimal practices.
4. To minimize patients' exposure to broad-spectrum antibiotics, hence reducing the likelihood of resistance development and its harmful consequences.
5. To advocate for the utilisation of the most precise and focused therapy available.
6. To enhance the standard of antimicrobial prescribing. Promote compliance with evidence-based guidelines.
7. To reduce the duration of hospital admissions and minimise healthcare expenses.
8. To minimise the likelihood of complications associated with intravenous procedures while ensuring the continued efficacy of treatment.

Synergy between infection prevention and control and antimicrobial stewardship

The synergy between IPC and AMS is a critical component of efforts to minimise infection incidence and antibiotic resistance in healthcare settings. In this section, we highlight the impact of the role of these interventions on each other as a means of mitigating AMR.

IPC's role in reducing the infection rate

Barrier methods and hand hygiene. To avoid disease transmission, IPC programs follow strict hand hygiene practices and use personal protective equipment (PPE). IPC reduces the spread of infectious organisms, which directly reduces the incidence of healthcare-associated infections (HAIs) such as catheter-associated urinary tract infections (CAUTIs), central line-associated bloodstream infections (CLABSIs), and ventilator-associated pneumonia (VAP).

Environmental cleaning and disinfection. IPC measures guarantee that the hospital environment, including surfaces, equipment, and patient rooms, is thoroughly cleaned and disinfected on a regular basis. This decreases the pathogen reservoir in the healthcare context, hence limiting the spread of illnesses.

Isolation and grouping. By separating patients with contagious infections and grouping patients with comparable infections, IPC helps to prevent pathogen spread within hospitals. This tailored approach aids in outbreak control and the prevention of cross-contamination among patients.

Impact on antibiotic usage

Reduced initial infections. By efficiently preventing infections, IPC decreases the requirement for antibiotics. Fewer illnesses mean fewer instances when antibiotics are prescribed, resulting in decreased overall antibiotic use.

Preventing subsequent infections. Effective IPC not only prevents primary infections, but also minimises the risk of subsequent infections that may result from the initial ones. For example, preventing surgical site infections (SSIs) lowers the probability of recurrent infections that may necessitate broad-spectrum antibiotics.

AMS's role in ensuring proper antibiotic use

AMS programs develop and enforce antibiotic prescribing standards, ensuring that antibiotics are used properly when necessary. This includes selecting the appropriate antibiotic, at the correct dose, for the appropriate time, and only when necessary. Two vital strategies employed by AMS are antibiotic time-outs and de-escalation strategies.

Antibiotic time-outs are AMS therapies that include reassessing antibiotic medication 48-72 hours after it is commenced. This enables therapy adjustment based on the most recent clinical data, including culture results, hence decreasing the use of unnecessary or excessively broad antibiotics.
De-escalation strategies. Once the causal pathogen has been identified, AMS recommends switching from broad-spectrum antibiotics to narrow-spectrum medicines. This focused approach reduces the likelihood of acquiring antibiotic resistance.

Impact on infection control
Preventing resistance development. AMS lowers the selective pressure that causes the evolution of antibiotic-resistant organisms by ensuring that antibiotics are only used when absolutely essential and in the most appropriate way. This is crucial for avoiding the development of MDROs, which are difficult to treat and control.
Reduced collateral damage. Inappropriate antibiotic treatment can cause collateral damage, such as disturbance of normal flora and the rise of resistant organisms such as multi-drug-resistant *Pseudomonas aeruginosa* (MDR-PA). AMS helps to reduce this danger by encouraging the prudent use of antibiotics, which aids IPC efforts to control these organisms.

Synergistic effects on healthcare outcomes
IPC prevents infections and resistance, reducing the need for antibiotics. This not only reduces overall antibiotic use, but also reduces the likelihood of incorrect use, which is a major generator of resistance.
AMS optimises antibiotic use. When antibiotics are required, AMS ensures that they are administered in a manner that reduces the risk of resistance. This includes avoiding needless broad-spectrum antibiotics, which are more likely to contribute to resistance, and instead opting for focused therapy based on precise diagnoses.
Improved patient outcomes. Fewer infections and improved recovery rates: The combined efforts of IPC and AMS result in fewer infections, which means shorter hospital stays, cheaper healthcare expenses, and improved patient outcomes. Patients are less prone to develop infection-related problems or to suffer negative consequences from needless antibiotic treatment.
Sustained antibiotic efficacy. By minimising needless antibiotic use and resistance, the synergy between IPC and AMS helps to retain the efficacy of existing antibiotics, ensuring that they remain useful treatment alternatives in the future.

Cost savings and resource optimisation

Reduced hospital burden
Lower infection rates. Fewer infections mean fewer expensive treatments and shorter hospital stays, lowering the total impact on healthcare resources.
Optimised antibiotic usage. AMS initiatives contribute to lowering the expenses associated with antibiotic overuse, such as the costs of treating antibiotic-resistant illnesses and managing the adverse effects of improper antibiotic usage.

Real global impact of IPC and AMS in hospital settings

The integration of IPC and AMS in various settings across the world has led to significant reductions in AMR. Although challenges such as limited resources and infrastructure exist in regions such as Africa, targeted efforts in various African countries have demonstrated the potential for substantial progress. Here are some real-world examples from Africa.

Reduction in HAI rate in Ghana's University Hospital, KNUST

At the University Hospital., KNUST in Ghana's Ashanti region, high levels of bacterial resistance to cephalosporins and meropenem in the hospital's antibiogram were reported. A bundled stewardship programme including AMS and IPC training and capacity building, resulted in reduced antibiotic use and a reduction in the HAI rate from 17.5% to 6.5% over a six-month period.

Controlling multi-drug-resistant tuberculosis (MDR-TB) in South Africa

Background. South Africa has one of the highest burdens of tuberculosis (TB) in the world, including multi-drug-resistant TB (MDR-TB). The spread of MDR-TB in healthcare settings has been a major public health challenge.

Integrated approach. The South African government and healthcare institutions employed an integrated IPC and AMS strategy to tackle MDR-TB. IPC measures include the use of negative pressure rooms, personal protective equipment (PPE), and patient isolation to prevent the transmission of TB in healthcare facilities. Simultaneously, AMS practices involve strict guidelines on the use of second-line anti-TB drugs, ensuring that they are only used when absolutely necessary and in an appropriate regimen.

Outcome. These efforts have led to a decrease in the transmission of MDR-TB within healthcare settings. For instance, in some hospitals in KwaZulu-Natal, the integration of IPC and AMS has significantly reduced the incidence of nosocomial MDR-TB, contributing to the broader control of drug-resistant TB in the region.

Reduction of neonatal sepsis in Kenya

Background. Neonatal sepsis, often caused by resistant bacteria, is a major cause of mortality in sub-Saharan Africa, including Kenya. The misuse of antibiotics has exacerbated the problem by fostering the emergence of resistant strains.

Integrated approach. In response, several hospitals in Kenya have implemented integrated IPC and AMS programs. IPC measures such as hand hygiene, sterilization of equipment, and proper waste disposal are coupled with AMS initiatives that focus on the rational use of antibiotics in neonatal care. These initiatives include the development of guidelines for antibiotic use and training healthcare workers in both IPC and AMS.

Outcome. A significant reduction in neonatal sepsis rates has been reported in hospitals where these integrated programs have been implemented. For example, in Kakamega County General Teaching and Referral Hospital (KCTRH) in Kenya, a coordinated IPC-AMS approach has led to a marked decrease in the incidence of maternal sepsis (one major cause of neonatal sepsis) caused by resistant pathogens, improving neonatal outcomes and reducing mortality rates.

Reduction of caesarean section surgical site infections in Tanzania

Background. SSIs are a common and serious complication in low-resource settings, including Tanzania. These infections often involve antibiotic-resistant bacteria, making them difficult to treat.

Integrated approach. Dodoma Regional Referral Hospital in Tanzania implemented an integrated IPC and AMS program to reduce SSIs. The program included measures such as preoperative antibiotic prophylaxis

according to AMS guidelines, strict adherence to sterilization protocols, and continuous monitoring and feedback on infection rates.
Outcome. The total number of post-caesarean section surgical site infections significantly decreased from 48% in the pre-intervention group to 17% in the post-intervention group. This reduction was statistically significant.

Coordinated Implementation of AMS and IPC

Coordinated execution of IPC and AMS initiatives is required to maximise the effectiveness of both programs. By combining these two crucial areas, healthcare facilities can develop a collaborative strategy for lowering healthcare-associated infections (HAIs) and combating antimicrobial resistance (AMR). Widely accepted strategies for coordinating IPC and AMS initiatives, with a focus on collaborative committees, include shared data metrics, and integrated educational programs.

Joint committees

Joint committees include individuals from the IPC and AMS teams, as well as essential stakeholders such as infectious diseases specialists, pharmacists, microbiologists, nursing leaders, and hospital management. This enables communication and cooperation between IPC and AMS teams, reducing silos in addition to streamlined decision-making. This facilitates faster and more coordinated responses to emerging infection and resistance risks. Such collaborative committees coordinate and reinforce efforts to avoid infections and manage antibiotic use through the use of comprehensive integrated approaches and strategies.

Shared data metrics
Another strategy is through shared data metrics such as integrating surveillance systems for AMS and IPC-related activities. Such integrated programmes measure antimicrobial consumption, infection rates, resistance patterns and compliance with AMS and IPC protocols and standards at the facility. The result is a comprehensive insight into understanding the impact of antimicrobial use on infection and resistance rates. It also promotes data-driven solutions for infection prevention and management as well as enabling early detection of outbreaks or resistance for prompt action. Embedding such shared data metrics into electronic health records can allow for real-time monitoring and reporting of vital metrics for AMS and IPC.

Integrated educational programs
Integrated educational programs that cover both IPC and AMS issues, helping healthcare personnel understand the link between infection prevention and effective antimicrobial use can also be used to leverage their synergy. This could include workshops and seminars where IPC and AMS experts lead sessions on antimicrobial resistance, infection control, and rational antibiotic prescribing. E-learning platforms as well as simulation exercises could offer flexible and thorough IPC and AMS training to all healthcare staff. They can also demonstrate how integrated IPC and AMS interventions impact patient outcomes and resistance patterns.
Other strategies include establishing a co-leadership structure for the IPC and AMS programs, joint policy and procedure development, collaborative quality improvement projects, and cross-departmental communication channels.

Outcomes of the synergy

Coordinated implementation of IPC and AMS increases the effectiveness of both IPC and AMS activities, resulting in larger reductions in HAIs and AMR. It also ensures that all areas of infection prevention and antimicrobial use are covered consistently, with no gaps. Additionally, sharing resources, such as staff, training materials, and technological platforms, allows for more efficient use of existing resources while avoiding duplication. Improved patient outcomes as well as a stronger organisational culture due to teamwork and shared responsibility are an additional impact of this synergy.

Healthcare facilities can achieve a unified strategy for infection prevention and antibiotic use by encouraging teamwork, leveraging shared resources, and maintaining constant communication. This collaborative effort not only improves patient outcomes and minimises the burden of HAIs and AMR, but it also fosters a culture of safety and continuous improvement in healthcare settings. To achieve long-term success, leaders of AMS and IPC teams must commit to these tactics, invest in resources, and conduct ongoing evaluations. However, the long-term benefits of combined IPC and AMS activities make it a worthy endeavour for any healthcare organisation that wants to offer high-quality, safe, and effective treatment to its patients.

Leveraging technology

The incorporation of digital technologies and health information technology into IPC and AMS programs is transforming how hospitals manage infections and antibiotic use. Electronic health records, predictive analytics, automated surveillance systems, clinical decision support, and telemedicine are just a few of the advancements that are increasing the effectiveness of these initiatives. By leveraging these technologies, healthcare facilities can increase the precision, speed, and consistency of their IPC and AMS operations, resulting in better patient outcomes, lower antibiotic resistance, and more effective resource utilisation. As healthcare evolves, the continuous development and acceptance of technological advancements will be important for developing IPC and AMS practices while also tackling the growing concerns of HAIs and AMR.

Challenges

Integrated AMS and IPC programs may be plagued by the same challenges faced by these interventions on their own as well as challenges unique to such integration. Examples of the major challenges of the integration of AMS and IPC and their respective solutions are outlined below:

- *Resource constraints*. Lack of trained workers and resources, which impedes integration efforts.
  Solution. Train healthcare professionals to do both IPC and AMS jobs while advocating for government and donor support.
- *Lack of coordination.* IPC and AMS teams sometimes function separately, with fragmented leadership.
  Solution. Create combined IPC-AMS committees and designate unified leadership to improve coordination.
- *Inadequate data systems*. Insufficient surveillance and lab assistance impede effective monitoring.
  Solution. Invest in electronic health records, enhance lab capacity, and collaborate with external laboratories.
- *Cultural barriers*. Staff resistance to change and a lack of AMS awareness, which affects adherence to integrated practices.

Solution. Implement behaviour change initiatives and recruit advocates to promote integrated IPC-AMS practices.

- *Competing priorities*. Healthcare staff prioritise urgent tasks over IPC-AMS activities.
  Solution. Create integrated procedures and streamline processes to make participation more efficient.
- *Training Gaps*. Inconsistent training and the absence of standardised rules inhibit integration.
  Solution. Offer unified training programs and standardise criteria for both IPC and AMS.
- *Policy challenges*. Weak, isolated policies and ineffective enforcement stymie successful implementation.
  Solution. To achieve compliance, IPC-AMS policies should be harmonised and regulatory enforcement strengthened.

Well-planned programs take these potential challenges into consideration with mitigation strategies developed in response. These integrated programs will therefore be able to surmount such hurdles together further strengthening their experience, organizational culture as well as the sustainable impact of AMS and IPC.

Conclusion

The synergy between IPC and AMS is critical in the fight against HAIs and AMR. IPC minimises the number of infections, reducing the need for antibiotics, whereas AMS guarantees that antibiotics are used appropriately when necessary, preventing the development and spread of resistance. This integrated strategy not only improves patient outcomes but also ensures that antimicrobials remain effective for future generations, resulting in a safer and more sustainable healthcare system. The future of combatting AMR and improving infection control is dependent on our dedication to continued research, innovation, and supportive policy. We can maintain and improve on IPC and AMS success by investing in new technologies, improving our understanding of resistance mechanisms, and encouraging international collaboration. A proactive and coordinated approach will be required to address growing difficulties and keep our healthcare systems resilient and effective in the face of changing threats.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 64

Education and training programs for infection prevention and control professionals

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Introduction

Throughout the first quarter of the 21st century, significant outbreaks and epidemics have been observed globally, including H1N1 influenza virus disease (2009), Ebola virus disease (2014-16), Middle East respiratory coronavirus syndrome (2012), as well as more recent occurrences such as coronavirus disease 2019 (COVID-19) and the 2022 monkeypox virus (2022-24). These public health crises have underscored deficiencies in infection prevention and control (IPC) programs at both national and facility levels worldwide, irrespective of a country's economic status or available resources. Furthermore, the increasing endemic burden of healthcare-associated infections (HAIs) and multidrug-resistant organisms (MDRO) which harms patients across the healthcare system in every country poses a significant threat to the healthcare system.

HAIs are infections acquired by patients while receiving medical treatment in healthcare facilities, and are one of the most common complications or adverse events affecting patients and healthcare workers. They result in increased morbidity and mortality and impact the capacity of health systems to function effectively by prolonging hospital stays and increasing healthcare costs. Furthermore, these infections can result in the increased usage of antimicrobial agents, thereby fueling the problem of antimicrobial resistance (AMR).

The emergence and spread of MDR and XDR organisms, such as carbapenem-resistant *Enterobacteriaceae* (CRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities, further complicates the treatment of HAIs. These organisms have developed resistance to multiple classes of antibiotics, making them difficult, and in some cases impossible, to treat with standard antimicrobial agents. This can result in treatment failures, prolonged illness, and increased risk of transmission to other patients. The global spread of MDR and XDR organisms poses a serious threat to public health by limiting treatment options, increasing the risk of healthcare-associated outbreaks, and contributing to the rise of AMR worldwide.

However, more than half of these threat can be prevented by implementing effective IPC interventions. These are set evidence-based practices that are designed to prevent the spread of HAIs and AMR among patients, healthcare workers and visitors in healthcare facilities. The World Health Organization (WHO) has formulated a set of recommendations referred to as the core components of effective IPC programs. These components are based on evidence-based findings on their efficacy in reducing HAIs, expert insights, and input from key stakeholders in the field. The core components are: 1) IPC programs; 2) IPC guidelines; 3) IPC education and training; 4) HAI surveillance; 5) multimodal improvement strategy implementation of IPC programs; and 6) IPC monitoring, auditing, and feedback at the national and facility-levels. And additional components at only the facility level include 7) workload, staffing, and bed occupancy and 8) the built environment, materials, and equipment for IPC.

A strong understanding of IPC principles and practices by healthcare workers (HCWs) are fundamental for effective implementation of IPC programs. As indicated above, IPC education and training is recommended by the WHO as one of the core components of IPC program that is required to improve compliance and implementation of effective IPC interventions both at national and healthcare facility level. Research has shown that HCWs who have received proper education and training in IPC practices play a vital role in breaking the chain of HAI transmission within healthcare settings, including the transmission of resistant organisms.

In the following sections we will discuss in detail how the national and healthcare facility IPC programs can effectively implement their IPC education and training program.

National and healthcare facility IPC programs

The role of national IPC program

One of the minimum requirements for the national IPC programs is to ensure the existence of a national IPC policy that mandates all healthcare workers receive both in-service and pre-service training.

IPC pre- and post-graduate and in-service training and education

IPC training and education are needed for effective implementation of IPC guidelines and standard operating procedures. Healthcare professionals who have received formal IPC training are more likely to comply with the standards of infection prevention and control. However, various studies have shown that; the education and training of IPC in undergraduate and postgraduate health science studies are insufficient and consequently, compliance of IPC practices among the students is poor. In addition, according to a 2019 survey on the implementation of IPC core components in healthcare facilities, IPC education and training received the lowest score.

The national Infection Prevention and Control program should develop IPC pre- and postgraduate as well as in-service curriculum in collaboration with the local academic institutions. These curriculums should cater to various groups, including IPC specialists, all HCWs engaged in service delivery and patient care, and other personnel such as administrative and managerial staff, auxiliary service staff, and cleaners. The program should ensure that the curriculums are comprehensive, relevant, and tailored to the specific needs of different roles within the healthcare setting. This approach will help in enhancing the knowledge and skills of a wide range of healthcare professionals and support staff, ultimately improving the overall effectiveness of infection prevention and control measures in healthcare facilities.

One of the most effective and sustainable way to improve the IPC practices across the healthcare system is to strengthen the IPC education and training in the pre and post graduate health science programs. The

national IPC team should work towards ensuring that the IPC training and education curriculums is well integrated into the national under and postgraduate health science education programs so that the future healthcare professionals are well equipped with knowledge and skills necessary to effectively prevent and control infection in healthcare settings.

IPC education and training can be delivered by incorporating IPC principles and practices into the curriculum of relevant courses or providing the IPC course as a standalone course. For post-graduate health science programs, the IPC training and education can be tailored to the specific needs of the program. In this regard, the WHO IPC core competencies for healthcare professionals can be used as a strong foundation, to design and develop IPC curriculums and delivering the IPC training and education.

Furthermore, tailored curricula designed to enhance in-service training and provide ongoing education for healthcare and support staff (such as nurses, doctors, allied health professionals, and cleaners) significantly enhances the efficiency and cost-effectiveness of implementation. It is essential that training programs are customized to suit the roles of different healthcare professionals and are accessible to all individuals working in health and care settings, including patient caregivers and personnel employed by external organizations.

Developing standardized training materials

Healthcare facilities, especially those in LMIC, are often challenged with resources and expertise to develop educational materials for the training of their health and care workers. On the other hand, the national program, through mobilizing resources and experts in the field, can develop standardized training material based on national and international guidelines for healthcare professionals at different level. Once the standardized training materials is developed, the healthcare facility IPC programs can adapt and train their healthcare workers on the latest protocols and best practices for preventing and controlling infections.

The national IPC program also plays a critical role in developing evidence-based IPC standard operating procedures (SOPs) that can be adopted by healthcare facilities. IPC SOPs are important for the training HCWs and to standardize the IPC practices across the healthcare system. The SOPs should be based on the national and international guidelines and should include all IPC practices that are categorized under standard precautions and transmission-based precautions. By incorporating these SOPs into their training programs, healthcare facilities can ensure that their HCWs are well-informed and equipped to implement best practices in their daily practice.

Supporting facility-level IPC training and education

Supporting IPC education and training of healthcare workforce is one of the core functions of the national programs. The national IPC program should provide guidance, resources and expertise for in-service training to be rolled out at the facility level to ensure that the IPC training and educations are being given based on evidence-based and ministry-approved guidelines, according IPC core competencies for healthcare workers and covering all professional categories.

In addition, the national IPC team plays a key role in monitoring and evaluating the implementation of IPC training at the facility level to identify area for improvement and provide targeted support. This can be done through conducting assessments, audits, and provide feedback to ensure that all front-line healthcare workers have received IPC training and education and they are adhering to IPC best practices.

Facility-level IPC training and education

- Training all front-line clinical staff (Healthcare professionals).
- Training of IPC Staff (focal/ IPC Team).
- Cleaners and other supportive staff.

IPC education and training is one of essential component of facility-level IPC program, contributing to the ultimate prevention of HAIs and AMR and the provision of high-quality health service delivery. Facility-level IPC programs should plan and implement IPC training and education for its health workforce to develop a skilled and knowledgeable health workforce with IPC basic competencies.

WHO recommends that all front-line clinical staff and cleaners must receive education and training on the facility IPC guidelines/SOPs upon employment for the effective implementation of IPC.

Three categories of human resources were identified by WHO as targets for IPC training and requiring different strategies and training content: these are

- IPC Professionals specialists;
- All HCWs involved in service delivery and patient care; and
- Other personnel that support health service delivery (administrative and managerial staff, auxiliary service staff, cleaners, etc.).

Training of IPC professionals

One of the fundamental requirements for the functional IPC program at healthcare facilities is to have a dedicated and trained IPC professional and team that implements and lead the efforts of preventing HAI and combating AMR through implementing IPC recommendations Medical and nursing staff, who trained and specialized in preventing and managing infections in healthcare settings, at a certified IPC course or equivalent; at least one professional per 250 beds is recommended to lead the IPC work of the facility IPC professionals work closely with healthcare teams to develop and implement strategies to prevent healthcare-associated infections, conduct surveillance for infectious diseases, investigate outbreaks, and educate healthcare staff and patients on infection control practices.

Countries like Sierra Leone and Ethiopia have developed a 6-month long course for the training of the IPC focal of their healthcare facilities, national and sub national IPC programs. They designed a unique course that combines classroom learning with hands-on training at the healthcare facilities. The trainings are designed and implemented by the national IPC programs in collaboration with partners and local academic institutions. It is reported that graduates of these training programs have played pivotal roles in implementing IPC activities across their health system like; in strengthening the national IPC program implementation, implementing HAI surveillance, providing IPC trainings, and participating in emergency response activities.

Infection prevention and control training delivery methods

- *Traditional classroom-based training*: is a vital method for educating IPC professionals, providing direct interaction and hands-on experiences that are often more engaging and effective than other learning methods.
- *Online and e-learning methods*: have become increasingly popular for training IPC professionals due to their flexibility, scalability, and accessibility. Properly designed online training programs can provide effective education that meets the diverse needs of healthcare workers across various settings.
- *Interactive online content for IPC training*: Creating engaging and interactive content is essential to keep learners motivated and ensure that they retain and apply IPC principles effectively.
- *Simulation and hands-on training for IPC professionals***;** simulation and hands-on training are critical components of IPC education that allow professionals to practice and refine their skills in a controlled, realistic environment. This approach bridges the gap between theoretical knowledge and real-world application, enhancing the competency and confidence of IPC professionals. These training methods are designed to

mimic clinical scenarios, enabling participants to develop problem-solving abilities, technical skills, and effective communication strategies essential for infection prevention.

- *Workshops and seminars for IPC professionals***;** workshops and seminars are pivotal in enhancing the skills and knowledge of IPC professionals. These interactive learning formats provide an opportunity for participants to engage with subject matter experts, share best practices, and address specific IPC challenges. Workshops focus on hands-on activities, group discussions, and problem-solving, while seminars typically involve presentations and lectures from experts. Both formats are essential for keeping IPC professionals updated on current trends, guidelines, and evidence-based practices.

Assessing learner competency in IPC education and training programs

Assessing the competency of IPC professionals is crucial for ensuring that training programs effectively impart the necessary knowledge and skills to prevent infections within healthcare settings. Competency assessment not only evaluates learning outcomes but also identifies areas requiring further development. These assessments provide valuable feedback to both learners and educators, fostering continuous improvement in IPC practices.

Current challenges and innovative approaches towards improving IPC education and training

Improving IPC education and training faces several challenges that hinder its effectiveness. One of the key obstacles is the limited availability of resources, especially in low-resource settings where funding, equipment, and materials for comprehensive IPC training are scarce. Another challenge is the inconsistency in training standards across different regions and facilities, leading to variations in the quality and content of IPC education.

Challenges in IPC training and education

There are some key highlighted challenges in IPC training and education for instance.

- *Rapid changes in IPC guidelines and practices*: Guidelines and best practices are constantly evolving, making it difficult for healthcare professionals to stay current with the latest information and procedures.
- *Inconsistent knowledge and practice across diverse healthcare settings*: IPC education and training need to be relevant to various healthcare environments and professionals at all level of healthcare system including from tertiary hospitals to primary healthcare and community level.
- *Bridging the knowledge gap among healthcare professionals*: There may be discrepancies in the training that newly hired employees and part-time employees get, and their levels of IPC knowledge may differ.
- *Behavioral and compliance challenges*: Some healthcare personnel may experience behavioral or motivational problems that make it difficult for them to follow IPC procedures, even with proper training.

IPC education and training can be greatly improved through innovative solutions, which improve patient safety, and protect the public's health while also resulting in better infection control practices and improved health outcomes.

Innovative approaches to improve IPC education and training

There are some key highlighted innovation modalities to improve IPC education and training.

- *Tailored modules*: Frequently updated, concise education for targeted units. This makes it possible for healthcare practitioners to become up-to-date on IPC guidelines.
- *Customized training programs*: Adapting instruction to particular contexts guarantees that the course covers the particular difficulties and resources of different environments.

- *Onboarding modules*: Integrated into the onboarding process, comprehensive IPC training modules guarantee that all new and part-time employees receive consistent training.
- *Behavioral nudges*: Improving compliance can be achieved by implementing minor adjustments to the work environment, such as posting reminders, using multimodal methods, and improving accessibility to hand hygiene stations.
- *Data analytics and feedback loops*: Monitoring compliance rates and getting staff input through data analytics enables you to pinpoint problem areas and design different interventions.

Digitalization and its impact on the IPC program

The discipline of IPC has seen innovations that are a reflection of both the evolving approaches to enhancing public health and safety and the ongoing advancements in technology. This session provides an overview of emerging technologies and their implications.

Machine learning and artificial intelligence (AI): These two fields are being utilized more to forecast epidemics, spot trends in infection data, and customize IPC procedures. Machine learning can also help with patient risk assessment using electronic health information, which can result in more focused IPC interventions. Improved surveillance technologies make it possible to monitor in real-time and react to infection responses more quickly. Furthermore, automated reporting systems help the speed and precision of epidemic detection using automated systems to gather and evaluate IPC data.

Research focus areas for the IPC program

To improve the IPC program and inform policymakers researching the following areas is very important:

- Evaluating how digital health technologies, including electronic health records and health information exchanges, can enhance IPC education, training and practices.
- Undertaking extended research projects to assess the efficiency of various IPC interventions and technology across a range of time periods.
- Monitoring how cultural and behavioral elements affect IPC practices and patient and healthcare staff compliance.
- Analyzing how IPC practices vary globally and the impact of socioeconomic factors on infection control.

Global perspectives on IPC education and training

Education and training programs for IPC professionals are essential to ensure effective management of infections and prevention of outbreaks. These courses are intended to give healthcare professionals and other pertinent staff members the information and capacities they need to establish and maintain IPC practice. An outline of the main elements and categories of IPC professional education and training programs can be found here.

Understanding the various IPC education and training methods used in different countries and promoting international cooperation will help the global community to share important knowledge and competency and improve infection control practices.

Common approach used in IPC education and training

- Certification programs.
- Degree programs.
- Specialized training workshops.
- Online training and e-learning modules.

- On-the-job training.
- Continuing education and learning collaborative.

Conclusion

Effective IPC education and training are critical for preventing HAIs and controlling AMR. National and healthcare facility programs must develop comprehensive, evidence-based training curricula, utilize innovative methods, and adapt to evolving digital technologies to enhance IPC practices globally and locally.

Competing interests

The authors have no financial and non-financial competing interests to declare.

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Chapter 65

Infection prevention and control in low resource settings: opportunities for improvement

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Introduction

Infection Prevention and Control (IPC) practices are critical in healthcare settings, especially in low-resource environments where the risk of infections can be higher due to limited infrastructure, inadequate supplies, and poor sanitation. Effective IPC measures are essential to reduce healthcare-associated infections (HAIs) and the spread of diseases, particularly in settings with constrained access to medical equipment, hygiene supplies, and trained personnel. Implementation of IPC remains a challenge in low-resource settings but with potential for improvement in low resource settings.

Water, sanitation and hygiene (WASH) is key in IPC and promotes hand hygiene including the use of soap and water or alcohol-based hand sanitizers to prevent infections. Consequently, in low-resource settings, access to clean water may be limited, so promoting proper handwashing with locally available resources and encouraging alternative methods like alcohol-based hand rubs where possible can significantly reduce infection rates. Evidence has demonstrated that healthcare facilities in low-resource settings often lack adequate waste disposal systems which affects the prevention of infections. Therefore, implementing simple waste segregation systems, such as separating infectious waste from non-infectious waste and providing safe disposal methods, can help prevent the spread of infections. Frequently touched surfaces, such as bed rails, doorknobs, and medical equipment, should be regularly disinfected using affordable and locally available disinfectants like chlorine-based solutions.

The use of personal protective equipment (PPE), such as gloves, masks, and gowns, is vital for protecting healthcare workers and patients. However, implementation of the use of PPE tends to be challenging in resource-limited countries because of shortage of PPE.

This chapter describes IPC practices in low resource settings and provided recommendations on strategies to mitigate these challenges. Articles relating to IPC in low resource settings were explored with no time limitation employed because of little information in the subject matter across low resource settings.

Infection prevention and control practices and burden of disease in low resource settings

The effective implementation of IPC measures in low resource settings is hindered by the high burden of diseases. The burden of infections in low-resource settings remains a significant global health challenge, disproportionately affecting vulnerable populations and contributing to high morbidity and mortality rates. These settings, often characterized by poor infrastructure, inadequate healthcare services, and limited access to clean water and sanitation, are breeding grounds for infectious diseases.

Barriers to implementing effective infection prevention and control in low-resource settings

Implementing effective IPC in low-resource settings faces numerous barriers that hinder the establishment and maintenance of robust IPC programs in such environments. Some of the key barriers to implementing effective IPC in low resource settings include:

Inadequate financial resources

One of the primary barriers to IPC implementation in low-resource settings is a lack of financial investment in healthcare systems. Many countries face budget constraints that limit their ability to invest in essential IPC materials, such as PPE, hand hygiene supplies, and disinfectants. Additionally, the absence of funds for constructing proper isolation facilities or purchasing sterilization equipment leaves healthcare systems ill-equipped to manage infection control effectively.

High burden of antimicrobial resistance (AMR)

A growing concern in low-resource settings is antimicrobial resistance (AMR), which occurs when pathogens develop resistance to drugs that were once effective against them. AMR complicates the treatment of infections and leads to higher rates of treatment failure, prolonged hospital stays, and increased healthcare costs. The misuse and overuse of antimicrobials, including antibiotics, in both human medicine and agriculture, is a primary driver of AMR in low-resource settings. Limited access to diagnostic services means that antibiotics are often prescribed without confirming bacterial infections, further fueling resistance.

Inadequate infrastructure to support infection prevention and control

Healthcare infrastructure in low-resource settings is often insufficient to support comprehensive IPC measures. Many hospitals and clinics lack proper ventilation systems, isolation wards, and basic sanitation facilities. For instance, clean running water, crucial for hand hygiene and cleaning, is not always available. Furthermore, electricity shortages make it difficult to maintain critical equipment like autoclaves for sterilization. Without an adequate infrastructure, healthcare workers struggle to adhere to IPC standards, increasing the risk of infection transmission.

Shortage of essential supplies for infection prevention and control

A consistent supply of essential IPC materials, including gloves, masks, gowns, and hand sanitizers, is often lacking in low-resource settings. This scarcity forces healthcare workers to reuse supplies or forego certain protective measures altogether, elevating the risk of HAIs. During disease outbreaks, such as COVID-19 or Ebola, these shortages are exacerbated, as global demand for these supplies spikes, further limiting access for low-resource regions.

Insufficient awareness and training on infection prevention and control

A lack of IPC training among healthcare workers and support staff is a significant barrier to infection control in low-resource settings. Many healthcare providers are not adequately educated on the importance of hand hygiene, proper PPE use, and sterilization techniques. Continuous training programs are often absent, and new staff may not receive any formal IPC education. Additionally, there may be a lack of awareness about the significance of IPC practices at the community level, which can lead to inconsistent application of preventive measures in healthcare and public settings.

Cultural practices and beliefs

In many low-resource settings, cultural practices and beliefs influence healthcare behaviors and can pose barriers to IPC implementation. For instance, in some cultures, caregivers may view self-medication or traditional healing practices as preferable to seeking professional healthcare, which can delay treatment and allow infections to spread. Moreover, resistance to wearing masks or reluctance to adhere to hygiene practices may be rooted in mistrust of the healthcare system or lack of education on disease prevention.

Inadequate human resource for effective infection prevention and control

A shortage of healthcare workers is a critical barrier to effective IPC. In many low-resource settings, the ratio of healthcare workers to patients is extremely low, and the few available workers are often overburdened. This leaves little time to focus on IPC protocols such as hand hygiene, proper waste disposal, and environmental cleaning. Overworked staff may also experience burnout, leading to lapses in infection control practices.

Inadequate waste management systems

There is often poor waste management is a major issue in many low-resource settings. Healthcare facilities often lack appropriate systems for disposing of medical waste, including sharps and biohazardous materials. Inadequate segregation of infectious waste from non-infectious waste can lead to increased exposure to infections for healthcare workers, patients, and the community. Open burning of medical waste is a common practice in some regions, posing additional health and environmental risk.

Lack of national infection prevention and control guidelines and policies

Many low-resource settings lack national IPC guidelines, policies, or enforcement mechanisms to ensure that infection control practices are standardized and followed across healthcare facilities. Inconsistent or outdated guidelines may not reflect the current best practices in infection control, leaving healthcare workers without a clear roadmap for implementing effective IPC measures. Additionally, without government enforcement or regulatory oversight, facilities may lack accountability in maintaining IPC standards.

Poor access to diagnostic and surveillance tools

Surveillance and diagnostics are essential for monitoring infection rates and identifying potential outbreaks, yet many low-resource settings lack the tools and technology to carry out these tasks. The absence of laboratory capacity to perform routine testing, such as AMR surveillance or pathogen identification, limits the ability of healthcare facilities to detect and respond to infections early. As a result, HAIs and infectious diseases can go unnoticed until they become widespread.

Inconsistent supply of clean water and sanitation

Clean water and sanitation are fundamental for IPC, but in low-resource settings, these basic necessities are often not consistently available. In many rural or underserved areas, healthcare facilities may operate without reliable access to clean water for handwashing, cleaning, and sterilization. The absence of proper sanitation also leads to increased rates of infections like cholera and typhoid, which further strain healthcare resources.

Lack of monitoring and evaluation systems

Ongoing monitoring and evaluation are critical for ensuring that IPC practices are followed and adapted as needed. Consequently, in low-resource settings, healthcare facilities often lack the capacity to monitor IPC compliance due to limited staffing or the absence of electronic health information systems. Without proper monitoring, it is difficult to assess the effectiveness of IPC interventions or identify areas for improvement.

Strategies to strengthen infection prevention and control in low-resource settings

Strengthening IPC in low-resource settings is crucial to preventing the spread of HAIs and improving patient safety. Despite the numerous challenges faced, there are effective strategies that can be implemented to enhance IPC practices. These strategies focus on improving resources, training, infrastructure, and awareness at both the facility and community levels.

Increase funding and resource allocation

One of the primary strategies for strengthening IPC is increasing financial investment in healthcare systems. This should first be done by engaging leadership in the development and implementation of the IPC program. Governments, international organizations, and donors need to prioritize IPC by allocating more resources for basic supplies such as PPE, hand sanitizers, disinfectants, and cleaning materials. Additionally, funding should be directed toward upgrading healthcare infrastructure, including WASH facilities, which are critical for effective infection control.

Strengthen healthcare infrastructure

Improving healthcare infrastructure is vital to enhancing IPC in low-resource settings. This includes upgrading facilities to ensure access to clean water, reliable electricity, and proper ventilation systems. Isolation wards should be created to prevent cross-contamination in hospitals and clinics, and autoclaves or other sterilization equipment should be made available for cleaning medical tools. Ensuring adequate waste disposal systems, including safe incinerators or waste management systems, is also essential for preventing the spread of infectious materials.

Implement cost-effective solutions

In low-resource settings, cost-effective and locally sourced solutions can play a significant role in strengthening IPC. For example, the use of locally produced alcohol-based hand sanitizers can help reduce the reliance on expensive imported products. Basic infection control measures like improving hand hygiene can be promoted through low-cost interventions such as tippy taps (simple handwashing stations) in areas where water supply is limited. Reusable PPE, when safely sterilized, can also reduce costs while maintaining IPC standards. In low-resource settings, healthcare workers often rely on locally available disinfectants like bleach or

chlorine-based solutions, which are effective and affordable. Some programs have implemented protocols that focus on disinfecting high-touch areas to reduce the spread of infections when resources are limited.

Enhance training and capacity building

Providing continuous education and training to healthcare workers is critical to strengthening IPC. Training programs should focus on proper hand hygiene, the correct use of PPE, and protocols for handling infectious materials. Developing simplified and culturally appropriate training materials can help ensure that healthcare workers, support staff, and even caregivers are well-informed. IPC training should also include strategies for detecting and managing outbreaks to improve early response.

Task-shifting, where certain responsibilities are transferred to lower-level healthcare workers or non-clinical staff, can also help mitigate the human resource shortage in low-resource settings. By empowering these workers to take on IPC roles, the burden on overworked clinical staff can be reduced, allowing for better adherence to infection control protocols.

Implement national IPC guidelines and policies

Strong national IPC guidelines and policies are essential for standardizing infection control practices across healthcare facilities. Governments and healthcare authorities need to develop and enforce national IPC standards based on global recommendations from organizations such as the WHO. These guidelines should be adapted to local contexts, considering available resources and healthcare infrastructure. Having clear policies in place helps hold healthcare facilities accountable and ensures that IPC practices are consistently followed.

Improve water, sanitation, and hygiene (WASH)

Improving WASH in healthcare settings is a fundamental part of strengthening IPC. Ensuring access to clean water for handwashing, sanitation, and cleaning is critical to preventing infections. Healthcare facilities should be equipped with reliable water supply systems and adequate sanitation infrastructure, including functioning toilets and waste disposal units. Community-level interventions that promote WASH practices, such as clean drinking water, proper sanitation, and safe hygiene habits, also contribute to reducing infection rates.

Develop community engagement and education programs

Engaging the community is crucial for promoting IPC beyond healthcare settings, similar to what was done during COVID-19. Community education programs can raise awareness about the importance of hand hygiene, safe caregiving practices, and proper waste disposal to prevent the spread of infections. In rural areas or informal settlements where healthcare access may be limited, community health workers (CHWs) can serve as valuable resources for disseminating IPC information and encouraging behaviors that reduce infection risks. Patients can also be engaged during hospital visits through group discussions concerning IPC.

Establish effective monitoring and evaluation systems

Evidence has shown that continuous monitoring and evaluation of IPC practices are essential for identifying areas of improvement and ensuring compliance with infection control standards. Healthcare facilities should implement surveillance systems to track the incidence of HAIs, AMR, and other infection-related issues. Regular audits of hand hygiene practices, cleaning protocols, and waste management can help identify gaps and improve IPC interventions. Data collected from monitoring systems can be used to inform policy decisions and guide resource allocation.

Leverage technology and innovation to improve infection prevention and control

The present Technological advancements can be leveraged to improve IPC in low-resource settings. For instance, mobile applications can be used to monitor compliance with hand hygiene protocols, while electronic health information systems can track infection rates and antimicrobial use. Telemedicine can be used to provide IPC training and support to remote or underserved healthcare workers. Additionally, simple diagnostic tools like rapid diagnostic tests (RDTs) for identifying infections can improve the timely detection of infectious diseases and reduce the spread of infections.

Integrate IPC into broader health systems strengthening

There is a need for IPC to be viewed as an integral part of broader health systems strengthening efforts. IPC measures need to be incorporated into routine healthcare delivery and linked with other public health initiatives, such as antimicrobial stewardship programs, maternal and child health services, and HIV/TB control efforts. By integrating IPC with other health programs, healthcare systems can create synergies that improve patient outcomes and reduce infection risks.

Foster international collaboration and support

Low-resource settings can benefit from international collaboration and support in implementing effective IPC measures. Global health organizations, donors, and non-governmental organizations (NGOs) can provide technical expertise, training, and funding to support IPC initiatives. Partnerships with international institutions can also facilitate knowledge sharing and the transfer of best practices, ensuring that low-resource settings can adopt effective, context-specific IPC interventions.

Way forward regarding infection prevention and control implementation in low resource settings

Low resource settings can instigate and improve their IPC by developing IPC programs and advocate with leadership, utilize external support, build resources gradually, connect with other programs, and involve national IPC associations and legal frameworks. Further, facilities need to develop guidelines and plan early for implementation, seek external technical assistance, and adapt to local needs. This should be followed by establishing training with a focus on effective methods, developing local leadership, and ensuring health system links, including creating an IPC career path. Furthermore, establishment of HAI surveillance is critical starting with practical, high-impact pilots, foster collaboration, mentorship, and focus on clear definitions, data quality, and using data for decision-making. Low resource settings must implement multimodal strategies and communicate clearly, focusing on key elements, and using impactful pilot projects. Alongside this, they should develop monitoring, audits, and feedback through implementing pilots, use positive incentives, and focus on data-driven actions. Low resource settings must improve staffing and bed occupancy and set national standards and use data to guide improvements. Additionally, there is a need to promote the built environment by involving IPC professionals in facility design and maintaining long-term advocacy. Low resource countries need to improve IPC practices by promoting hand hygiene initiatives, local PPE production, innovative waste management solutions, improved sterilization practices, community health worker engagement, and vaccination programs.

Conclusion

This paper discussed numerous barriers that hinder the implementation of effective IPC in low-resource settings. However, there are also opportunities for improvement through innovation, capacity building, and international support. Addressing financial constraints, improving healthcare infrastructure, and enhancing training and awareness can help strengthen IPC measures and reduce the burden of infections in low resource settings. Additionally, there must be ongoing education and training of healthcare workers in IPC practices in resource-limited settings to sustain IPC interventions. Fostering a culture of infection prevention through awareness and knowledge sharing can significantly improve healthcare outcomes.

Competing interests

The author has no financial and non-financial competing interests to declare.

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Chapter 66

Personalized medicine in managing infectious diseases

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Introduction

Infectious diseases have long posed significant global health challenges, with pathogens constantly evolving and presenting diverse clinical manifestations across different populations. Traditional approaches to managing infectious diseases, while effective in many cases, often rely on broad-spectrum treatments and generalized public health strategies that may not account for the variability in individual patient responses, pathogen characteristics, or environmental factors. This is where personalized medicine comes into play—ushering in a paradigm shift in the way we diagnose, treat, and manage infectious diseases.

Personalized medicine, also referred to as precision medicine, tailors healthcare interventions to the unique biological and genetic characteristics of individual patients. Advances in genomics, proteomics, and bioinformatics, along with the increasing availability of high-throughput technologies, have facilitated a more precise understanding of host-pathogen interactions. The integration of genetic data and biomarkers is crucial for understanding susceptibility to infections. Advances in genomics and proteomics allow for the identification of specific markers associated with disease severity and treatment response, paving the way for more individualized management of infectious diseases. These developments enable clinicians to customize therapies based not only on the genetic profile of the patient but also on the molecular features of the infectious agent, drug susceptibility patterns, and patient-specific factors such as immune response, age, comorbidities, and lifestyle.

In the context of infectious diseases, personalized medicine offers the potential for more accurate diagnostics, targeted therapies, and optimized treatment regimens, reducing the risk of drug resistance and adverse effects while improving patient outcomes. Moreover, it enhances the ability to predict which populations are at higher risk of infection or severe disease, enabling tailored preventive strategies, such as vaccines or prophylactic treatments, based on individualized risk profiles. The application of precision medicine in public health can improve trust in healthcare systems by ensuring that interventions are effective and tailored to

community needs. This is particularly relevant in the context of emerging infectious diseases, where rapid identification and response are critical.
This chapter delves into the evolving role of personalized medicine in managing infectious diseases, exploring its current applications, challenges, and future potential. By integrating cutting-edge genomic technologies, molecular diagnostics, and computational tools, personalized medicine promises to revolutionize the management of infections, moving beyond the one-size-fits-all approach toward a more tailored, patient-centered framework for treatment and prevention.

Antibiotic stewardship in the era of precision medicine

Antibiotic stewardship refers to a systematic approach to optimise the use of antibiotics to treat infections, with the primary goal of improving patient outcomes, reducing antibiotic resistance, and minimizing adverse effects. Current policies aim to reduce the use of antibiotics and promote the development of new antimicrobials, but these efforts alone are not enough to fully address the problem. Precision medicine provides various strategies to enhance antibiotic use and fight against antibiotic resistance. The main approaches in antibiotics stewardship of precision medicine: prediction of disease susceptibility, personalized diagnostics, and tailored treatment planning.
Prediction of disease predisposition using genomic data, followed by the development of individualized prevention plans, and personalized diagnostics, shifting from traditional clinical diagnostics to approaches that integrate individual patient data, including various molecular biomarkers, with provisions for the long-term storage of biomaterials. Treatment planning is based on the patient's unique characteristics, utilizing biomarkers to monitor therapeutic progress, and pharmacological strategies, involving the personalized selection of drugs through a combination of genomic insights and therapeutic drug monitoring. The rapidly advancing field of personalized medicine increasingly focuses on proteomics. To establish criteria that differentiate between a healthy state and disease, proteomics aims to identify the complete set of proteins associated with specific physiological or pathological conditions. It is considered a key area for the identification of biomarkers. One promising approach involves measuring the expression of host genes in peripheral blood.
Biomarkers play a pivotal role in precision medicine. A biomarker is defined as "a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention".
In addition to biomarkers, another promising approach in precision medicine that can enhance the effectiveness of antibiotics is the use of phages to identify bacterial pathogens. Techniques have been developed to detect a variety of human pathogens, including *Escherichia coli*, *Listeria*, *Bacillus anthracis* (anthrax), and others, through the use of reporter phages. This approach has also been applied to *Mycobacterium* species. Further advancements in these methods are anticipated through genetic engineering, which holds the potential to significantly improve their accuracy and efficacy.
Artificial intelligence and machine learning algorithms hold significant potential for enhancing antibiotic stewardship. Researchers are concentrating on three primary areas: predicting antimicrobial susceptibility profiles using genomic data, analyzing disruptions in cellular functions caused by antibiotics to gain a deeper understanding of their mechanisms of action and facilitate the development of new antibiotics, and making informed management decisions regarding antimicrobial use based on data from electronic medical records.
Optimizing antibiotic dosages for individual patients can not only reduce toxicity but also help curb the spread of antimicrobial resistance. Therapeutic drug monitoring (TDM) enables more precise use of antibiotics to achieve pharmacokinetic/pharmacodynamic goals aimed at preventing the emergence of resistance. Studies

have shown that targeted dosing, supported by dosing software, can reduce nephrotoxicity and shorten the duration of therapy.

While broad-spectrum antibiotics are often essential in the early stages of infection when the pathogen is not yet identified, they can also negatively impact the host microbiome and exert selective pressure that promotes the development of resistant bacteria. Transitioning from broad-spectrum to narrow-spectrum antibiotics based on susceptibility testing is a key priority in antibiotic stewardship. Precision antimicrobials offer an alternative to broad-spectrum agents, specifically targeting stages of pathogenesis that disrupt the pathogen's maintenance or persistence in the host, or selectively eliminating the pathogen with minimal side effects.

How personalized medicine prevents drug-resistant infections

Antimicrobial resistance (AMR) is a significant global health concern. According to the World Health Organization, AMR is one of the top public health threats of our time. Antibiotic resistance arises from various factors, including inadequate surveillance systems, overuse of antimicrobials, insufficient infection control measures, and a lack of awareness among both the public and patients. Additionally, the absence of up-to-date data on AMR and limited diagnostic capabilities further exacerbate the issue. The COVID-19 pandemic has contributed to the increase in antibiotic resistance due to heightened antibiotic consumption, breakdowns in surveillance and preventive measures, and a slowdown in the research and development of new antibiotics.

Personalized medicine holds significant potential to address these challenges effectively. By tailoring treatments to individual patient characteristics—such as genetic profile, metabolism, and specific pathogen traits—personalized medicine can optimize antimicrobial use, thereby reducing the risk of overuse and misuse. This approach enhances treatment efficacy, minimizes adverse effects, and helps curb the development of drug resistance.

Therapeutic drug monitoring (TDM) is a critical tool for optimizing antibiotic dosing in critically ill patients, enhancing the likelihood of overcoming infections caused by multidrug-resistant (MDR) bacteria. Nanobiotechnology presents an innovative solution to mitigating antimicrobial resistance by employing nanobiosensors to detect antibiotics in patients' blood plasma. These devices facilitate rapid, on-site quantification of antibiotics from small sample volumes, enabling clinicians to make informed treatment decisions more efficiently. By improving the precision of antibiotic use, nanobiosensors contribute to reducing the burden of MDR infections, playing a vital role in the global fight against AMR. Nanobiotechnology presents an innovative solution to mitigating antimicrobial resistance by employing nanobiosensors to detect antibiotics in patients' blood plasma. These devices facilitate rapid, on-site quantification of antibiotics from small sample volumes, enabling clinicians to make informed treatment decisions more efficiently. By improving the precision of antibiotic use, nanobiosensors contribute to reducing the burden of MDR infections, playing a vital role in the global fight against antimicrobial resistance. There is growing interest in using microneedle-based transdermal electrodes for molecular probing and drug delivery. These sensors only penetrate the stratum corneum layer of the skin, so they do not cause pain or bleeding. They do not reach nerve endings or capillary blood vessels in the dermis, making them a minimally invasive method for taking a sample of interstitial fluid to monitor drugs or metabolites. Measuring antibiotic doses with microneedles can help optimize the concentration of other drugs in the body, including in the blood serum. The concentration of a drug in its free form, not bound to other substances, is currently considered the gold standard, as it provides a balance

between the body's components such as blood and extracellular fluid. Therefore, the development of minimally invasive microneedle sensors can provide a means to optimize drug delivery in blood vessels.
Personalized medicine offers a promising solution for addressing the global challenge of antimicrobial AMR by tailoring treatments to individual patient's characteristics and the specific traits of pathogens. By using tools such as TDM and nanobiotechnology, clinicians can optimize antibiotic dosing, reduce the risk of drug overuse, and improve treatment efficacy.

Personalized medicine in the prevention of hospital infections

Personalized medicine has the potential to significantly enhance the prevention of hospital infections by tailoring infection control strategies to individual patient profiles. Here are some key aspects of how personalized medicine is applied in this context. Personalized medicine allows for the identification of patients at higher risk for healthcare-associated infections (HAIs) based on their clinical, biological, and epidemiological characteristics. By utilizing advanced predictive algorithms that analyze patient data, healthcare providers can determine which individuals require targeted preventive measures. This approach optimizes resource allocation and enhances the effectiveness of infection control interventions. The implementation of personalized infection prevention and control (IPC) measures involves customizing interventions based on individual risk factors. For instance, patients with specific comorbidities or genetic predispositions may benefit from enhanced hygiene protocols, isolation procedures, or tailored antibiotic prophylaxis. This targeted approach not only reduces the incidence of infections but also minimizes unnecessary interventions that could lead to adverse effects or increased healthcare costs.
Advancements in genomics enable the assessment of both patient susceptibility to infections and the characteristics of pathogens. By understanding the molecular resistance mechanisms and virulence factors of infectious agents, clinicians can make informed decisions regarding prophylactic treatments and select appropriate antibiotics that are less likely to contribute to resistance development.
Personalized medicine incorporates real-time monitoring of patient health data, allowing for dynamic adjustments in infection prevention strategies. For example, if a patient shows signs of infection or an increase in risk factors, clinicians can promptly modify their care plan to implement more stringent IPC measures. This adaptability enhances overall patient safety and reduces the likelihood of occurring during hospitalization. By involving patients in their care through personalized medicine approaches, healthcare providers can educate them about their specific risks and empower them to engage in preventive practices. This may include guidance on hygiene practices, awareness of symptoms, and adherence to prescribed prophylactic measures, which collectively contribute to reducing hospital infections.

Personalized medicine in the prevention of drug-resistant tuberculosis

Personalized medicine offers innovative strategies for preventing drug-resistant tuberculosis (TB) by tailoring treatment and prevention approaches to individual patient characteristics and specific strains of *Mycobacterium tuberculosis*. Advanced genetic screening techniques, such as next-generation sequencing, enable rapid identification of drug-resistant strains, allowing healthcare providers to determine the most effective antibiotic regimen based on the pathogen's resistance profile. This customization of treatment regimens considers individual pharmacogenomics, enabling adjustments in drug dosage and selection to enhance efficacy and

minimize side effects, thereby reducing the likelihood of treatment failure and subsequent resistance. Additionally, predictive models can assess an individual's risk of developing drug-resistant TB based on factors like genetic predispositions and previous treatment history, allowing for targeted preventive measures for high-risk patients. Personalized medicine also emphasizes host-directed therapies that enhance the immune response or mitigate harmful immune reactions, improving treatment outcomes and further reducing the chances of resistance development. The integration of TMD allows for real-time adjustments to treatment based on individual responses, ensuring informed decisions about modifying regimens to prevent resistance emergence. Overall, personalized medicine represents a significant advancement in TB management, optimizing treatment efficacy and minimizing adverse effects while contributing to global efforts to control tuberculosis.

Conclusion

The integration of personalized medicine into infection prevention strategies represents a paradigm shift in how hospitals manage HAIs. By focusing on individual risk profiles and tailoring interventions accordingly, healthcare systems can improve patient outcomes, reduce the incidence of infections, and enhance the overall efficiency of infection control practices.

Competing interests

The author has no financial and non-financial competing interests to declare.

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