

Chapter 1

The Burden of Healthcare-Associated Infection

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KEY MESSAGES

- The World Health Organization (WHO) estimates that hundreds of millions of patients are affected by healthcare-associated infection (HAI) worldwide each year, leading to significant mortality and financial losses for health systems, but precise data of the global burden are not available.
- Of every 100 hospitalized patients at any given time, 6 to 7 will acquire at least one HAI in developed countries and 10 in developing countries.
- In low- and middle-income countries, HAI frequency, especially in high-risk patients, is at least two to three times higher than in high-income countries, and device-associated infection densities in intensive care units are up to 13 times higher.

Healthcare-associated infections (HAIs) affect patients in hospitals and other healthcare settings. These infections are not present or incubating at time of admission, but include infections appearing after discharge, and occupational infections among staff. HAIs are one of the most frequent adverse events during healthcare delivery. No institution or country can claim to have solved this problem, despite many efforts. Healthcare workers' (HCWs') hands are the most

common vehicle of microorganisms causing HAI. The transmission of these pathogens to the patient, the HCW, and the environment can be prevented through hand hygiene best practices.

WHAT WE KNOW – THE EVIDENCE

Although a national HAI surveillance system is in place in most high-income countries, only 23 developing countries (23/147 [15.6%]) reported a functioning system when assessed in 2010.¹ In 2010, all 27 European Union (EU) Member States and Norway contributed to at least one of the four components of the Healthcare-Associated Infections Surveillance Network (HAI-Net), coordinated by the European Centre for Disease Prevention and Control (ECDC). Among these, 25 and 23 countries participated in the point prevalence surveys of HAI and antimicrobial use in long-term care facilities (LTCF) and acute care hospitals, respectively; 13 countries participated in the surveillance of surgical site infections (SSI); 14 in surveillance of HAI in intensive care units (ICUs); and 7 countries contributed to all surveillance components.²

Based on a 1995–2010 systematic review and meta-analysis of national and multicenter studies from high-income countries conducted by the WHO, the prevalence of hospitalized patients who acquired at least one HAI ranged from 3.5% to 12%. Pooled HAI prevalence was 7.6 episodes per 100 patients (95% confidence interval [CI], 6.9–8.5) and 7.1 infected patients per 100 patients admitted (95% CI, 6.5–7.8).¹ Very similar data were issued in 2008 by the ECDC based on a review of studies carried out between 1996 and 2007 in 19 countries.³ Mean HAI prevalence was 7.1%; the annual number of infected patients was estimated at 4,131,000 and the annual number of HAI at 4,544,100.³ In 2011–2012, a point prevalence study coordinated by ECDC in 29 countries indicated that, on average, 6% (range, 2.3%–10.8%) of admitted patients acquired at least one HAI in acute care hospitals.⁴ Based on these data, ECDC estimated that approximately 80,000 patients in Europe on any given day develop at least one HAI for a total annual number of 3.2 million patients (95% CI 1.9–5.2) with a HAI.⁴

The estimated HAI incidence in the United States was 4.5% in 2002, corresponding to 9.3 infections per 1000 patient-days and 1.7 million affected patients.⁵ In the United States and Europe, urinary tract infection (UTI) used to be considered the most frequent type of infection hospital-wide (36% and 27%, respectively).^{3,5} In the recent European point prevalence study, lower respiratory tract infection (23.4%) was the most frequent HAI, followed by SSI (19.6%) and UTI (19%).⁴ According to several studies, the frequency of SSI varies between 1.2% and 5.2% in high-income countries.¹ In European countries, SSI rates varied according to the type of operation; the highest were in colon surgery (9.9%) and the lowest in knee prosthesis (0.7%).⁴

HAI incidence is much higher in severely ill patients. In high-income countries, approximately 30% of ICU patients are affected by at least one episode of

HAI with substantial associated morbidity and mortality.⁶ Pooled HAI cumulative incidence density in adult high-risk patients was 17 episodes per 1000 patient-days (range 13.0–20.3) in a meta-analysis performed by WHO.¹ Incidence densities of device-associated infections in ICUs from different studies including WHO reviews are reported in Table 1.1. In a large-scale study conducted in some middle-income countries in Latin America, HAIs were the most common type of incidents occurring in hospitalized patients; the most frequent were pneumonia and SSI.⁷

According to a systematic review, WHO reported that HAIs are at least two to three times more frequent in resource-limited settings than in high-income countries.^{1,8} In low- and middle-income countries, HAI prevalence varied between 5.7% and 19.1% with a pooled prevalence of 10.1 per 100 patients (95% CI, 8.4–12.2); the reported prevalence was significantly higher in high-quality studies (15.5% vs. 8.5%, respectively).⁸ In contrast to Europe and the United States, SSI was the leading infection hospital-wide in settings with limited resources, affecting up to one-third of patients exposed to surgery; SSI was the most frequently surveyed HAI in low- and middle-income countries.^{1,8} The reported SSI incidence ranged from 0.4 to 30.9 per 100 patients undergoing surgical procedures and from 1.2 to 23.6 per 100 surgical procedures, with pooled rates of 11.8 per 100 patients exposed to surgery (95% CI, 8.6–16.0) and 5.6 per 100 surgical procedures (95% CI, 2.9–10.5).⁸ This is up to nine times higher than in high-income countries.

In low- and middle-income countries, the proportion of patients with ICU-HAI ranged from 4.4% to 88.9% with an infection incidence as high as 42.7 episodes per 1000 patient-days (Table 1.1).¹ This is almost three times higher than in high-income countries. The cumulative incidence of specific device-associated HAI in low- and middle-income countries was estimated by WHO and is regularly reported by the International Nosocomial Infection Control Consortium (INICC), a surveillance network comprising ICUs from 36 low- and middle-income countries. Again, the incidence was found to be at least two to three times higher than in high-income countries and even up to 13 times higher in some countries (Table 1.1). Newborns are also at higher risk in low- and middle-income countries with infection rates 3 to 20 times higher than in high-income countries. Among hospital-born babies in developing countries, HAIs are responsible for 4% to 56% of all causes of death in the neonatal period, and as much as 75% in Southeast Asia and Sub-Saharan Africa.¹ HAIs are not limited to the hospital setting. They are a major problem in LTCF and nursing homes with high levels of antimicrobial resistance and can also result from any type of outpatient care (see Chapters 42C and 42D).

According to available data, the burden of endemic HAI is very significant in terms of excess costs, prolonged hospital stay, attributable mortality, and additional complications and related morbidities. European estimates indicate that HAIs cause 16 million extra days of hospital stay and 37,000 attributable deaths annually, but they also contribute to an additional 110,000 deaths; the annual economic impact in Europe is as high as £7 billion.³ In the United States, around

Table 1.1 Cumulative Incidence Density of HAI and Device-Associated Infections in Adult ICU Patients in High-, and Low/Middle-Income Countries

Surveillance Networks/ Reviews, Study Period, Country	HAI/1000 Patient-Days (95% CI)	Patient-Days	CR-BSI/1000 Central Line-Days (95% CI)	CR-UTI/1000 Urinary Catheter-Days (95% CI)	Urinary Catheter-Days	VAP/1000 Ventilator-Days (95% CI)	Ventilator-Days
WHO meta-analysis, high-income countries, 1995–2010, NHSN, 2006–2008, USA [#]	17.0 (14.2–19.8)	32,537,324	3.5 (2.8–4.1)	4.1 (3.7–4.6)	13,614,567	7.9 (5.7–10.1)	5,339,322
WHO meta-analysis, low- and middle-income countries, 1995–2010, INICC, 2004–2009, 36 developing countries [#]	42.7 (34.8–50.5)	193,139	12.2 (10.5–13.9)	8.8 (7.4–10.3)	970,710	23.9 (20.7–27.1)	679,950
	/	/	2.1	3.4	546,824	2.9	383,068
	/	/	6.8 (6.6–7.0)	7.1 (6.9–7.3)	535,414	18.4 (17.9–18.8)	357,214

Source: Adapted with permission from reference 1.

HAI, healthcare-associated infection; CR-BSI, central-venous catheter-related bloodstream infection; CR-UTI, catheter-related urinary tract infection; VAP, ventilator-associated pneumonia; NHSN, National Healthcare Safety Network; INICC, International Nosocomial Infection Control Consortium.

[#]Medical/surgical ICUs in major teaching hospitals.

[†]Argentina, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Egypt, Greece, India, Jordan, Kosovo, Lebanon, Lithuania, Macedonia, Malaysia, Mexico, Morocco, Pakistan, Panama, Peru, Philippines, Puerto Rico, El Salvador, Saudi Arabia, Singapore, Sri Lanka, Sudan, Thailand, Tunisia, Turkey, Venezuela, Vietnam, Uruguay. In: Rosenthal VD et al., *Am J Infect Control* 2012;**40**:396–407.

99,000 deaths were attributed to HAI in 2002.⁵ According to the Centers for Disease Control and Prevention (CDC), the overall annual direct medical costs of HAI to US hospitals ranges from US\$36 to US\$45 billion; of these, from US\$25 to US\$32 billion would be avoidable when considering that up to 70% of HAIs are preventable.⁹

Very limited data are available at the national level to assess the impact of HAI in low- and middle-income countries. According to a WHO review, increased length of stay associated with HAI in low- and middle-income countries varied between 5 and 29.5 days.¹ Crude excess mortality rates of 18.5%, 23.6%, and 29.3% for catheter-related UTI, central venous catheter-related bloodstream infection, and ventilator-associated pneumonia, respectively, were reported by INICC in adult patients in 173 ICUs in Latin America, Asia, Africa, and Europe.¹ Wide variations in cost estimates associated with HAI were observed between countries. Methods used to estimate excess costs associated with HAIs also varied substantially among studies published in different countries. For instance, in Mexican ICUs, the overall average cost of a HAI episode was US\$12,155; in Argentina, overall extra-costs for catheter-related bloodstream infection and healthcare-associated pneumonia were US\$4,888 and US\$2,255 per case, respectively.¹ In a recent case-control study from Brazil, overall costs of hospitalization for methicillin-resistant *Staphylococcus aureus* bacteremia reached US\$123,065 for cases *versus* US\$40,247 for controls.¹⁰

WHAT WE DO NOT KNOW – THE UNCERTAIN

Despite dramatic data related to specific countries or regions, HAI is not included in the list of diseases for which the global burden is regularly estimated by WHO or the Institute for Health Metrics and Evaluation. Precise estimates of the number of patients affected by HAI and the number of episodes occurring worldwide every year, or at a certain moment in time, are not available. Similarly, estimating the number of deaths attributable to HAI is extremely difficult because co-morbidities are usually present, and HAIs are seldom reported as the primary cause of death. Disability-adjusted life years estimates attributable to HAI are not available. Indeed, for instance, it is complex to calculate years of life lost due to a HAI in a cancer patient dying of HAI. In addition, little is known about the occurrence of HAI complications and associated temporary or permanent disabilities. Finally, the available information regarding indirect attributable costs associated with HAI is limited, in particular regarding the extent of economic losses potentially avoidable through better infection control.

Although the number of publications on HAI surveillance in settings with limited resources has increased over the last few years, the picture of the endemic burden of HAI and antimicrobial resistance patterns in low- and middle-income countries remains very scattered. Data from these countries are hampered in all

the aforementioned areas, and HAI surveillance is not a priority in most countries. There is a need to identify simplified, but reliable protocols and definitions for HAI surveillance in settings with limited resources. In addition, standardized approaches are very much required to facilitate the best use of data to inform policy makers, raise awareness among frontline staff, and identify priority measures.

RESEARCH AGENDA

Further research is needed to:

- Identify reliable and standardized epidemiological models to estimate the global burden of HAI in terms of proportion of affected patients and number of HAI episodes, attributable mortality, length of stay, disability-adjusted life years, and costs per year saved.
- Develop and validate approaches to estimate the HAI incidence and disease burden using International Classification of Diseases codes and additional information available from computerized patient records.
- Develop and validate protocols and definitions suitable for HAI surveillance in settings with limited resources.
- Identify risk factors for HAI, in particular potential differences between high-income and low- and middle-income countries.

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