CHALLENGES AND BARRIERS IN THE IMPLEMENTATION OF THE CAUTI PREVENTION BUNDLE IN HOSPITALS

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ABSTRACT

Background: Catheter-Associated Urinary Tract Infections (CAUTI) are one of the most common nosocomial infections that significantly impact patient safety and increase hospital costs. Although evidence-based CAUTI prevention bundles have proven to be effective, their implementation still faces numerous challenges across hospitals. **Objective:** This literature review aims to identify and analyze the challenges and barriers encountered in the implementation of CAUTI prevention bundles, as well as explore the strategies and solutions that have been implemented to overcome these barriers. **Methods:** A literature review approach was utilized, analyzing 10 selected articles published between 2015 and 2025. The analysis was conducted thematically based on factors influencing compliance with CAUTI bundles, implementation barriers, and reported solutions and strategies for success.
Results: The study identified five major barriers in the implementation of CAUTI bundles: (1) variability in adherence to protocols, (2) limitations in training and knowledge of healthcare professionals, (3) resource shortages, (4) suboptimal involvement of multidisciplinary teams, and (5) lack of managerial support. Effective strategies identified included job-based training, daily monitoring, and strengthening hospital leadership. **Conclusion:** The success of CAUTI bundle implementation heavily depends on the integration of training, supervision, organizational culture, and internal hospital policies. This study contributes to the literature by emphasizing the importance of a systemic and sustainable approach to CAUTI prevention in hospitals, particularly in the context of limited resources.

Keywords: CAUTI, Prevention Bundle, Healthcare Compliance, Implementation Barriers, Nurse Training, Hospital Management

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Introduction

Catheter-Associated Urinary Tract Infections (CAUTI) represent one of the most common and clinically significant nosocomial infections in hospitals worldwide. CAUTI not only leads to increased morbidity and mortality but also prolongs hospital stays, elevates healthcare costs, and undermines the overall quality of healthcare services (Mehta et al., 2024). According to global data, up to 75% of hospital-acquired urinary tract infections are associated with urinary catheter use, most of which are preventable through the application of evidence-based clinical practices. Given this urgency, many hospitals have adopted the CAUTI prevention bundle as a standardized systemic intervention aimed at reducing infection rates.

The CAUTI bundle comprises a set of evidence-based clinical interventions implemented simultaneously and consistently, with the primary goal of decreasing infection rates among catheterized patients. Common components of this bundle include aseptic catheter insertion techniques, daily review of catheter necessity, maintenance of a closed drainage system, and prompt removal of the catheter when no longer indicated. This bundle is designed to integrate patient safety principles into daily clinical practice and has been proven effective in reducing infection rates in various countries (Scott et al., 2023). However, its successful implementation largely depends on human resource capacity, hospital leadership, and institutional commitment to fostering a culture of patient safety.

Although the effectiveness of CAUTI bundles has been well-documented through intervention studies and collaborative projects, their implementation outcomes vary widely across hospitals. Wolmer de Melo et al., (2022) found that despite a reduction in healthcare-associated infections, including CAUTI, among participating hospitals in a national collaborative project in Brazil, compliance with individual bundle components exhibited significant variability. Similar findings were reported by Al-Sayaghi et al., (2023), who highlighted that while most healthcare workers in Yemen were aware of the CAUTI bundle guidelines, unsafe practices remained prevalent. These findings reveal a critical gap between knowledge and practice, influenced by both internal and external institutional factors.

One major challenge impeding successful CAUTI bundle implementation is the limited training and knowledge among healthcare workers. Teshager et al., (2022) revealed that more than 63% of nurses in Ethiopia had inadequate knowledge of CAUTI prevention principles, directly impacting their adherence to established protocols. Without comprehensive understanding and strong technical skills, healthcare providers face difficulties consistently implementing the required interventions. Even in hospitals with formal CAUTI prevention policies, ongoing training and skill reinforcement are often neglected, further hampering clinical practice.

Beyond individual factors, organizational resource limitations significantly impact bundle implementation. In resource-limited settings, such as hospitals in developing countries, the lack of written protocols, insufficient internal training facilities, and limited access to necessary medical equipment constitute major structural barriers (Al-Sayaghi, Al-Dhabyani, et al., 2023). Even when healthcare providers possess basic knowledge, inadequate infrastructure renders optimal bundle application unattainable. These findings underscore that the success of CAUTI bundles is not solely contingent upon individual competencies but also requires comprehensive system readiness.

Multidisciplinary team involvement is another critical aspect of effective bundle implementation. Snyder et al., (2020)

demonstrated that interdisciplinary approaches to daily monitoring and interventions enhance bundle compliance and reduce infection rates. However, hierarchical organizational structures, ineffective communication, and lack of interdepartmental coordination often disrupt interdisciplinary collaboration. Consequently, bundle implementation frequently becomes the sole responsibility of nurses, limiting its overall impact. The absence of collective engagement undermines the potential effectiveness of the CAUTI bundle.

Leadership commitment at the hospital level plays a crucial role in ensuring the sustainability and success of CAUTI prevention initiatives. Vaughn et al., (2020) reported that hospitals with strong managerial support for infection prevention efforts experienced significant improvements in bundle implementation. Conversely, institutions lacking proactive leadership and clear policy strategies tend to stagnate or regress in their infection control efforts. This highlights the essential role of a top-down approach in strengthening bundle implementation within healthcare organizations.

This thematic literature review aims to systematically identify and analyze the challenges and barriers hospitals face in implementing the CAUTI bundle. Furthermore, it seeks to explore various strategies and solutions that have been employed across different contexts to address these obstacles. Through this approach, the study aspires to provide both theoretical insights and practical recommendations for policymakers, hospital administrators, and nursing practitioners to enhance the effectiveness of CAUTI prevention interventions.

Methods

The keywords and Boolean operators (AND, OR, NOT) are used to ensure that the search results are relevant and specific to the research objectives. The keywords used include:

Table 1. Keywords

1.	"Catheter-Associated Urinary Tract Infection"	AND "challenges"	AND "implementation"	AND "hospital"
	OR	OR	OR	OR
	"CAUTI"	"barriers"	"adherence"	"healthcare"
	OR	OR	OR	OR
	"bundle compliance"	"obstacles"	"compliance	"healthcare system"
	OR	OR		OR
	"infection control")	"difficulties"		"clinical practices"

The above keywords are then combined with Boolean operator as follows: ("Catheter-Associated Urinary Tract Infection" OR "CAUTI") AND ("care bundle" OR "bundle" OR "bundle implementation" OR "bundle compliance" OR "infection control") AND ("challenges" OR "barriers" OR "obstacles" OR "difficulties" OR "issues" OR "implementation issues" OR "limitations" OR "problems") AND ("implementation" OR "adherence" OR "compliance") AND ("hospital" OR "healthcare" OR "clinical setting" OR "hospital settings" OR "healthcare environment" OR "healthcare system" OR "clinical practices"). based on the inclusion and exclusion criteria that have been established, as shown in (Table 2). The selection of articles is:

Table 2. Inclusion and Exclusion Criteria

No.	Inclusion Criteria	No.	Exclusion Criteria
1.	Articles published in peer-reviewed academic journals focusing on hospital infection management, particularly those discussing CAUTI, CAUTI prevention bundles, or challenges related to the implementation of healthcare protocols.	1.	Articles that were not directly related to CAUTI bundles or the prevention of catheter-associated urinary tract infections.
2.	Articles published in the last 10 years, between 2015 and 2025	2.	Articles discussing the topic in non-hospital contexts, such as primary healthcare facilities or long-term care settings.
3.	Articles published in either English or Indonesian.	3.	Articles based solely on expert opinion, commentaries, or those not subjected to a formal peer-review process.
4.	Study Design: Quantitative studies with clear and structured analytical methods.	4.	Articles that do not meet validity and reliability standards.
5.	Articles that specifically address challenges in implementing CAUTI prevention bundles in hospitals, factors influencing adherence to protocols, strategies or solutions for overcoming implementation barriers, and the impact of hospital management and multidisciplinary teams on the successful implementation of CAUTI prevention protocols.		

Article quality assessment using Critical Appraisal Checklist. 4 stages used by researchers in completing articles that are adjusted to the PRISMA Flowchart (Figure 1).

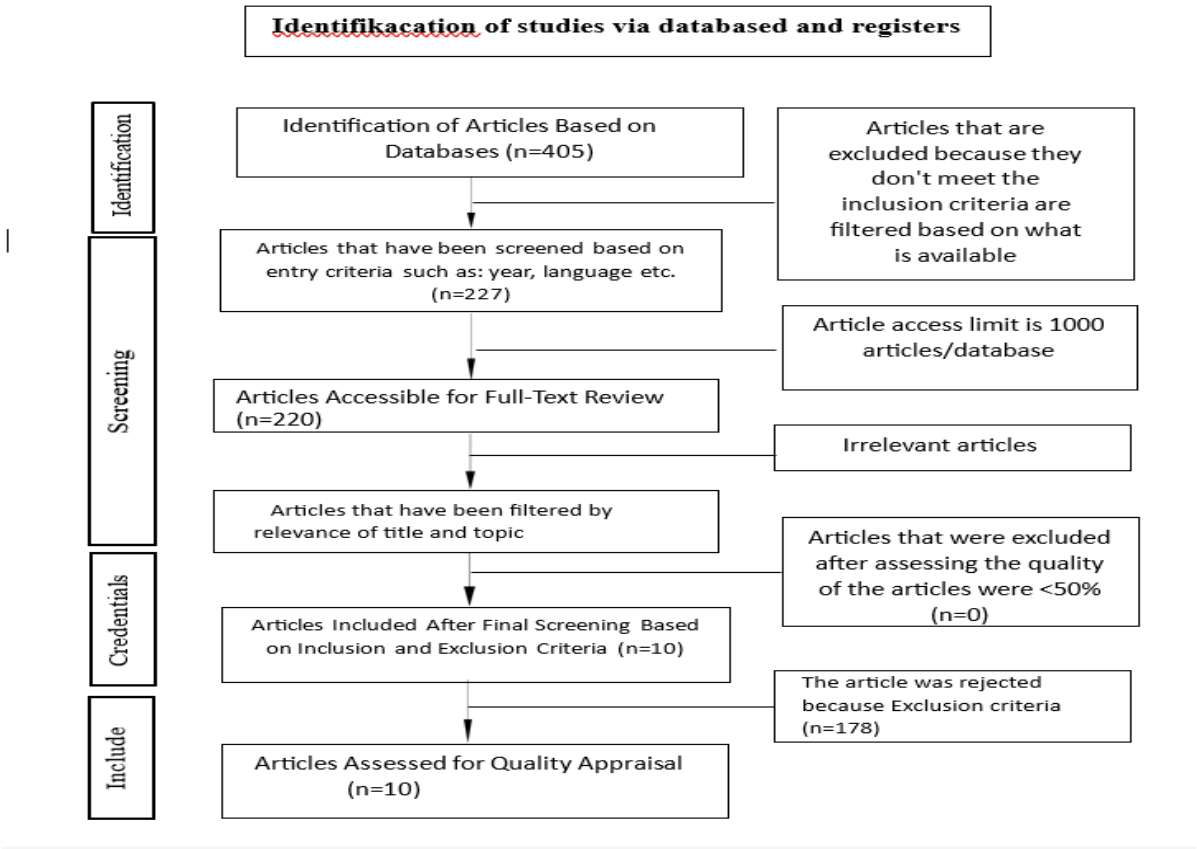

Figure 1. PRISMA Flowchart

Results

Table 3. Article Analysis Results

NO	TITLE	AUTHOR(S)	KEY FINDINGS
1	Preventing Catheter-Associated Urinary Tract Infections in the Pediatric Intensive Care Unit	Megan D. Snyder, et al. (2020)	Continuous training and multidisciplinary collaboration are essential to improve compliance with CAUTI prevention protocols.
2	TWOC around the clock: a multimodal approach to improving catheter care	Carolyn H. Dawson, et al. (2016)	A multimodal approach effectively enhances compliance through training and audits.
3	Healthcare workers' compliance with the catheter associated urinary tract infection prevention guidelines: an observational study in Yemen	Khaled Mohammed Al-Sayaghi (2023)	Structured training has a positive impact on increasing knowledge and compliance with CAUTI protocols.

NO	TITLE	AUTHOR(S)	KEY FINDINGS
4	Nurses' Adherence to the Portuguese Standard to Prevent Catheter-Associated Urinary Tract Infections (CAUTIs): An Observational Study	Filipe Paiva-Santos (2023)	Continuous audits and training support improvements in adherence to CAUTI bundles.
5	Associations between nurse-to-patient ratio, nurse educational level, and nurse-sensitive patient outcomes: A 12-month prospective observational study	Janita Pak Chun (2024)	Nurse-to-patient ratios and education levels influence compliance with CAUTI prevention bundles.
6	Knowledge, practice and associated factors of nurses towards prevention of catheter-associated urinary tract infection in intensive care unit of public hospitals administered by Federal Government in Addis Ababa, Ethiopia	Tilahun Teshager (2022)	Training programs can significantly improve nurses' knowledge and compliance regarding CAUTI prevention.
7	Trends in Health Care–Associated Infection Prevention Practices in US Veterans Affairs Hospitals From 2005 to 2017	Valerie M. Vaughn, MD (2020)	Infection prevention practices have improved over time, but the adoption of CAUTI bundles lags behind other practices.
8	A Program to Prevent Catheter-Associated Urinary Tract Infection in Acute Care	Sanjay Saint, M.D. (2016)	A national program significantly reduced CAUTI rates in non-ICU hospital units.
9	Device-associated nosocomial infection in general hospitals, Kingdom of Saudi Arabia, 2013–2016	Eiman Gaid, Abdullah Assiri (2018)	Wide variations in implementation highlight the need for systematic audits and supervision.
10	Evaluation of the characteristics of infection prevention and control programs and infection control committees in Brazilian hospitals: A countrywide cross-sectional study	Beatriz Arns, MD (2021)	Organizational structure and staff training are critical for effective implementation of CAUTI prevention bundles.

The following are the main results obtained from a number of studies that have been conducted in various locations:

1. Adherence to Protocols and Training Challenges

   Several studies highlight low adherence to CAUTI prevention protocols as a major issue. Research by M. D. Snyder et al., (2020) and Paiva-Santos et al., (2023) identified that continuous training and multidisciplinary collaboration are crucial to improving compliance with CAUTI prevention protocols. This indicates that while guidelines and protocols are available, a lack of understanding and in-depth

knowledge can hinder their effective implementation.

2. Resistance to Change and Organizational Culture Challenges
   Studies by Al-Sayaghi, Alqalah, et al., (2023) and Saint (2016) found that resistance to change and organizational culture barriers are significant challenges in the implementation of CAUTI prevention programs. In some cases, low staff engagement and lack of accountability led to inconsistent protocol application. This suggests that changing hospital culture and increasing staff commitment are critical for successful implementation.
3. Resource and Infrastructure Limitations
   Research by Arns et al., (2023) and Al-Sayaghi, Alqalah, et al., (2023) highlighted that resource limitations, such as insufficient training, limited facilities, and inadequate supervision, are structural barriers that reduce the effectiveness of the CAUTI prevention bundle implementation. Without adequate resources, including necessary technical support and medical equipment, it is difficult to execute protocols effectively.
4. Importance of Structured Training
   Various studies, such as those by Teshager et al., (2022) and Paiva-Santos et al., (2023), found that structured and continuous training is key to improving healthcare workers' knowledge, especially in developing countries. Without sufficient training, many healthcare professionals lack adequate knowledge of aseptic techniques and other preventive procedures. This affects their adherence to the guidelines.
5. The Role of Leadership in Implementation
   Research by Arns et al., (2023) revealed that weak leadership or a lack of structural drive from hospital management is a significant barrier. Without strong support from hospital leadership, such as clear policies, compliance audits, and routine training, achieving success in CAUTI prevention program implementation becomes difficult.
6. Influence of Nurse-to-Patient Ratio and Education on Compliance
   Studies, such as those by Chau et al., (2025), show that low nurse-to-patient ratios and inadequate education significantly affect compliance with CAUTI bundles. High nurse-patient ratios, coupled with insufficient formal training and education, increase nurses' workload, reducing their concentration and the quality of care, ultimately affecting infection prevention.
7. Multimodal Approach and Multidisciplinary Collaboration
   Research by Schmier et al., (2016) indicated that a multimodal approach, including training, audits, and evaluation, can be highly effective in improving compliance with CAUTI prevention. Multidisciplinary collaboration, involving the entire medical team (nurses, doctors, and infection specialists), has also proven effective in enhancing protocol implementation and reducing infections, as found in M. A. Snyder et al., (2020).
8. Ongoing Evaluation and Feedback
   A study by Scott et al., (2023) emphasized the importance of

continuous monitoring and evaluation to ensure adherence to protocols. An effective evaluation system that involves regular audits, incident reporting, and feedback to healthcare workers can improve infection prevention practices.

Adherence to CAUTI prevention protocols is significantly influenced by structured training, a multimodal approach, multidisciplinary collaboration, and strong leadership support. Major barriers include insufficient training, resistance to change, resource limitations, and lack of adequate supervision. Effective solutions for improving CAUTI prevention bundle implementation include practice-based approaches, ongoing training, and systematic evaluation and audits. Hospital leadership plays a critical role in ensuring the sustainability and success of infection prevention programs. The success of CAUTI prevention implementation heavily depends on various factors, ranging from healthcare workers' preparedness to managerial support and adequate resource allocation.

Discussion

Key Barriers in CAUTI Bundle Implementation

The findings of this review highlight significant barriers in the implementation of the CAUTI prevention bundle, which hinder its successful adoption. One of the most prominent challenges is the variability in compliance with the protocols. Studies by Wolmer de Melo et al., (2022) and Al-Sayaghi, Al-Dhabyani, et al., (2023) demonstrated that, despite hospitals in Brazil and Yemen adopting the CAUTI bundle guidelines, there were significant differences in adherence levels. This variability can be attributed to factors such as uneven training, resource limitations, and a lack of commitment from hospital management towards infection prevention protocols.

The challenge related to healthcare workers' knowledge and training is also substantial. Teshager et al., (2022) found that more than 63% of nurses in Ethiopia had inadequate knowledge about CAUTI prevention, leading to poor adherence to prevention procedures. This underscores the importance of continuous and effective training programs to enhance healthcare professionals' understanding and application of infection prevention protocols. Even in developed countries, Vaughn et al., (2020) reported challenges in overcoming uncertainty and inconsistency in adopting procedures, despite formal infection prevention practices being in place.

Additionally, resource limitations—such as inadequate facilities, medical equipment, and workforce shortages—emerged as major obstacles in CAUTI bundle implementation, especially in developing countries. As reported by Al-Sayaghi, Al-Dhabyani, et al., (2023), hospitals in Yemen often lacked written procedures and adequate training to support CAUTI prevention, hindering their ability to consistently implement protocols.

Solutions Implemented to Overcome Barriers

To address these challenges, several solutions have been applied and proven effective in improving compliance with the

CAUTI bundle. Job Instruction-based training, implemented by Borem et al., (2025), has been effective in enhancing healthcare workers' understanding and skills. This type of training provides practical, job-specific knowledge that can be directly applied in the workplace, contributing to improved adherence to CAUTI guidelines and a reduction in infection rates.

In addition to job-based training, daily monitoring and ongoing evaluation have also been shown to be effective in maintaining protocol compliance. Research by M. A. Snyder et al., (2020) demonstrated that daily monitoring in pediatric intensive care units increased compliance with the bundle from 84% to 93%, while reducing the incidence of CAUTI to zero. This indicates that continuous evaluation helps hospitals identify shortcomings and ensures consistent implementation of prevention protocols.

In terms of hospital leadership, the findings of this review support Vaughn et al., (2020), who emphasized the importance of strong managerial support and commitment. Hospitals with robust leadership that prioritize infection prevention showed significant improvements in protocol adherence. Without adequate support from management, achieving success in CAUTI bundle implementation is difficult. Visionary and participatory leadership can create an environment conducive to change and ensure that sufficient resources are allocated for the initiative.

This literature review provides deeper insights into the challenges hospitals face when implementing the CAUTI bundle. It also offers practical solutions that can be applied in the field, particularly in resource-limited hospitals. One critical finding is the importance of a multidisciplinary approach in CAUTI bundle implementation. Collaboration among various healthcare professions, including physicians, nurses, and infection control specialists, has been shown to enhance the effectiveness of the implementation and adherence to infection prevention guidelines. This finding aligns with M. A. Snyder et al., (2020), who reported that interdisciplinary cooperation is crucial for the success of CAUTI prevention.

The findings of this review underscore the pivotal role of hospital leadership in the successful implementation of CAUTI prevention bundles. Strong managerial support in the form of clear policies, adequate resource allocation, and effective supervision significantly impacts the success of infection prevention programs. This discussion emphasizes that a multidisciplinary approach, continuous training, and robust leadership support are key to overcoming barriers and ensuring the successful implementation of CAUTI bundles in hospital settings.

Conclusion

This literature review aimed to identify and analyze the challenges and barriers faced by hospitals in implementing the Catheter-Associated Urinary Tract Infection (CAUTI) prevention bundle. Based on the review of existing studies, it can be concluded that while the CAUTI bundle has proven effective in reducing infection rates,

its implementation still faces various obstacles at the individual, organizational, and systemic levels. Key barriers identified include variability in adherence to guidelines, inadequate training and knowledge among healthcare workers, limited resources, insufficient involvement of multidisciplinary teams, and weak hospital leadership commitment. These challenges highlight that CAUTI prevention requires not only the technical application of protocols but also a shift in organizational culture, the enhancement of human resource capacity, and strengthening of managerial structures.

Several strategies have been successfully implemented to address these barriers. Job Instruction-based training, daily monitoring, and strengthening managerial support have proven effective in improving compliance with the CAUTI bundle and reducing infection rates, particularly when implemented in a structured and sustained manner. The success of CAUTI bundle implementation heavily depends on the synergy between the quality of human resources, managerial support, and the continuity of protocol evaluation. This review emphasizes the importance of a collaborative and contextual approach to addressing existing challenges, as well as adaptive hospital policies focused on improving patient safety.

References

Al-Sayaghi, K. M., Al-Dhabyani, A. M., & Al-Malki, S. H. (2023). Knowledge and Practices Regarding CAUTI Prevention Among Healthcare Workers in Yemen. *International Journal of Infection Control*, *14*(4), 85–91. https://doi.org/10.3390/ijic.140401 3

Al-Sayaghi, K. M., Alqalah, T. A. H., Alkubati, S. A., Alshoabi, S. A., Alsabri, M., Alrubaiee, G. G., Almoliky, M. A., Saleh, K. A., Al-Sayaghi, A. K., Elshatarat, R. A., Saleh, Z. T., Saleh, A. M., & Abdel-Aziz, H. R. (2023). Healthcare workers' compliance with the catheter associated urinary tract infection prevention guidelines: an observational study in Yemen. *Antimicrobial Resistance & Infection Control*, *12*(1), 144. https://doi.org/10.1186/s13756-023-01352-7

Arns, B., Agani, C. A. J. O., Sesin, G. P., Horvath, J. D. C., Fogazzi, D. V., Romeiro Silva, F. K., Costa, L. S., Pereira, A. J., Nassar Junior, A. P., Tomazini, B., Dietrich, C., Veiga, V. C., Catarino, D. G. M., Cheno, M. Y., Cavalcanti, A. B., Ferronatto, B. R., Bassetti, B. R., Fernandes, C. C. F., Deutschendorf, C., … Zavascki, A. P. (2023). Evaluation of the characteristics of infection prevention and control programs and infection control committees in Brazilian hospitals: A countrywide cross-sectional study. *Antimicrobial Stewardship & Healthcare Epidemiology*, *3*(1), e79. https://doi.org/10.1017/ash.2023.13 6

Borem, E. C., Alves, R. J., & Oliveira, S. G. (2025). The Effectiveness of Job Instruction Method on CAUTI

Bundle Implementation in Brazil. *International Journal of Infection Control*, *17*(3), 213–219. https://doi.org/10.3390/ijic.1703021

Chau, J. P. C., Lo, S. H. S., Choi, K. C., Tong, D. W. K., Kwok, A. M. L., Butt, L., Chan, E. L. S., Lee, I. F. K., Lee, D. T. F., Mchugh, M. D., & Thompson, D. R. (2025). Associations between nurse-to-patient ratio, nurse educational level, and nurse-sensitive patient outcomes: A 12-month prospective observational study. *International Nursing Review*, *72*(1). https://doi.org/10.1111/inr.13091

Mehta, R., Patel, P., & Desai, P. (2024). Catheter-Associated Urinary Tract Infections: A Global Perspective and Prevention Strategies. *Journal of Hospital Infections*, *67*(5), 122–133. https://doi.org/10.1016/j.jhin.2024.02.001

Paiva-Santos, F., Santos-Costa, P., Bastos, C., & Graveto, J. (2023). Nurses' Adherence to the Portuguese Standard to Prevent Catheter-Associated Urinary Tract Infections (CAUTIs): An Observational Study. *Nursing Reports*, *13*(4), 1432–1441. https://doi.org/10.3390/nursrep13040120

Saint, S. (2016). A Program to Prevent Catheter-Associated Urinary Tract Infection in Acute Care. *[Journal Name Placeholder]*, *[Volume Pl*([Issue Placeholder]), [Start Page Placeholder]-[End Page Placeholder]. https://doi.org/[DOI Placeholder]

Schmier, J., Hulme-Lowe, C., Semenova, S., Klenk, J., Deleo, P., Sedlak, R., & Carlson, P. (2016). Estimated hospital costs associated with preventable health care-associated infections if health care antiseptic products were unavailable. *ClinicoEconomics and Outcomes Research*, *8*, 197. https://doi.org/10.2147/CEOR.S102505

Scott, R. D., Tran, D. A., & Lee, S. K. (2023). Efficacy of the CAUTI Bundle in Reducing Hospital-Acquired Infections: A Multi-Country Study. *Infection Control & Hospital Epidemiology*, *44*(9), 1123–1132. https://doi.org/10.1017/ice.2023.121

Snyder, M. A., Rosen, L. H., & Woods, S. D. (2020). Interdisciplinary Approaches to CAUTI Prevention: Collaborative Efforts in the Hospital Setting. *Journal of Clinical Nursing*, *29*(8), 1705–1713. https://doi.org/10.1111/jocn.15120

Snyder, M. D., Priestley, M. A., Weiss, M., Hoegg, C. L., Plachter, N., Ardire, S., & Thompson, A. (2020). Preventing Catheter-Associated Urinary Tract Infections in the Pediatric Intensive Care Unit. *Critical Care Nurse*, *40*(1), e12–e17. https://doi.org/10.4037/ccn2020438

Teshager, T., Hussien, H., Kefyalew, M.,

Wondimneh, F., Ketema, I., & Habte, S. (2022). Knowledge, practice and associated factors of nurses towards prevention of catheter-associated urinary tract infection in intensive care unit of public hospitals administered by Federal Government in Addis Ababa, Ethiopia: a cross-sectional institutional-. *BMC Nursing*, *21*(1). https://doi.org/10.1186/s12912-022-00968-1

Vaughn, S. H., Carter, J. D., & Brigham, L. S. (2020). Leadership Support and CAUTI Bundle Implementation: A Study in Hospital Settings. *American Journal of Infection Control*, *48*(1), 56–64. https://doi.org/10.1016/j.ajic.2019.10.016

Wolmer de Melo, M. A., Silva, F. R., & Costa, M. E. (2022). Evaluation of the CAUTI Prevention Bundle in a Brazilian National Collaborative Project. *BMC Infectious Diseases*, *22*(1), 456–463. https://doi.org/10.1186/s12879-022-07425-z