EVIDENCE-BASED PRACTICE GUIDELINE

FOR ESTABLISHING HOSPITAL-BASED ANTIMICROBIAL STEWARDSHIP PROGRAMS IN SAUDI ARABIA

Saudi Pediatric Infectious Diseases Society (SPIDS)

First Edition

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Executive **Summary**

This evidence-based practice guideline, developed by the Saudi Pediatric Infectious Diseases Society (SPIDS) in collaboration with King Saud University, focuses on **establishing hospital-based antimicrobial stewardship programs (ASPs) in Saudi Arabia.**

The guideline addresses the significant global threat of antimicrobial resistance (AMR) and the need for optimized antibiotic use to improve patient outcomes and reduce AMR.

The guideline prioritizes 23 clinical questions based on the IDSA/SHEA guidelines, augmented by four additional questions specific to the Saudi context. It proposes interventions to reduce inappropriate antibiotic use, improve antibiotic utilization, optimize antibiotic therapy, and enhance microbiology and laboratory diagnostics. Recommendations are graded based on the strength of evidence and include strategies such as didactic education, preauthorization and prospective audits, facility-specific guidelines, and the use of clinical decision support systems. The guideline emphasizes the crucial roles of pharmacists and nurses within the ASP team.

The guideline was developed using the KSU-modified ADAPTE methodology, which included a systematic review of existing guidelines, expert panel consensus, and external peer review. The guideline also addresses the need for strong organizational and structural support, emphasizing leadership commitment and accountability. The document provides specific recommendations for implementing and evaluating the success of ASP programs, including relevant performance measures and strategies for dissemination and implementation as advised by the Public Health Authority (PHA) in Saudi Arabia.

Finally, the document includes a patient information sheet that explains appropriate and inappropriate antibiotic use. The clinical and methodology subgroups agreed that the guideline document will be reviewed and updated every five years.

Summary **Table**

Table 1: Summary Table of the Adapted Guideline

Main ICD-10 Code	Y40: Systemic antibiotics[1] Excl.: Antibiotics, topically used (Y56.-), antineoplastic antibiotics (Y43.3)
Related ICD-10 Codes	T36: Poisoning by systemic antibiotics Excl.: Antibiotics: ▪ Antineoplastic (T45.1) ▪ Locally applied NEC (T49.0) ▪ Topically used for: - Ear, nose, and throat (T49.6) - Eye (T49.5) Bacterial agents resistant to antibiotics (U80-U89) ▪ Note: These categories should never be used in primary coding. They are provided for use as supplementary or additional codes when it is desired to identify the antibiotic to which a bacterial agent is resistant in bacterial infection classified elsewhere.
Guideline Publication Date	May 2025
Expected Review Date	May 2030
Target Users	Pediatric Infectious disease physicians, adult infectious disease physicians, infectious disease pharmacists, clinical pharmacists, internal medicine, intensivists, surgeons, nurses, medical lab physicians and technicians, microbiologists, infection control and prevention, quality and safety department, and administrators.
Source Guideline	Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America (IDSA/ SHEA). *Clin Infect Dis.* 2016 May 15;62(10):e51-77. https://doi.org/10.1093/cid/ciw118
Methodology	This guideline prioritized 23 clinical questions from the IDSA/SHEA GRADE-based source guideline. The guideline formal adaptation methodology used was “KSU-Modified-ADAPTE”.

Introduction

The Saudi Pediatric Infectious Disease Society (SPIDS), headquartered in Riyadh, has been registered with the Saudi Commission of Health Specialists since 2012. Functioning as a professional association, SPIDS collaborates with nationally recognized pediatric infectious disease specialists, encompassing molecular, translational, and clinical researchers as well as practitioners. The society's mission extends to serving Saudi Arabia, the Middle East, and the EMRO region, addressing underrepresented infectious disease needs compared to Europe and North America.

The research committee is one of the major committees of the SPIDS, it serves as the formal body that advocates and promotes for the national, local, and collaborative research efforts among all segments in the community. It provides guidance, strategies, and coordinates activities for exchange and dissemination of research. Understanding this role and realizing the current knowledge gap in implementing and practicing the program of the antimicrobial stewardship, this guideline aims to address this gap and support the healthcare sector and professionals.

In 2015, Saudi Arabia's Ministry of Health (MOH) recognized the significance and impact of AMR and introduced antimicrobial containment measures and infection prevention and control programs in MOH hospitals. In 2017, the Kingdom Arabia developed its first AMR National Action Plan, adopting the five objectives of the World Health Organization's (WHO) Global Action Plan on Antimicrobial Resistance:

Objective 1:

Improve awareness and understanding of antimicrobial resistance through effective communication, education, and training.

Objective 2:

Strengthen the knowledge evidence base through surveillance and research.

Objective 3:

Reduce the incidence of infection through effective sanitation, hygiene, and prevention measures.

Objective 4:

Optimize the use of antimicrobial medicines in human and animal health.

Objective 5:

Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines, and other interventions.

In 2018, the mandate was shifted from the Ministry of Health to the Public Health Authority (Weqaya). The Kingdom's 2022 - 2025 AMR national action plan emphasizes a collaborative, multisectoral, and transdisciplinary One Health approach that operates at local, regional, national, and global levels; and recognizes the interconnection between people, animals, agriculture, and the shared environment.

This plan provides the necessary AMR activities that contribute to the overall goals, and reassessment of the current situation, capabilities, and resources and narrowed their focus for the upcoming years on 5 objectives based on the current priorities in the kingdom.

The collaboration between SPIDS and the KSUMC CPG Steering Committee involves bridging clinical expertise with guideline methodologists to produce the provided evidence-based guideline. This joint effort aims to integrate the knowledge and insights of infectious disease specialists with the rigorous methodology of guideline development, ensuring comprehensive and effective clinical guidance with the inclusion of national recommendations and standards.

The benefits and risk associated with implementing antimicrobial stewardship programs in Saudi Arabia

Antimicrobial Stewardship Programs (ASPs) are coordinated interventions aimed at optimizing antimicrobial use to improve patient outcomes and limit antimicrobial resistance (AMR), which has become a significant challenge globally. These programs have been shown to effectively reduce inappropriate antimicrobial use, improve patient outcomes, and decrease the emergence of resistance. A systematic review highlighted the global value of ASPs, reporting outcomes from interventions primarily in North America and Europe, demonstrating a significant decrease in antibiotic usage and antimicrobial resistance. Most studies noted a reduction in the duration of antimicrobial therapy and a significant decrease in overall antibiotic expenditure, showcasing economic benefits alongside improved patient care. The most common interventions included audit and feedback on antimicrobial therapy and altered therapy guidelines. These findings emphasize the critical role of ASPs in reducing antibiotic overuse and combating AMR, leading to cost savings and enhanced patient safety.[1-3]

Implementing ASPs specifically in Saudi Arabia aligns with global efforts to curb antimicrobial resistance and optimize antibiotic use. Although specific studies in Saudi Arabia were not directly reviewed, the global evidence supports the universal benefits of such programs. Pharmacist-led services in ASPs have been shown to play a crucial role in improving clinical outcomes, including reducing mortality rates and inappropriate antimicrobial prescribing. These programs help in the rational prescription of antimicrobial drugs, leading to significant cost savings and reduced resistance. Given the shared challenges of AMR worldwide, Saudi Arabia can likely experience similar positive outcomes through the implementation and enhancement of ASPs, leveraging the expertise of pharmacists and infectious disease specialists to promote judicious antibiotic use and improve patient care outcomes.[4-7]

Guideline **Adaptation Group**

The ASP guideline adaptation group (GAG) or task force included eight pediatric infectious diseases' specialists from across the Kingdom as well as a medical microbiologist and an infectious disease clinical pharmacist, and three guideline methodologists.

To make the best use of recent high-quality efforts locally and internationally, the guideline development/ adaptation process followed the King Saud University (KSU) Modified ADAPTE methodology, one of the formal methodologies for guideline adaptation.[8,9] Detailed process is reported in the appendices.

Table 2: Guideline Development/Adaptation Group

Full Name	Affiliation(s)	Role/Clinical Specialty
Clinical Panel (Subject Matter Experts)		
1. **Dr. Rana Hassan Almaghrabi (RHA)**	Consultant, Pediatric Infectious Diseases, Adjunct Assistant Professor at Al Faisal University, President, SPIDS, Scientific Board Director, Pediatric Infectious Diseases Fellowship Program at SCFHS, MAD-ID Antimicrobial Stewardship certification, Prince Sultan Military Medical City, Riyadh, Saudi Arabia	Clinical Chair Clinical Content Expert
2. **Dr. Fatimah Abullah Aldubisi (FAA)** MBBS, FRCPC	Consultant Pediatric Infectious Diseases and Antimicrobial Stewardship, MAD-ID Antimicrobial Stewardship Certificate, Riyadh Second Health Cluster, Ministry of Health, Vice President and Chair Scientific and Research Committees at SPIDS, Riyadh, Saudi Arabia	Clinical Chair Clinical Content Expert
3. **Dr. Sahar Althawadi**	Consultant Medical Microbiologist, Section Head, Microbiology Laboratory King Faisal Specialist Hospital and Research Center (KFSHRC) - Riyadh, Saudi Arabia	Clinical Content Expert
4. **Dr. Omar Alzomor**	Pediatric Infectious Diseases Consultant, Pediatric Infectious Diseases Department, Children Hospital, King Saud Medical City, Riyadh, Saudi Arabia	Clinical Content Expert

Full Name	Affiliation(s)	Role/Clinical Specialty
Clinical Panel (Subject Matter Experts)		
5. **Dr. Tasneem Ahmed Almubayedh**	Pediatric Infectious Disease Consultant MBBS, Maternity, and Children Dammam, Saudi Arabia	Clinical Content Expert
6. **Dr. Sameera Mohmmed Aljehani**	Consultant Pediatric and Pediatric Infectious Diseases, King Abdulaziz Hospital-Moh-Jeddah, Saudi Arabia	Clinical Content Expert
7. **Prof Mohammed Saeed AlAyed**	Pediatric Infectious Diseases Consultant, Pediatric Department, College of Medicine Najran University, Saudi Arabia	Clinical Content Expert
8. **Dr. Bashayer M. AlShehail**	Infectious Disease Clinical Pharmacist Consultant Pharmacy Practice Department, College of Clinical Pharmacy, Imam Abdulrahman Bin Faisal University, Dammam 31441, Saudi Arabia	Clinical Content Expert
9. **Dr. Mona Ahmed Bahasan**	Pediatric Infectious Disease Assistant Consultant, Pediatric Department, KFSHRC-Jeddah, Saudi Arabia	Clinical Content Expert
10. **Dr. Ghofran Waleed Sabbahi**	Infectious Diseases Fellow, Department of Pediatric Infectious Diseases, Ministry of Health, Western Region, Saudi Arabia	Clinical Content Expert
Methodology Subgroup		
11. **Dr. Ghada A. Bawazeer** MSc, PharmD, BCPS, BCMTMS (GAB)	College of Pharmacy, KSU, Riyadh, Saudi Arabia CPG Steering Committee, KSUMC Guidelines International Network Cochrane Member	Methodology Chair, Methodology Subgroup, Associate Professor of Pharmacy, Consultant Ambulatory Clinical Pharmacist, Guideline Methodologist
12. **Dr. Yasser S. Amer** MBBCh, MSc, FISQua, CPHQ, IPFPH	Quality Management Department, KSUMC CPG Steering Committee, KSUMC Research Chair for EBHC-KT, KSU Guidelines International Network Cochrane Member	Methodology Co-Chair, Methodology Subgroup, Pediatrician, Guideline Methodologist
13. **Prof. Lubna A. Al-Ansary** MBBS, FRCGP	Family and Community Medicine, Department, College of Medicine, KSU, Riyadh, Saudi Arabia CPG Steering Committee, KSUMC. Guidelines International Network Cochrane Editor	Member, Methodology Subgroup, Professor and Consultant of Family and Community Medicine, Guideline Methodologist

Scope and **Purpose**

Disease/Condition: Antibiotic Stewardship Practices

Guideline Objective(s): The objective of this guideline is to evaluate interventions aimed at optimizing antibiotic use across various levels of care and to address approaches to measure successful implementation.

Health or Clinical Questions (PIPOH Model)

Table 3: PIPOH Question of the Guideline

P: Patient (Target Population):	Hospitalized children and adults receiving antimicrobial agents. This guideline excludes antibiotic use in long term care facilities, outpatient care, primary care services, dental setting, home healthcare, and emergency department.

I: Interventions and Practices Considered/ CPG Category:	- **Interventions to reduce inappropriate use**
	  ▪ Didactic Education
	- **Interventions to improve antibiotic utilization and patient outcomes**
	  ▪ Preauthorization and prospective audit and feedback
	  ▪ Facility-specific clinical practice guidelines for common infectious diseases syndromes
	  ▪ Targeting patients with specific infectious diseases syndromes
	  ▪ Reduce the risk of use of antibiotics with a high risk of CDI
	  ▪ Prescriber-led review
	  ▪ Use of computerized clinical decision support systems
	  ▪ Cycling or mixing in antibiotic selection to reduce antibiotic resistance
	- **Interventions to optimize antibiotic use**
	  ▪ Allergy assessment
	  ▪ Shortening antibiotic duration of therapy
	  ▪ Dedicated Pharmacokinetic (PK) monitoring and adjustment program
	  ▪ De-escalation of therapy
	  ▪ Parenteral to oral antibiotics switching

	- **Microbiology & lab diagnostics**
	  ▪ Facility-specific antibiograms
	  ▪ Selective or cascade reporting of antibiotic susceptibility test
	  ▪ Rapid viral testing for respiratory pathogens
	  ▪ Rapid diagnostic testing on blood specimens
	  ▪ Procalcitonin (PCT) testing
	  ▪ Use of nonculture-based fungal markers
	- **Best measures to track the success of the program**
	  ▪ Defined Daily Dose (DDD)
	  ▪ Day of Therapy (DOTs)
	  ▪ Expenditure on antibiotic
	- ASP implementation for specific population (hematology/oncology patients, immunocompromised, NICU, patients)
	- Optimal ASP structure and team to influence better implementation of ASP to improve outcomes and reduce cost

P: Professionals (Intended/Target Users or Stakeholders)/Clinical Specialties:	Pediatric Infectious disease physicians, adult infectious disease physician, infectious disease pharmacists, clinical pharmacists, internal medicine, intensivist, surgeons, nurses, medical lab physicians and technicians, microbiologists, infection control and prevention, quality and safety department, health informatics and administrators.
O: Major Outcomes Considered:	- Reducing or preventing antimicrobial resistance patient safety
H: Healthcare Settings:	- Hospitals in Saudi Arabia

Questions and **Recommendations**

The GAG adopted and prioritized 23 clinical questions from the IDSA/SHEA guideline together with associated clinical outcomes and excluded four because they fell outside the scope of target implementation sites of this CPG adaptation project (Table 4). In addition to four additional questions based on the local needs and context in Saudi Arabia. The evidence base for each question was updated in May 2024 in line with the source guideline's search strategies. Additional literature searches were run on the local contextual factors (epidemiology, values and preferences, equity, acceptability, feasibility, implementation, and cost). The GAG did not create new GRADE Evidence-to-Decision (EtD) frameworks for each question.
(For more details on the guideline adaptation methodology refer to the Methods and Appendices sections).

Table 4: Guideline Clinical Questions and Recommendations

1. Interventions to Improve Antibiotic Use	
Is didactic education a useful antibiotic stewardship intervention for reducing inappropriate antibiotic use? **1.1.** We suggest **against** relying solely on didactic educational materials for stewardship.	Weak recommendation, low-quality evidence
Does the use of preauthorization and/or prospective audit and feedback interventions by antibiotic stewardship programs (ASPs) improve antibiotic utilization and patient outcomes? **1.2.** We recommend preauthorization and/or prospective audit and feedback over no such interventions.	Strong recommendation, moderate-quality evidence
Should ASPs develop and implement facility-specific clinical practice guidelines for common infectious diseases syndromes to improve antibiotic utilization and patient outcomes? **1.3.** We suggest ASPs develop facility-specific clinical practice guidelines coupled with a dissemination and implementation strategy.	Weak recommendation, low-quality evidence
Should ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes? **1.4.** We suggest ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes.	Weak recommendation, low-quality evidence
Should ASPs implement interventions designed to reduce the use of antibiotics-associated with a high risk of Clostridium Difficile Infection (CDI)? **1.5.** We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics-associated with a high risk of CDI compared with no such intervention.	Strong recommendation, moderate-quality evidence

Do strategies to encourage prescriber-led review of appropriateness of antibiotic regimens, in the absence of direct input from an antibiotic stewardship team, improve antibiotic prescribing? **1.6.** We suggest the use of strategies (e.g., antibiotic time-outs, stop orders) to encourage prescribers to perform routine review of antibiotic regimens to improve antibiotic prescribing.	Weak recommendation, low-quality evidence
Should computerized clinical decision support systems integrated into the electronic health record at the time of prescribing be incorporated as part of ASPs to improve antibiotic prescribing? **1.7.** We suggest incorporation of computerized clinical decision support at the time of prescribing into ASPs.	Weak recommendation, low-quality evidence
Should ASPs implement strategies that promote cycling or mixing in antibiotic selection to reduce antibiotic resistance? **1.8.** We suggest against the use of antibiotic cycling as a stewardship strategy.	Weak recommendation, low-quality evidence
2. Interventions Targeting Optimization of Antibiotic Therapy	
In hospitalized patients requiring intravenous (IV) antibiotics, does a dedicated pharmacokinetic (PK) monitoring and adjustment program lead to improved clinical outcomes and reduced costs? **2.1.** We recommend that hospitals implement PK monitoring and adjustment programs for aminoglycosides.	Strong recommendation, moderate-quality evidence
2.2. We suggest that hospitals implement PK monitoring and adjustment programs for vancomycin.	Weak recommendation, low-quality evidence
In hospitalized patients, should ASPs advocate for alternative dosing strategies based on pk/pharmacodynamic principles to improve outcomes and decrease costs for broad-spectrum ß-lactams and vancomycin? **2.3.** In hospitalized patients, we suggest ASPs advocate for the use of alternative dosing strategies vs standard dosing for broad-spectrum β-lactams to decrease costs.	Weak recommendation, low-quality evidence
Should ASPs implement interventions to increase use of oral antibiotics as a strategy to improve outcomes or decrease costs? **2.4.** We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics.	Weak recommendation, low-quality evidence
In patients with a reported history of ß-lactam allergy, should ASPs facilitate initiatives to implement allergy assessments with the goal of improved use of first-line antibiotics? **2.5.** In patients with a history of β-lactam allergy, we suggest that ASPs promote allergy assessments and penicillin (PCN) skin testing when appropriate.	Weak recommendation, low-quality evidence
Should ASPs implement interventions to reduce antibiotic therapy to the shortest effective duration? **2.6.** We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration.	Strong recommendation, moderate-quality evidence

3. Interventions Targeting Microbiology and Laboratory Diagnostics

Should ASPs work with the microbiology laboratory to develop stratified antibiograms, compared with non-stratified antibiograms? **3.1.** We suggest development of stratified antibiograms over solely relying on non stratified antibiograms to assist ASPs in developing guidelines for empiric therapy.	Weak recommendation, low-quality evidence
Should ASPs work with the microbiology laboratory to perform selective or cascade reporting of antibiotic susceptibility test results? **3.2.** We suggest selective and cascade reporting of antibiotics over reporting of all tested antibiotics.	Weak recommendation, low-quality evidence
Does the use of antibiotic de-escalation interventions by antibiotic stewardship programs (ASPs) improve antibiotic utilization and patient outcomes? **3.3.** We suggest that ASP team implement antibiotic de-escalation strategy, especially in the ICU setting, and following microbiology test results to reduce the emergence of multidrug-resistant bacteria associated with the empirical use of broad-spectrum antibiotics.	Good practice statement
Does the use of comments or additional messages enhance microbiology report interpretation and guide therapy? **3.4.** We suggest including comments or a relevant alert in the microbiology report may be useful and could lead to a more appropriate antibiotic selection.	Good practice statement
Should ASPs advocate for use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics? **3.5.** We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics.	Weak recommendation, low-quality evidence
Should ASPs advocate for rapid diagnostic testing on blood specimens to optimize antibiotic therapy and improve clinical outcomes? **3.6.** We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation	Weak recommendation, moderate-quality evidence
In adults in intensive care units (ICUs) with suspected infection, should ASPs advocate procalcitonin (PCT) testing as an intervention to decrease antibiotic use? **3.7.** In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use.	Weak recommendation, moderate-quality evidence
In patients with hematologic malignancy, should ASPs advocate for incorporation of nonculture-based fungal markers in interventions to optimize antifungal use? **3.8.** In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), we suggest incorporating nonculture-based fungal markers in ASP interventions to optimize antifungal use.	Weak recommendation, low-quality evidence

4. Interventions of Implementing ASP in Special Populations

Should ASPs develop facility-specific clinical guidelines for management of fever and neutropenia (F&N) in hematology-oncology patients to reduce unnecessary antibiotic use and improve outcomes? **4.1.** We suggest ASPs develop facility-specific guidelines for F&N management in hematology-oncology patients over no such approach.	Weak recommendation, low-quality evidence
In immunocompromised patients receiving antifungal therapy, do interventions by ASPs improve utilization and outcomes? **4.2.** We suggest implementation of ASP interventions to improve the appropriate prescribing of antifungal treatment in immunocompromised patients.	Weak recommendation, low-quality evidence
In neonatal intensive care units (NICUs), do ASPs reduce inappropriate antibiotic use and/or resistance? **4.3.** We suggest implementation of antibiotic stewardship interventions to reduce inappropriate antibiotic use and/or resistance in the NICU.	Good practice statement

5. Measurements to Assess Impact of ASP on Expenditure and Patient's Outcomes

Which overall measures best reflect the impact of ASPs and their interventions? **5.1.** We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to defined daily dose (DDD).	Weak recommendation, low-quality evidence
Who are the key stakeholders who should receive reports on antimicrobial stewardship program performance? **5.2.** We suggest that ASP leader regularly reports the progress of the program to the hospital leaderships, and to stakeholders.	Good practice statement

6. Organizational and Structural Support
What Organizational and Structural Support Should Exist to Support?

6.1. We suggest engagement of leadership commitment at all levels of the institution to ensure the ASP has sufficient budget, technology, time, authority, and resources to succeed.	Good practice statement
6.2. We suggest appointing leaders and co-leaders who are responsible for program outcomes provides accountability for ASP activities.	Good practice statement
6.3. We suggest integrating a qualified clinical pharmacist as member of ASP team to promote optimal antimicrobial use, to reduce the transmission of infections, and to educate other healthcare professionals, patients, and the public.	Good practice statement
6.4. We suggest integrating a qualified nurse as member of ASP team to promote appropriate antimicrobial use, during patient admission, daily progress monitoring, clinical progress, quality monitoring, and patient education and discharge.	Good practice statement

Background

Antimicrobial resistance (AMR) poses a significant global threat and is listed among the top ten public health challenges by the World Health Organization.[10] The increased use of antimicrobials in hospitals leads to a higher prevalence of resistant bacteria, causing hospital-associated infections with significant morbidity and mortality.[11] The prominent cause contributing to AMR crisis remains to be the overuse and misuse of antimicrobials, particularly the inappropriate usage of antibiotics. Economically, the global estimates place the cost of capital loss due to antibiotic resistance at $300 billion and $1 trillion by 2050.[12]

A 5-year resistance trend in pathogens at a multi-hospital healthcare system in Saudi Arabia between 2015-2019 showed a rising rate in antimicrobial resistance.[13] Gram negative pathogens were four times more likely to cause nosocomial infections compared with Gram-positive bacteria. The most common resistant pathogens were extended-spectrum cephalosporin-resistant *E. coli* (37.1%), extended-spectrum cephalosporin-resistant *Klebsiella* (27.8%), carbapenem-non-susceptible *Acinetobacter* spp. (19.5%), carbapenem-non-susceptible *Pseudomonas aeruginosa* (19.2%) and methicillin-resistant *S. aureus* (18.6%).

To address these challenges, optimizing antibiotic use is crucial. Antibiotic Stewardship Programs (ASPs) play a pivotal role in optimizing antimicrobial use, improving patient outcomes, reducing adverse events, and combating antibiotic resistance.[14] ASPs follow the consensus statement from infectious disease organizations, focusing on appropriate antibiotic selection, dosing, duration, and administration. The implementation of ASPs is encouraged and, in some cases, mandated by governmental and regulatory agencies. In line with national standards, healthcare institutions in Saudi Arabia, as mandated by the Saudi Central Board for Accreditation of Healthcare Institutions (CBAHI), are required to establish infection prevention and control programs. These programs aim to identify, reduce, and eliminate infection risks, ensuring a clean environment and patient safety. The recommendation includes developing and regularly updating an antibiogram, reviewed by an infection prevention and control committee at least annually.

This comprehensive approach aligns with global efforts to combat AMR and enhance patient safety. Although ASPs have been implemented in several Saudi tertiary hospitals and medical cities, a nationwide study published in 2021, revealed that just 26% of Saudi MOH facilities have adopted ASPs.[15] Indeed, the antimicrobial resistance (AMR) national action plan was developed by WEQAYA in collaboration with various health sectors and stakeholder to implement the five objectives of the World Health Organization's (WHO) Global Action Plan on Antimicrobial Resistance.[16]

These Objectives Include:

Objective 1:

Improve awareness and understanding of antimicrobial resistance through effective communication, education, and training.

Objective 2:

Strengthen the knowledge evidence base through surveillance and research.

Objective 3:

Reduce the incidence of infection through effective sanitation, hygiene, and prevention measures.

Objective 4:

Optimize the use of antimicrobial medicines in human and animal health.

Objective 5:

Develop the economic case for sustainable investment that takes account of the needs of all countries and increase investment, new medicines, diagnostic tools, vaccines, and other interventions.

The implementation of ASP is associated with major healthcare cost. Al-Omari et al. showed that the across four tertiary hospitals, antimicrobial costs decreased by 28.45 % in the first year of the ASP implementation.[17] This remained relatively stable in subsequent years, with overall cumulative cost savings estimated at 6,286,929 SAR and negligible expenses of 505,115 SAR. Moreover, ASPs also resulted in significant reduction in healthcare associate infections. However, there is still a need for a national guideline in place to promote standardized approaches to antimicrobial stewardship. These guidelines aim to optimize the use of antimicrobial agents, improve patient outcomes, and reduce the emergence of antimicrobial resistance across the kingdom. Moreover, the Public Health Authority (PHA) in Saudi Arabia has produced a guidance to antimicrobial stewardship implementation in hospitals that was released. The SPIDS ASP guideline is a complementary and integrated with the upcoming PHA implementation guidance.

Target **Population**

Hospitalized children and adults receiving antimicrobial agents. This guideline excludes antibiotic use in long term care facilities, outpatient care, primary care services, one-day surgery, day care units, dental setting, home healthcare, and emergency departments.

Recommendations and Evidence Summaries

1. Interventions to Improve Antibiotic Use

Didactic Education

Is didactic education a useful antibiotic stewardship intervention for reducing inappropriate antibiotic use?

1.1. We **suggest against** relying solely on didactic educational materials for stewardship.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Antimicrobial stewardship programs (ASPs) commonly use education to improve antibiotic prescribing practices. Educational strategies include didactic lectures, distribution of educational pamphlets and materials, and educational meetings. Didactic education alone is not an effective way to reduce inappropriate antibiotic use or sustain improvements in antibiotic prescribing habits. However, it can be a useful part and more effective if combined with comprehensive antibiotic stewardship program such as prospective audit and feedback.[2] Educational strategies should target all healthcare professionals, including physicians, pharmacists, physician assistants, nurse practitioners, and healthcare students and trainees. Medical schools and teaching hospitals should ensure that their curriculum includes instruction on fundamental antibiotic stewardship principles.[18]

Several studies from Saudi Arabia highlight the use of education and training as a component of ASP interventions.[15,19] Studies also, emphasized on tailoring the educational program to the action(s) most relevant to the provider group.[20-22] At the education level, studies highlighted the need for optimal under- and postgraduate education stewardship-curriculum.[23,24] In addition, there is still limited research specifically addressing the impact of education on antimicrobial stewardship outcomes in Saudi Arabia.

Preauthorization and/or Prospective Audit and Feedback Interventions

Does the use of preauthorization and/or prospective audit and feedback interventions by antibiotic stewardship programs (ASPs) improve antibiotic utilization and patient outcomes?

1.2. We **recommend** preauthorization and/or prospective audit and feedback over no such interventions.

Strong recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Preauthorization:

Preauthorization requires prescribers to gain approval prior to the use of certain restricted antibiotics. The use of antibiotic must be optimized in order to successfully treat infections, protect patients from the harms brought on by overuse of antibiotics, and combat antibiotic resistance.
Preauthorization has the advantage of enabling the manager to choose which patients need to receive antibiotic administration before it is given. It decreases unnecessary antimicrobial use, costs reduction, and increases the potency of initial empirical therapy. In addition, it can induce a change in prescription patterns in the early stage.[25] A regional survey of ASPs in Makkah region (KSA) hospitals at the pharmacy level review showed that formulary restrictions (89%) and feedback on prescribing to physicians (68%) as most common ASP interventions with high suggested success in hospitals.[19]

Decisions on which antibiotics to preauthorize should be made in consultation with ASP team which could improve the empiric use rather than focusing on the cost of drug. This intervention necessitates the availability of specialists and people who can expeditiously fulfill authorizations. In order to adopt preauthorization and avoid delaying treatment for severe infections, hospitals may alter the agents, circumstances, and procedures (e.g. preauthorization through an electronic order entry system). Based on the center protocols and resources, some centers permit the use of the first empiric dose of the antibiotics and require preauthorization afterward, others may allow an extended supply of the empiric antibiotics for 24 -48 hours. Stewardship programs need to keep an eye on any unintended implications of preauthorization, particularly any delays in treatment.

Prospective Audit with Intervention and Feedback (PAF):

An important ASP strategy that involves a case-by-case review of patients prescribed antibiotics, typically by an infectious diseases (ID) physician or clinical pharmacist.[2] Cases are reviewed for antibiotic appropriateness and feedback is delivered directly to the provider caring for the patient, prospective (real-time) audit is preferred over the retrospective assessment of antibiotic. One of the most effective ways to deliver the feedback is the “handshake” stewardship (H-AS) which is a rounding-based, real-time assessment approach that prioritizes face-to-face or live communication and engages frontline providers into the PAF process. A quasi-experimental study conducted in a tertiary hospital Jeddah-Saudi Arabia on non-ICU patients for whom a restricted antibiotic was ordered showed that prospective audit and feedback implemented within a multidisciplinary antimicrobial stewardship program (ASP) was associated with positive outcomes.[26] There was lower daily dose and days of therapy per 100 patient days, more de-escalation and higher clinical cure rates with significantly shorter Hospital and ICU length of stay. In-hospital mortality and 30-day readmission were also significantly lower in the intervention group.

Preauthorization and PAF both have their merits and shortcomings.[27] The PAF had the capacity to reveal patterns in antibiotic usage within institutions and promote the development of relationships among the different stakeholders. But PAF is a time-consuming process, associated with high administrative burden and healthcare provider load, potential delay in patient care and potential for overuse of alternative therapies. Conversely, preauthorization effectively decreased the utilization of broad-spectrum antimicrobials, but it provided only limited educational chances. This can be overcome by incorporating clinical guidelines, antibiotic stewardship training, feedback and data analysis, case-based learning, and continuous professional development. As many experts believe that both interventions should be given top priority, a hybrid approach may allow ASPs to capitalize on the merits of one while mitigating the shortcomings of the other.[28] More research is needed to assess satisfaction with, and perceived efficacy of each strategy based on local data and experience.

Facility-Specific Clinical Practice Guidelines for Common Infectious Diseases Syndromes

Should ASPs develop and implement facility-specific clinical practice guidelines for common infectious diseases syndromes to improve antibiotic utilization and patient outcomes?

1.3. We **suggest** ASPs develop facility-specific clinical practice guidelines coupled with a dissemination and implementation strategy.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Implementing facility-specific clinical practice guidelines can be very helpful and lead to significant improvements in antibiotic use for illnesses commonly treated in both pediatric and adult infections. The Implementation of facility-specific guidelines have been associated with a better and more appropriate antibiotic utilization.[29-36] The interdisciplinary guideline formulation process as well as a multidimensional distribution and implementation strategy are very important to boost guideline knowledge and uptake. Guideline dissemination in electronic or hard-copy formats, provider education, engagement of peer champion advocates, audit and feedback of prescribing practices to providers, checklists, and implementation of recommendations into electronic order sets were examples of such efforts.

The Saudi Pediatric Infectious Diseases Society (SPIDS) is highly active in producing and endorsing several published clinical practice guidelines in Saudi Arabia on topics covering community-acquired pneumonia (CAP),[37] Diagnosis and management of community-acquired urinary tract infection in infants and children,[38] Brucellosis in children,[39] and guidelines for the secondary prevention of rheumatic heart disease.[40]
The Saudi Ministry of Health has set sepsis, community-acquired pneumonia (CAP) in adults and children, and acute gastroenteritis in children as priority themes for clinical practice guidelines and these guidelines are supposed to be released soon. Moreover, a qualitative study conducted in Saudi hospitals, revealed that one of the barriers to the adoption and implementation of ASPs include concerns among physicians regarding lack of enforcement of policies and guidelines by governing bodies.[5]
A systematic review mapped 11 studies published from Saudi Arabia about the level of ASP implementation within acute care setting compared to CDC guidelines.[41] Only 5 studies reported on the use of facility-specific guidelines,[5,20,42-44] among those, only one study monitored the adherence to facility-specific treatment guidelines.[42]
Further research is needed to assess the level of implementation and adherence to facility-specific guidelines and the targeted outcomes should be tracked within the local context.

Targeting Antibiotics Use in Patients with Specific Infectious Diseases Syndromes

Should ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes?

1.4. We **suggest** ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Targeting antibiotic use and clinical outcomes for a specific infectious diseases issue has been found to be beneficial in addition to hospital-wide actions such as preauthorization or the formulation of clinical guidelines.[45] For example, Community acquired pneumonia, urinary tract infection, skin, and soft tissue infections are important opportunities to improve the use of antibiotics in pediatric population. Recommendations may be based on national guidelines but should reflect hospital treatment preferences based on local susceptibilities, and formulary options. Currently the Saudi Pediatric Infectious Diseases Society (SPIDS) is highly active in producing and endorsing several clinical practice guidelines targeting rheumatic heart disease, community acquired pneumonia, Brucellosis and urinary tract infections.[37-40]

Reduce the Use of Antibiotics-Associated with a High Risk of CDI

Should ASPs implement interventions designed to reduce the use of antibiotics-associated with a high risk of Clostridium Difficile Infection (CDI)?

1.5. We **recommend** antibiotic stewardship interventions designed to reduce the use of antibiotics-associated with a high risk of CDI compared with no such intervention.

Strong recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Clostridium difficile (CD) is one of the leading causes of healthcare-associated infection.[46] The use of antibiotics is strongly associated with this infection, particularly the use of clindamycin, cephalosporins, macrolides, and fluoroquinolones.[47] Therefore, ASP is a strong first-practical step in CD prevention.[48,49] Surveillance program for CDI is an essential component of prevention of healthcare-associated CDI (HC CDI) to monitor its rate and identifying pending outbreak. A statistically significant reduction in healthcare associated infections including healthcare CDIs and improved patient's outcomes had been reported in many studies with ASP implementation including meta-analysis studies.[2,50]
A case control study in a major tertiary hospital showed that targeted ASP interventions for antibiotics highly associated with CDI was effective in reducing inappropriate antibiotic and reducing direct cost.[51] Another study by Aldeyab et al, described successful implementation of ASP intervention targeting high-risk antibiotics (second-generation cephalosporins, third generation cephalosporins, fluoroquinolones and clindamycin) resulted in CDI incidence rate decreased by 0.0047/100 bed-days per month.[52] There is a lack of published data on CDI prevalence at the national level, conducting research specific to the local context is essential to gain a comprehensive understanding of the problem and develop effective ASP interventions in Saudi Arabia. However, PHA Currently monitors CDI rate is monitored nationwide as an indicator, and mandates its collection and follow-up from all hospital.

Prescriber-Led Review of Appropriateness of Antibiotic Regimens

Do strategies to encourage prescriber-led review of the appropriateness of antibiotic regimens, in the absence of direct input from an antibiotic stewardship team, improve antibiotic prescribing?

1.6. We **suggest** the use of strategies (e.g., antibiotic timeouts, and stop orders) to encourage prescribers to perform a routine review of antibiotic regimens to improve antibiotic prescribing.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Antibiotic timeout is a provider-led reassessment of the continuing need and choice of antibiotics when the clinical picture is clearer and more diagnostic information, especially when the results of cultures and rapid diagnostics, is available (often 48 -72 hours after initiation of therapy).[53,54] An antibiotic "time out" is a term used by the Centers for Disease Control and Prevention and is listed as a key intervention for improving antibiotic use. It promotes the concept of "self-stewardship" in healthcare settings.[55] The idea is that the most responsible physician takes the time (i.e., a "time out") to do this reassessment. The reassessments may be scheduled for additional intervals, such as on days 5, 7, etc. of the therapy. Antibiotic timeout is critical and has shown to be an effective component of ASP. To maximize the effectiveness, it has to be suitable with the available resources.[50] In some centers, the antibiotic timeout can be led by the designated stewardship lead if provider-led reassessment is not feasible. A single-center, retrospective, before and after study conducted in Jeddah-Saudi Arabia, implemented re-authorization intervention as an alternative to the time-out strategy of restricted antibiotics that were continuing on day 3.[56] The study found a significant reduction in overall consumption of restricted antibiotics and length of hospital stay without adversely affecting hospital mortality. More research is needed to identify the best approach to implementing a prescriber-led review of prescribed antimicrobials, outcome, and cost-effectiveness.

Computerized Clinical Decision Support Systems Integrated into the Electronic Health Record at the Time of Prescribing

Should computerized clinical decision support systems integrated into the electronic health record at the time of prescribing be incorporated as part of ASPs to improve antibiotic prescribing?

1.7. We **suggest** the incorporation of computerized clinical decision support at the time of prescribing into ASPs.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Computerized decision support systems (CDSS) and surveillance systems are designed to help clinicians prescribe antibiotics more effectively. Computerized decision support system provides treatment recommendations at the time of prescribing,[57-63] while computerized surveillance systems help to identify and track antibiotic use patterns by facilitating more prospective audits with feedback interventions and minimizing the time for interventions.[64-66]

Applying both CDSSs and surveillance systems for prescribers has been shown to have a number of benefits including minimizing the use of broad-spectrum antibiotics, more appropriate antibiotic selection, improving antibiotic dosing, decreasing antibiotic resistance, lower prescribing errors, decreasing adverse effects, lowering antibiotic costs, decrease length of stay, decrease mortality. However, there are some potential drawbacks to CDSS and surveillance systems, they are expensive and time-consuming to set up and maintain, also they can generate a lot of alerts, which can be overwhelming for doctors and may lead to "alert fatigue". The implementation cost might significantly limit the wide use of this system. In 2021, it was reported that 44% of hospitals in Saudi Arabia have computerized prescriber order entry (CPOE) system functionality for formulary system management.[67] There is a lack of research on the impact of the use of computerized systems to support ASP activities in Saudi Arabia.

Cycling or Mixing in Antibiotic Selection to Reduce Antibiotic Resistance

Should ASPs implement strategies that promote cycling or mixing in antibiotic selection to reduce antibiotic resistance?

Weak recommendation, low-quality evidence

1.8. Suggest **against** the use of antibiotic cycling as a stewardship strategy.

Evidence Summary & Local Considerations

Since the 1980s, the concept of rotating antibiotic treatments for patients with bacterial infections has been viewed as a potential strategy for reducing antibiotic resistance rates in hospitals. This approach is known as antibiotic cycling and it involves using a specific antibiotic as a first-line therapy for all patients for a defined period, replacing that antibiotic with a drug of a different class but a similar spectrum of activity for the same duration, and then repeating the cycle. More than two different antibiotics can be part of this rotation.

Antibiotic mixing, on the other hand, takes a less structured approach, with each consecutive patient on a ward being treated with an alternative class of antibiotics. Clinical studies have produced inconclusive results on the efficacy of antibiotic cycling or mixing, in addition to limitations regarding logistics, patient-specific considerations, and resource availability.[68] Further research on tailoring such strategies to local resistance patterns and their impact on patient outcomes and antibiotic resistance is warranted.

2. Interventions Targeting Optimization of Antibiotic Therapy

Dedicated Pharmacokinetic (PK) Monitoring and Adjustment Program

In hospitalized patients requiring intravenous (IV) antibiotics, does a dedicated pharmacokinetic (PK) monitoring and adjustment program lead to improved clinical outcomes and reduced costs?

2.1. We recommend that hospitals implement PK monitoring and adjustment programs for aminoglycosides.

Strong recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Hospital implementation of PK monitoring program for aminoglycoside is recommended and endorsed by many guidelines.[2,69] Furthermore, the updated 2023 IDSA Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections has added a supplement for PK monitoring of aminoglycoside.[70] Having monitoring programs for aminoglycoside is highly encouraged since it has been associated with improved outcomes in terms of efficacy and safety.[71,72] Pharmacists' involvement in running PK programs has been linked to less nephrotoxicity, reduced length of stay, and cost reduction.[73] The value of pharmacist-led therapeutic drug monitoring services demonstrated a valuable impact on appropriate dosing and monitoring of antibiotics such as vancomycin, amikacin, and gentamicin.[74] The study was conducted in a tertiary hospital in Jeddah, Saudi Arabia, and showed a significant impact on optimal initial dosing. In addition, optimal dose adjustments and correct drug level ordering were also observed.

Dedicated Vancomycin Monitoring and Adjustment Program

2.2. We **suggest** that hospitals implement PK monitoring and adjustment programs for vancomycin.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Vancomycin requires therapeutic drug monitoring since it can increase the rate of Acute kidney injury (AKI) in patients with high serum concentrations. On the other hand, the subtherapeutic level is associated with the risk of treatment failure.[75] Having a PK monitoring program for Vancomycin is linked to less incidence of nephrotoxicity and cost reduction in some studies.[76] In a recent quasi-experimental study that evaluated pharmacist-directed vancomycin therapeutic drug monitoring in pediatric patients, they reported that implementation of pharmacist-led PK service achieved a higher number of patients dosed optimally both initially and in subsequent dose adjustment. Additionally, it improved the ordering of vancomycin trough levels at the correct time.[77] However, many of those studies failed to correlate the PK monitoring programs to therapeutic outcomes.[78] Further research is warranted to improve vancomycin monitoring and impact on patient outcomes.

Alternative Dosing Strategies Based on PK/Pharmacodynamic Principles for Broad-Spectrum ß-Lactams and Vancomycin

In hospitalized patients, should ASPs advocate for alternative dosing strategies based on pk/pharmacodynamic principles to improve outcomes and decrease costs for broad-spectrum ß-lactams and vancomycin?

2.3. In hospitalized patients, we **suggest** ASPs advocate for the use of alternative dosing strategies vs standard dosing for broad-spectrum β-lactams to decrease costs.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

β-lactams are broad-spectrum antibiotics that are considered one of the most used antibiotics for treating many bacterial infections. They exhibit time-dependent antimicrobial activity and can be optimized by maximizing the period during which the free drug concentration exceeds the organism's minimum inhibitory concentration (MIC).[79] Continuous infusion of β-lactams is more efficacious than intermittent infusion, according to PK/PD studies. Therefore, one of the approaches that are proposed as an optimization strategy for dosing these antibiotics is prolonged/extended infusion of β-lactams instead of bolus administration.[80] However, the evidence in improving clinical outcomes conflicts with some studies demonstrating no benefits in outcome.[81] Nevertheless, the administration of β-lactams as a continuous infusion can lead to cost savings by decreasing drug costs and pharmacy /nursing labor time.[82] A study conducted at Johns Hopkins Aramco Healthcare in Saudi Arabia using a retrospective drug utilization evaluation methodology revealed that 34% of the patients were switched to extended infusion of piperacillin/tazobactam in a timely manner.[83] This was improved to 86% following the implementation of extended infusion protocol supervised by a clinical pharmacist.

However, no outcome data was described in the study. A cost-effectiveness study from Egypt demonstrated the superiority of extended infusion of piperacillin/tazobactam compared to the intermittent infusion regarding cost-effectiveness ratio ($1835.41 and $1914.09/expected success, respectively) attributed to fewer days required for clinical success and fewer days spent on the antibiotic.[84] Larger, prospective, and high-quality studies are needed to compare the effectiveness and cost-effectiveness of the two dosing strategies in different patient population groups and hospital settings in Saudi Arabia.

Increase Use of Oral Antibiotics Use

Should ASPs implement interventions to increase use of oral antibiotics as a strategy to improve outcomes or decrease costs?

2.4. We recommend ASPs implement programs to increase both the appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics.

Evidence Summary & Local Considerations

IV to PO switching is a cost-saving approach used in ASP programs. Certain antimicrobials with good oral bioavailability can be switched from IV to oral in stable patients without contraindications.[85] This includes drugs like fluoroquinolones, linezolid, Bactrim, and fluconazole. In some cases, IV antibiotics can be switched to oral agents with similar activity, such as Cefazolin to Dicloxacillin.[86] Hospital guidelines with defined criteria can help guide prescribers in making timely switches which will result in a reduction in cost, IV line-related complications, and length of hospital stay.[87,88] In a recently published systematic review discussing the effectiveness of antimicrobial stewardship interventions on the early switch from intravenous-to-oral antimicrobials, they reported that IV to PO switch has a positive impact on both clinical such as length of hospital stay and economic outcomes without increasing the risk of mortality, readmission, and adverse drug reaction.[89] At the local level, a single center, a prospective quasi-interventional study conducted at a tertiary academic hospital in Jeddah, Saudi Arabia showed that a Pharmacist-managed early switch from IV-PO therapy was associated with a significant reduction in IV medication use and an overall cost-saving of 50,960.8 SAR ($13,589.5).[90] More research is still needed to further explore this intervention based on available resources and expertise.

In Patients with a Reported History of ß-Lactam Allergy, Should ASPs Facilitate Initiatives to Implement Allergy Assessments with the Goal of Improved Use of First-Line Antibiotics?

In patients with a reported history of ß-lactam allergy, should ASPs facilitate initiatives to implement allergy assessments with the goal of improved use of first-line antibiotics?

2.5. In patients with a history of ß-lactam allergy, we recommend that ASPs promote allergy assessments and penicillin (PCN) skin testing when appropriate.

Strong recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Up to 90% of self-reported penicillin allergies are incorrect, inaccurate, and misrepresent patient allergy data. This may lead to needless escalation to a wider range of antibiotics and second-line drug selection, hindering antimicrobial stewardship initiatives.[91]

Allergy assessment and policies are challenging and need multidisciplinary teams, including ASP, infectious disease physicians, clinical pharmacists, and immunology/allergy experts.[92]

First and foremost, in screening a patient for penicillin allergy is the evaluation of the allergic response history, followed by risk stratification.[93] Risk stratification recommendations are an ASP activity that may enhance antimicrobial usage. Roberts et al. found that computerized algorithms may assist pediatricians in identifying low-risk penicillin allergy patients.[94] A recent national study in Saudi Arabia investigated self-reported penicillin allergy and found that the prevalence was 9.5%.[95] Skin testing was reported in 35.6%, 46.1% described anaphylaxis reaction with only 43.82% receiving epinephrine or antihistamine injection, while 11.4% are less likely to have true penicillin allergy. Another small cross-sectional questionnaires-based study from a major tertiary hospital In Jeddah found that patient-reported allergy was higher than the penicillin allergy risk tool (PEN-FAST) score; 4% vs 2% respectively.[96] The scarcity of data from Saudi Arabia on the use of allergy assessments as part of stewardship initiatives emphasizes the need for more study.

Implementing Interventions to Reduce Antibiotic Therapy to the Shortest Effective Duration

Should ASPs implement interventions to reduce antibiotic therapy to the shortest effective duration?

2.6. We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration.

Strong recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Shortening the duration of antibiotic treatment is important for optimizing antibiotic use, as it reduces unnecessary antibiotic exposure and thus decreases the emergence of resistance and adverse side effects, including clostridioides difficile infections (CDIs).[97] Having ASP guidelines that are easily accessible to all healthcare providers regarding the recommended duration for common infectious diseases is considered an important component in ASP activates.[2] Furthermore, implementing and defining discontinuation criteria either through guidelines or prospective audit and feedback has been a successful ASP approach.[98] Using computerized physician order entry systems to ensure that the prescriber has entered the antimicrobial stop date is another useful tool that can be used as well.[99] A study from a major tertiary hospital in Riyadh, Saudi Arabia showed that the utilization of prospective audit and feedback resulted in a shorter duration of antibiotic therapy, less inappropriate antimicrobial use, fewer antibiotic adverse events, and a neutral effect in nosocomial infection rates, and length of ICU stay or mortality.[51] Furthermore, a reduction in antimicrobial utilization by 11% to 38% DDD/1000 patient-days and lower total antimicrobial costs (US$ 5–10/patient-day) was also reported.

3. Interventions Targeting Microbiology and Laboratory Diagnostics

Microbiology Laboratory-Developed Stratified Antibiograms, Compared with Non-stratified Antibiograms

Should ASPs work with the microbiology laboratory to develop stratified antibiograms, compared with non-stratified antibiograms?

3.1. We suggest the development of stratified antibiograms over solely relying on non-stratified antibiograms to assist ASPs in developing guidelines for empiric therapy.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Cumulative antibiograms can help prescribers choose effective therapy when culture results are pending, inform, and update local guidelines for empirical treatment of common infection syndromes, update per procedural or perioperative prophylaxis recommendations, rationalize antimicrobial formulary selection, survey local resistance and benchmarking, identify stewardship intervention targets, and provide context for new drug susceptibility testing results. The Clinical Laboratory Standard Institute issued guidance on cumulative susceptibility test data analysis and presentation.[100,101] The guidance recommends an annual data analysis and presentation focusing on diagnostic isolates and species with ≥30 isolates. Also, instead of hospital-wide antibiograms, stratified antibiograms by service, unit, resistance mechanisms, body areas, or specimens are more relevant and are recommended. The stratified antibiogram will assist in building empiric therapy recommendations in each institution and identify important discrepancies in susceptibility testing across hospital units, which will help optimize treatment. In the context of Saudi Arabia, a case study from a medical city hospital showed that one of the biggest challenge to ASP implementation was the incompatibility of the electronic medical system and the need to generate and share manual data manually.[102] However, several studies showed the usage of antibiograms to guide therapy and monitor antimicrobial sensitivity and emerging resistance.[103-105] Further research is still needed to explore stratified antibiogram impact on clinical effectiveness and emerging of antibiotic resistance.

Perform Selective or Cascade Reporting of Antibiotic Susceptibility Test Results by Microbiology Laboratory

Should ASPs work with the microbiology laboratory to perform selective or cascade reporting of antibiotic susceptibility test results?

3.2. We suggest selective and cascade reporting of antibiotics and over-reporting of all tested antibiotics.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Cascade or selective reporting can be used to promote the judicious use of antimicrobials. Cascades consist of algorithm-driven reports that provide only a limited number of tested antimicrobial susceptibilities based on formulary availability, local cumulative susceptibilities, and cost for isolates with no or low levels of resistance and reporting of susceptibility to broader-spectrum drugs only when isolates are resistant to drugs in the first "cascade". Careful selection of reported susceptibilities and frequent re-evaluation are necessary to ensure the continued value and reliability of the cascade and the quality of the reporting. Unreleased susceptibility data should also be readily available upon clinician request. Several studies suggest an association between the antibiotics listed in antimicrobial susceptibility reporting and the use of these antibiotics by prescribers with an impact on the appropriateness of antibiotic selection.[106-109] For example, providing only susceptibilities to narrow-spectrum urine agents such as nitrofurantoin and trimethoprim-sulfamethoxazole when organisms isolated from midstream urine cultures are susceptible to these agents and releasing other agents such as quinolones or cephalosporin only when resistance to the former is demonstrated. Only one study from a tertiary hospital in Dhahran, Saudi Arabia, found that selective reporting helped physicians choose the most appropriate antibiotics for their patients within a stewardship program, and reduced C. difficile infection.[44] Additional research on the extent of using selective and/or cascade reporting for antimicrobial stewardship among Saudi hospitals and its impact on patient outcomes, cumulative antibiograms, and resistance surveillance is needed.

Antibiotic De-escalation.

Does the use of antibiotic de-escalation interventions by antibiotic stewardship programs (ASPs) improve antibiotic utilization and patient outcomes?

Good practice statement

3.3. We suggest that ASP team implement antibiotic de-escalation as one of the main antimicrobial stewardship strategies in health care settings.

Evidence Summary & Local Considerations

Antibiotic de-escalation is a crucial strategy within antibiotic stewardship programs aimed at optimizing antibiotic use. It involves discontinuing at least one empirically prescribed antimicrobial agent, resulting in a reduced number of administered antibiotics, or switching to an antibiotic with a narrower spectrum of activity within 3–5 days after the initiation of empirical therapy.[27] De-escalation aims at combating antibiotic resistance and reducing the overall use of antibiotics. It should be done based on clinical judgment and supported by microbiological data.[110] A case-control study from a tertiary hospital in Riyadh, Saudi Arabia showed inappropriate antimicrobial use due to inappropriate de-escalation of empiric broad-spectrum antibiotics in 46% of the cases (33.3% for meropenem, 54.8% for vancomycin, and 31.3% for piperacillin/tazobactam).[111] Another single-center study showed that although de-escalation was associated with reduced hospital length of stay in patients admitted due to UTIs, the rate of successful de-escalation was only 29.7%.[112]. Other studies from Saudi Arabia also demonstrated a low rate of de-escalation.[83,113-117] Moreover, in one study, the calculated burden of direct costs resulting from delayed de-escalation and delayed discontinuation was $18,706 over three months, which would equate to a cost saving of about $74,824 per year if broad-spectrum antibiotics were used properly.[115] The studies identified several challenges such as the absence of timely culture, shortage of ASP team members, and reluctance of prescribers to make modifications to clinically unwell patients. Further research is still needed to identify strategies to overcome barriers in implementing successful de-escalation interventions.

Use Comments or Additional Messages to Enhance Microbiology Reports and Guide the Therapy

Does the use of comments or additional messages enhance microbiology report interpretation and guiding therapy?

3.4. Including comments or a relevant alerts in the microbiology report may be useful and could lead to a more appropriate antibiotic selection.

Good practice statement

Evidence Summary & Local Considerations

Using comments or additional messages to enhance microbiology reports is a widely used approach, but its benefits and pitfalls have not been extensively studied. Clear and concise messages on patient reports can provide valuable guidance to healthcare professionals in selecting appropriate antimicrobial therapy.[118] The CLSI also recommends therapy-related comments.[119] Messages can highlight important considerations and recommendations based on the specific microorganism identified and its susceptibility profile.[120]

For example, resistance mechanism characterization, diagnosis issues, culture interpretation, probable contamination or colonization, new interpretation criteria, dosing recommendations, and suggestions for alternatives, etc. Automated messages, available in many laboratory systems, reduce the inherent complexity of managing this process and enhance communication. There is a need for research from Saudi Arabia to explore the use and impact of specific comments on laboratory reports within ASP bundle package.

Use of Rapid Viral Testing for Respiratory Pathogens

Should ASPs advocate for use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics?

3.5. We suggest the use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Respiratory viral infections, including influenza, are common mimics of bacterial syndromes that can lead to increased bacterial resistance when inappropriately treated with antibiotics to reduce inappropriate antibiotics usage in respiratory infections. Rapid molecular assays are extremely sensitive and may detect organisms that would not generally be detected or considered clinically significant by the current gold standards of traditional microbiology.[121,122] Laboratorians have had to deal with similar situations regularly since the beginning of molecular testing. If used, ease of availability, rapid turnaround time, and prompt notification of results are essential for promoting appropriate antiviral therapy and timely discontinuation of antibacterial when not otherwise indicated. Combined with active ASP support and interpretation where it is applicable to optimize antibiotic therapy and improve clinical outcomes.

Although rapid vial testing has the potential to diminish the inappropriate use of antibiotics, results have been inconsistent. Very limited studies from Saudi Arabia, one local study assessed the clinical and financial impact of utilizing GeneXpert MRSA/SA in combination with criterion-based testing. The test significantly shortened the time to optimal antimicrobial therapy by 1.7 days (2.5 vs. 44 hr, $p < 0.0001$), also, the cost saved was $4,121.[123] More research is needed to assess this ASP intervention in Saudi Arabia.

Rapid Diagnostic Testing on Blood Specimens

Should ASPs advocate for rapid diagnostic testing on blood specimens to optimize antibiotic therapy and improve clinical outcomes?

3.6. We suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation.

Weak recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

The key to successful rapid diagnostic testing is the twinning of these technologies to an antimicrobial stewardship team that can notify clinicians about test results and guide their use in initiating or modifying antimicrobial therapy. Most published studies have been performed in larger tertiary-care centers with multiple resources and direct communication of results with guidance on management and therapy provided by clinical pharmacists and/or consultant ID physicians.[124-126] When combined within stewardship programs, multiple studies have demonstrated important benefits when these technologies are used.[121,127,128] Clinical microbiologists must collaborate with the rest of the antimicrobial stewardship team to achieve a consensus on the rules of usage and the presentation and interpretation of the results. Clinicians should receive appropriate information and training before microbiology laboratories go live with rapid diagnostic testing, especially when multiplex platforms are used as large amounts of information are available at one time. Microbiology laboratories may want to put in place strategies to identify, track, and analyze discrepant results, especially in the implementation phase of new tests. Interpretation of individual results should always be done in the light of a clinical evaluation of the patient and other available results. We recommend that clinical microbiologists contact prescribers or coordinate responses with antimicrobial stewardship teams in these situations, especially when discrepant results are found in critical specimens, to guide the most appropriate therapeutic strategy. When suspicion of infection is low and the patient is stable, a “wait-and-see” strategy may be the best option. It is worth mentioning that Rabid diagnostic testing is not always available, and their wide use is still limited to the tertiary and more specialized centers.

Procalcitonin (PCT) Testing as an Intervention to Decrease Antibiotic Use in Intensive Care Units (ICUs)

In adults in intensive care units (ICUs) with suspected infection, should ASPs advocate procalcitonin (PCT) testing as an intervention to decrease antibiotic use?

3.7. In adults in ICUs with suspected infection, we suggest the use of serial PCT measurements as an ASP intervention to decrease antibiotic use.

Weak recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin. PCT serum concentration increases in response to Infectious stimuli, fungal infections, trauma, and surgery. Serum PCT is detectable as soon as 4 h and peaks between 12 and 48 h after infection onset. PCT is a prognostic scoring to detect infection, make a diagnosis, determine the severity of disease, and assess a patient's outcome.[129] Most studies have focused on its use for respiratory infections and sepsis, and data support its use more often as an indicator to stop, rather than start therapy. A Cochrane review on the use of PCT algorithms in acute respiratory infections found that the median exposure to antimicrobials was reduced from 8 to 4 days without any adverse impact on the mortality rate. Similar data were found in patients with sepsis in intensive care units.[130] Several clinical recommendations advocate PCT as one of the supplementary clinical interventions that can be employed for the management of pneumonia based on the clinical evidence and research that is done. In the case of CAP, the 2019 Infectious Diseases Society of America (IDSA) guideline supports initiating antibiotic therapy with radiographic confirmation regardless of initial levels of PCT.[131] Serial PCT levels, on the other hand, may be useful for antibiotic treatment in clinical scenarios where the duration of antibiotic therapy for CAP exceeds the normal suggested period (5 to 7 days). Based on clinical trial findings, the FDA approved the use of PCT for antibiotic withdrawal advice in sepsis therapy in the United States in 2017.[132] Furthermore, the Society of Critical Care Medicine (SCCM) Surviving Sepsis Campaign Guidelines 2021 advocate PCT as one of the methods that can be used to examine the feasibility of discontinuing antibiotic medication in conjunction with clinical evaluation.[133] However, as advised by the guidelines, cautious use of PCT-guided antibiotic therapy in conjunction with clinical assessment is still mandated.[134] At a local level, the use of procalcitonin has grown significantly over the last years, however consistent with other international reports, the use of PCT should be contingent on the clinical assessment.[135-137] Further large studies are warranted in this area.

Incorporation of Nonculture-Based Fungal Markers to Optimize Antifungal Use

In patients with hematologic malignancy, should ASPs advocate for incorporation of nonculture-based fungal markers in interventions to optimize antifungal use?

3.8. In patients with hematologic malignancy at risk of contracting invasive fungal disease (IFD), we suggest incorporating nonculture-based fungal markers in ASP interventions to optimize antifungal use.

Weak recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

Utilization of Rapid fungal markers such as (fungal PCR) has been used in the practice to optimize antifungal use. For example, aspergillus galactomannan, fungal PCR, and 3 β-d-glucan.[138-142] There are currently no local studies to evaluate the value of using non-culture-based antifungal markers as ASP intervention in Saudi Arabia.

4. Interventions of Implementing ASP in Special Populations

Facility-Specific Clinical Guidelines for Management of Fever and Neutropenia (F&N) in Hematology-Oncology Patients

Should ASPs develop facility-specific clinical guidelines for management of fever and neutropenia (F&N) in hematology- oncology patients to reduce unnecessary antibiotic use and improve outcomes?

4.1. We suggest ASPs develop facility-specific guidelines for F&N management in haematology-oncology patients over no such approach.

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Although data are limited, implementing therapeutic pathways for F&N management can reduce needless antibiotic use without poor outcomes in pediatric hematology-oncology departments. Adherence to treatment guidelines has been found in studies to improve significant clinical outcomes. A quality improvement practice project aimed at reducing antibiotic delivery delays in pediatric febrile neutropenic patients visited King Faisal Specialist Hospital and Research Centre (KFSH&RC) in Saudi Arabia has been published.[143] Following implementation, a clinical audit revealed a reduction in antibiotic administration time as well as greater self-efficacy and knowledge among nursing staff in managing the treatment of febrile neutropenic patients. Another from the same institution showed that de-escalation of carbapenem in patients with febrile neutropenia was not associated with increased resistant microorganisms and there was no difference in mortality and ICU admission rate before and after the implementation of the de-escalation protocol.[144] More research is still needed on clinical guidelines development with an implementation strategy in the care of cancer patients with F&N.

Implementation of ASP In Immunocompromised Patients Receiving Antifungal Therapy

In immunocompromised patients receiving antifungal therapy, do interventions by ASPs improve utilization and outcomes?

4.2. We suggest the implementation of ASP interventions to improve the appropriate prescribing of antifungal treatment in immunocompromised patients.

Weak recommendation, moderate-quality evidence

Evidence Summary & Local Considerations

In view of the continuous expanding of the Immunocompromised population at risk of invasive fungal infections (IFI), the emergence of new species, the diagnostic challenges, and the limited antifungal medications, the demand for having antifungal stewardship program (AFS) in each institution dealing with immunocompromised patients is very clear.[145-147] There is limited data on effective AFS interventions in immunocompromised patients, however, the interventions mirror principles of general ASPs (e.g., PAF, preauthorization, handshake stewardship, education.[146] A study from King Khalid University Hospital in Riyadh, Saudi Arabia investigated the appropriateness of caspofungin prescriptions.[148] The study found that 76.1% of the patients received empirical prescriptions, of which 74.4% had the appropriate dose, and 56.3% had received it for more than five days, despite no proven Candida infection. Only 39% of patients who received definitive prescriptions met all four study criteria for appropriate prescription. More research from Saudi Arabia on AFS to investigate the scope, the AFS strategies implemented, and the impact on clinical outcomes, antimicrobial resistance, and expenditures.

Implementation of ASP In Neonatal Intensive Care Units (NICUs)

In neonatal intensive care units (NICUs), do ASPs reduce inappropriate antibiotic use and/or resistance?

4.3. We suggest the implementation of antibiotic stewardship interventions to reduce inappropriate antibiotic use and/or resistance in the NICU.

Good practice statement

Evidence Summary & Local Considerations

Excessive use of antibiotics is common in the NICU. Many well-appearing infants received empirical treatment based on perinatal risk factors only. Most antimicrobial prescribing in NICU is empiric and requires guidance.[149] Limited evidence is available to determine the most effective ASP strategies in the NICU, but general principles should apply. A 33-month surveillance study was conducted in King Abdulaziz Medical City, Riyadh, Saudi Arabia. The study showed that the most frequent antibiotic utilized in the NICU is the aminoglycoside (45.4%), and that the local consumption of cephalosporins and carbapenems is probably higher than international levels.[150]

Antimicrobial Stewardship Program (ASP) is a key strategy to optimize antibiotic use in the NICU similar to pediatric and adult population. Strategies may include authorization, electronic order sets, use of procalcitonin and guidelines for the common neonatal syndromes and hospital Acquired infections use of antibiograms, pharmacy-driven stewardship efforts have been utilized in NICU-specific stewardship initiatives. A retrospective study at a tertiary care hospital in Bisha Southwest Saudi Arabia showed that Klebsiella pneumonia is common in the NICU and that there was a high resistance to trimethoprim/sulfamethoxazole (71.8%), cefotaxime (71.4%) and aztreonam (65.2%).[151] Another retrospective study over 5 years from Hail a Maternity Hospital in Hail, Northern Saudi Arabia, showed similar pattern of Klebsiella pneumonia isolate in NICU.[152] There is still a need to investigate implementation and impact of ASP strategies in NICU in Saudi Arabia.

5. Best Measurements to Assess Impact of ASP on Expenditure and Patient's Outcomes

Which Overall Measures Best Reflect the Impact of ASPs and Their Interventions?

Which overall measures best reflect the impact of ASPs and their interventions?

5.1. We suggest monitoring antibiotic use as measured by days of therapy (DOTs) in preference to a defined daily dose (DDD).

Weak recommendation, low-quality evidence

Evidence Summary & Local Considerations

Two measures are widely accepted to measure antimicrobial consumption, these are DOTs and DDDs.[153] DDDs, calculated from aggregated dispensing data, and DOTs, calculated from patient-level prescription data, both measures can be used to examine the overall use of antimicrobials or specific use by the unit, provider, or service in the hospital and each has its advantages and disadvantages.[154] DOT which is defined as the number of days that a patient receives an antimicrobial agent regardless of dose.[153]

The measure can be used for adult and pediatric populations. It is not affected by dose adjustments such as that required for patients with renal diseases. However, DOT is more complex to measure and requires patient-level antibiotic use data, which may not be easily available in every hospital [180–182]. DDD which is the summed average maintenance dose per day for a drug used for its main indication. DDD has several limitations. DDD assumes the standard dose as per indication and doesn't recognize the need for higher dose adjustment such as in obese patients or lower doses such as in renal impairment. It is limited for adults and since pediatric doses are often weight-based.

Finally dosing is not recommended as the first method for measuring antibiotic utilization in such a population.[153] IDSA and the National Healthcare Safety Network (NHSN) prefer the use of DOT over DDD. However, PHA adopts DDD for antimicrobial consumption collection and analyses, while DDD is not recommended for pediatric hospitals, hospitals that are mainly for patients with renal dysfunction, where we advise to adopt Days of Therapy (DoT) measures.[155]

Other additional metrics have been used and they are divided into 3 main categories: Outcome measures, process measures, and structure measures. The outcome measures evaluate the patient, microbial, or financial effects related to the ASP process or interventions, for example: The length of stay (LOS), primarily because of timely switching from IV to oral antibiotics or by stopping unnecessary IV antibiotics. Other examples are reduction in CDI rates and antibiotic resistance which are relatively insensitive metrics because of the effects of other confounding variables. It is worth mentioning that although ASP might lead to a reduction in cost, and it is useful to monitor cost savings, it should not be a primary measure of the success of an ASP. The process measures are indicators that assess the interventions, strategies, and other activities of the ASP program. An example of this is determining compliance with facility-specific antibiotic treatment guidelines. The structure measures describe the characteristics and components of the ASP program. Such as having designated leaderships in place, institutional guidelines, and all the CDC ASP core elements, or the governance structure of the program. These measures are not always considered one of the metrics, but they are still valid. Different metrics have advantages and disadvantages, and no ideal metric exists. When choosing metrics to be used, it is most important the metric be measured reliably and consistently over time.[156] Several studies from Saudi Arabia, reported evaluation of both measures when reporting antimicrobial stewardship outcome.[26,102,150,157-163]

Reporting ASP Program Performance

Who are the key stakeholders who should receive reports on antimicrobial stewardship program performance?

Good practice statement

5.2. We suggest that ASP leaders regularly reports the progress of the program to the hospital leaderships, and to stakeholders.

Evidence Summary & Local Considerations

Information summarizing the hospital ASP should be regularly shared with the hospital leaders such as the chief executive officer, Hospital director, medical director, or the director for the pharmacy and therapeutics (PT) committee. Although a leader in higher authority is preferred, the ultimate reporting path depends on the structure and leadership hierarchy of the facility. Reports to leadership should include information about the progress of the program, challenges faced, and the needs. Program outcomes such as antimicrobial use, resistance, cost, and other facility-specific ASP outcomes should also be shared. Reporting must be conducted at a regular and pre-specified timeline.

ASP reports should also be regularly shared with stakeholders and prescribers who expect program results to justify their work and support to the ASP team. Prescribers' reports should include performance and outcome measures such as the rate of adherence to hospital antibiotic guidelines, the ASP intervention acceptance rate, and the rate of antimicrobial resistance. Performance feedback can motivate the prescribers not only to improve their prescription practices but also to continue to support the ASP team.

Staff in the microbiology laboratory, the infection control department, and the medical epidemiology department in the hospital should collaborate in preparing reports on antimicrobial resistance. Early program reports ≤1 year after implementation, should focus on process-related measures to show that the program is well implemented, for example, the number of recommendations made, proportion of recommendations accepted, use of audited antibiotics, compliance with hospital guidelines, and antibiotic cost savings. These metrics should be included in quarterly and annual reports. Some outcome measures, such as total antibiotic consumption and antimicrobial resistance, may require ≥1 year to show changes from baseline. These metrics should be included in full annual or interim reports when appropriate.[55,153,164]

6. Organizational and Structural Support for ASP

What Organizational and Structural Support Should Exist to Support?

Hospital Leadership Commitment

6.1. Hospital leadership support is very important and a prerequisite for the success of any ASP program.

Good practice Statement

Evidence Summary & Local Considerations

Leadership support is very important for the success of an ASP. It is one of the core elements of Hospital Antibiotic Stewardship Programs published by the Centers for Disease Control and Prevention in 2019. Support from the senior leadership of the hospital, especially the Chief Executive Officer, can play a critical role in helping the stewardship program get the resources needed to accomplish its goals and the program's success overall. Moreover, having the support from other hospital leaders such as the Medical Director, Director of Pharmacy, Director of Quality and Patient Safety, and the head of nursing office, are also very crucial and key to the success of the program.[165]

In general, the CDC core elements have categorized the leadership commitments into two groups, priority commitments and others.

Examples of Priority Leadership Commitment Include:

- Giving stewardship program leader(s) time to manage the program and conduct daily stewardship interventions.
- Ensuring program leadership has regularly scheduled meetings with the senior executives and hospital board to report stewardship activities, resources, and outcomes, and provide advice.
- Providing essential financial and staffing resources and supporting them to operate the program effectively.

Other Examples of Leadership Commitment That Are Included in Leading ASP References Include:

- Promoting ASP as a quality improvement and patient safety goal of the organization and incorporating the program into the strategic planning of the organization.
- Making formal statements of support for efforts to improve and monitor antibiotic use.
- Supporting the ASP team and committee in promoting accountable clinical practice across the organisation.
- Include the ASP-related duties officially in the job description and annual performance reviews for ASP program leads and key support staff.
- Ensuring staff in the ASP program and from relevant departments are given adequate time to contribute to stewardship activities.
- Supporting training and education for program leaders (e.g. attendance of stewardship training courses and meetings) and hospital staff, for example ensuring that clinicians (prescribers, pharmacists, nurses, and midwives) receive appropriate orientation on the AMS program at the start of their employment in the organization.
- "Non-compliance" action
- Appointment letter
- Education

An exploratory case study in a tertiary hospital in Riyadh, Saudi Arabia, found that strong management support secured funds for ID clinicians and locum ASP pharmacist recruitment.[102] Senior managers also instructed hospital departments to participate in educational events and adapt to process changes.

Accountability

6.2. Leadership accountability is an essential component of any ASP, the presence of accountable leader and co-leader for the program is recommended.

Good practice statement

Evidence Summary & Local Considerations

Leadership accountability is essential for the success of any antimicrobial stewardship program (ASP). This means having designated leaders or co-leaders either physicians, pharmacists, or non-physician leaders with supporting physicians who are responsible for the program's management and outcomes.[25,81,166] Effective ASP leaders must have strong leadership, management, and communication skills who are accountable for the program, and should work collaboratively with other healthcare professionals as it is essential for the success of (ASP).
An infectious diseases physician, or clinical pharmacist preferably with infectious diseases training is well-placed to lead the ASP program. If these experts are not available, a general practitioner, general physician, or surgeon should be supported to lead and manage the program.
Regular leaders/co-leader stewardship rounds provide an opportunity to discuss antibiotic use with medical staff who prescribe antibiotics and identify areas for improvement to ensure that antibiotics are used appropriately and that patients receive the best possible care which is a valuable tool for improving antibiotic use and enhancing the visibility and support of the antimicrobial stewardship program.[166-169]
A systematic review mapped hospital antimicrobial stewardship programs in the Gulf Cooperation Council states against international standards and found that leadership and accountability are not adequately addressed.[41]

The Role of Pharmacist in the ASP

6.3. Pharmacists are at the forefront of the creation, growth, development, and promotion of ASP by influencing the antimicrobial prescription to improve patient outcomes.

Good practice statement

Evidence Summary & Local Considerations

The CDC emphasizes the importance of pharmacist expertise as a priority for Hospital Core Element for successful stewardship program implementation. The American Society of Health-System Pharmacists (ASHP) and the Society of Infectious Diseases Pharmacists (SIDP) both hold the opinion that a pharmacist plays a significant role in an antibiotic stewardship program. They are at the forefront of the creation, growth, development, and promotion of AMS by influencing antimicrobial prescription to improve patient outcomes, lowering adverse events related to antimicrobials, encouraging cost-effective care, and reducing the development of antimicrobial resistance. Currently, there is a considerably greater demand for pharmacists due to the fact that every hospital now employs a pharmacist with ID training. Hence, to fill this gap, formal training programs are available locally and internationally. In Saudi Arabia, Infectious diseases pharmacists play major roles as members of the multidisciplinary ID team and pharmacy experts' members of the ASP or antimicrobial committee.[170] A study from Makkah, Saudi Arabia, found that clinical pharmacists reduced the antimicrobial therapy duration using imipenem and meropenem.[171] Pharmacists are actively involved in effective hospital ASPs, either as the program's leader or co-leader. It is crucial to find a pharmacist who is empowered to supervise implementation efforts to improve the usage of antibiotics. There are several roles that pharmacists can adapt to assist the ASP program which can be incorporated within different ASP interventions such as formulary restriction, time to stop, and others.[6,26,83,114,172-174]

A survey of 64 hospitals from the Gulf Cooperation Councils countries delineated the evolving roles of pharmacy professionals in the prescribing and transcribing process.[67] About 65% of hospitals has a stewardship program. Pharmacists' role included leadership and accountability (28.6%), data analysis (28.6%), and Clinical support (40.5%).

The Role of Nurses in the ASP

6.4. We suggest including nursing's perspectives and actively engage the nursing staff in ASP initiatives, strategies, and solutions to combat antibiotic resistance and improve care.

Good practice statement

Evidence Summary & Local Considerations

Multidisciplinary approaches are necessary for effective AMS activities to maintain their relevance and sustainability. A scoping review of 43 ASP guidelines, found that only 32.5% of these guidelines recommended a role for the bedside nurse in antibiotic stewardship, which highlights unacknowledged their important role.[175] The potential opportunities for nurses in ASP are significant, even though their involvement in stewardship programs is still very low and primarily focused on clinical issues.[2,176] The roles of nurses as executives, leaders, and policymakers can be expanded.[177] Nurses are usually engaged in educating patients, communicating with and managing other staff, assessing, monitoring, and reviewing prescriptions, durations, and dosage, initiating antimicrobials for septic patients, and initiating intravenous to oral switch. In Saudi Arabia, limited studies investigated the role of nursing staff in ASP. More research is needed to explore the hidden potential of nursing staff to support ASP interventions in Saudi Arabia.

Methods

Organizations, Taskforce Composition, and Coordination

The Saudi Pediatric Infectious Disease Society (SPIDS) sponsored this national guideline project. The key stakeholders have been identified and included in the Guideline Development/Adaptation Group or the External Review Group as feasible. The steering committee for this CPG adaptation project included the two clinical chairs, methodology chair, and methodology co-chair.

Adaptation Process Methodology

Phase One – Set-Up

1. Checking the feasibility of CPG adaptation

The preliminary rapid search showed a large number of published CPGs addressing this topic.

2. Establishing a Guideline Adaptation Group (GAG)

This CPG project was commissioned by SPIDS in collaboration with the KSUMC CPG Steering Committee (Guideline Methodologists). A group of clinical experts was formulated by the SPIDS to be members of the GAG (for details refer to the Guideline Adaptation Group).
The methodology followed was according to the 'KSU-Modified-ADAPTE' method.[8,9]

3. Selecting and prioritizing the CPG health topic

The topic was selected and prioritized by SPIDS group.

4. Identifying necessary resources and skills

The methodology team conducted capacity-building sessions for the GAG members on the CPG adaptation methodology in addition to technical support.

5. Completing the tasks of the set-up phase

All members of the GAG declared their conflicts of interest (COI). The completed COI forms can be made available from the SPIDS.

6. Writing up the CPG adaptation working plan

A timeline for the CPG adaptation project was outlined and agreed upon by all GAG members.

Phase Two – Adaptation

7. Determining the health questions

Refer to the scope and purpose section. The PIPOH Model was used to identify the health questions that guided the search and screening process.

8. Searching for source CPGs and other relevant documents

A systematic review of evidence-based CPGs for antimicrobial stewardship guidelines in addition to published systematic reviews and AGREE II appraisal of ASP guidelines.

9. Screening retrieved source CPGs

See PRISMA[178] 2020 Flow chart (Appendices)

10. Reducing the large number of retrieved CPGs

The GAG relied on the inclusion and exclusion (eligibility) criteria for screening and filtration as shown in the PRISMA flowchart.

11. Inclusion / Exclusion CPGs Selection Criteria

a. Inclusion criteria

i. **Methods of Development:** Evidence-Based CPGs: (Detailed Methodology of Development Documented; link Recommendations with Evidence; link to Systematic Reviews) rather than Non-Evidence-Based -based CPGs (Expert opinion). Published GRADE-based guidelines were given a preference for inclusion.
ii. **Author(s) Organization (CPG development group)** from CPGs Database (Producer or Finder) and Specialized Society (clinical specialty) rather than single authors.
iii. **Country:** International or national CPGs.
iv. **Date of Publication:** Any CPG published on or after October 2018.
v. **Language:** English and Arabic CPGs only.
vi. **Status:** Only original source CPG (de novo developed) rather than adapted CPGs.
vii. **Additional criteria:** The document is described as a CPG in the title, abstract or methodology section.

b. Exclusion Criteria

i. **Any document that was:**
   1. Described as a review article, randomized controlled trial or consensus statement.
   2. No methodology section.
   3. No English abstract.
   4. Published before 2016.
   5. Written to patients only.
   6. Target tertiary healthcare settings.

12. Assessment of the quality of the source CPGs using the AGREE II Instrument

Refer to the results of Appraisal of Guidelines Research & Evaluation II (AGREE II) Instrument appraisal conducted by Rennert-May, et al (2019) for the first 5 CPGs.[179] The AGREE II assessment results of the Guidelines on Implementing Antimicrobial Stewardship Programs in Korea: Domain 1 (78%), Domain 2 (67%), Domain 3 (51%), Domain 4 (83%), Domain 5 (31%), Domain 6 (83%). The first overall assessment was 58%, and the second overall assessment (Yes = 0, Yes with modifications =2, No =0).

13. Recommendation formulation methodology

The guideline adaptation group conducted an informal consensus process after reviewing the recommendations of the source high-quality CPG developed by the IDSA in consideration for their nation-wide applicability, acceptability, and implementability in line with the national health system in Saudi Arabia.

14. Assessing the currency of the selected source CPG

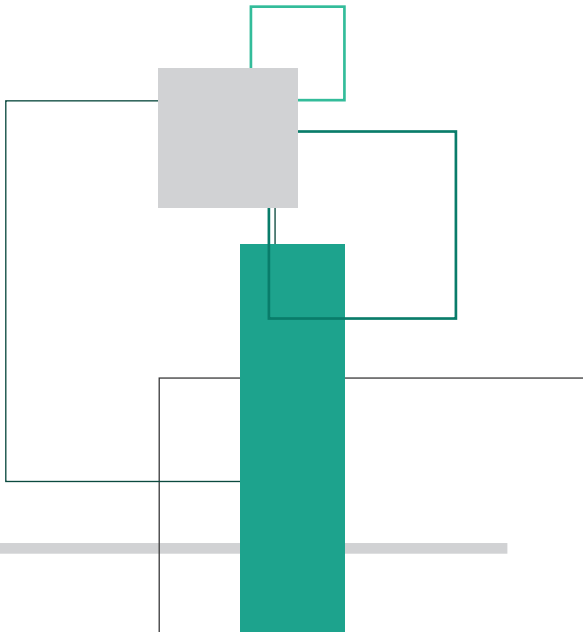
The following questions were used to assess the currency of source guideline:

a. Are you aware of any new evidence relevant to this CPG statement? No
b. Is there any new evidence to invalidate any of the recommendations comprising the CPG? No
c. Are there any plans to update the CPG in the near future? No
d. When was the CPG last updated? Published: April 13, 2016, and Last Updated: August 16, 2018
e. What is the citation for the latest version? (Reference 2)
https://www.idsociety.org/practice-guideline/implementing-an-ASP/

Steps from 13-15 were not conducted as the GAG relied on the results of the AGREE II assessment to reach the required assessments of CPG content, consistency, acceptability, and applicability. Steps 16 and 17: The AGREE II assessments were discussed among the members of the GAG. Therefore, the CPG adaptation group decided to select the relevant recommendations from one source CPG.[2]

15. Step 18 Preparing the draft adapted CPG.

The first draft of the adapted CPG was prepared and sent for external review via email with the related clinical review and methodology review forms.



Phase Three – Finalization

16. Step 19. External review (Clinical Content and Methodology)

Details of the members of the external review group (Refer to the Peer Review section).

17. Step 20. Consulting with endorsement bodies

The adapted CPG **was developed and approved by** the Saudi Pediatric Infectious Diseases Society (SPIDS).

18. Step 21. Consulting with the source CPG developer(s)

Permission for adapting the IDSA CPG was granted on (May 3, 2023).

19. Step 22. Acknowledging the source documents

The source CPG, relevant articles, and websites have been clearly acknowledged in the adapted CPG document.

20. Step 23. Planning for aftercare of the adapted CPG

The GAG decided on a plan for reviewing and updating the adapted CPG using the CheckUp tool that is freely provided by AGREE Enterprise.[180]

21. Step 24. Producing the final adapted CPG document

This document represents the finalized adapted CPG full document.

Guideline Development

The CPG steering committee recruited the rest of the 8 clinical panel members of the GDG/ GAG based on their subject matter expertise and relevance to antimicrobial stewardship multidisciplinary team from the SPIDS network through email invitations and zoom meetings. The clinical chairs were FAA and RHA.
The following main health sectors were involved: Universities, the Ministry of Health, and KFSHRC from Riyadh, Jeddah, Dammam, Najran, and the Western Region.

The three members of the CPG methodology subgroup are trained and expert guideline methodologists. For full details, refer to the Guideline Adaptation Group section. The Methodology Chair was GAB and co-chair was YSA.

Guideline Support Team

This SPIDS guideline adaptation project was supported and guided by guideline methodologists from the King Saud University Medical City CPGs Steering Committee, Riyadh, Saudi Arabia. The recent templates released by the Saudi Health Council National EBM center were considered as well. The methodology experts provided technical support and guidance throughout the guideline adaptation process.

The communication pathway between the different components of the GDG/GAG including the members of the clinical panel and the methodology subgroup was via Zoom online meetings and a dedicated WhatsApp group titled: ASP Guideline SPIDS. The GAG conducted nine virtual and two face-to-face joint meetings (clinical/ methodology), with seven additional meetings for the clinical panel group.
All meetings (N=18) were conducted remotely on a bi-weekly or monthly basis, and the rest of the communication or queries were answered through the WhatsApp group, including exchanging Microsoft Word and PDF files and templates for editing and completing, links to relevant publications and/ or websites, meetings arrangements links, queries and feedback, etc. Two face-to-face meetings were conducted. All meetings were coordinated by the SPIDS Committees. The outcomes of these meetings included filling out the COI forms, identifying the PIPOH health questions to be included in the guideline scope, reviewing the published and the conducted AGREE II appraisals, formulation of the adapted recommendations, identifying and identifying guideline implementation strategies and tools, and drafting and finalization of the full CPG document.
Moreover, a preliminary version of this adapted guideline was presented as an oral presentation (by GAB and YSA) and a panel discussion in the SPIDS 2024 Week in Riyadh.

Guideline Funding and Management of Conflict of Interest

This guideline project was funded by the Saudi Pediatric Infectious Diseases Society (SPIDS) that did not interfere with the formulation of recommendations or any other step of the guideline adaptation process. There was no relation with any pharmaceutical or industrial company. The permission to use the IDSA source guideline for the adaptation process was granted free of charge after an email thread and a couple of online meetings with the IDSA team (namely Jon Heald, Dana Wollins, and Genet Demisashi) to explain the scope and the objective of this national guideline project.

We used the policy and form for managing conflicts of interest proposed by the National Center for EBM-SHC. All the GAG members and Guideline Support Team members received honoraria for participating in the Guideline development process from the SPIDS.
There were no financial or non-financial conflicts of interest to declare. The COI forms filled by all contributors can be made available from the SPIDS.

Selection of Questions and Determining Outcomes of Interest

The following 27 health questions (23 questions were adopted and prioritized from the source IDSA/SHEA guideline using a voting and consensus process by the GAG through several meetings, and 4 additional questions were added by the clinical panel (Table 5). The outcomes were identified, reported, and prioritized as well from the source guideline in line with the national health priorities and national accreditation standards. For the related definitions and considerations, refer to the **glossary of terms section.**

Table 5: Prioritized Health Questions

Question	Prioritized Outcome
1. Is didactic education a useful antibiotic stewardship intervention for reducing inappropriate antibiotic use?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Adverse events ▪ Antibiotic cost savings
2. Does the use of preauthorization and/or prospective audit and feedback interventions by antibiotic stewardship programs (ASPs) improve antibiotic utilization and patient outcomes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
3. Should ASPs develop and implement facility-specific clinical practice guidelines for common infectious diseases syndromes to improve antibiotic utilization and patient outcomes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
4. Should ASPs implement interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases syndromes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
5. Should ASPs implement interventions designed to reduce the use of antibiotics-associated with a high risk of Clostridium Difficile Infection (CDI)?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes

6. Do strategies to encourage prescriber-led review of appropriateness of antibiotic regimens, in the absence of direct input from an antibiotic stewardship team, improve antibiotic prescribing?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic cost savings
7. Should computerized clinical decision support systems integrated into the electronic health record at the time of prescribing be incorporated as part of ASPs to improve antibiotic prescribing?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic cost savings
8. Should ASPs implement strategies that promote cycling or mixing in antibiotic selection to reduce antibiotic resistance?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Antibiotic cost savings
9. In hospitalized patients requiring intravenous (IV) antibiotics, does a dedicated pharmacokinetic (PK) monitoring and adjustment program lead to improved clinical outcomes and reduced costs?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
10. In hospitalized patients, should ASPs advocate for alternative dosing strategies based on pk/pharmacodynamic principles to improve outcomes and decrease costs for broad-spectrum ß-lactams and vancomycin?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
11. Should ASPs implement interventions to increase use of oral antibiotics as a strategy to improve outcomes or decrease costs?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
12. In patients with a reported history of ß-lactam allergy, should ASPs facilitate initiatives to implement allergy assessments with the goal of improved use of first-line antibiotics?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use
13. Should ASPs implement interventions to reduce antibiotic therapy to the shortest effective duration?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Clinical outcomes

14. Should ASPs work with the microbiology laboratory to develop stratified antibiograms, compared with non-stratified antibiograms?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events
15. Should ASPs work with the microbiology laboratory to perform selective or cascade reporting of antibiotic susceptibility test results?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance
16. Does the use of antibiotic de-escalation interventions by antibiotic stewardship programs (ASPs) improve antibiotic utilization and patient outcomes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Antibiotic cost savings ▪ Clinical outcomes
17. Does the use of comments or additional messages enhance microbiology report interpretation and guiding therapy?	▪ Audit and feedback ▪ Implementation
18. Should ASPs advocate for use of rapid viral testing for respiratory pathogens to reduce the use of inappropriate antibiotics?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events
19. Should ASPs advocate for rapid diagnostic testing on blood specimens to optimize antibiotic therapy and improve clinical outcomes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
20. In adults in intensive care units (ICUs) with suspected infection, should ASPs advocate procalcitonin (PCT) testing as an intervention to decrease antibiotic use?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use
21. In patients with hematologic malignancy, should ASPs advocate for incorporation of nonculture-based fungal markers in interventions to optimize antifungal use?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events
22. Should ASPs develop facility-specific clinical guidelines for management of fever and neutropenia (F&N) in hematology- oncology patients to reduce unnecessary antibiotic use and improve outcomes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)

23. In immunocompromised patients receiving antifungal therapy, do interventions by ASPs improve utilization and outcomes?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance ▪ Adverse events ▪ Antibiotic cost savings ▪ Clinical outcomes ▪ Patient Reported Outcome Measures (PROMs)
24. In neonatal intensive care units (NICUs), do ASPs reduce inappropriate antibiotic use and/or resistance?	▪ Antibiotic utilization ▪ Unnecessary/inappropriate antibiotic use ▪ Antibiotic resistance
25. Which overall measures best reflect the impact of ASPs and their interventions?	▪ Effectiveness ▪ Efficacy ▪ Audit and feedback ▪ Implementation
26. Who are the key stakeholders who should receive reports on antimicrobial stewardship program performance?	▪ Effectiveness ▪ Efficacy ▪ Audit and feedback ▪ Implementation
27. What organizational and structural support should exist to support?	▪ Effectiveness ▪ Efficacy ▪ Audit and feedback ▪ Implementation

Evidence Synthesis and Inclusion of Local Data

The guideline methodology team was responsible for conducting a thorough review of published evidence and guidelines. A recently published systematic review of ASP guidelines was retrieved and used as a key article,[179] in addition to an updated search that retrieved only one published guideline.[164]

Development of Recommendations

The ASP that received the highest AGREE II score in domain 3 by Rennert-May et al., the IDSA/ SHEA guideline, was identified and reviewed.[2,179] Twenty-three questions and 24 recommendations of the IDSA/ SHEA guidelines were reviewed and adopted after reviewing the relevant published evidence available from recent local studies from KSA. In addition, the clinical panel identified 4 clinical questions and 7 recommendations. The GAG considered the local contextual factors like feasibility, applicability, acceptability, equity, national policies and programs, national accreditation standards, healthcare transformation program, cost, resources, patient values and preferences, implementation, etc.

The evidence summary and rationale for each recommendation, given the local literature, were discussed and finalized among the GAG members. Patients preferences and values were identified from the clinical experience of GAG members in ASPs, and informed by patient experience and stories, later used as implementation tools. The agreement process was conducted by voting and consensus during online and physical meetings. The consensus was considered with a cut-off point of 70% of the GAG members.

Strength of Recommendations

The source guideline IDSA used the approach and implications to rate the quality of evidence and strength of recommendations according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Table 6).

Table 6: Classification of the Quality of Evidence and Strength of Recommendations

Quality of Evidence	Recommendations
Strong	Strong recommendation, strong-quality evidence
Moderate	Strong recommendation, moderate-quality evidence
Moderate	Weak recommendation, moderate-quality evidence
Low	Weak recommendation low-quality evidence
———	Good practice statement

Guideline Drafting and Review

The first draft of the adapted ASP guideline was prepared during the process by both subgroups of the GAC (i.e., the clinical experts and the methodology experts) based on the input from the source IDSA/SHEA guideline, literature review, and GAG discussions during the meetings. The GAG was guided by the two clinical chairs in addition to the methodology chair and co-chair. There were no disagreements among the group. The draft guideline, which included recommendations and implementation tools, was then shared with the peer/ external review group that included clinical and subject matter experts in addition to a guideline methodology expert, and their feedback and comments were brought to the main GAG and further discussed against the same contextual factors considered before. The finalized guideline full document was prepared after a consensus process from the main GAG.

Peer Review

The peer review or external review process was conducted by clinical experts in implementing ASPs in addition to one guideline methodology expert (Table 7). This group was not involved in the production of the first draft of the guideline. All peer reviewers were required to complete the declaration of COI form that was proposed by the National EBM Center, Saudi Health Council.

Table 7: External Reviewers of the Adapted Guideline

External Expert Name	Affiliation	Response (date)
Prof. Abdulrahman Alnemri (Clinical expert)	Professor of Pediatrics, Consultant Neonatologist, Pediatric Department, College of Medicine, King Saud University, Neonatal Intensive Care Unit (NICU), King Saud University Medical City, Riyadh	30/ 6/2024
Dr. Abdulrahman Bin Mohanna (Clinical expert)	BSc, MSc, PhD Senior Health Expert at the Saudi Public Health Authority, AMR Division, Riyadh	29/7/2024
Dr. Fatimah Alshahrani (Clinical expert)	Associate Professor, College of Medicine, King Saud University and Director, Infection Prevention and Control Department, King Saud University Medical City, Riyadh	19/8/2024
Dr. Hiba AlTarrah (Clinical expert)	MD, FRCPC, Consultant Pediatric Hematology/Oncology King Fahad Specialist Hospital, Dammam	23/6/2024
Dr. Yang Song (Guideline methodology expert)	Assistant Professor, School of Medicine, Chinese University of Hong Kong, Shenzhen, China Co-chair, Adaptation Working Group, Guidelines International Network	11/8/2024
Dr. Zainab Al Duhailib (Clinical expert)	MBBS, EDIC, MSc (epid) Critical Care Medicine Department, King Faisal Specialist Hospital & Research Centre College of Medicine, AlFaisal University Riyadh, Saudi Arabia	1/7/2024

The guideline's peer review aimed to provide input about the following:

- Validate the accuracy of the evidence base of the recommendations.
- Assess the rationale of each recommendation.
- Provide clarity, feasibility, and implementability feedback on the recommendations.
- Support recommendation adoption, recognition, and acceptance upon publication.
- Gather suggestions for local performance measures to support implementability of the guideline.

Approvals

- The finalized guideline was approved by the board of the SPIDS society.
- Future plans is to submit the guideline to Saudi Health Council's (SHC), National EBM Center's Scientific Committee for review.

How to Use

This guideline serves as an evidence-based clinical practice decision tool for facilitating decision-making within antimicrobial stewardship programs in Saudi Arabia and is not intended to set a rigid standard of care. Therefore, the recommendations provided should not be interpreted as advocating for a singular approach to managing the local ASPs. Given the diverse healthcare landscape and patient populations in Saudi Arabia, variations in practice are expected. Clinicians are encouraged to consider the unique needs, values, and preferences of patients, as well as the resources and limitations specific to their institutions or practice settings when implementing these recommendations. Healthcare professionals involved in antimicrobial stewardship programs should exercise judgment in adapting these guidelines to their local contexts and clinical practices.

Performance Measures

Performance measures, also known as key performance indicators (KPIs), are measurable objectives that evaluate structures, processes, and outcomes. They define numerator and denominator criteria to evaluate the adherence of a patient population to a specific clinical practice guideline.[181]

Aligning KPI development with evidence-based recommendations is a priority in guideline development, adaptation, and implementation.
The required data for auditing ASPs is called the "antibiotic use data" and it refers to estimates derived from individual patient data and may include information on patient characteristics and indications for treatment.[182] Audit and feedback for ASPs refers to the assessment of prescribed antibiotic treatment, with feedback on antibiotic treatment considered as inappropriate. Prospective (preferred) or retrospective assessment of antibiotic therapy in in-patients, performed by trained HCWs or AMS team members this intervention has advantages and disadvantages.[182]
Furthermore, the following outcomes were reported from implemented ASPs by Ababneh et al.; 1) Change in susceptibility rate in Multidrug-resistant pathogens;
2) De-escalation and discontinuation rate of restricted antimicrobials; 3) Consumption of antimicrobials pre and post ASP implementation policy; 4) Mortality rate; 5) Expenditures; and 6) Length of stay (LOS).[183]
According to the GIN performance measures' standards, KPIs based on clinical practice guidelines should stem from strong recommendations.[181]

This adapted guideline included five strong recommendations.

1. We recommend preauthorization and/or prospective audit and feedback over no such interventions.
2. We recommend antibiotic stewardship interventions designed to reduce the use of antibiotics-associated with a high risk of Clostridium Difficile Infection (CDI) compared with no such intervention.
3. We recommend that hospitals implement pharmacokinetic (PK) monitoring and adjustment programs for aminoglycosides.
4. We recommend ASPs implement programs to increase both appropriate use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics.
5. We recommend that ASPs implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration.

Guideline Dissemination **and Implementation**

Several implementation frameworks and manuals have recommended the following guideline implementation strategies or interventions:

1. Leadership commitment, engagement, and support.
2. Local clinical and quality champions.
3. Dissemination (printed and electronic).
4. Regular training and education.
5. Regular audit and feedback along with regular review and update promotes the concept of the 'living CPGs'.
6. Networking with relevant existing projects.
7. Parents or carers as champions for changes.

1. The Saudi Public Health Authority (Weqaya)

PHA had recently published a guidance for Antimicrobial Stewardship Implementation in Hospitals, to provide practical recommendations for healthcare workers in hospitals to improve the quality of antimicrobial prescribing and thereby improve patient clinical outcomes.

2. CDC Core Elements:

The CDC Core Elements for Antimicrobial Stewardship Programs (ASPs) Include:

- **Leadership Commitment:** Dedication from organizational leaders to support and prioritize antimicrobial stewardship initiatives.
- **Accountability:** Assigning responsibility for implementing and overseeing the ASP to qualified individuals or teams.
- **Drug Expertise:** Ensuring access to personnel with expertise in antimicrobial management, including pharmacists and infectious disease specialists.
- **Action:** Implementing interventions to optimize antimicrobial use, such as formulary restriction, preauthorization, and dose optimization.
- **Tracking:** Monitoring antimicrobial prescribing practices and resistance patterns to inform intervention strategies.
- **Reporting:** Regularly communicating antimicrobial use and resistance data to clinicians, stakeholders, and leadership.
- **Education:** Providing ongoing education and training on antimicrobial stewardship principles and practices to healthcare personnel.
- **Research:** Conducting research to evaluate the impact of antimicrobial stewardship interventions and identify areas for improvement.

These core elements serve as a framework for healthcare facilities to establish and maintain effective antimicrobial stewardship programs, ultimately aiming to optimize antimicrobial use and combat antimicrobial resistance. For further details, refer to the USA CDC official website: https://www.cdc.gov/antibiotic-use/hcp/core-elements/health-departments.html

3. ASP Committee Structure

Table 8: The Recommended Structure of the ASP Committee

Team members	Note*
Core Teams Members	
Leader of the committee	Based on the facility and the leadership structure, the leader of the ASP committee can be one of the following: CEO (preferred), medical director, the director of the pharmacy and therapeutics (P&T) committee, and the Infectious disease physician. (ASP team leader)
Co-leader	The co-leader usually comes next in hierarchy to the leader of the committee, therefore appointing the co-leader depends on the chosen leader. For instance, an ID physician should be appointed if the CEO was the ASP committee leader, and a clinical pharmacist might be assigned if the leader was an infectious diseases physician
Pharmacist	FTE clinical pharmacists are preferred, and Infectious diseases training is strongly recommended but not a prerequisite
Consultants from medical/ surgical and intensive care units	Consultants from different hospital department should be included in the committee to represent their own departments in term of ASP implantations and outcomes
Microbiologist	Consultant microbiologist is an essential member of the team to ensure timely communication of issues and action plans about resistance patterns and diagnostics.
Nurse	There is growing recognition of the importance of engaging nurses in the hospital ASP efforts
Ad Hoc members	
Infection Prevention and Control (IPC)	An essential member of the committee, the head of the Infection Prevention and Control or one of his team should work in tandem with the ASP team
Quality improvement and patient safety teams	Can advocate for resources dedicated to stewardship interventions
IT department	If available, IT team can facilitate and increase the efficiency of the ASP work

*Adopted from Nelosn study: Principles and Practice of Antimicrobial Stewardship Program Resource Allocation[184]

4. ASP Actions (Antimicrobial Stewardship Interventions/Strategies)

There are multiple ASP strategies that may be chosen. Different references use different ways to categorize these strategies:

1. Core vs supplemental strategies:

The widely used classification is the one that stratifies the interventions into core or major actions and supplemental or minor actions. The two core strategies that are strongly recommended in the guidelines of the IDSA/SHEA and considered as a A-I level recommendation, are the prospective audits and feedback, and the pre-authorization with formulary restriction. Published evidence demonstrates that they are the two most effective antibiotic stewardship interventions in hospitals (CDC), see Table 9.

Table 9: Examples of ASP Interventions

Core Strategies		Prospective audit and feedback
		Pre-authorization and formulary restriction
Supplemental strategies*	Process/structural strategies	Automatic stop order
		Hospital-wide introduction of rapid diagnostic technology in the laboratory
		Clinical decision support (CDSS) systems/ computerized physician order entry
		Antimicrobial order form and documentations
		Systematic antibiotic allergy verification
	Pharmacy/formulary strategies	Formulary automatic substitution
		Automatic changes from IV to PO
		Formulary review/streamlining
		Therapeutic drug monitoring
		Dose optimization/adjustments
		Time-sensitive automatic stop orders
		Duplicative therapy alerts
		Documentation of indications for antibiotics
	Prescribing guidance strategies	Disease-specific treatment guidelines/ pathways/ algorithms
		Empiric antibiotic prescribing guidelines
		IV-PO switch
		Duration of therapy
	Clinical strategies	De-escalation and streamlining
		Dose optimization
		Antibiotic-time outs
		Bug-drug mismatch
		Preventing treatment of non-infectious conditions
		Targeted review of patients with specific infections
	Microbiology-related strategies	Antibiograms
		Cascading and selective reporting of antimicrobial susceptibility testing results
		Selective Improved diagnostics
		Strategic microbiology results reporting
	Nursing-based interventions	Optimizing microbiology cultures
		Intravenous to oral transitions reminder
		Prompting antibiotic reviews (timeouts):

*Some differences exist between references in the classification of the interventions among the different categories. Overlaps of the interventions between the categories also exists.

2. Pre-authorization vs post-authorization strategies:

Based on the timing of the interventions, strategies can be either pre-authorization, also called a "front-end strategy" i.e., happens before antibiotic prescription (e.g., pre-authorization and formulary restriction) or post-authorization or "Back-end" strategy which happen after antibiotic prescription (e.g., prospective audit and feedback). Broadly speaking, post-authorization strategies are more acceptable by the prescribers.

3. Persuasive vs restrictive strategies

ASP interventions can be persuasive, restrictive, or combination of both.

Persuasive Strategies: These are strategies that attempt to educate and persuade the clinicians to prescribe appropriately, or to give feedback on their prescribing e.g., prospective audits and feedback.

Restrictive Strategies: Include strategies that prevent or provide a 'barrier' to prescribing antibiotics, such as by limiting access to specific antibiotic agents, or by instituting automatic stop orders or time limits for antibiotic treatments.

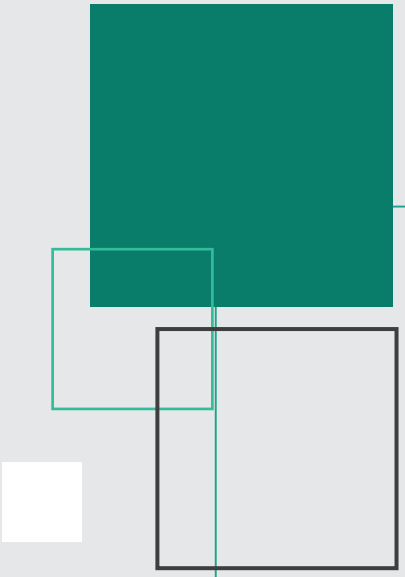
Available data suggest that persuasive interventions are less effective in the short term than restrictive methods but may have a greater long-term effect on prescribing practices.

4. Common infection-based interventions (disease-based interventions)

Some infections account for the majority of antibiotic prescribed in the hospitals, such as lower respiratory tract infections (e.g., community acquired pneumonia), urinary tract infections and skin and soft tissue infections. Interventions targeting these infections and aiming to optimize the antibiotic selection, dose and duration and are potential opportunities for ASP team. Other examples of Infection-based Interventions include sepsis, *Staphylococcus* aureus infection, C. difficile infection, and others.

Another way of categorizing the ASP intervention is based on the process, or the department/section involved e.g., Structural or process-related strategies, nursing, pharmacy, clinical/ provider, and microbiology-based strategies. Some references also broadly classify the interventions as active or passive. The primary active strategy recommended in IDSA/SHEA stewardship guidelines is prospective audit and feedback.[2,3] Active intervention is effective because it is patient-specific, but often is time and resource consuming and requires clinical expertise. Passive initiatives can be applied broadly because it is not specific to one patient. Examples include providing education, developing an institutional guideline, or an algorithm in the electronic medical record.

The selection between these interventions depends on many factors. Each ASP is unique and should be tailored based on the identified priorities within the hospital and the resources available. When establishing a new stewardship program, it is best to start with the core strategies and focus on achieving and maintaining them before adding some of the supplemental strategies. In real life, often a combination of the above strategies will be employed.



5. Microbiology role in "ASP" sample cascade reporting

Table 10: Sample of Antibiotic Cascade Reporting by Microbiology Lab

Tire 1: Antimicrobial agents that are appropriate for routine, primary testing, and reporting	Tire 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tire 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tire 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tires are not optimal because of various factors
Ampicillin			
Cefazolin	Cefuroxime		
Cefotaxime or ceftriaxone	Cefepime		
	Ertapenem Imipenem Meropenem	Cefiderocol	
		Ceftazidime-avibactam	
		Imipenem-relebactam	
		Meropenem-vaborbactam	
Amoxicillin -clavulanate Ampicillin-tazobactam			
Gentamicin	Tobramycin	Plazomicin	
	Amikacin		
Ciprofloxacin Levofloxacin			
Trimethoprim-sulfamethoxazole			
	Cefotetan Cefoxitin		
	Tetracycline		
			Aztreonam
			Ceftaroline
			Ceftazidime
			Ceftolozane-tazobactam
Urine only			
Cefazolin (surrogate for uncomplicated UT)			
Nitrofurantoin			
		Fosfomycin (*Escherichia coli*)	

Table obtained from antimicrobial stewardship in Australian health care.[185]

6. Outcome measures, hand on practice:

Table 11: Examples of Metrics Used for Measuring the Outcome of the ASP Program

Outcome measures	Process measures	Structure measures
Antimicrobial resistance rate	Antimicrobial consumption e.g., DDD and DOT	Components of the stewardship program e.g., CDC core elements
Length of stay (LOS)	Compliance with the guidelines	
C. difficile rate	Time to appropriate therapy	
Clinical success/cure	Documented indication for antimicrobial therapy	
Readmission rates		
Infection related mortality		

Days of therapy (DOT)

DOT is the number of days a single antimicrobial is administered regardless of the number of doses administered or dosage strength.

Calculation of DOT for an individual patient (a single treatment episode):

DOT: The number of days that a patient receives an antimicrobial agent (regardless of dose), or any dose of an antibiotic that is received during a 24 hour period represents 1 DOT.
Data from such DOT calculations can provide the contribution of a treatment episode to overall antibiotic use in both hospital and community settings (future learn).

DOT per 1000 patient days using a denominator:

DOT is also used for comparison purposes such as antibiotic use over time, before and after interventions or changes in practice. Using a denominator will allow a more meaningful comparison over time and locations even between hospitals within a geographic area or between countries. The most commonly used denominators in hospital ASPs are the number of patient days (occupied bed days).
Furthermore, to allow comparison between hospitals or services of different sizes, DOT are often standardized to 100 or 1000 patient days (per UK and National). The Infectious Disease Society of America and Society for Healthcare Epidemiology of America recommends DDD/1000 patient days as a metric for hospital-based antimicrobial stewardship programmes.

Examples:
Cefazolin 2 g q 8h IV X 1 day = 1 DOT
Cefazolin 1 g IV X 1 dose = 1 DOT
The DOT for a given patient on multiple antibiotics will be the sum of DOT for each antibiotic that the patient is receiving.
Examples
During his illness, a patient received a combination of Amoxicillin 500 mg Q 8 hours and azithromycin 500 mg for the first 3 days, but then continued on Amoxicillin alone for 4 more days.
DOT of amoxicillin = 7 DOT
DOT azithromycin = 3 DOT
Total DOT for the course of the treatment: 7 + 3 = 10 DOT

DOT Per 1000 patient-days:

The number of days antibiotics received during specific period x 1000 = DOT per patient-days

Number of patient-days (or bed-days) during the same period

However, many hospitals are unable to easily calculate DOT, which requires patient-level data, ideally from electronic medical records. 11 Hospitals without electronic medical records and data-mining software may be able to manually count DOT for targeted antibiotics in specific hospital locations or patient populations.

Example:
In a referral center, ASP team was attempting to calculate the DOT for ceftriaxone for the month of July (total patient days/bed occupied 360)
The following were found:
Ceftriaxone 1 gm IV every 12 hours for 40 days
Ceftriaxone 1 gm every 24 hours for 20 days
Ceftriaxone 2 gm every 24 hours for 30 days
Total days ceftriaxone used = Total DOT for ceftriaxone for that month = 40 + 20 + 30 = 90
DOT per 1000 patient-days
90/360 X 1000 = 250 DOT/ 1000 patient-days for ceftriaxone in the month of July

Defined Daily Dose (DDD)

The basic definition for a defined daily dose is the assumed average maintenance dose per day for a drug used in its main indication in adults (FL) DDD is generally less accurate than DOT and not applicable to pediatric patients. It is primarily used by antimicrobial teams to monitor trends within a ward, hospital, or primary care setting. To calculate the DDDs the total number of grams of each antibiotic used in a ward (or whole hospital) during a defined period is divided by the WHO assigned DDD value for that antibiotic e.g., the DDD for ceftriaxone is 2 gm.

DDDs for all medicines are assigned by the WHO and have been used as a standardised measure since the 1970s (www.whocc.no/atc_ddd_index). DDD is therefore often an easier way of measuring KPIs for ASPs in hospitals with pharmacy systems that cannot calculate DOT.
For additional examples of DDD calculations for other antimicrobials process and outcome KPIs please refer to Weqaya guidance.[155]

Calculation of DDD for an individual patient (a single treatment episode):
DDD is defined by WHO the total antibiotic consumption (in gm or mg)

Example:
A patient is receiving an oral amoxicillin 500 mg three times per day for 5 days.
To calculate the DDD for this individual patient:
Daily dose 3 X 500 mg = 1.5 gm
Amoxicillin DDD by the WHO: 1 gm
DDD for 1 day: 1.5/ 1 = 1.5 DDD
Total DDD for the course of 5 days for this individual patient: 5 X 1.5 = 7.5 DDD
i.e., this patient has contributed with 7.5 DDD to the overall all hospital use of the antibiotics

Calculating Defined daily DDDs per 1,000 patient days using a denominator:

Like in the case of DOT, DDD is often standardized to 100 or 1000 patient days (DOT/1000 patient days) to allow comparison between hospitals or services of different sizes.

DDD per 1000 patient days

Total antibiotic consumption (g or mg) x 1000 = DDD per 1000 patient-days

WHO DDD value (g or mg) x patient-days (or bed-days) during the same period

Example (1):
A local hospital dispensed 12,000 grams of meropenem in the yeas of 2022. The hospital records indicated a 346,112 bed occupied during this period of time. What is the total DDD of meropenem in the year 202?
To calculate the DDDs per 1000 patient days in the year 2022:
12,000 gram/2 grams (WHO DDD for meropenem) = 6000 DDD
6000 DDD/346,112 (patient days) X 1000 = 17.3 DDD/1000 patient days

Example (2):
A medical word dispensed 220 doses of IV levofloxacin (750 mg) and 120 doses of PO levofloxacin (500 mg) in the month of June. (Total bed occupied in the same month was 32,124).
What is the total DDD of levofloxacin in the month of June?
To calculate the total DDDs of levofloxacin per 1000 patients in the month of June:
Total amount of dispensed levofloxacin= IV levofloxacin (220 X 750) + PO levofloxacin (120 X 500) = 225,000 mg = 225 gm
Levofloxacin DDD = 225/0.5 (WHO DDD for levofloxacin) = 450 DDD of levofloxacin
DDD per 1000 patient days = 450/32,124 X 1000 = 14 DDD per 1000 patient days

Table 12: Comparison Between DOT and DDD for Measuring the Outcome of the Antimicrobial Stewardship Program

DOT	DDD
The most accurate and preferred measure of antibiotic use	Useful measure of ASP progress when using consistent methodology over time
Can be used in adult and pediatric populations	Easy to calculate. Can be calculated in the absence of computerized pharmacy records by using purchasing data
Provide method for comparisons and benchmarking within and between institutions and countries	Allows comparisons and benchmarking within and between institutions and countries
NOT affected by change in dosing (e.g., Levofloxacin 500mg vs. 750 mg), or WHO DDD	Internationally recognized as assigned and published by the WHO, and updated annually
No subject to differences in institutional preferences	Enables comparison of antibiotic use over time, thereby identifying areas for further investigation using audit and quality improvement methods
Disadvantages	
Relatively more difficult to measure as they require patient-level information	Inaccurate in certain populations e.g., renal impairment and pediatrics
Requires computerized pharmacy records to obtain data. Manual determination, although more precise, is not practical	Can over or underestimate antibiotic use as do not account for alternative dosing regimes due to renal dysfunction, obesity etc.
Favours the use of broad-spectrum monotherapy over narrow spectrum combination therapy. e.g., meropenem x 7 d = 7 DOTs while Ceftriaxone + metronidazole x 7 d = 14 DOTs	Create some bias in combination therapy e.g., for the same infection, the use of 3 narrow spectrum antibiotics will result in 3 times as many DDD of one broad spectrum antibiotic
Overestimation with one-time doses (one dose counted the same as multiple doses) e.g., cefazolin OD for surgical prophylaxis equals to cefazolin 3 times/day for 24 hours	It may not reflect the dose used for particular infection
	DDD can change with time
1 DOT is any dose of antibiotic during a 24-hour period, the DOT for a dosing interval >24 hours (e.g., in renal failure) do not reflect patient exposure; it only reflects antibiotic administration	Doses used for the DDD may not be the currently recommended doses for optimization of the antibiotic activities e.g., levofloxacin of 500 Vs 750 mg dosing used by different centers

Table 13: Days of Therapy (DOT) KPI Data Sheet

DOT			
Functional area	Antimicrobial stewardship	ICD Code:	Refer to Table 1
Name	Days of Therapy per 1000 patients' days		
Definition	Is the number of days a single antimicrobial is administered regardless of the number of doses administered or dosage strength.		
Rational	Individual-level data make it possible to assess the duration of treatment, redundant therapy, etc.		
Classification	Outcome (quantitative)	Quality dimensions	Medication Management/safety
Calculation			
Calculation formula			
Numerator	The number of days antibiotics received during specific period	Denominator	Number of patient-days (or bed-days) during the same period
Exclusion criteria	Not applicable	Exclusion Criteria	Not applicable
Unit of measure	Per 1000 patient-days		
Target Setting			
Target	Variable (to be decided by site of implementation)	Data collection	Electronic or manual
Benchmark	Variable	Reporting frequency	Quarterly reporting
Data Collection and Administration			
Data source	Pharmacy Data and Medical Records		
Reference	• WHO Antimicrobial Stewardship Programmes[182] • Antimicrobial Stewardship Programmes in Saudi Hospitals: Evidence from a National Survey[15]		

Table 14: Defined Daily Dose (DDD) KPI Data sheet

DDD			
Functional Area	Antimicrobial stewardship	ICD Code:	Refer to Table 1
Name	Defined daily dose per 1000 patient-days		
Definition	Assumed average maintenance dose per day for a medicine used for its main indication in adults.		
Rational	DDD per 100(0) patient-days is the most commonly used quantity measure of antibiotic use, because the data needed to calculate it are available in many settings (unlike days of therapy, DOTs); no individual-level data are needed. It should, however, be noted that differences in data sources and definitions may influence this indicator.		
Classification	Outcome (quantitative)	Quality dimensions	Medication Management/safety

Calculation			
Calculation formula			
Numerator	Total antibiotic consumption (g or mg)	Denominator	Total number of patient-days within that period of time
Exclusion criteria	Not applicable	Exclusion Criteria	Not applicable
Unit of measure	Per 1000 patient-days		
Target Setting			
Target	Variable (to be decided by site of implementation)	Data collection	Electronic or manual
Benchmark		Reporting frequency	Quarterly reporting
Data Collection and Administration			
Data source	Pharmacy Data and Medical Records		
Reference	• WHO Antimicrobial Stewardship Programmes[182] • Antimicrobial Stewardship Programmes in Saudi Hospitals: Evidence from a National Survey[15]		

Patient **Information**

1. What are antibiotics?

Antibiotics are medicines that fight bacterial infection only, by either killing the bacteria or making it difficult to grow and multiply so our immunity can overcome these types of diseases.

2. How can reduce the rate of bacterial infection before antibiotics use?

Before using antibiotics, simple respiratory etiquette can keep you healthy and reduce the spread of infection to others like cough cover and hand cleaning. Also, staying home when you are sick reduces the spread of infection. Furthermore, vaccines are the most effective way to keep your health and other health safe and reduce the need for antibiotics use.

3. What do antibiotics treat?

Antibiotics only treat infections that are caused by bacterial causes. And your knowledge about the difference between bacterial and viral diseases can protect you from inappropriate antibiotic use sequelae because a clinical evaluation by a health care professional is required to determine if your disease is caused by viral or bacterial infections. Urinary tract infections and sore throats caused by streptococci are examples of bacterial infections which required antibiotic therapy.

4. What do not antibiotics treat?

Most infections are caused by viruses such as cold and flu and no need for antibiotics in such cases.
Examples of viral infections:

- Sore throat.
- Common cold and flu.
- Gastroenteritis.

Other diseases may not need to be treated with antibiotics because mostly caused by viruses like
Ear infections, sinusitis and bronchitis.

5. What's the harm of taking antibiotics even if they might not be helpful?

- Overuse of antibiotics can lead to antibiotic resistance.
- Non-appropriate antibiotics use can lead to unnecessary side effects. However, when there are indications to use antibiotics, the benefits outweigh the risks of side effects. The side effect includes:
  - Rash and anaphylactic reaction.
  - Nausea, abdominal cramps, and diarrhea.
  - Increase liability of fungal infection.
  - Affect your immunity by killing your microflora.
  - Other serious side effect includes C. diff colitis can damages your bowel and cause fatal diarrhea, and severe allergic reaction like Steven Johnsen Syndrome.
- Improper duration of therapy can cause treatment failure.

6. What is the impact of antibiotic resistance?

Antibiotic resistance is a global and institutional emergent health problem in our days. It is caused by bacteria, not our body, and makes that bacteria able to fight the most commonly used antibiotics. Antibiotic resistance can impact our health and can lead to serious and fatal infections. The appropriate use of antibiotics and proper prescription can lessen this burden.

7. What is the meaning of appropriate antibiotic use?

- Use antibiotics for bacterial indications after clinical evaluation by a health care professional.
- Use the dose of antibiotics as prescribed by a health care professional.
- Use antibiotics for a total duration of therapy that is prescribed by a health care professional.
- Do not store antibiotics at home for later use and share them with family members without a medical prescription.

8. What is the meaning of inappropriate antibiotic use?

- Unnecessary antibiotics use for non-bacterial causing disease.
- Using antibiotics without medical prescription and clinical evaluation.
- Using improper doses of antibiotics.
- Using antibiotics for the wrong duration.
- Using the stored antibiotics at home or sharing them with family members without a medical prescription.

Patients Experience **Stories**

قصة تجربة المريض

القصة الأولى

- في صيف عام ٢٠٢٣، كانت الطفلة (م) طفلة مرحة سعيدة سليمة تذهب إلى أحد دور الحضانة النهارية، حيث لاحظت مربيتها وجود احمرار في ساعد الطفلة الأيمن، ولكن لكون الطفلة هادئة ولم تشكِ من أي ألم، أو تثر أي ضجة، لذلك لم تكن المربية قلقة بشأن الاحمرار وظنّت أنه مجرّد احمرار عارض سيزول خلال فترة وجيزة.
- تدهورت حالة الطفلة بعد يومين، وتحولّ مكان الاحمرار إلى تقرّح، مما استدعى مراجعة الطفلة برفقة والدها للطبيب، حيث قام الطبيب بفحصها وأخذ مزرعة من مكان التقرّح، وبدأ استخدام مضاداً حيويّاً (الكليندامايسين) كعلاج تجريبي لالتهاب النسيج الخلوي، ريثما تظهر نتائج الزرع الجرثومي.
- أظهرت نتائج الزرع الجرثومي إصابة الطفلة بجرثومة المكورات العنقودية الذهبية الحساسة للميثيسيلين (MSSA).
- عُولجت الطفلة في المستشفى لمدة أسبوعين باستخدام المضاد الحيوي (الكليندامايسين) مع تحسن سريري واضح. ولكنها بدأت تعاني خلال فترة مكوثها في المستشفى من إسهال دموي وألم في البطن، مما استدعى إجراء مزرعة من البراز والتي أظهرت نتيجتها وجود عدوى بجرثومة المطثية العسيرة التي تتسبب بأحد أنواع التهاب القولون (التهاب القولون الغشائي الكاذب).
- أوقف الطبيب الكليندامايسين على الفور.
- باستعراض الحالة يتبين لنا أن التهاب القولون الغشائي الكاذب هو أحد نتائج سوء استخدام المضادات الحيوية، ويمكن للاستراتيجيات والتداخلات المتعددة المضادة للميكروبات أن توقف ذلك؛ على سبيل المثال (التدقيق والمراجعة ووجود الدلائل الإرشادية الخاصة بالمرض).

القصة الثانية

- لم يعاني مريضنا البالغ من العمر ١٤ شهرًا من أي شكاية صحيّة من قبل، ولكنه بدأ يعاني في فصل الشتاء من السعال والزكام. لاحظت والدته أثناء نومه تسرعاً بالتنفس مما أثار قلقها، حيث طلبت من الأب في اليوم التالي اصطحاب الطفل إلى أحد المراكز الصحيّة، وبعد معاينته من قبل طبيب الأطفال، شخّص الطبيب إصابة الطفل بعدوى فيروسية، ونصح الوالدين بإعطائه خافض الحرارة فقط بسبب ارتفاع درجة حرارته التي وصلت إلى 39 درجة مئوية ليلاً.
- ولسبب معاناة الأم من الربو فقد كانت قلقة من احتمال أن يكون ابنها يعاني من نفس المرض، لكن الطبيب قال إن رئتيه تبدو سليمة.
- وفي اليوم التالي، كان نشاط الطفل منخفضاً وحيويته أقل من المعتاد، مع ضيق في التنفّس مما استدعى مراجعة الأهل لغرفة الطوارئ.
- الذي يتسبب بالتهاب RSV أظهر اختبار التحري السريع لفيروسات الجهاز التنفسي إيجابية الفيروس التنفسي المخلوي الشعب الهوائية عند الأطفال في فصل الشتاء.
- التوصيات: طمأنة الأهل والعلاج الداعم.
- يفيد الاختبار السريع في ضبط الاستخدام العشوائي للمضاد الحيوي وعدم استخدام المضاد الحيوي الا في حال وجود استطباب واضح له.

Guideline Updating **and Localization**

The CPG Adaptation Group decided to review this adapted CPG for updates after five years from its publication date (2025) which should be on (2030) after checking for updates in the source guidelines, consultation of expert opinion on the changes needed for updating according to the newest evidence and recommendations published in this area and the clinical audit and feedback from implementation efforts. The guideline update process will be guided by the Checklist for the Reporting of Updated Guidelines (CheckUp).[180]

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Appendices

Abbreviations

Terms	Full name
ASP	Antimicrobial Stewardship Program
AMR	Antimicrobial Resistance
AMS	Antimicrobial Stewardship
AGREE II	Appraisal of Guidelines for Research & Evaluation II
CDI	Clostridium Difficile Infection
CDSS	Computerized Decision Support System
COI	Conflict of Interest
CPG	Clinical Practice Guideline
DDD	Defined Daily Dose
DOT	Days of Therapy
EBHC-KT	Evidence-Based Health Care-Knowledge Translation
EMRO	World Health Organization (WHO) Regional Office for the Eastern Mediterranean
EtD	Evidence-to-Decision
F&N	Fever and Neutropenia
GAG	Guideline Adaptation Group
GIN	Guidelines International Network
HC CDI	Healthcare-Associated Clostridioides Difficile Infection
H-AS	Handshake Stewardship
IFI	Invasive Fungal Infection
ID	Infectious Diseases
IDSA	Infectious Diseases Society of America
ICU	Intensive Care Unit
IFD	Invasive Fungal Disease
IV	Intravenous
KFSHRC	King Faisal Specialist Hospital and Research Center
KSU	King Saud University
KSUMC	King Saud University Medical City
LoE	Level of Evidence
MAD-ID	Medication-Assisted Drug-Induced Disease
MBS	Maternity, and Children
MIC	Minimum Inhibitory Concentration
MOH	Ministry of Health
NICU	Neonatal Intensive Care Unit
PAF	Prospective Audit with Intervention and Feedback
PCN	Penicillin
PCT	Procalcitonin
PHA	Public Health Authority (Weqaya), Saudi Arabia
PK	Pharmacokinetic
PIPOH	Patient, Intervention, Population, Outcome, Healthcare context
PROMs	Patient Reported Outcome Measures
RSV	Respiratory Syncytial Virus
SCFHS	Saudi Commission for Health Specialties
SHEA	Society for Healthcare Epidemiology of America
SoR	Strength of Recommendation
SPIDS	Saudi Pediatric Infectious Diseases Society
SWAB	Dutch Working Party on Antibiotic Policy
WHO	World Health Organization

Glossary of Terms

Antimicrobial stewardship (AMS)
refers to the optimal selection, dosing, and duration of antimicrobial treatment resulting in the best clinical outcome with minimal side effects to the patients and minimal impact on subsequent resistance.[186]
Another proposed definition: AMS is a systematic approach to educate and support health care professionals to follow evidence-based guidelines for prescribing and administering antimicrobials.[187]

Antimicrobial resistance (AMR)
is the resistance of a microorganism to an antimicrobial medicine to which it was previously sensitive. It develops when a microorganism mutates or acquires a resistance gene.[188]

Antibiotic use or utilization
was defined in a recent study as antimicrobial administration (i.e., receipt of at least one antibiotic) per patient. A prescription was defined as the use of one substance by one route of administration. Antimicrobial prescription rates were expressed as a percentage of patients receiving antimicrobials, or as a percentage of all antibiotic prescriptions (proportional use).[189]

Search Methods

CPG databases:
Guidelines International Network (GIN) International Guidelines Library (n=5). ECRI Guidelines Trust (USA) (n=0). National Institute of Clinical and Health Excellence (NICE) UK (n=2). Scottish Intercollegiate Guidelines Network (SIGN) UK (n=0). EBSCO DynaMed (USA) (n=29).

Bibliographic databases:
- PubMed/ MEDLINE (n=215). Google Scholar (n=295). LILACS (n=85), TRIP (n=252).

Specialized professional societies:
- The American Association of Neuromuscular & Electro-diagnostic Medicine (AANEM). American Physical Therapy Association (APTA). American Family Physician (AFP). Canadian Chiropractic Guidelines Initiative (CCGI). Orthopaedic Division Clinical Update. The American Society of Regional Anesthesia and Pain Medicine and the American Academy of Pain Medicine. The Royal College of Chiropractors (RCOC)

Other Publications
- Systematic reviews: Rennert-May E, Chew DS, Conly J, Guirguis M, Slobodan J, Fryters S, Bresee L. Clinical practice guidelines for creating an acute care hospital-based antimicrobial stewardship program: A systematic review. *Am J Infect Control*. 2019 Aug;47(8):979-993 https://doi.org/10.1016/j.ajic.2019.02.010

Search Keywords
- Antimicrobial stewardship, guideline
- PubMed search: "Antimicrobial Stewardship"[MeSH Terms], "Guideline"[Publication Type] OR "Guidelines as Topic"[MeSH Terms].

A total of 883 records were retrieved, 850 were excluded by title and abstract and 27 were excluded after full-text review according to the health questions and the eligibility criteria. Only 6 source original CPGs were found to be eligible for the quality assessment step. The GAG relied on the results of the published systematic review of the ASP CPGs.[179] The Korean antimicrobial stewardship CPG, developed by the Korean Society for Antimicrobial Therapy, the Korean Society of Infectious Diseases, and the Korean Society of Health-System Pharmacists, was appraised by two independent reviewers (YA, GB) and any discrepancies were resolved by discussions.[164]

List of eligible source CPGs for quality appraisal:

1. German Society for Infectious Diseases (GSID)[190]
2. Infectious Diseases Society of America (IDSA)/ Society for Healthcare Epidemiology of America (SHEA)[2]
3. National Institute for Health and Care Excellence (NICE)[191]
4. Strategy for the control of Antimicrobial Resistance in Ireland (SARI)[192]
5. Dutch Working Party on Antibiotic Policy (SWAB)[193]
6. Guidelines on Implementing Antimicrobial Stewardship Programs in Korea[164]

Forest Plots

Not Applicable

Guideline Recommendations, Evidence Profiles and Evidence-to-Decision Frameworks

Not Applicable

Evidence-to-Decision frameworks and Summary of Findings Tables

Not Applicable

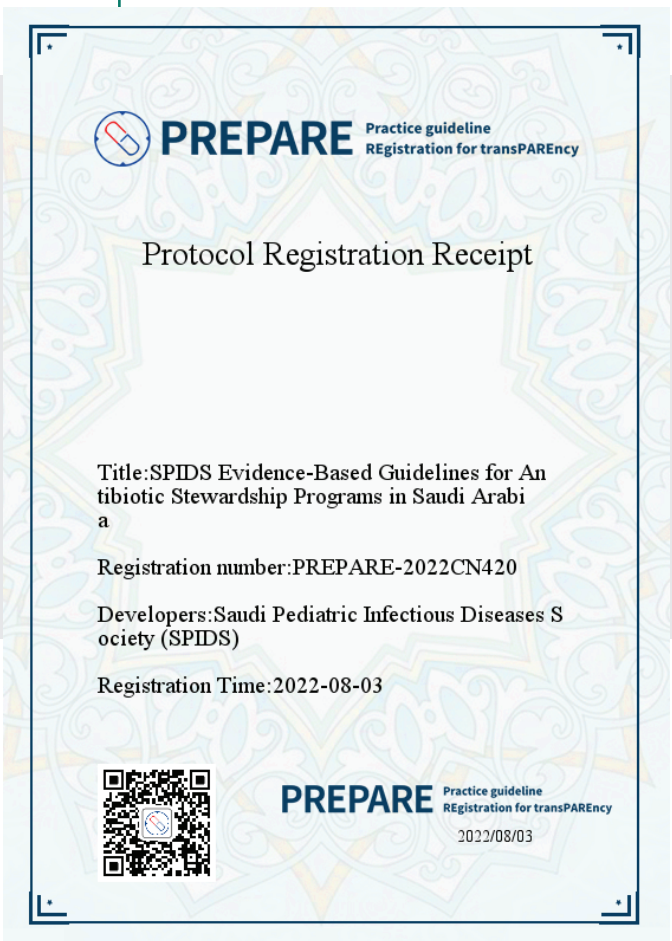
Acknowledgments

We gratefully acknowledge the invaluable contributions of the Guideline Development/Adaptation Group, the Guideline Support Team, and the external reviewers. Their expertise, dedication, and hard work were essential to completing this guideline. We also extend our sincere appreciation to the Saudi Pediatric Infectious Diseases Society (SPIDS), the Saudi Commission for Health Specialties (SCFHS), the National Center for Non-Profit Sector, King Saud University (KSU), King Saud University Medical City (KSUMC), and the Public Health Authority(s) for their generous support and funding which made this project possible. Finally, we thank all individuals who participated in developing and reviewing this guideline.

Guideline **Registration**

The guideline was registered with the Practice guideline REgistration for transparency (PREPARE) accessed through http://www.guidelines-registry.org

Registration Number: **PREPARE-2022CN420**
Registration Date: **03/08/2022**


PREPARE Practice guideline REgistration for transPAREncy

Protocol Registration Receipt

Title:SPIDS Evidence-Based Guidelines for Antibiotic Stewardship Programs in Saudi Arabia

Registration number:PREPARE-2022CN420

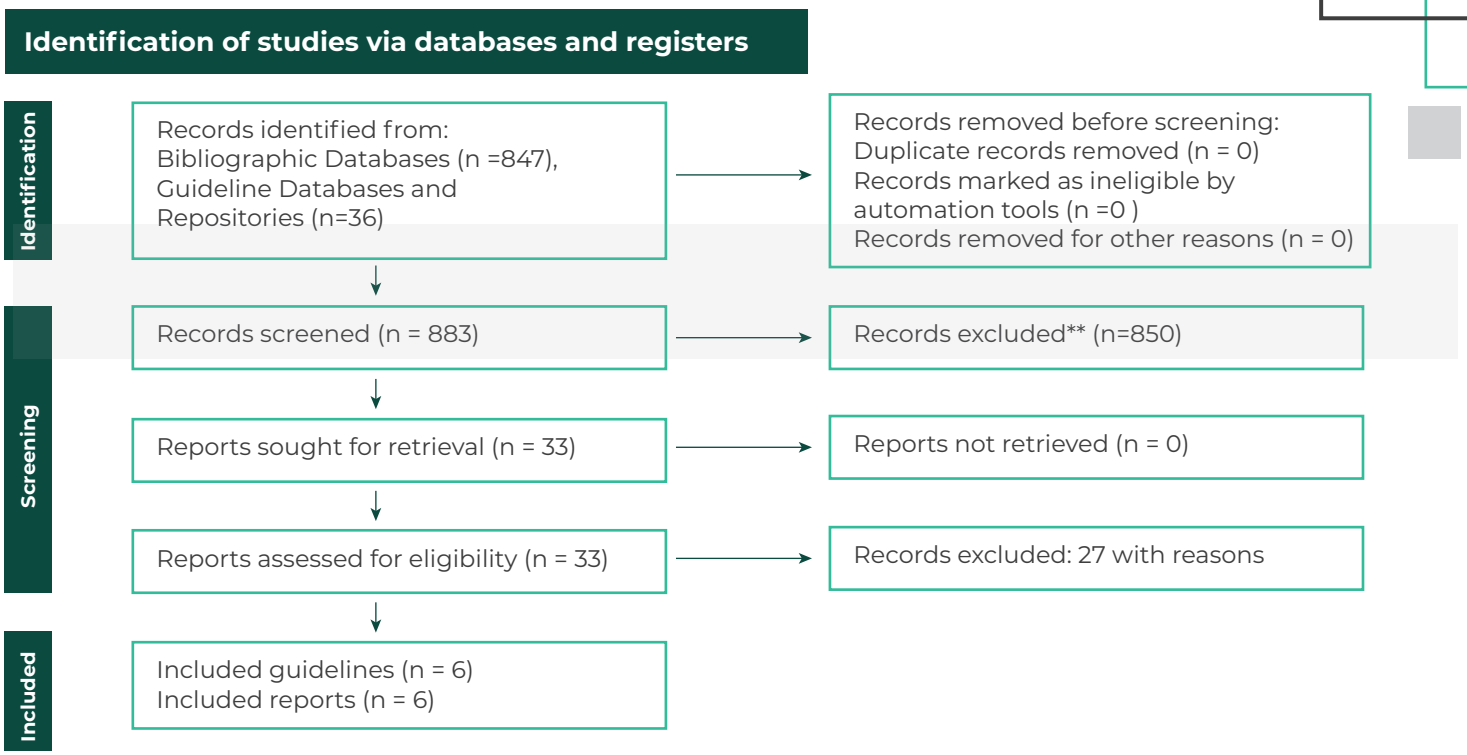
Developers:Saudi Pediatric Infectious Diseases Society (SPIDS)

Registration Time:2022-08-03

PREPARE Practice guideline REgistration for transPAREncy

2022/08/03

PRISMA 2020 Flowchart



Appendix Figure: PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registries only.

RIGHT-Ad@pt Reporting Checklist

7 sections, 27 topics, and 34 items	Assessment	Page(s)	Note(s)
Basic information			
Title/subtitle			
1. Identify the report as an adaptation of practice guideline(s), that is include "guideline adaptation", "adapting", "adapted guideline/recommendation(s)", or similar terminology in the title/subtitle.	✓ Yes ☐ No ☐ Unclear		
2. Describe the topic/focus/scope of the adapted guideline.	✓ Yes ☐ No ☐ Unclear		
Cover/first page			
3. Report the respective dates of publication and the literature search of the adapted guideline.	✓ Yes ☐ No ☐ Unclear		
4. Describe the developer and country/region of the adapted guideline.	✓ Yes ☐ No ☐ Unclear		
Executive summary/abstract			
5. Provide a summary of the recommendations contained in the adapted guideline.	✓ Yes ☐ No ☐ Unclear		

Abbreviations and acronyms

6. Define key terms and provide a list of abbreviations and acronyms (if applicable).

- ✓ Yes
- ☐ No
- ☐ Unclear

Contact information of the guideline adaptation group

7. Report the contact information of the developer of the adapted guideline.

- ✓ Yes
- ☐ No
- ☐ Unclear

Scope

Source guideline(s)

8. Report the name and year of publication of the source guideline(s), provide the citation(s), and whether source authors were contacted.

- ✓ Yes
- ☐ No
- ☐ Unclear

Target population(s)

9. Provide the basic epidemiological information about the problem (including the associated burden), health systems relevant issues, and note any relevant differences compared to the source guideline(s).

- ✓ Yes
- ☐ No
- ☐ Unclear

Aim(s) and specific objectives

10. Describe the aim(s) of the adapted guideline and specific objectives, and note any relevant differences compared to the source guideline(s).

- ✓ Yes
- ☐ No
- ☐ Unclear

Brief description of the health problem(s)

11. Describe the target population(s) and subgroup(s) (if applicable) to which the recommendation(s) is addressed in the adapted guideline, and note any relevant differences compared to the source guideline(s).

- ✓ Yes
- ☐ No
- ☐ Unclear

End-users and settings

12. Describe the intended target users of the adapted guideline, and note any relevant differences compared to the source guideline(s).

- ✓ Yes
- ☐ No
- ☐ Unclear

13. Describe the setting(s) for which the adapted guideline is intended, and note any relevant differences compared to the source guideline(s).

- ✓ Yes
- ☐ No
- ☐ Unclear

Rigor of development

Guideline adaptation group

14. List all contributors to the guideline adaptation process and describe their selection process and responsibilities.

- ✓ Yes
- ☐ No
- ☐ Unclear

Adaptation framework/methodology

15. Report which framework or methodology was used in the guideline adaptation process.

- ✓ Yes
- ☐ No
- ☐ Unclear

Source guideline(s)

16. Describe how the specific source guideline(s) was(were) selected.

- ✓ Yes
- ☐ No
- ☐ Unclear

Key questions

17. State the key questions of the adapted guideline using a structured format, such as PICO (population, intervention, comparator, and outcome), or another format as appropriate.

- ✓ Yes
- ☐ No
- ☐ Unclear

18. Describe how the key questions were developed/modified, and/or prioritized.

- ✓ Yes
- ☐ No
- ☐ Unclear

Source recommendation(s)

19. Describe how the recommendation(s) from the source guideline(s) was (were) assessed with respect to the evidence considered for the different criteria, the judgements and considerations made by the original panel.

- ✓ Yes
- ☐ No
- ☐ Unclear

Evidence synthesis

20. Indicate whether the adapted recommendation(s) is/are based on existing evidence from the source guideline(s), and/or additional evidence.

- ✓ Yes
- ☐ No
- ☐ Unclear

21. If new research evidence was used, describe how it was identified and assessed.

- ✓ Yes
- ☐ No
- ☐ Unclear

Assessment of the certainty of the body of evidence and strength of recommendation

22. Describe the approach used to assess the certainty/quality of the body/ies of evidence and the strength of recommendations in the adapted guideline and note any differences (if applicable) compared to the source guideline(s).

- ✓ Yes
- ☐ No
- ☐ Unclear

Decision-making processes

23. Describe the processes used by the guideline adaptation group to make decisions, particularly the formulation of recommendations.

- ✓ Yes
- ☐ No
- ☐ Unclear

Recommendations

24. Report recommendations and indicate whether they were adapted, adopted, or *de novo*.	✓ Yes ☐ No ☐ Unclear
25. Indicate the direction and strength of the recommendations and the certainty/quality of the supporting evidence and note any differences compared to the source recommendations(s) (if applicable).	✓ Yes ☐ No ☐ Unclear
26. Present separate recommendations for important subgroups if the evidence suggests important differences in factors influencing recommendations and note any differences compared to the source recommendations(s) (If applicable).	✓ Yes ☐ No ☐ Unclear

Rationale/explanation for recommendations

27. Describe the criteria/factors that were considered to formulate the recommendations or note any relevant differences compared to the source guideline(s) (if applicable).	✓ Yes ☐ No ☐ Unclear

External review and quality assurance

External review

28. Indicate whether the adapted guideline underwent an independent external review. If yes, describe the process.	✓ Yes ☐ No ☐ Unclear

Organizational approval

28. Indicate whether the adapted guideline obtained organizational approval. If yes, describe the process.	✓ Yes ☐ No ☐ Unclear

Funding, declaration, and management of interest

Funding source(s) and funder role(s)

30. Report all sources of funding for the adapted guideline and source guideline(s), and the role of the funders.	✓ Yes ☐ No ☐ Unclear

Declaration and management of interests

31. Report all conflicts of interest of the adapted and the source guideline(s) panels, and how they were evaluated and managed.	✓ Yes ☐ No ☐ Unclear

Other information

Implementation

32. Describe the potential barriers and strategies for implementing the recommendations (if applicable).	✓ Yes ☐ No ☐ Unclear

Update

31. Briefly describe the strategy for updating the adapted guideline (if applicable).	✓ Yes ☐ No ☐ Unclear

Limitations and suggestions for further research

34. Describe the challenges of the adaptation process, the limitations of the evidence, and provide suggestions for future research.	✓ Yes ☐ No ☐ Unclear

RIGHT: Reporting Items for Practice Guidelines in HealThcare[194]