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Core Elements for Implementing Antimicrobial Stewardship Programs in Korean General Hospitals

1C Infection & Chemotherapy

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ABSTRACT

Currently, antimicrobial resistance (AMR) is a major threat to global public health. The antimicrobial stewardship program (ASP) has been proposed as an important approach to overcome this crisis. ASP supports the optimal use of antimicrobials, including appropriate dosing decisions, administration duration, and administration routes. In Korea, efforts are being made to overcome AMR using ASPs as a national policy. The current study aimed to develop core elements of ASP that could be introduced in domestic medical facilities. A Delphi survey was conducted twice to select the core elements through expert consensus. The core elements for implementing the ASP included (1) leadership commitment, (2) operating system, (3) action, (4) tracking, (5) reporting, and (6) education. To ensure these core elements are present at medical facilities, multiple departments must collaborate as teams for ASP operations. Establishing a reimbursement system and a workforce for ASPs

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Conflict of Interest

BWE is editorial board of Infect Chemother; however, he did not involve in the peer reviewer selection, evaluation, and decision process of this article. Otherwise, no potential conflicts of interest relevant to this article was reported.

Author Contributions

Conceptualization: KTK, HSC, KP. Funding acquisition: KTK. Investigation: BK, CM, MSL, YKY, SJJ, YCK, BWE, HK, ISH, CP, HL. Methodology: KTK, JS. Supervision: HBK, SK, and MSL. Writing - original draft: HSC and KP. Writing - review & editing: HSC, KP, HBK, SK, BK, CM, MSL, YKY, SJJ, YCK, BWE, HK, ISH, CP, KTK. are prerequisites for implementing ASPs. To ensure that ASP core elements are actively implemented in medical facilities, it is necessary to provide financial support for ASPs in medical facilities, nurture the healthcare workforce in performing ASPs, apply the core elements to healthcare accreditation, and provide incentives to medical facilities by quality evaluation criteria.

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Keywords: Antimicrobial resistance; Leadership; Multidisciplinary; Financial support; Accreditation

INTRODUCTION

1. Background and Purpose

Antimicrobial agents have profoundly impacted the development of medicine. Their development enabled the treatment of many infectious diseases and contributed to the development of high-tech medical interventions, including chemotherapy and organ transplantation. However, currently, antimicrobial resistance (AMR) is emerging as a serious global health concern.

The inappropriate use of antimicrobials is the major cause of antimicrobial resistance (AMR) and adverse drug reactions [1]. As per a report published in 2014, AMR will be responsible for 10 million deaths worldwide by 2050. This is higher than the predicted number of deaths from cancer [2]. In Korea, a qualitative evaluation of antimicrobial prescriptions at medical facilities nationwide in 2019 revealed that 26.1% of all antimicrobial prescriptions were inadequate [3, 4]. In a survey of antimicrobial awareness among healthcare physicians in 2020 in Korea, over 35% of physicians reported unawareness of the lack of requirement for antimicrobials, but had still prescribed them in some cases [5].

To overcome the increase in antimicrobial-resistant bacteria, various strategies are required to minimize the inappropriate use of antimicrobial agents. The antimicrobial stewardship program (ASP) is an integrated intervention strategy to establish optimal antimicrobials for patients requiring antimicrobial treatment at the appropriate dose and for the requisite period [6, 7]. It enables the effective treatment of infectious diseases, protects patients from the damage caused by the unnecessary use of antimicrobials, and minimizes the risk of AMR [8].

In May 2015, the World Health Organization (WHO) declared AMR a public health crisis facing humanity, and the Global Action Plan on AMR was approved by the World Health Assembly [9]. In Korea, the use of antimicrobials is 1.6 times higher than the Organization for Economic Co-operation and Development (OECD) average, and a government-led AMR management policy has been implemented since 2016. In 2016, at the National Policy Coordination Meeting at the government level, the First Korean Action Plan on AMR (2016 - 2020) was presented to provide management measures. However, the improvement in human antimicrobial use or resistance was insufficient compared to the initial expectation, with a continuous increase in resistance to major antimicrobials being observed. Currently, the Second Korean Action Plan on AMR (2021 - 2025) is being implemented, and the settlement of ASP at domestic medical facilities is a key strategy for overcoming AMR [10, 11]. The first step is to define ASP at domestic medical facilities by developing core elements of ASP applicable to general hospitals or higher-grade medical facilities, which

are acute care hospitals. Considering differences across types of medical facilities and the ability to invest in the workforce or cost to implement ASP, subdivisions of the core elements should be made based on the type of medical facility or situation.

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2. Scope

Based on a systematic literature review, this guideline presents the rationale for the core elements of ASP implementation for the optimal use of antimicrobials. This guideline is subject to future revisions based on changes in domestic circumstances.

3. Organization of the Korean ASP Core Elements Development Committee

The Korean ASP Core Elements Development Committee was established in November 2021. Fifteen experts recommended by the Korean Society for Antimicrobial Therapy, Korean Society of Infectious Diseases, Korean Society for Healthcare-associated Infection Control, Korean Society of Pediatric Infectious Diseases, and Korea Society of Health System Pharmacists, as well as external advisory organizations, including the Korea Institute for Healthcare Accreditation and the Health Insurance Review and Assessment Service (HIRA), participated in the development of guidelines with evidence-based and multidisciplinary approaches.

4. Literature review and analysis of introduction cases in Korea and other countries

ASP-related literature and cases of ASP introduction in Korea and other countries were investigated through systematic literature searches, and the existing clinical treatment guidelines were reviewed. For international literature, PubMed (www.pubmed.gov), Cochrane Library (www.cochranelibrary.com), and EMBASE (www.embase.com) were used as the main search databases to establish clinical practice guidelines. For the Korean literature, KMBase (www.kmbase.medric.or.kr) and the Research Information Sharing Service were used. In addition, guidelines from other countries were reviewed to analyze the ASP introduction cases, and 135 references were cited.

5. Process of selecting the core elements of Korean ASP implementation

This guideline focused on developing a checklist for each medical facility to check the application, along with developing core elements of the implementation of ASP. A Delphi survey was conducted to reach agreement between the participating researchers and advisors on the feasibility, importance, and possible implementation period of the prepared checklist items.

6. External expert review

A second opinion was collected from the expert group on the guideline recommendations prepared through the internal discussion of the ASP Core Elements Development Committee, and the contents were revised and supplemented through additional meetings. Additionally, opinions of the Korean Society for Antimicrobial Therapy were collected, and the guidelines were completed accordingly.

This guideline was reviewed and approved by the Korean Society for Antimicrobial Therapy, Korean Society of Infectious Diseases, Korean Society of Health System Pharmacists, Korean Society for Healthcare-associated Infection Control, and Korean Society of Pediatric Infectious Diseases before publication.



7. Glossary of terms and abbreviations

The academic terms related to this guideline were written in Korean based on the 6th edition of the medical glossary (published by the Korean Medical Association, revised in March 2020), and terms whose meanings were not clearly conveyed in Korean were written in Korean, with the English terms in parentheses. Terms that could not be expressed in Korean, such as pathogen names, proper nouns, drug names, and units were written in English.

CORE ELEMENTS OF ASP

1. Leadership commitment

(1) Concept

Hospital leadership is responsible for operating ASP to help different departments cooperate in the program. The hospital leadership should recognize the importance of ASP and provide sufficient resources, such as necessary organizations, workforce, budgets, and information technology.

(2) Checklist

- 1. Regulations to operate the ASP committee with the participation of hospital leadership are established, and regular meetings are held.
- 2. Hospital leadership allocates the budget and workforce necessary to implement the ASP.
- **3.** Hospital leadership sets the implementation of the ASP as the priority goal of the facility and manages indicators to measure program performance.

(3) Usage examples

- ① Hospital leadership that can support the necessary resources (workforce, organization, budget) for ASP activities and take responsibility for the results should participate in the ASP committee.
- ② The ASP committee should hold regular meetings to deliberate and decide on the contents, results, and necessary resources of the ASP.
- ③ The ASP committee can be operated independently according to the circumstances of the medical facility in the form of a drug management (pharmacist) committee, an infection control committee, or a subcommittee of the Quality Improvement and Patient Safety Committee. If the ASP committee is not operated independently, the ASP agenda must be carried out as a fixed and separate item.
- ④ The index for measuring the performance of ASP can be selected and set according to the circumstances of the medical facility from the components of the tracking among the core elements of ASP implementation.

(4) Evidence-based description

The support of the senior leadership of the hospital, particularly the head of the medical institution, director of nursing, and director of the pharmaceutical department, is critical to the success of ASP. This plays an important role in securing the human and material resources necessary to achieve its goals [7]. The head of the facility should make efforts, such as providing enough time for those in charge of the ASP to manage and implement it every day and holding regular meetings to evaluate the resources necessary to achieve the goals of the hospital to improve antimicrobial use. Therefore, work related to ASP should be officially



included in the job description of employees engaged in ASP, and sufficient time should be guaranteed to engage in related work.

To incentivize medical facilities to invest workforce and finances in ASP, government agencies should compensate medical facilities by setting an appropriate fee for ASP activities. An appropriate ASP is effective in optimizing antimicrobial use and minimizing antibiotics resistance and *Clostridioides difficile* infection (CDI) [12, 13]. Additionally, since ASP reduces the use of hospitals and healthcare resources, ultimately reducing medical costs and enabling such savings to be used to support the workforce involved in ASP and the finances necessary operating of the program, hospital leadership must be willing to fully support it, considering its positive effects [14]. In addition, for continuous ASP activities, hospital leadership should receive regular reports on the content and results of the activities and provide support to improve the system.

2. Operating system

(1) Concept

Hospital leadership is responsible for organizing and operating a multidisciplinary antimicrobial stewardship team (hereinafter the "dedicated team"). The dedicated team comprises a physician with expertise in antimicrobial use in charge, a dedicated pharmacist with knowledge of antimicrobial use, and the workforce necessary for other medical facilities to operate ASP.

(2) Checklist

- 1. There are departments as well as dedicated employees and teams that implement ASP with regulations for the individual roles and ASP procedures.
- 2. The dedicated team that conducts ASP should be a multidisciplinary team involving physicians, pharmacists, nurses, clinical microbiologists, infection control professionals, and information system professionals.
- 3. There should be a leader in charge of the operation of ASP.
- 4. There is a dedicated pharmacist who has completed ASP training and participates in its activities.

(3) Usage examples

- ① Dedicated employees who operate ASP refer to employees who do not perform any tasks other than ASP tasks, with related tasks officially included in their job description.
- ② Dedicated employees must periodically complete education on ASP.
- ③ To successfully implement ASP, physicians, pharmacists, nurses, clinical microbiologists, infection control professionals, and information system professionals must form a multidisciplinary team for collaboration.
- ④ Based on clinical experience, leadership experience, extensive multidisciplinary relationships, and training, an adult or pediatric infectious disease specialist is recommended as the leader of the multidisciplinary ASP team.
- (5) The composition, roles, procedures, and working hours of a dedicated team operating an ASP were stipulated in an official document.
- (6) A pharmacist trained in ASP is a key member of the ASP team. The pharmacist supports appropriate antimicrobial use, including a prospective audit through intervention and feedback, education, work structure development and tracking for antimicrobial use, and the establishment of antimicrobial and infectious disease-related policies and guidelines.



(4) Evidence-based description

The routine collaboration of physicians, pharmacists, nurses, clinical microbiologists, infection control professionals, and information technology professionals is a core activity in ASP [7]. Successful implementation of ASP requires a multidisciplinary team that can leverage its expertise, with hospital leadership and related committee members supporting and collaborating with the ASP team (Fig. 1) [15].

Infectious disease and pediatric infectious disease specialists routinely perform tasks such as diagnosing and treating complex infectious diseases, prescribing appropriate antimicrobials, and managing the effects of antimicrobial use. Their leadership competencies are recognized in many facilities for their roles as infection control directors or quality improvement and patient safety directors [16]. Infectious disease specialists develop guidelines for the use of antimicrobials based on antimicrobial susceptibility data and research results on antimicrobial treatment and interventions, providing direct feedback to the prescribing physician on antimicrobial selection. Considering clinical experience, leadership experience, wide multidisciplinary relationships, and training processes, an infectious disease specialist is suitable as a leader of the ASP team that can effectively implement ASP by maximizing the potential of ASP team members [16].

The United States Center for Disease Control and Prevention (CDC) recommends that a clinician or pharmacist be appointed as the director or co-director of an ASP to be responsible for the operation and outcome of the program for its successful implementation [17]. According to a 2019 National Healthcare Safety Network (NHSN) survey, 59% of hospitals in the United States had ASPs jointly led by physicians and pharmacists. The directors of ASPs regularly report the results to hospital leadership and committees and can improve antimicrobial use through regular ASP rounds and discussions with the physician who prescribe antimicrobials [18, 19].

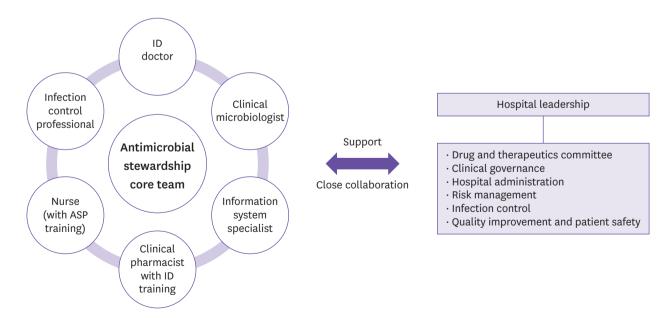


Figure 1. Multidisciplinary team responsible for implementing antimicrobial stewardship. Adapted from Yoon YK, et al. Infect Chemother. 2021;53(3):617-59, according to the Creative Commons license.

ID, infectious diseases; ASP, antimicrobial stewardship program.



In Australia, it is recommended to form a multidisciplinary antimicrobial stewardship team, including at least one physician and a pharmacist in charge, for ASP implementation. For medical facilities that lack professional manpower and financial resources, the manpower and role of the ASP team depend on the type and size of the medical facility. While the director of an ASP is supposed to be an infectious disease specialist, a pharmacist specializing in infectious diseases, or a clinical microbiologist, the director of the medical facility can undertake the role of a director and operate the ASP with the advice of a local pharmacist, an infectious disease specialist, or a clinical microbiologist through the local network, or with the help of a visiting physician or pharmacist [20].

In Canada, it is recommended that a pharmacist be appointed along with a clinician as the director or co-director of an ASP. However, if professional manpower is not available at a facility, the ASP can be operated through the participation of local and external experts [21]. In an observational study of 73 hospitals in Canada implementing ASPs, the use of antimicrobials tended to decrease when a professional was in charge of the program. Nonetheless, the adjusted analysis revealed no significant differences. It is necessary for the effective operation of the ASP for professional personnel such as clinicians and pharmacists to be in charge of the ASP, but time and financial support to carry out the ASP work must be guaranteed [22].

The ASP guidelines by the Infectious Disease Society of America (IDSA) recommend that an infectious disease specialist with expertise and experience in ASPs or a pharmacist specializing in infectious diseases play a key role in the operation of an ASP [23]. Many developed countries that introduced and applied ASPs before Korea emphasized the need to expand the professional workforce essential to operate ASPs [24-28]. In Japan, a nationwide survey in 2018 identified the status of healthcare human resources related to ASPs, confirming that the number of full-time equivalent (FTE) experts in ASP independently related with the implementation and improvement of ASP [28, 29]. In addition, the medical reimbursement system was improved to add the ASP implementation fee calculated based on multidisciplinary healthcare workers participating in ASP in 2018, relative to the existing infection control fee [28].

In Korea, calculating the human resources required to operate ASPs at eight medical facilities in 2020 revealed a median FTE required per 100 beds of 1.2 (interquartile range [IQR]:1.02 - 1.38) and an FTE per 100 patients using antimicrobials of 2.28 (IQR:1.93 - 2.62) [30]. Considering the domestic reality, appointing an ASP director with expertise is difficult even at the medical facilities of general hospitals or higher grades. The situation of the professional workforce is poor, with difficulties in seeking help from local healthcare networks, unlike overseas. To effectively implement ASP in domestic medical facilities, it is necessary to expand the relevant professional workforce. Therefore, long-term educational and economic support is required. The shortage of a professional workforce cannot be solved by a short-term method using only temporary support or evaluations. Conversely, an inappropriate change may be introduced in the formal mobilization of nonprofessional personnel who cannot fulfill the role of the actual director of ASP at a medical facility. To encourage professional personnel to participate in ASP activities actively, the fee for ASP activities of the infectious disease specialist in charge should be granted, and a reasonable system and economic compensation should be provided to motivate physicians to select an infectious disease department when selecting the specialization subject. In addition, human resource education should be imparted to pharmacists specializing in the infectious disease division by preparing a support system, such as a fee for administering antimicrobials.

Dedicated pharmacists participating in the ASP team are responsible for managing antimicrobial use, developing antimicrobial use guidelines, participating in antimicrobial stewardship committees, participating in rounds and conferences, monitoring and reporting the adverse effects of antimicrobials, identifying and providing information on the latest treatment trends, education and academic research, and quality improvement (**Table 1**) [31].

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Table 1. Role of the dedicated pharmacist in charge of antimicrobial stewardship programs

The pharmacists' role	Activities
Antimicrobial usage	- Monitoring and assessment of antimicrobial usage.
management	- Quarterly assessment of antimicrobial usage.
	- Quarterly assessment of the appropriate use of prophylactic antimicrobials for in-hospital surgery.
	- ASP in collaboration with relevant committees and other professions.
	- Monitoring the period of antimicrobial use and intervening prescriptions for unnecessary long-term use.
	- Intervention of conversion from parenteral to oral therapy.
	- Promoting appropriate use of antimicrobials and minimizing misuse of antimicrobials.
Antimicrobial use guideline development	- Participating in the development of clinical guidelines with relevant departments in consideration of the status of identification of antimicrobial-resistant bacteria for infectious diseases in the hospital.
	- Development of guidelines for the use of antimicrobials against diseases and drugs that can cause prescription errors.
	- Recommending antimicrobials suitable for each disease and an appropriate dosage regimen by managing and updating the in- hospital antimicrobial prescription system.
	- Providing the latest information on antimicrobials and managing the antimicrobial prescription system.
	- Managing the application, development, tracking, and reporting trends of ASPs with responsible companion leaders in ASP outcomes.
Preparation of the ASP	- Composition of the ASP committee (name may differ across hospitals)
committee	- Establishment and implementation of policies for the proper use of antimicrobials.
	- Education on the antimicrobial use and review of the antimicrobial prescription system management.
	- Participation in the review and implementation of antimicrobials and vaccines.
	- Report on the occurrence of antimicrobial resistance.
	- Review and publication of the activities of the ASP team.
	- Reporting the work of the ASP team to the hospital management through committee activities.
Participation in rounds	- Collaboration with healthcare workers on antimicrobial treatment
and conferences	- As a member of the ASP team, attending rounds and conferences to understand the patient condition and treatment plan and sharing the latest information necessary for patient treatment.
	- Providing healthcare workers with information on drugs, adjusting and intervening for drug treatment, and providing additional pharmaceutical services, such as pharmacokinetic consultation and intensive nutrition, if necessary.
	- Antimicrobial-related drug interaction monitoring and information provision.
Monitoring and reporting antimicrobial adverse	- Identifying the causal relationship of drug adverse effects by identifying symptoms suspected of drug adverse effects in the history of patients or during inpatient care and collecting and evaluating information.
effects	- Reporting according to the adverse effect reporting system at the hospital, recommending countermeasures and alternative drugs to healthcare workers, and necessary intervention.
	- Antimicrobial adverse reaction monitoring and information provision.
	- Management of history such as antimicrobial-related allergic reactions.
Identifying and providing	- Understanding domestic and international guidelines related to infectious diseases and treatment and identifying the occurrences
information on the latest	or introduction of new drugs in South Korea, changes in insurance benefits, etc.
treatment trends	- Providing up-to-date information to healthcare workers, if necessary.
	- Management of the prescription antimicrobial list and formulary at the hospital.
Conducting educational	- Providing education and information on infectious drugs to healthcare workers, pharmacists, and pharmacy students.
and academic research	- Conducting research of infectious drugs and publishing academic papers.
and quality improvement	- Newsletter publication.
activities	- Education for patients, guardians, and visitors.
	- Promoting efficient ASP activities by participating in work improvement activities of relevant in-hospital committees and councils.
	- Provision of important information and advice on antimicrobials for patients and healthcare professionals.
	- Participation in antimicrobial-related public campaigns at local and national levels.
Local pharmacy	- Management of antibiotic education, taking history, adverse reactions, etc. by utilizing the advantage of easy access to patients in the community.
	- Recognizing the symptoms of infectious diseases that require a hospital visit and recommending treatment.
	- Public health hygiene education.
	- Providing information on vaccination programs, such as influenza vaccination.

ASP, antimicrobial stewardship program.



In the United States, pharmacists can effectively operate ASP in hospitals by actively participating as leaders or co-leaders [32]. In a study by Waters et al., pharmacists specializing in infectious diseases became the head of ASP and conducted team rounds with other medical staff; 2,457 prescription interventions were performed in 33 months, and the prescription intervention acceptance rate was 91.8%. In addition, these activities significantly reduced the duration of hospital stay for patients hospitalized for community-acquired pneumonia, thereby saving \$355,000 (58%) over two years [33]. A Japanese study by Niwa et al. reported the effect of promoting the optimal use of antimicrobials, reducing costs, and reducing hospital stays through pharmacist activities in ASP [34]. A study conducted in Thailand by Apisarnthanarak et al. compared the group that consulted a pharmacist specializing in infectious diseases after education with the group that did not, reporting that the use of inappropriate antimicrobials and length of hospital stay was significantly reduced in the consultation group [35]. A meta-analysis on the effect of ASP led by pharmacists in the Middle East reported a significant decrease in inappropriate antimicrobial prescriptions in the group that implemented ASP (relative risk = 0.36, 95% confidence interval:0.32 - 0.39) [36].

3. Action

(1) Concept

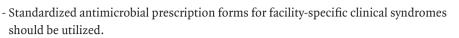
Various interventions are required to support optimal antimicrobial prescriptions. Intervention activities included evaluation and feedback on whether antimicrobial administration was necessary, the selection of appropriate antimicrobials, correct use, and appropriate administration period.

(2) Checklist

- 1. Audit and feedback on the use of antimicrobials are under implementation.
- 2. Antimicrobial restriction and authorization of prescription for specific antimicrobials are under implementation.
- 3. An antimicrobial prescription form or a computerized antimicrobial prescription system recommends and supports antimicrobial prescriptions based on ASP guidelines at medical facility.
- 4. Interventions for major infectious diseases or other supplementary ASP interventions are conducted.
 - Major infectious diseases include urinary tract infection, community-acquired pneumonia, bloodstream infection, and *Clostridioides difficile* infection (CDI).
 - Supplementary ASP interventions include minimizing antimicrobial combination therapy, antimicrobial de-escalation, recommending optimal duration of treatment, changing intravenous antimicrobials to oral antimicrobials, utilizing therapeutic drug monitoring (TDM) for specific antimicrobials, and rapid reporting of microbiological results.

(3) Usage examples

- ① Core interventions
 - For antimicrobials requiring special management, pre-authorization is performed to ensure that optimal antimicrobials are administered for appropriate indications.
 - Antimicrobial restriction and authorization programs for antimicrobials that require special management should be utilized.
 - Facility-specific antimicrobial treatment guidelines should be developed based on domestic guidelines or local antimicrobial susceptibility data.



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- The Korean Society for Antimicrobial Therapy (KSAT) antimicrobial prescription support program is available on the KSAT website.
- Relevant departments collaborate to develop an optimized antimicrobial prescription protocol for patients with major infectious diseases (*e.g.*, collaboration with the ASP team and intensive care unit).
- Face-to-face consultation regarding patient care with a physician from the ASP team should be implemented.
- ② Supplementary interventions
 - Allergies before administering antimicrobials should be assessed.
 - A process to evaluate the adequacy of prescribed antimicrobials 48 72 h after the initial prescription of antimicrobials should be introduced.
 - Antimicrobial treatment guidelines for conversion from parenteral to oral therapy should be utilized.
 - Guidelines to recommend doses based on the weight, renal and liver function of patients should be used.
 - Guidelines recommending simplified or antimicrobial de-escalation, according to the antimicrobial susceptibility of the causative microorganisms, should be utilized.
 - An automatic alert system based on the duplicative spectrum of antimicrobials or drugdrug interactions should be utilized.
 - Automatic antimicrobial timeouts should be implemented (*e.g.*, surgical prophylactic antimicrobials and empirical antimicrobials).
 - TDM for specific antimicrobials should be utilized.
 - A rapid diagnosis system for the rapid reporting of microbiological reports and selective antimicrobial susceptibility testing results should be established.
 - Biomarkers such as procalcitonin should be introduced and used to shorten the duration of antimicrobial administration.
 - Microbiological culture sample collection and real-time transportation systems before antimicrobial administration should be implemented appropriately.
 - Evidence-based measures to improve the use of antimicrobials in certain infectious diseases and facility-specific situations should be shared (*e.g.*, community-acquired pneumonia, urinary tract infection, skin and soft tissue infections, intra-abdominal infections, sepsis, bloodstream infections [central venous catheter infections], surgical prophylactic antimicrobials, surgical site infection, suspected methicillin-resistant *Staphylococcus aureus* [MRSA] infection, evaluation of antimicrobial therapy used for other purposes in patients with novel CDI, and inappropriate use of antimicrobials for contaminated specimens or colonization).

(4) Evidence-based description

① Core strategies

The ASP has two main strategies: prospective audit with feedback (back-end) programs, and antimicrobial restriction and preauthorization (front-end) programs [15].

Prospective audits with feedback programs have the advantage of partially guaranteeing the autonomy of the prescribing physicians, and the effects of positive relationship formation and education are expected as the manager and the prescribing physician communicate. A manager's workload can be adjusted to the level of available resources by controlling the



timing and type of antimicrobial administration. Interventions can be provided based on the results of the culture to increase the prescribing physician's acceptance, and antimicrobial de-escalation and duration of treatment can be discussed. Depending on how effectively the manager communicates with the medical staff, adherence to the appropriate antimicrobial prescription may vary, and the manager may perform labor-intensive tasks [7, 23, 37, 38]. The recently introduced handshake stewardship approach provides immediate, individualized feedback to medical staff through a round-based, individualized approach [19].

Antimicrobial restriction and preauthorization programs are strategies by which medical staff obtain preauthorization for a specific antimicrobial before prescribing it to a patient. Prospective audits with feedback programs are strategies in which the administrator evaluates the appropriateness of antimicrobial prescription after a certain period since the antimicrobial has been prescribed.

Antimicrobial restriction and pre-authorization programs have the advantage of reducing antimicrobial use by reducing the frequency of unnecessary antimicrobial administration. They can increase the likelihood of appropriate empirical antimicrobials being administered from the beginning and change the antimicrobial prescription pattern within a short period. The disadvantage is that the autonomy of the medical staff may be lost as the ASP team directly controls the overall use of antimicrobials. Although various interventions are likely to be implemented depending on the proficiency of the ASP manager, negative interactions may occur because of the conflicting relationship between the prescribing physician and the manager. Furthermore, as the workload of ASP managers increases, handling preauthorization requests that occur during off-hours becomes a problem, leading to delayed antimicrobial administration [7, 23, 37]. To overcome such disadvantages, the use of antimicrobials is occasionally restricted to 3 - 5 days after the prescription, when the results of microbiological tests are confirmed and the clinical response to empirical antimicrobials can be evaluated [39].

The two ASP strategies are mutually exclusive and choosing one is not necessary. Considering the characteristics and unique culture of the hospital, attitudes of medical staff, available resources, and strengths and weaknesses of each core strategy, strategies can be selectively mixed and implemented according to the antimicrobial or patient group [40].

② Supplementary strategies

- Physician-led intervention

Antimicrobial streamlining or de-escalation is a strategy to reduce unnecessary antimicrobial combination therapy and switch to an antimicrobial with a narrow spectrum [41]. In most cases, the use of broad-spectrum antimicrobials or antimicrobial combination therapy is common, with empirical antimicrobials administered for severe infections. To support antimicrobial streamlining or de-escalation, the causative organism and antimicrobial susceptibility should be actively identified [42, 43].

Education is an important component of ASP interventions because it directly affects antimicrobial prescription behavior [44]. Education through face-to-face discussions on antimicrobial prescriptions has a relatively more lasting effect than passive activities such as delivering lectures or circulating printed materials or e-mails [45]. Education should be provided to various healthcare workers such as physicians, pharmacists, physician assistants, and nurses. In particular, the need for education of medical and nursing students has been emphasized [46].



Practical guidelines and clinical pathways for each infectious disease tailored to the characteristics of medical facilities are shared in a multifaceted manner to improve the treatment behavior of the medical facility in accordance with the guidelines and increase the frequency of appropriate initial empirical antimicrobial administration [47-49]. Prescription sets and checklists for best practice alerts can be used to incorporate treatment guidelines or policies into the prescription process [50]. When creating clinical guidelines or treatment policies, the ASP team and various healthcare workers should actively communicate and participate. In addition, if it is difficult to use internal guidelines at medical facilities, empirical antimicrobial recommendations can be used for each clinical disease/syndrome and suspected infection situation according to the KSAT antimicrobial prescription support program available on the KSAT website. A specific syndrome-based ASP using these guidelines may be more effective in reducing antimicrobial use or CDI than interventions through a prospective audit with feedback programs [51-53].

Antimicrobial combination therapy can be expected to have a synergistic effect on each antimicrobials as well as to reduce the development of resistance or to expand the antimicrobial range before confirming the causative bacteria and antimicrobial susceptibility. It is also recommended as an empirical antimicrobial treatment for ventilator pneumonia, infective endocarditis, and multidrug-resistant organism (MDRO) infections [54-57]. However, treatment with a single antimicrobial is generally recommended for identification of causative organisms [58].

- Pharmacist-led intervention

Optimization of dosage and duration for infectious syndromes maximizes the effectiveness of antimicrobial treatment and minimizes adverse effects [7, 23, 37]. Therefore, physicians should administer antimicrobials based on clinical guidelines and actively utilize TDM [59]. When prescribing antimicrobials, it may be useful to use dose optimization software that considers the site of infection, antimicrobial susceptibility, and kidney or liver function of the patient. Shortening the duration of antimicrobial administration in various infectious diseases positively affects treatment results for pneumonia, skin and soft tissue infections, urinary tract infections, intra-abdominal infections, and gram-negative bacteremia [60-64]. To optimize the duration of antimicrobial administration, a computerized antimicrobial prescription program may be used to stop the prescription after administration of a certain antimicrobial for a certain duration. Alternatively, an alert program could be used.

Conversion from parenteral to oral therapy is part of the intervention method that applies a unified clinical pathway by establishing a protocol for the use of appropriate antimicrobials according to the characteristics of the hospital or patient, enabling the replacement of parenteral antimicrobials with oral antimicrobials in a timely manner [65]. The use of oral antimicrobials can reduce hospital stays, costs, and adverse effects of injections [66, 67]. A strategy should be employed to encourage outpatient treatment with ertapenem or teicoplanin, which can be administered once a day [68, 69], or to switch to oral linezolid instead of vancomycin or teicoplanin in patients with MRSA infection [70].

- Microbiological test-based intervention

Rapid diagnostic testing requires fostering a cooperative relationship between the ASP teams and microbiological laboratories. The sooner culture results are reported, the sooner appropriate antimicrobials can be prescribed [71-74]. Rapid diagnostic testing for respiratory viruses or respiratory virus polymerase chain reaction (PCR) can help avoid additional test



prescriptions, reduce unnecessary antimicrobial use, and help select appropriate therapeutic agents such as antiviral agents [75, 76]. Antimicrobial prescription can be improved by conducting a causative bacteria test using multiplex PCR on respiratory samples from patients with ventilator-associated pneumonia [77]. In addition, the GeneXpert MRSA/SA (Cepheid, Sunnyvale, CA, USA), Verigene nucleic acid microarray assay, or matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry allows early identification of pathogens, and applying it to ASP may enable early administration of optimal antimicrobials [71, 78, 79].

When antimicrobial susceptibility to the causative organism is reported, selective reports of the specific antimicrobial susceptibility are more helpful than providing the susceptibility results of all antimicrobial susceptibility results simultaneously [80-82].

The use of biomarkers such as procalcitonin can shorten the duration of antimicrobial administration in patients with sepsis or community-acquired pneumonia [83-85]. In particular, the procalcitonin test and PCR for detecting of respiratory viruses can be used for computerized ASP based on an alarm in the computerized medical record to reduce the use of antimicrobials [86].

- System to support ASP interventions

The antimicrobial order forms are standardized to include the name of the drug, dose, usage, administration duration, and infectious disease for prescribing antimicrobials, and antimicrobial order forms for specific clinical syndromes can be used to improve the appropriate antimicrobial prescription rates. In addition, guidelines for evaluating antimicrobial allergy before administration may be applied [7, 23].

Electronic medical record tools with clinical decision support systems can help administer doses tailored to patients' age, renal function, and specific infectious diseases, and help prescribe antimicrobials suitable for AMR patterns [87]. If medical records are computerized with physicians entering antimicrobial prescriptions, the appropriateness of a specific antimicrobial prescription can be evaluated more effectively, shortening the time required for management [88]. Recently, mobile devices have been used for ASP [78, 79], followed by the development of customized smartphone clinical decision support software, enhancing accessibility to intranet-based guidelines [89-91].

4. Tracking

(1) Concept

Tracking refers to a series of survey activities performed to identify the status of antimicrobial use and to evaluate ASP. Through tracking, areas requiring improvement related to antimicrobial prescriptions were identified, and the effectiveness of antimicrobial prescription interventions was evaluated.

(2) Checklist

- 1. The use of antimicrobials within a medical facility is being tracked regularly.
- 2. The status of the occurrence of six multidrug-resistant organisms (methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-intermediate/resistant S. aureus [VISA/VRSA], vancomycin-resistant Enterococci [VRE], multidrug-resistant *Acinetobacter baumannii*



[MRAB], multidrug-resistant *Pseudomonas aeruginosa* [MRPA], and carbapenemresistant *Enterobacteriaceae* [CRE]), which are designated as communicable diseases in Korea are tracked regularly (at least once every quarter).

- 3. The incidence of CDI is tracked regularly.
- 4. The antimicrobial susceptibility results for frequently isolated bacteria are tracked regularly.
- 5. The occurrence of antimicrobial adverse events is tracked regularly.
- 6. The acceptance of recommendations based on audit and feedback on the use of antimicrobials is tracked regularly.
- 7. The degree of approval of antimicrobial restriction and prescription authorization of for specific antimicrobials are tracked regularly.
- 8. Antimicrobial prescription interventions for major infectious diseases or other supplementary ASP interventions are tracked regularly.
- Major infectious diseases include urinary tract infection, community-acquired pneumonia, bloodstream infections, and CDI.
- Supplementary ASP interventions include minimizing redundant antimicrobial combination, antimicrobial de-escalation, recommending optimal duration of treatment, switching parenteral antimicrobials to oral antimicrobials, utilizing TDM for specific antimicrobials, and rapid reporting of microbiological results.

(3) Usage examples

1 Antimicrobial usage measurement

Measurement of antimicrobial usage includes measuring antimicrobial usage by category, measuring changes in antimicrobial usage over time within medical facilities (internal benchmarking), comparative analysis of antimicrobial usage with other facilities (external benchmarking), and identifying antimicrobial usage patterns using antimicrobial usage indicators (*e.g.*, Standardized Antimicrobial Administration Ratio [SAAR]).

② ASP outcome measurement

The ASP outcome measurement includes measurements of the AMR rate, CDI rate, cost reduction by ASP, adverse reactions caused by antimicrobials, and prognosis of infectious diseases.

③ Assessing the process of antimicrobial prescribing intervention activities Assessing the process of antimicrobial prescription intervention activities includes measuring the acceptance of the audit with feedback activities, measuring the degree of restriction or approval of antimicrobials included in antimicrobial restriction and authorization activities, measuring the adherence to antimicrobial treatment guidelines within the facility, measuring the degree of conversion from parenteral to oral therapy, measuring any redundant antimicrobial combination, and measuring the duration of antimicrobial administration.

(4) Evidence-based description

① Antimicrobial usage measurement

After examining overseas cases, monitoring the use of antimicrobials at medical facilities basically comprises the "evaluation of antimicrobial usage at medical facilities nationwide," using various datasets, such as medical insurance claims, electronic health records, and drug distribution data [92-95]. In some developed countries, including the United States, a benchmarking system that performs comparisons with external hospitals, measures



changes in antimicrobial usage over time inside the hospital, and provides feedback is being operated at the national level to evaluate the level of antimicrobial use at individual medical facilities along with the evaluation of antimicrobial usage at medical facilities nationwide and to efficiently set improvement goals [93]. In Korea, the Korea National Antimicrobial Use Analysis System (KONAS), a benchmarking system that allows individual facilities to measure the amount of antimicrobials used within their facilities and compare and analyze them with those of other facilities, has been established in 2021, and it is necessary to promote each medical facility to actively utilize the system [96]. When an individual hospital applies for KONAS participation and agrees to transfer health insurance claim data from HIRA to KONAS, antimicrobial usage by class within the medical facilities is provided by days of therapy and daily defined doses, respectively. Simultaneously, by providing SAAR, which is an index comparing the expected antimicrobial use with the actual antimicrobial use of the facility, the level of antimicrobial use at the facility can be efficiently determined [96, 97].

According to the Roadmap of Antimicrobial Usage Monitoring System Applicable to Domestic Medical Facilities in Korea, which was developed in 2021, tertiary hospitals should first be included in the monitoring system to benchmark the use of antimicrobials, followed by expansion to secondary and primary (hospitals and long-term care facilities) hospitals in five to ten years [98]. Appropriate data sources were identified to include health insurance claims and electronic health records from each hospital. The health insurance claims data currently being used for KONAS cover almost all healthcare institutions in Korea and enable the operation of a monitoring system. However, the data are slightly different from the actual antimicrobial prescription data, and a relatively long time lag (approximately 1.0 - 1.5 years) from the time of prescription to the time of data generation exists [98]. Electronic health records in hospitals best reflect actual antimicrobial usage, but in Korea, no unified computerized system exists among hospitals, and most hospitals do not have a system measuring the antimicrobial usage or workforce to analyze the amount of antimicrobial use, making it difficult to use electronic health records. From a long-term perspective, a system should be established that can analyze and monitor antimicrobial usage based on electronic health records led by the KDCA [93, 96].

② ASP outcome measurement

ASP can reduce the rates of AMR and CDI, medical expenses, and frequency of adverse antimicrobial reactions while improving the prognosis of patients with infectious diseases [15]. According to the Core Elements of Hospital Antibiotic Stewardship Programs:2019, published by the CDC in the United States in 2019, the AMR rate, incidence of CDI, and effect of ASP on medical costs are presented as performance indicators for ASP [99].

In several studies, including Korean studies, an increase in the use of antimicrobials has been reported as a major risk factor for colonization or infection by antimicrobial-resistant bacteria [100-102]. According to several recently published studies, ASP reduces the amount of antimicrobial use, selection pressure of antimicrobials, and AMR rate at individual facilities by implementing an audit with feedback of antimicrobial prescriptions or infection control activities [103, 104]. In a study at a university hospital with 800 beds in Korea, antimicrobial restriction programs for broad-spectrum antimicrobials, including carbapenems and glycopeptides, led by infectious disease specialists, and an audit with feedback for redundant combinations of antimicrobials with anti-anaerobic activities tended to decrease the ciprofloxacin and oxacillin resistance rates of *S. aureus* and carbapenem resistance rates of *P. aeruginosa* in intensive care units [105]. Currently, national AMR



monitoring systems, such as the Korea Global Antimicrobial Resistance Surveillance System (Kor-GLASS) and the Korean Antimicrobial Resistance Monitoring System (KARMS), monitor antimicrobial-resistant bacteria in Korea. However, determining the status of AMR at individual facilities remains difficult. Since each facility is obligated to collect data and report MRSA, VISA/VRSA, MRAB, MRPA, VRE, and CRE to the KDCA as communicable diseases, such data may be used to evaluate the outcome of ASPs at facilities.

Antimicrobial exposure is a risk factor for CDI. Third generation cephalosporins, fluoroquinolones, and clindamycin are closely associated with the occurrence of CDI [106, 107]. Limiting exposure to these high-risk antimicrobials through ASP efficiently prevented CDI. Applying ASP to the use of clindamycin and broad-spectrum antimicrobials, particularly cephalosporins and fluoroquinolones, is effective in decreasing CDI [108-110]. Although various diagnostic tools for CDI exist, a single test for diagnosis is not recommended, and even in large hospitals in Korea, the diagnostic method for CDI varies slightly across hospitals [110]. In the United States, it is recommended to monitor the status of hospitalacquired CDI to measure the effectiveness of ASP and monitor the prevalence of CDI in hospitals. According to the NHSN of the CDC, CDI that occurs at or after four days of admission is defined as hospital-acquired CDI [111, 112]. Therefore, a system should be established for systematic CDI surveillance in Korea.

The CDC in the United States suggests that it is not appropriate to establish cost savings as an important outcome measure of antimicrobial use management program success, but it can be helpful if cost reduction is used as a necessary resource for ASP [99]. The reduction in the medical cost of ASP mainly results from the decreased use of antimicrobials. Performing an audit with feedback activities or antimicrobial restriction and preauthorization activities markedly reduces the use of antimicrobials, thereby leading to cost savings [113-115]. A Korean study that conducted a program that recommended switching to oral therapy for patients who met certain conditions among inpatients receiving fluoroquinolone injections reported that the cost of fluoroquinolone in the patient group who accepted the recommendation was approximately 35% lower than that of those who did not [116]. In addition to reducing drug costs, many factors can reduce medical costs. However, there is no way to measure these factors easily, so it seems difficult to apply the indicator smoothly at this point.

(3) Assessment of the process of antimicrobial prescription intervention activities Assessment of the process of antimicrobial prescription interventions to improve antimicrobial prescribing-related quality may focus on specific interventions performed in hospitals [15, 99]. Tracking the type and acceptance of audits with feedback can help identify areas where additional education and interventions may be useful. The degree of prospective audit with feedback was evaluated along with monitoring whether treatment was postponed. In addition, adherence to antimicrobial treatment guidelines within the facility, whether antimicrobial time is performed, conversion from parenteral to oral therapy, and redundant antimicrobial combination therapy can be tracked, and whether the duration of antimicrobial administration is appropriate can be reviewed.

5. Reporting

(1) Concept

Antimicrobial use, antimicrobial resistance, and antimicrobial prescription intervention activities are regularly reported to the hospital leadership, who share them with all medical staff involved in antimicrobial prescription to promote appropriate antimicrobial prescription.



(2) Checklist

- 1. The information on antimicrobial use (changes in dosage and prescription patterns based on ASP) is reported to the hospital leadership and the ASP committee and shared with relevant employees.
- 2. The information on antimicrobial resistance is reported and shared.
- 3. The information on antimicrobial prescription by individuals or groups compliant with the medical facility's guidelines for the treatment of infectious diseases is reported and shared.
- 4. The information on antimicrobial restriction and prescription authorization for specific antimicrobials is shared with prescribing medical staffs.
- 5. The adherence to recommendations based on audit and feedback interventions on the use of antimicrobials is shared with prescribing medical staffs.

(3) Usage examples

- ① Reporting antimicrobial usage and sharing with employees: Antimicrobial usage of the entire hospital or group (*e.g.*, emergency department, intensive care unit, division of high antimicrobial use, specific diseases, such as sepsis, etc.) and individual antimicrobial usage are reported. Antimicrobial usage amounts and prescription patterns according to ASP were reported to the ASP committee and shared with relevant employees.
- ② Reporting antimicrobial resistance and sharing with employees: Information on the antimicrobial resistance of specific bacteria is reported, and information on antimicrobial resistance obtained from the entire hospital or group (*e.g.*, intensive care unit, frequent use of antimicrobials, and antimicrobial-resistant bacteria) is shared with relevant employees. The antimicrobial resistance rates of specific bacteria and patterns according to ASP were reported to the ASP committee and shared with the relevant employees.
- ③ Reporting adherence to antimicrobial treatment guidelines and sharing with employees: Whether the antimicrobials prescribed by groups (*e.g.*, emergency room, intensive care unit, divisions frequently using antimicrobials, specific diseases, such as sepsis) and individuals meet the antimicrobial treatment guidelines is shared.
- ④ Reporting antimicrobial prescribing intervention activities and sharing with employees: Through antimicrobial restriction and authorization or audits with feedback programs, the list of actively prescribed antimicrobials is shared with all medical staff. Details of the activity and adherence to recommendations were shared with the prescribing medical staff.

(4) Evidence-based description

1 Reporting AMR and sharing with employees

Information on antimicrobial use (changes in antimicrobial usage amount and prescription pattern induced by ASP) is reported and shared to improve antimicrobial prescriptions by motivating and changing behaviors across hospitals and related employees. This activity is an easy and simple way to improve antimicrobial prescriptions, as it respects individual and group autonomy as much as possible without imposing any restrictions [6, 15]. Few studies have confirmed whether reporting and sharing antimicrobial use within hospitals can improve antimicrobial use in healthcare settings. However, sharing information on individual antimicrobial usage in primary hospitals can provide an opportunity to benchmark and improve antimicrobial use, and similar effects are expected in other hospitals [117, 118].

Depending on the hospital, proper reporting of the current status of antimicrobial use may be impossible because of the difficulty in collecting or analyzing data related to the use of



antimicrobials due to a lack of resources or finances. In this case, a system such as KONAS was used to easily obtain and report data on antimicrobial usage in the entire hospital. Hospitals capable of sufficiently collecting and analyzing data on antimicrobial use can carry out a higher level of reporting. These hospitals are recommended to share information on antimicrobial use collected over a short period as often as possible to help physicians prescribe antimicrobials to track previous antimicrobial prescriptions. If reporting in a short period is difficult, reporting once or twice a year may be considered. Therefore, reporting the status of antimicrobial use by individuals may be effective. However, group reports can be submitted if an individual report on the status of antimicrobial use is mistaken for a punitive measure, causing antipathy for the prescribing physician, or if individual reporting is impossible because of a change in the physician in charge or rotational work. Finally, reports on the use of antimicrobials should provide customized data. For example, reporting prophylactic antimicrobial use in surgery rather than providing data on total antimicrobial use to surgeons may be effective in improving the use of antimicrobials in surgery [119].

② Reporting antimicrobial resistance and sharing with employee

Since information on antimicrobial resistance of bacteria influences antimicrobial selection, antimicrobial resistance information at medical facilities must be provided periodically (quarterly or twice a year) [7, 120]. The ASP team can work with the person in charge of the microbiological laboratory to report the antimicrobial susceptibility of the strains that can be analyzed and the change in the antimicrobial resistance of the bacteria according to the ASP. Even within a single medical facility, antimicrobial susceptibility patterns can vary greatly, depending on the location of the bed (*e.g.*, intensive care unit), patient age (*e.g.*, children), type of infection (*e.g.*, bloodstream infection), and source of infection (*e.g.*, community-acquired infection). Reporting antimicrobial susceptibility results by grouping in this manner can provide important information for creating institutional antimicrobial treatment guidelines.

In the absence of in-hospital microbiological laboratories or limited personnel available to report antimicrobial resistance information, intra-organizational reporting of regional antimicrobial susceptibility patterns using existing systems such as KARMS or Kor-GLASS may be considered (**Table 2**) [120, 121].

③ Reporting antimicrobial prescribing intervention activities

Reviewing the contents of antimicrobials requested during antimicrobial restriction and authorization activities, compliance with recommendations during audits with feedback interventions, adherence to antimicrobial treatment guidelines at medical facilities, and sharing problems emerging in this process with the prescribing physician can help improve antimicrobial prescriptions.

As the second Korean action plan on AMR emphasizes the proper use of antimicrobials by focusing on small-, medium-, and long-term care facilities that had been lacking in antimicrobial use management, it is necessary to improve the reporting system that these hospitals can utilize to improve the use of antimicrobials. In the plan to support antimicrobial management at primary and secondary hospitals by operating a pilot project to establish a network of tertiary hospitals with primary and secondary hospitals, as in the Duke Antimicrobial Stewardship Outreach Network (DASON) model, it is also necessary to support the reporting system [122, 123].



Table 2. Comparison of Korea Global Antimicrobial Resistance Surveillance System and Korean Antimicrobial Resistance Monitoring System

Surveillance system	Kor-GLASS	KARMS
Target institution	Tertiary or quaternary/nursing hospitals	Primary or secondary/nursing hospitals
Target strains	Staphylococcus aureus	Staphylococcus aureus
	Enterococcus faecalis	Enterococcus faecalis
	Enterococcus faecium	Enterococcus faecium
	Streptococcus pneumoniae	Streptococcus pneumoniae
	Escherichia coli	Escherichia coli
	Klebsiella pneumoniae	Klebsiella pneumoniae
	Pseudomonas aeruginosa	Enterobacter cloacae
	Acinetobacter spp.	Pseudomonas aeruginosa
	Salmonella spp.	Acinetobacter baumannii
	Shigella spp.	Non-typhoidal Salmonella
	Neisseria gonorrhoeae	Salmonella typhi
	Clostridioides difficile	Shigella spp.
		Campylobacter jejuni
		Vancomycin-resistant S. aureus
		Neisseria gonorrhoeae
Target specimens	Blood	Blood
	Urine	Urine
	Feces	Feces
	Urogenital specimen	Urogenital specimen
		All specimens
Susceptibility testing laboratory	Microbial characteristic analysis center	Each collection agency
Test method	Disk diffusion method	Microbiology total laboratory automation system
	Agar dilution method	
	Broth microdilution method	
Resistance rate calculation	Calculation of the resistance rate by directly analyzing non-repetitive strains	Arithmetic mean of the resistance rates reported by the surveillance body; repetitiv strains not removed (probably higher than actual resistance rates offered)
Collected strain	Non-repetitive	Strain not collected

Kor-GLASS, Korean Antimicrobial Resistance Surveillance System; KARMS, Korean Antimicrobial Resistance Monitoring System.

Studies on the effects of reporting antimicrobial use submitted by Korean medical facilities are insufficient and require future research to establish evidence.

6. Education

(1) Concept

All activities that include education of medical staff on optimal prescription of antimicrobials and antimicrobial-resistant bacteria and patient education on antimicrobials being used are a core element of a comprehensive effort to improve antimicrobial use.

(2) Checklist

- 1. Regular education on clinical practice guideline or antimicrobial treatment guidelines is provided to ensure proper antimicrobial prescription by medical staffs.
- 2. Regular ASP education is provided to the hospital leadership and healthcare workers.
- 3. Regular education on collection (blood culture, etc.), transport, management, and
- results interpretation for clinical microbiological specimen is provided to medical staffs. 4. Promotion and education on ASP are provided for patients and their caregivers to allow
- them to speak up for the appropriate use of antimicrobials.

(3) Usage examples

① There are methods of application, including material-based education (*e.g.*, antimicrobial use guidelines, including national guidelines, lectures, posters, flyers, newsletters, and



- alerts via email), face-to-face education or rounds (handshake stewardship), and casebased education.
- ② The education target is medical staff including students, patients, and caregivers.

(4) Evidence-based description

Education is most effective when the interventions and outcomes are evaluated together. Case-based education is particularly effective, and an audit with feedback strategies, antimicrobial restrictions, and authorization strategies are good ways to provide education on antimicrobial use. Lectures, handouts related to instructions, and email alerts are passive educational activities, and such training is most effective when combined with interventions and outcome measures in ASP [44, 124, 125]. Education is an essential component for improving antimicrobial use in hospitals. However, education alone is ineffective [7]. In a meta-analysis, passive education by distributing educational booklets or delivering lectures through campaigns may show some effect [126]. Nonetheless, the effect is temporary, and observed during the intervention period. It also does not last for over one year [127].

Material-based education (*e.g.*, antimicrobial use guidelines, including national guidelines, lectures, posters, flyers, newsletters, alerts via email, etc.) provides physicians with guidelines for clinical practice or antimicrobial prescription or trains nurses on culture techniques, which include educating patients about the signs and symptoms of adverse effects of antimicrobials. In a study comparing the groups that received an educational intervention, including lectures, meetings, and expert advice counseling via emails and phone calls, and those that did not, the annual antimicrobial prescription rate significantly decreased in the group that received educational intervention, and this effect was confirmed to last up to four months [128]. Another study confirmed that the distribution of user-friendly guidelines for physicians and dentists in Quebec, Canada, decreased the doses of prescribed antimicrobials compared to other regions of Canada [129]. In addition, a study demonstrated that the total prescription of antimicrobials was reduced by pediatricians who participated in meetings, seminars, and campaigns compared with those who did not [130].

Intervention methods included face-to-face education or rounds (handshake stewardship). Face-to-face education, or rounds, is a training method in which an ASP team of physicians and pharmacists reviews all prescribed antimicrobials, providing direct, individualized feedback through rounds. It is particularly effective when providing feedback to an individual using handshake stewardship.

Case-based education is an educational method that reviews and discusses de-identified cases with physicians, making it easier to recognize the process of changing antimicrobial treatments. The reviewed cases included signs, symptoms, test results, treatment processes, and clinical outcomes of patients, and case presentations were recommended in an iterative manner with regular meetings and discussions with other departments within the facility.

Education should be provided to various healthcare workers such as clinicians, pharmacists, physician assistants, clinical nurses, nursing students, and residents. In particular, the need for education of medical students has been emphasized [46].

Patient education plays an important role in ASP. The patients should know which antimicrobials they are using for what indication and should be educated regarding the signs and symptoms of adverse effects caused by the antimicrobials. They must be encouraged to



share the information with their providers. This corresponds to the "speak-up" movement of the quality improvement department and can be emphasized at inpatient, outpatient, and medical facilities of all sizes, and the participation of quality improvement officers is beneficial. In addition, patients should be aware of the adverse effects that may occur even after they stop taking antimicrobials after discharge. Nurses also play an essential role in patient education. Since educational materials designed for patient participation are more effective, patient participation should be encouraged when developing educational materials for patients on the appropriate use of antimicrobials.

Data on the effects of education on antimicrobial use in Korean medical facilities are insufficient and require future research to establish evidence.

I. ASP ACTIVATION PLAN IN KOREAN MEDICAL FACILITIES

1. Application of ASP to healthcare institution accreditation criteria

(1) Examples of foreign countries

The major domains related to ASP are the medicine management domain in the United States and Canada, and the prevention and control of infection domains in Australia and Taiwan. Commonly, the importance of leadership at medical institutions, close connection with infection prevention and control (IPC) systems, and participation of employees and patients are emphasized for the appropriate implementation and operation of ASP.

① United States (The Joint Commission [TJC])

The criteria related to ASPs were established independently of drug management. The seven core elements related to ASP should be specifically documented, and items that require leaders to prioritize ASP for their organizations are linked to leadership criteria that require the highest decision-making body to provide necessary resources. Furthermore, a multidisciplinary protocol approved by medical facilities is required to form a multidisciplinary team. The item to check the results of areas that require improvement related to the operation of ASP is linked to the criteria for evaluating the effectiveness of the drug management system. Among the core elements, education is linked to the infection control criteria, and the application of ASP is integral to IPC activities. In connection with the infection control criteria, it is necessary to monitor whether implementing ASP reduces MDRO, central line-associated bloodstream, catheter-associated urinary tract, and surgical site infections.

2 International Organization (Joint Commission International)

The Joint Commission International is an international organization established by the TJC in the United States. Criteria related to ASP were independently prepared as criteria for managing and using medicines. To reduce the occurrence, spread of antimicrobial-resistant bacteria, and improve patient conditions, hospitals have implemented measures to ensure the optimal use of antimicrobials and support (staffing, financial resources, evidence-based data, information technology, etc.) through leadership to ensure effective ASPs. In addition to IPC professionals, physicians, nurses, pharmacists, and other professionals should operate a coordination mechanism in which trainees, patients, and family members are encouraged to participate. However, appointing a pharmacist as the person in charge of ASP operation has not been specifically mentioned.



③ Australia (National Safety and Quality Health Services [NSQHS])

Criteria related to ASPs are established independently under the prevention and control of healthcare-associated infections and comprise four main categories. The first is the improvement of clinical governance and quality to support the prevention and control of healthcare-associated infections and ASP; the second is the IPC system; the third is the reprocessing of reusable medical devices; and the fourth is ASP. Under these criteria, medical institutions are required to establish a system to improve ASP, emphasizing that it should be applied, particularly along with clinical governance, drug management, and partnerships with healthcare consumers. As hospitals are mandated to obtain accreditation according to the NSQHS criteria, guidelines on these criteria would be useful for medical facilities by suggesting key tasks and strategies for improvement to meet the criteria.

④ Canada (Accreditation Canada)

In the Qmentum of Accreditation Canada, criteria related to ASP are independently constituted as essential criteria in drug management. The Qmentum criteria were developed for each service or healthcare facility type, but the connection among the criteria was not confirmed.

(2) Korean status and development direction

Since the International Standard for Accreditation Criteria of the International Society for Quality in Health Care (ISQua) included content related to ASP, Korea has also tried to include it in the revision of acute hospital infection-related criteria (version 2.1) after the Middle East respiratory syndrome outbreak, but the government or academia has not yet been sufficiently prepared to reduce AMR.

In August 2016, the first Korean Action Plan on AMR was prepared in Korea, and a second-phase accreditation survey of acute-stage hospitals was in progress. Among the resistance management measures, the detailed implementation plan for the optimal use of antimicrobials included the development and spread of antimicrobial usage guidelines, with no specific mention of ASP. No Korean guidelines have been established for the application of ASP. Therefore, to meet the ISQua criteria related to ASP, the third-phase acute hospital accreditation criteria in 2018 were revised to the level of the management system for the appropriate use of antimicrobials (8.1 ME. 5).

The criteria applied to the fourth-phase acute hospital accreditation survey, starting around September 2022, were announced in 2021. However, the contents related to ASP did not change significantly. The reason for this is like that in the third phase. Guidelines to be applied were not finalized, and preparations for healthcare institutions were insufficient. In particular, there was a professional workforce shortage (pharmacists, infectious disease experts, etc.).

When revising the criteria to reflect ASP in the future, the first thing to consider is whether to keep them under the infection control domain as they are now or move them to the drug management domain. As the core elements are like those of the United States guidelines, the United States accreditation criteria seem convenient to follow. However, as emphasized in most countries, drug management, leadership and quality improvement systems, close linkages with IPC systems, and patient participation measures should be included for the appropriate implementation and operation of ASP. If acute-stage hospital accreditation criteria are revised in relation to ASP, they should be reflected in the fifth phase. If pending issues, such as disagreement between authorities and key stakeholders and no groundwork for application (particularly the preparation of compensation measures related to program application), are resolved, revisions can be made, even in the middle of the fourth phase. Details to be included in the accreditation and judgment criteria should be prepared through a pilot project for ASP applications.

1C Infection & Chemotherapy

2. Introduction of the national health insurance fee for ASP

The ASP aims to improve the quality of medical care for infectious diseases and maintain patient safety by preventing AMR, reducing drug-related adverse reactions, shortening hospital stays by implementing appropriate ASP activities at medical facilities, reducing unnecessary misuse of antimicrobials without adverse effects on the treatment progress of infectious diseases, and inducing and maintaining proper use of antimicrobials. The need for a new ASP fee, which is a fee to support domestic antimicrobial use management program activities centered on infectious disease physicians, is increasing, with concerns about the operational purpose of the existing IPC fee and the added burden on the person in charge also being raised. Therefore, the differences between the two management fees should be discussed.

In September 2016, the IPC fee was newly established to compensate for the cost of managing infectious diseases to prevent the occurrence and spread of infections at medical facilities in advance and to support the establishment of an infection control infrastructure. The IPC fee is paid by the establishment and operation of the infection control team and committee at the hospital for the efficient operation of IPC programs, such as healthcare-associated infections. If IPC is performed at a facility with a dedicated workforce for each licensed bed, a fee may be applied for each grade. The IPC fee supports IPC activities, such as (1) IPC team composition and operation, (2) IPC policy and operating system development at hospitals, (3) in-hospital administrative support for IPC, (4) core IPC execution, and (5) investigation and reporting of healthcare-associated infections.

Among the various activities aimed at improving the quality of healthcare and ensuring patient safety, IPC activities are being implemented to manage and prevent healthcareassociated infections, whereas ASP is being implemented to support quality management activities for the use of antimicrobials. Since the domains of IPC and ASP activities are related to healthcare, tasks between them, particularly in managing antimicrobial-resistant bacteria, overlap but not in a mutually exclusive or hierarchical relationship. Conversely, IPC and ASP activities are complementary to each other, having a cooperative relationship to prevent the spread of MDROs caused by inappropriate use of antimicrobials, within medical facilities, between facilities, and to the local community through ASP activities by managing the cause of antimicrobial-resistant bacteria and through IPC activities.

The CDC presents seven items as core elements of ASP activities, using which the difference between IPC activities can be explored. The seven core elements are: (1) leadership commitment, (2) accountability, (3) pharmacy expertise, (4) action, (5) tracking, (6) reporting, and (7) education.

Achieving the purpose of each activity requires organizing an ASP team separately from the infection control team to operate the ASP. The dedicated ASP team should be a multidisciplinary team of clinical microbiologists, nurses, and information system specialists, under the responsibility of qualified physicians and pharmacists. Many developed countries that have introduced and applied ASP programs before Korea emphasize the need to expand the professional workforce essential to operating ASP. Guidelines for the



application of ASP by the United States CDC and the IDSA recommend an infectious disease specialist or a pharmacist specializing in infectious diseases with expertise and experience in antimicrobial management to operate ASP. The infection control team also comprises multidisciplinary healthcare workers such as qualified clinicians, infection control nurses, clinical microbiologists, and specialized administrative personnel. However, infection control activities in most medical facilities are in charge of IPC, and ASP activities are mainly carried out by physicians at the Department of Infectious Diseases and Pediatric Infectious Diseases, in collaboration with the pharmaceutical department. The team leader and key practitioners of each activity may vary.

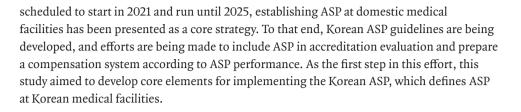
The core problem of ASP operations is the dearth of relevant experts, such as those in charge of ASP and pharmacists responsible for effectively leading ASP at domestic medical facilities. Long-term educational and economic support should be the basis for expanding the relevant professional workforce that plays a key role. As for the support method, the fee for each activity, such as consultation fees, incentives based on evaluation using various evaluation indicators, and the establishment of a separate ASP fee can be considered. In the long term, considering the participation of tertiary hospitals, an ASP fee should be established to secure professional workforce. Like the IPC fee that has been newly established to compensate for the cost of infectious disease control and support establishing of an infection control infrastructure, a new fee for ASP activities is necessary to build the infrastructure necessary to manage the use of antimicrobials required to treat infectious diseases, particularly to support the expansion of related specialists. Infection control activities in Korea, which are currently subject to IPC fees, experience difficulties in securing manpower and performing activities. Since increasing the number of skilled personnel does not increase a hospital's income, adding and strengthening items, such as the ASP committee, ASP physician, infectious disease specialist or pharmacist, and restricted antimicrobial approval system, to the evaluation items for hospitals induces each hospital to recruit specialized personnel.

3. Effect of prediction and cost-effectiveness analysis of ASP

According to a 2018 survey, 85% of acute care hospitals in the United States had seven core elements, an increase from 41% in 2014 [99]. A study in the United States revealed that a 1% increase in the proportion of hospitals performing core elements was associated with a 0.3% lower incidence of hospital-acquired CDI [131]. In this study, the performance of the core elements and MRSA showed no significant correlation [131]. The advantages of meeting the core elements include reducing the use of antimicrobials for acute upper respiratory tract infections in outpatients and improving the appropriateness of use and cost-effectiveness [132]. Implementing ASP with core elements reduced treatment costs per patient by \$37 (7%), increased quality-adjusted life years by 0.001 (1.2%) and reduced the hospitalization rate by 0.3%, compared to cases without implementation. In a study conducted by the Veterans Health Administration in the United States, institutions that implemented ASP with core elements effectively lowered the antimicrobial use rate in outpatients with acute upper respiratory tract infections compared to those that did not, thereby increasing antimicrobial prescription adequacy and reducing the hospitalization rate [133].

CONCLUSION

To overcome the problem of AMR at the national level, Korea has been preparing a national action plan on AMR since 2016. In the second national action plan on AMR, which is



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This study confirmed six core elements (leadership commitment, operating system, action, tracking, reporting, and education), and 28 checklist items were developed to evaluate each core element. The main details of each core element are summarized below.

In leadership commitment, participation of the hospital leadership in Korea is essential for the success of ASP, as in overseas guidelines. Hospital leadership should prioritize the implementation of ASP for medical facilities and actively support human and material support for the successful implementation of the program. In addition, the ASP committee should be operated and the program should be managed properly by holding regular committee meetings. The operating system corresponds to accountability and pharmacy expertise, a core element of the ASP program of the CDC, which was applied to foreign cases with abundant manpower, and it was judged that it should be applied differently in Korea. Therefore, we attempted to present the structural aspects for the application of ASP. Considering the situation of domestic medical facilities with an insufficient professional workforce, forming a dedicated team, and designating dedicated employees has been recommended to expand the professional workforce operating the program. This aids in avoiding the formal mobilization of the existing workforce. The dedicated team must include an infectious disease specialist (or a clinician with training of more than a certain period) and a pharmacist specializing in infectious disease, and multidisciplinary operation must be performed in cooperation with professionals in other fields. In this action, the core of interventions for the appropriate prescription of antimicrobials is the prospective audit with feedback activities, antimicrobial restriction, and preauthorization activities. However, the shortage of a professional workforce, such as infectious disease specialists and pharmacists, should be considered. Therefore, instead of a prospective audit with feedback on the use of antimicrobials, an audit with feedback was suggested according to the situation at each medical facility. For other supplementary interventions, each medical facility selected and implemented applicable items. Tracking was performed to evaluate the ASP. It measured antimicrobial usage at medical facilities, with regular follow-ups on intervention items being implemented at each facility. Reporting, as in overseas guidelines, involves sharing information on antimicrobial use and the ASP outcome of each medical facility with management and related healthcare workers. Finally, education entails repeated education on the need for ASP and clinical guidelines for antimicrobial use and clinical microbiological specimen collection methods for medical staff. This would encourage active participation in the treatment process by informing patients and caregivers of the importance of appropriate antimicrobial use.

As an external driving force to actively introduce ASPs at medical facilities in Korea, it should be considered in foreign countries that ASPs are included in the accreditation criteria for healthcare institutions. The main reason that ASP has not been actively reflected in the accreditation criteria to date is the lack of guidelines and professional workforce related to domestic ASP [134]. Overcoming these problems would allow ASP items to be actively reflected in the fifth phase of healthcare institution accreditation. Although there are concerns that the health insurance fee for ASP overlaps with the existing IPC fee, ASP activities are quality control activities for using antimicrobials, with clear differences from IPC activities supported by IPC fees. For ASP to be fully established in medical facilities in Korea, the workforce should be secured through financial assistance. Appropriate compensation measures, such as calculating separate fees for ASP activities, should be actively considered.

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The core elements derived from this study were discussed by experts after reviewing the literature of various countries, and the checklist items used to evaluate each core element were established by applying them to the domestic situation. In this study, core elements applicable to general hospitals, particularly tertiary hospitals, were developed. Considering the difference in human resources and financial capacity of each facility, even in tertiary hospitals at the same level, each core element is refined for appropriate application, even at medical facilities with limited resources. Considering the high antimicrobial prescription and inappropriate antimicrobial prescription rates [135] at primary or secondary hospitals, and the high detection rate of antimicrobial-resistant bacteria at primary, secondary, and long-term care facilities, preparing separate guidelines for core elements of small- and medium-sized hospitals and clinics in the long term may be necessary.

1. Limitations of the guideline and future challenges

The guideline development process is difficult owing to the scarcity of evidence-based studies in this field. Most clinical studies on which the recommendations of these guidelines are based have been conducted abroad. As some applied Korean research results were prepared in only a few situations, caution should be taken when applying them to actual medical institutions. The core elements are intended to be applied in acute care hospitals that are general hospitals or higher grades. The development of core elements of ASP for primary or secondary hospitals and long-term care facilities must be accomplished. In addition, research should be conducted to verify the effectiveness of the developed core elements applied to domestic medical facilities when applying ASP.

2. Conflict of Interest

This guideline was prepared through a policy R&D project sponsored by the KDCA, and the guidelines were developed independently by a development committee. The development process was not affected by government agencies, pharmaceutical companies, hospital groups, or interest groups, including KDCA.

3. Plan for guideline revision

These guidelines will be revised periodically to reflect the results of major recent research in Korea and abroad in the future to maintain suitability for the domestic situation.

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Core elements for implementing ASP



Appendix. Antimicrobial stewardship program (ASP) Checklist

Core element	Checklist items	Yes	No
Leadership Commitment	1. Regulations to operate the ASP committee with the participation of hospital leadership are established, and regular meetings are held.		
	2. Hospital leadership allocates the budget and workforce necessary to implement the ASP.		
	Hospital leadership sets the implementation of the ASP as the priority goal of the facility and manages indicators to measure program performance.		
Operating System	1. There are department as well as dedicated employees and teams that implement ASP with regulations for the individual roles and ASP procedures.		
	 The dedicated team that conducts ASP should be a multidisciplinary team involving physicians, pharmacists, nurses, clinical microbiologists, infection control professionals, and information system professionals. 		
	3. There should be a leader in charge of the operation of ASP.		
	4. There is a dedicated pharmacist who has completed ASP training and participates in its activities.		
Action	1. Audit and feedback on the use of antimicrobials are under implementation.		
	2. Antimicrobial restriction and authorization of prescription for specific antimicrobials are under implementation.		
	An antimicrobial prescription form or a computerized antimicrobial prescription system recommends and supports antimicrobial prescriptions based on ASP guidelines at medical facility.		
	4. Interventions for major infectious diseases or other supplementary ASP interventions are conducted.		
	A. Urinary tract infection		
	B. Community-acquired pneumonia		
	C. Bloodstream infection		
	D. Clostridioides difficile infection (CDI)		
	E. Minimizing antimicrobial combination therapy F. Antimicrobial de-escalation		
	G. Recommending the optimal duration of antimicrobial administration		
	H. Changing intravenous antimicrobials to oral antimicrobials		
	I. Utilizing of therapeutic drug monitoring (TDM) for specific antimicrobials		
	J. Rapid reporting of microbiological results		
Tracking	1. The use of antimicrobials within a medical facility is being tracked regularly.		
	2. The status of the occurrence of six multidrug-resistant organisms (MRSA, VISA/VRSA, VRE, MRAB, MRPA, and CRE), which are designated as communicable diseases in Korea are tracked regularly (at least once in each quarter).		
	3. The incidence of CDI is tracked regularly.		
	4. The antimicrobial susceptibility results for frequently isolated bacteria are tracked regularly.		
	5. The occurrence of antimicrobial adverse events is tracked regularly.		
	6. The acceptance of recommendations based on audit and feedback on the use of antimicrobials is tracked regularly.		
	7. The degree of approval of antimicrobial restriction and prescription authorization for specific antimicrobials are tracked regularly.		
	8. Interventions for major infectious diseases or other supplementary ASP interventions are tracked regularly.		
	A. Urinary tract infection		
	B. Community-acquired pneumonia		
	C. Bloodstream infection		
	D. CDI		
	E. Minimizing antimicrobial combination therapy		
	F. Antimicrobial de-escalation		
	G. Recommending the optimal duration of antimicrobial administration		
	H. Changing intravenous antimicrobials to oral antimicrobials I. Utilizing of TDM for specific antimicrobials		
	J. Rapid reporting of microbiological results		
Reporting	 The information on antimicrobial use (changes in dosage and prescription patterns based on ASP) is reported to the hospital leadership and the ASP committee and shared with relevant employees. 		
	2. The information on antimicrobial resistance is reported and shared.		
	 The information on antimicrobial resistance is reported and shared. The information on antimicrobial prescription by individuals or groups compliant with the medical facility's guidelines for the treatment of infectious diseases is reported and shared. 		
	 The information on antimicrobial restriction and prescription authorization for specific antimicrobials is shared with prescribing medical staffs. 		
	 The adherence to recommendations based on audit and feedback interventions on the use of antimicrobials is shared with prescribing medical staffs. 		

(continued to the next page)



Appendix. (Continued) Antimicrobial stewardship program (ASP) Checklist

Core element	Checklist items	Yes	No
Education	 Regular education on clinical practice guideline or antimicrobial treatment guidelines is provided to ensure proper antimicrobial prescription by medical staffs. 		
	2. Regular ASP education is provided to the hospital leadership and healthcare workers.		
	Regular education on collection (blood culture, etc.), transport, management, and results interpretation for clinical specimen is provided to medical staffs.		
	 Promotion and education on ASP are provided for patients and their caregivers to allow them to speak up for the appropriate use of antimicrobials. 		

MRSA, methicillin-resistant *Staphylococcus aureus*; VISA/VRSA, vancomycin-intermediate/resistant *Staphylococcus aureus*; VRE; vancomycin-resistant Enterococci, MRAB, multidrug-resistant *Acinetobacter baumannii*; MRPA, multidrug-resistant *Pseudomonas aeruginosa*; CRE, carbapenem-resistant *Enterobacteriaceae*.