Review

Antimicrobial Stewardship in Pediatrics
How Every Pediatrician Can Be a Steward

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Antimicrobial stewardship (AS) programs are effective in improving clinical outcomes associated with antimicrobial therapies while improving patient safety by reducing adverse events and development of bacterial resistance. Understanding the basic principles of AS is essential to the successful development and implementation of AS strategies. Identifying and developing strategies to address barriers and challenges to AS can facilitate the establishment of financial, administrative, and organizational support, and agreement and participation by individual prescribers. Review of published outcomes of AS demonstrates the effectiveness in reducing unnecessary antimicrobial use and adverse events such as *Clostridium difficile* infections. We also illustrate the need for further research and expansion of AS activities to office-based practices and communities by using novel and innovative AS strategies and by influencing regional and national policies.

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During the past 2 decades, a significant increase in the prevalence of multidrug-resistant bacterial infections has occurred in children. This problem is observed for community-onset and health care–associated infections (HAIs).[1] Important pathogens include methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, and gram-negative bacteria producing extended-spectrum β-lactamases and carbapenemases.[1-4] Concurrently, the development and availability of new antibiotics are experiencing significant shortages.[5] As a result, implementation of strategies to preserve the activity of existing antimicrobial agents by preventing development of bacterial resistance has become an urgent public health priority. Antimicrobial stewardship (AS) is one such approach that can prevent emergence of antibiotic resistance while improving patient outcomes and safety.

What Are the Goals of AS?

In 2007, the Infectious Diseases Society of America (IDSA) and the Society for Healthcare Epidemiology of America (SHEA) published guidelines for developing institutional AS programs. These guidelines defined the primary goal of stewardship as "to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use, including toxicity, the selection of pathogenic organisms, and the emergence of resistance."[6(p159)] This broad and inclusive definition has served as the basis for the establishment of formal AS programs at many acute care institutions primarily structured as formulary restrictions, preauthorization, and prospective audit and feedback programs. The definition has also provided guidance in the development of AS protocols that ensure appropriate antibiotic selection, dosing, and administration and educational programs on appropriate antibiotic use for patients, families, and prescribers. In addition, with increasing resistance seen in community-acquired pathogens, AS programs are now applying efforts to outpatient and office-based practice settings and long-term care facilities.[7-9] Recognition of the high prevalence of inappropriate or unnecessary antimicrobial use in outpatient settings has led to such initiatives as the Centers for Disease Control and Prevention's Get Smart Program for outpatients, which provides education for physicians and patients alike with the goal of reducing inappropriate antimicrobial use in the community.[10]

State of Pediatric AS

Initial AS efforts were centered on adult patient populations. Owing to an increasing recognition of the unique aspects of antimicrobial use and challenges associated with pediatric patient populations, a more concerted effort for widespread implementation of formal AS programs in pediatrics has occurred in recent years. In 2010, the Pediatric Infectious Diseases Society (PIDS) formed the Pediatric Committee on Antimicrobial Stewardship with the mission of advancing pediatric AS in various clinical settings, promoting research in pediatric AS, and developing AS educational programs. PIDS also sponsors and organizes an annual conference on pediatric AS.[9] The American Academy of Pediatrics also has recommended implementation of AS programs for health care organizations that provide inpatient and outpatient pediatric care.[11]

Adoption of AS in free-standing children's hospitals in the United States has accelerated in the past few years. A recent survey of 43 children's hospitals showed that 16 institutions (37%) of institutions currently have an established AS program supported by full-time equivalents for a pediatric infectious diseases physician and/or clinical pharmacist.[12] More than half of these established programs

Table 1. Principles and Strategies for AS Programs

Principles	Examples of Strategies
Timely antibiotic therapy management	Ensuring prompt initiation of antibiotic therapy when indicated Critical illness such as sepsis High-risk patients with serious bacterial infections Avoiding use of antibiotics when not indicated Viral upper or lower respiratory tract infections Asthma exacerbations Viral pharyngitis Use of clinical guidelines and algorithms that facilitate provider recognition of clinical syndromes that do and do not require antibiotics
Appropriate selection of antibiotics	Ensuring that proper antibiotic regimens are selected for specific clinical syndromes and infections Minimizing redundant antibiotic regimens for gram-negative or anaerobic bacterial infections Use of antibiograms and clinical guidelines to optimize antibiotic selections
Appropriate administration and de-escalation of antibiotic therapy	Ensuring proper dosing of antibiotics Peer review of antibiotic use at 48-72 h after initiation to determine if therapy should be continued, changed, or discontinued Monitoring for serum therapeutic levels of antibiotics Proper administration of antibiotics for surgical prophylaxis
Use of expertise and resources at point of care	Formation of multidisciplinary AS committees Obtaining administrative and leadership support
Continuous and transparent monitoring of antibiotic use	Auditing antibiotic use to identify opportunities for stewardship and education Prospective monitoring to assess efficacy of AS program

Abbreviation: AS, antimicrobial stewardship.

were implemented after 2008. Another 15 children's hospitals (35%) are in the preparatory stage of implementing AS programs. Among the 16 established AS programs, 15 (94%) used a prospective audit with feedback and/or formulary restriction.

Because a significant proportion of antibiotic use is found in community hospitals, pediatric wards within larger medical centers, and outpatient and office-based practice settings, continuing expansion and adoption of pediatric AS programs and activities beyond the walls of free-standing children's hospitals and inpatient settings are essential to achieving the goals of AS. For successful implementation of pediatric AS on these new frontiers, paradigm changes are necessary, including hospitalists and general pediatricians taking on leadership roles in AS initiatives and developing practical solutions rooted in the general principles of AS.

What Are the Principles and Strategies of AS?

Antimicrobial stewardship strategies and protocols incorporate 1 or more of the core principles exemplified in the Centers for Disease Control and Prevention's Get Smart Program for health care providers.[13] The 5 core principles are (1) timely management of antimicrobial therapy, (2) appropriate selection of antimicrobials, (3) appropriate administration and de-escalation of antimicrobial therapy, (4) use of available expertise and resources at the point of care, and (5) transparent monitoring of antimicrobial use data (**Table 1**). Understanding these core principles can help identify opportunities for AS and to develop strategies to facilitate appropriate antibiotic use (Supplement [eCase 1]).

Appropriate and Prompt Antimicrobial Therapy Initiation

Timely management of antimicrobial therapy consists of prompt initiation of antimicrobial therapy in critical situations such as sepsis. Patients with risk factors for serious bacterial infections, such as central venous catheters or immunocompromising conditions, should receive prompt and appropriate antimicrobial therapy when they present with signs or symptoms of suspected infection. For febrile patients and those with neutropenia, AS protocols and interventions have been shown to be effective in reducing time to antibiotic administration by addressing barriers to prompt physician order entries after documentation of fevers and by improving access to the supply of antibiotics by stocking them in the emergency carts within the unit.[14,15] A recent study of critically ill children with community-acquired bacterial pneumonia demonstrated that longer times to initiation of parenteral antibiotic therapy to which subsequently cultured organisms were susceptible resulted in longer durations of mechanical ventilation, intensive care unit (ICU) stays, and overall hospitalization[16] and underscored the importance of timely initiation of therapy. Antimicrobial stewardship programs can facilitate prompt initiation of therapy by developing protocols and guidelines based on evidence and best practices.

Conversely, studies have demonstrated overuse of antibiotics in clinical situations where antibiotics are not indicated, for example, in children with asthma, pharyngitis, and viral respiratory infections, including bronchiolitis secondary to respiratory syncytial virus infection.[17-20] A Cochrane review evaluating the effectiveness of AS interventions in reducing unnecessary ambulatory antibiotic use showed that multifaceted approaches combining elements such as prescriber audit and feedback, interactive educational meetings for prescribers, and educational outreach for patients and the public were more likely than single-strategy approaches to reduce inappropriate antibiotic use.[21] In addition, use of clinical guidelines and algorithms that facilitate provider recognition of clinical syndromes that necessitate antibiotic treatment promotes timely antibiotic management.[22] Such interventions may be supported by computerized physician orders.

Appropriate Selection of Antibiotics

Selection of the appropriate antimicrobial regimen is another central AS principle. In adult patients with sepsis, bacteremia, and ventilator-associated pneumonia, empirical antimicrobial therapies using agents that lacked activity against subsequently cultured organisms or lacked coverage for specific clinical syndromes led to increased mortality and morbidity.[23-26] Choosing the appropriate empirical antimicrobial regimen requires a good understanding of the bacterial resistance rates, epidemiology, and pathophysiology in the relevant patient population. Local antibiograms that can provide pathogen-specific resistance rates for children are invaluable resources and guide the clinicians in selecting effective antimicrobials for their patients. Unfortunately, resistance rates reported in many institutional antibiograms represent all isolates and do not assess potential variability in resistance rates in specific patient care units, patient populations, or body sites. For example, isolates from ICUs or units caring for patients with chronic conditions are expected to have higher resistance rates than isolates from units caring for patients with a lower acuity of illness.[27] Resistance rates in pediatric wards within adult-centered medical centers or community hospitals may not be reflected in the institutional antibiogram.[28] Simi-

larly, clinicians in outpatient settings must consider that institutional antibiograms contain isolates from HAIs and thus reflect higher resistance rates than those typically seen in community-acquired infections. Finally, antibiograms should be interpreted within the clinical context of the patient because most antibiograms do not provide syndrome- or infection-specific resistance data for each pathogen. As an example, *Escherichia coli* isolated from a child with a first episode of urinary tract infection is more likely to be susceptible to commonly used antibiotics, such as a combination of trimethoprim and sulfamethoxazole, than an *E coli* strain isolated from a child with vesicoureteral reflux and a third urinary tract infection, which may express resistance to third-generation cephalosporins. These limitations underscore the need for the development of clinically relevant antibiograms. Recent studies in adult and pediatric patients have shown that antibiograms structured around clinical syndromes, such as urinary tract infections or intra-abdominal infections, can assist the prescriber in selecting appropriate empirical antibiotic regimens for specific infections.[29,30]

Appropriate antibiotic selection also means minimizing redundant antimicrobial regimens. In the past, use of 2 antimicrobials for the treatment of gram-negative bacterial infections had been widely recommended because it was believed to improve outcomes and prevent antimicrobial resistance. However, large meta-analyses have demonstrated that monotherapy resulted in comparable morbidity and treatment failure rates and reduced nephrotoxic effects owing to avoidance of aminoglycoside agents when compared with dual therapies.[31] In critically ill children with suspected gram-negative bacterial infections, dual antimicrobial therapy is fitting to ensure appropriate coverage while culture data are pending. However, once the organism is identified and susceptibility is determined, only 1 agent is needed to complete therapy in most instances.

Appropriate Administration and De-escalation of Antibiotic Therapy

Ensuring proper dosing and administration of the appropriately selected antibiotic is another essential principle of AS. Pediatric AS programs using prospective surveillance of antibiotic use and therapeutic level monitoring have been effective in identifying and correcting dosing.[32-34] Use of agents such as vancomycin hydrochloride, aminoglycosides, and voriconazole can benefit from the pharmacologic expertise provided by AS programs. Surgical antimicrobial prophylaxis is another area in which AS can have an impact through the design of protocols and standardized prescription orders to ensure that antibiotics are administered before incision, readministered every 3 to 4 hours intraoperatively during prolonged cases, and discontinued 24 to 48 hours later to avoid future infections with resistant pathogens.[35]

Appropriate and timely de-escalation or discontinuation of antimicrobial therapy is probably the best recognized and most widely adopted principle of AS. Prospective audit and feedback strategies are commonly used by institutional stewardship programs through which antimicrobial use is monitored and peer reviewed to assess whether therapy should be continued, adjusted, de-escalated, or discontinued on the basis of clinical and microbiological data. De-escalation of therapy can be achieved by reducing the number of antibiotics, selecting narrow- over broad-spectrum antibiotics, or converting parenteral to oral therapy. This strategy has been proven to be effective in pediatric institutions and has significantly decreased unnecessary antimicrobial use.[32,33,36]

Use of Expertise and Resources at Point of Care

Owing to the continued increases in antimicrobial-resistant pathogens in health care and community settings and resultant changes in treatment recommendations, access to expertise in clinical pharmacology and infectious diseases is critical to ensure that the most appropriate and effective therapy is provided. As recommended in the IDSA and SHEA guidelines for developing AS programs, development of local AS teams or committees composed of experts from multiple fields, including infectious diseases, pharmacy, microbiology, infection control, and information technology (**Figure**), can help provide the needed guidance and resources to hospitals, offices, and communities.[6] In addition, support from hospital administration and medical staff leadership in establishing appropriate authority and securing financial resources for an AS program is essential to its success. Potential strategies to promote AS in smaller facilities and community-based settings with fewer resources are provided in **Table 2**.

Continuous and Transparent Monitoring of Antibiotic Use

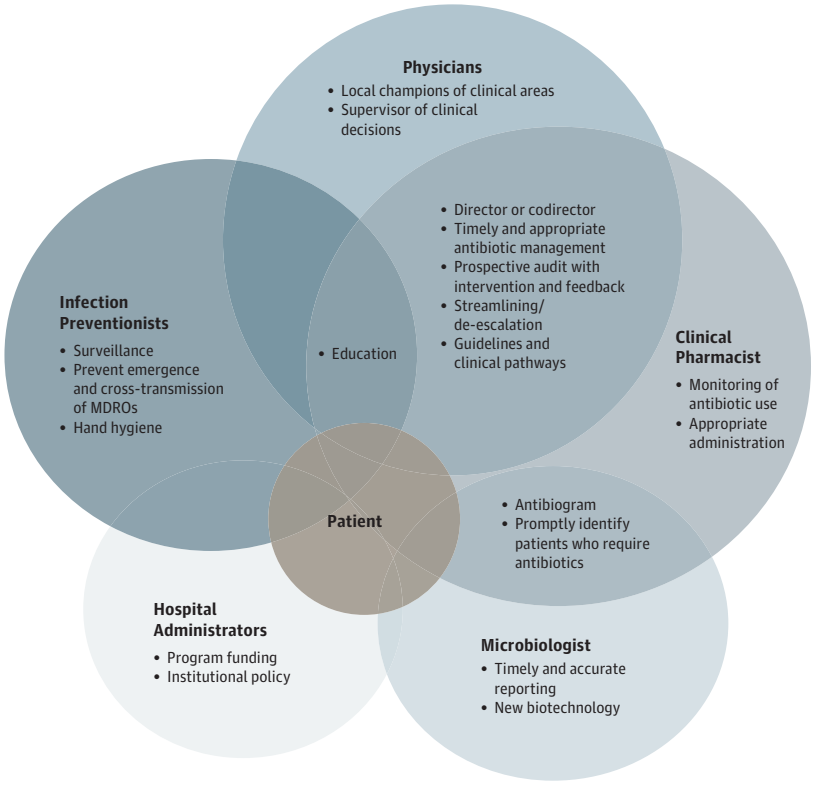
Finally, the appropriate use of antimicrobials cannot be fully realized without continuous and transparent monitoring of antimicrobial use to assess how and why certain antimicrobials are being used and to identify specific opportunities for AS intervention and education. In addition, monitoring can enable prospective evaluations of the effectiveness of active AS programs and assist in making modifications to existing protocols to improve performance. Consistent and standardized surveillance at institutions can provide the foundation for benchmarking antimicrobial use and providing comparisons between hospitals. Controlling for differences between hospitals and applying risk adjustments remain a challenge for such benchmarking efforts. Recently, the National Healthcare Safety Network of the Centers for Disease Control and Prevention launched the medication-associated module that is intended to monitor institutional antimicrobial use and resistance. This tool has the potential to address the questions of appropriate antimicrobial use on regional and national levels and help develop benchmarks.[37]

What Are the Common Barriers to Development and Implementation of AS Programs?

A number of well-recognized barriers may hinder the development and growth of AS programs. Understanding these barriers and identifying potential strategies to overcome these challenges is valuable for practitioners seeking to start a new AS program or to expand or improve existing programs (Supplement [eCase 2]).

Much of the data regarding barriers to AS implementation and development are derived from surveys of infectious disease specialists. In one survey, more than 80% of respondents and 100% of respondents currently involved in developing an AS program reported the existence of significant barriers.[38] The most frequently cited barriers included lack of funding or time to support a program, lack of hospital administration awareness of the value of AS programs, and concerns about the effect of the stewardship program on physician autonomy, such as potential antagonism be-

Figure. The Antimicrobial Stewardship Team



A Venn diagram demonstrates overlapping specialist responsibility for guidance and for providing resources to hospitals, offices, and communities. MDRO indicates multidrug-resistant organism.

tween physician groups. This study also suggested that some of the current pediatric AS programs are extensions of adult-centered programs and thus may not be tailored to the specific needs of pediatric patients. A potential strategy to overcome these barriers is to use a conceptual framework that identifies potential categories of barriers as knowledge, attitude, and practice barriers (**Table 3**).

Knowledge Barrier: Lack of Knowledge and Awareness by Administrative Leadership

- Example: During a meeting, your institutional leadership is unfamiliar with AS and is questioning its value.

A growing evidence base supports the value of AS in pediatrics. Highlighting AS as a program of patient quality improvement and safety intervention with secondary benefits of cost savings is likely to be a winning strategy. This strategy may require additional work, but the evidence is on your side. Begin by reviewing evidence-based guidelines for AS[6] and strategies for overcoming the reluctance of administrative leaders to invest in AS.[39] In addition, identifying and arranging a face-to-face meeting with an effective physician champion within the leadership can be a key strategy in educating key decision makers about the importance of AS programs.

Attitude Barrier: Lack of Agreement About Clinical Management

- Example: Your AS program makes recommendations for treatment of sepsis caused by gram-negative bacilli. You find that the primary service disagrees with the recommendation to discontinue dual coverage because these care providers are concerned about the efficacy of single-agent therapy and the potential for the emergence of resistance.

This example provides an opportunity to form a multidisciplinary group to review existing evidence and develop consensus. Some clinicians may not be familiar with current evidence. In addition, a significant gap in the available clinical evidence could lead to opportunities to design a clinical research study or to survey and review local practices and clinical outcomes. Demonstrating variability in local practice can be a powerful motivator to develop practice guidelines. Engaging all relevant and invested clinicians, including infectious diseases specialists, is a key step in this process.

Attitude Barrier: Loss of Physician Autonomy and Creation of Antagonism

- Example: Your AS program frequently provides recommendations to the staff in various specialty units about changing or discontinuing antimicrobial therapy. However, you find that compliance with your recommendations is relatively low and sense that the recommendations are causing antagonism because they challenge long-standing clinical practices within the units.

The structure and approach in which an AS program is implemented can significantly affect the perception and acceptance of the program by clinicians. Any new intervention that is perceived by front-line clinicians as interfering with their routine practices or adding to the complexity of delivery of care will undoubtedly be questioned.

Table 2. Potential Strategies to Promote AS Programs in Community-Based Settings

Key Elements	Outpatient Settings	Community Inpatient Settings
Establish need for AS program	Provide evidence-based data to implement AS program to leadership, management, and peers	Provide evidence-based data to implement AS program to leadership, management, and peers
Establish team and resources	Identify local physician champion (eg, general pediatrician) Identify potential resources (eg, pharmacy records, microbiology results, relevant information technology) Establish dissemination and education strategies for peers, patients, and families	Identify local physician champion (eg, hospitalist or general pediatrician) Solicit representation from key admitting practices Identify potential resources (eg, pharmacy records, infection-control practitioners, pharmacist, microbiologist, microbiology results, information technology)
Prioritize AS program activities to generate data	Develop treatment guidelines for common infections (antibiotic indications and regimens for pharyngitis, otitis) Develop treatment guidelines to avoid unnecessary antibiotics (eg, for RSV, asthma) Examine susceptibility profiles of common pathogens (eg, *Staphylococcus aureus* and *Escherichia coli*)	Establish restrictive formulary Develop pediatric antibiograms Develop treatment guidelines (empirical regimens for pneumonia and cellulitis; no antibiotics for RSV) Review of select antibiotics (eg, linezolid, carbapenems) Facilitate conversion of intravenous to oral antibiotic therapy Identification of "drug-bug" mismatch (resistant pathogens treated with ineffective antibiotics)
Set AS program goals for agreed-on process measures	Adherence to guidelines (eg, avoid antibiotic use for viral infections) Changes in antibiotic selection and use (eg, increased use of narrow-spectrum agents or decreased days of therapy per patient) Antimicrobial costs Appropriate cultures obtained before antibiotic therapy initiation Provider acceptance of recommendations	Changes in antibiotic use Formation of AS team with resources allocated as promised Timely administration and appropriate duration of antibiotics Appropriate cultures obtained before antibiotic therapy initiation Provider acceptance of recommendations
Set AS program goals for agreed-on outcome measures	Reduction in adverse events Rate of hospitalization	Reduction in adverse events Antibiotic resistance trends Reduction in *C difficile* rates

Abbreviations: AS, antimicrobial stewardship; RSV, respiratory syncytial virus.

Table 3. Barriers to AS Programs

Category	Barriers	Examples
Knowledge	Lack of awareness Lack of familiarity	No knowledge of AS guidelines Unfamiliar with guidelines in general or with specific guideline(s)
Attitude	Lack of agreement Lack of self-efficacy Lack of outcome expectancy	Disagreement with specific guidelines Perceived lack of confidence or preparation to implement guidelines Lack of belief that guideline will lead to an important health outcome
Practice	External factors	Lack of time, staff, administrative support, reimbursement, supplies, educational materials to support stewardship program

Abbreviation: AS, antimicrobial stewardship.

Local champions identified within various clinical care areas (eg, ICUs, surgical services) who are supportive of the goals and mission of AS can be extremely effective in successful implementation of program activities. These champions can bridge the gap between the AS team and their colleagues. Clinicians and practitioners whose patients can be affected in the initial development of clinical practice guidelines or pathways must be engaged. When implementing an AS program, members of the stewardship team should meet with these stakeholders to introduce the anticipated program protocols and activities and to seek and identify additional areas in which AS programs can provide targeted assistance. For example, the oncology service may indicate that they are seeking to shorten the time to receipt of the first dose of antibiotic for patients hospitalized with fever and neutropenia. Finally, development of alternative or creative AS strategies may be necessary beyond the conventional prospective audit and feedback mechanism. For certain special populations (eg, patients undergoing bone marrow transplant), focusing AS activities on the development of consensus guidelines and care pathways for fever and neutropenia may be more effective. Strategies tailored to specific patient populations and practice patterns of a specific group of clinicians can enhance acceptance and improve compliance.

Practice Barriers: Lack of Funds, Resources, and Time

- Example: Your institution supports establishing an AS program, but no resources are available to support physician or pharmacist efforts.

Despite many reports demonstrating cost savings associated with AS programs, frequently cited barriers to program development include financial, personnel, and resource limitations.

When developing a proposal for an AS program to your leadership, it should be framed as a "business case."[39] The return on investment from AS programs typically can be seen within a short time, with cost savings routinely achieved within 1 year of implementation owing to the reduction of unnecessary antimicrobial use and decrease in the pharmacy budget. However, the short-term cost savings from reduction of antimicrobial use may not be sufficient for long-term financial justification and does not reflect the full economic impact of AS. Building a business case that demonstrates the economic benefits of improved patient outcomes secondary to AS, such as decreased lengths of stays in the ICUs and hospitals, HAIs, and antibiotic-associated adverse events, can lead to a stronger economic argument for long-term funding. Scrutiny of other nonantibiotic high-cost therapies, such as palivizumab, can be incorporated into the scope of AS activities for a larger effect on cost savings.

Practice Barriers: Lack of Technical Resources and Infrastructure to Implement a Comprehensive AS Program

- Example: You are aware that many AS programs incorporate technology to assist in daily surveillance of antimicrobial use and to identify "bug-drug" mismatches, but you will not have access to these resources as you begin your AS program.

When building an AS program, leaders must recognize the limitations of technical or infrastructure resources and develop activities and protocols that account for these limitations and carry realistic chances of achieving their goals. This strategy often requires identifying "low-hanging fruit" after auditing antimicrobial use and developing AS projects that are smaller in scope. For

example, a single antibiotic that is frequently used inappropriately can be identified and targeted for intervention to help facilitate timely and appropriate de-escalation of therapy. In addition, strategies can be developed to facilitate transition from intravenous to oral therapy. Developing a clinical practice guideline or pathway for commonly treated conditions is another way to create a large effect on antimicrobial use in settings of limited resources. Success from smaller stewardship projects and activities can be the basis for increased funding and support through evidence- and data-driven promotion and education about AS programs to leadership.

What Outcomes Can Be Measured to Monitor Successful AS?

Efforts have been made to measure and quantify the impact and outcomes of AS programs. Initial studies reported on process measurement outcomes, such as decreased use of antimicrobials and subsequent reduction in costs owing to decreases in unnecessary or inappropriate antimicrobial therapies after implementation of AS protocols.[32,33] Antimicrobial stewardship has been shown to reduce prescription errors by incorporating clinical guidelines and standardized computerized provider order entries to ensure therapeutic and safe dosing.[34] In addition, AS protocols have been effective at promoting safe and appropriate transitions from inpatient to outpatient management of infections that require parenteral antimicrobial therapy.[40]

In contrast, relatively fewer studies have examined patient-oriented clinical outcomes of AS programs, such as lengths of hospital or ICU stays, HAIs, readmissions, mortality, *Clostridium difficile* infections, and adverse events associated with antibiotic therapy. Several studies have described significantly decreased *C difficile* infection rates in adults after implementation of AS programs, especially those targeting fluoroquinolone use.[41-44] A Cochrane review in 2005 evaluated 60 studies of interventions targeting antibiotic prescribing in inpatient settings and identified only 9 that included clinical outcome measures.[45] Of these 9 studies, clinical outcomes were improved in 3, unchanged in 4, and worsened in 2.[46] Another systematic review of AS programs in critical care settings concluded that most studies reported unchanged mortality rates, HAI rates, and lengths of ICU and hospital stays after AS implementations.[47] One recent study demonstrated decreased HAI rates but unchanged lengths of stay and readmission rates after AS implementation.[48] Another study reported increased cure and decreased treatment failure rates for infections as a result of AS.[49] These variations of clinical outcomes reported from a small number of adult studies highlight the need for further research and data to assess the impact of AS. As a result, outcome research has been identified as one of the research priorities for AS by IDSA, SHEA, and PIDS to address the lack of standardization and validation of outcome measures, suboptimal study designs, and small samples that have plagued many studies.[9] Antimicrobial stewardship programs can play an important role in organizing and coordinating research efforts to address these deficiencies.

Antibiotic exposure is a recognized risk factor for the emergence of bacterial resistance.[50-52] Efforts to reduce the prevalence of antibiotic resistance by AS seek to decrease the level of exposure and limit antibiotic use. However, studies attributing decreased antibiotic resistance directly to AS programs have been relatively lacking, likely owing to the difficulty of controlling for confounding variables and interventions other than AS that affect resistance prevalence and the limitations of nonrandomized study designs.[44,53] In addition, evaluation of resistance prevalence as an outcome of AS requires long-term measurements. Studies have shown decreased resistance in gram-negative bacilli after implementation of AS targeting the use of third-generation cephalosporins, fluoroquinolones, and carbapenems.[54-58]

Table 4. Minimum Requirements for AS Program Outlined by SHEA, IDSA, and PIDS

Requirement	Details
Creation of a multidisciplinary interprofessional AS team	Physician directed or supervised At least 1 member with training in AS Team should include physician, pharmacist, clinical microbiologist, and infection preventionist
Formulary restriction	Limit duplicative antibiotics
Develop institutional clinical guidelines	Management of common infection syndromes
Stewardship interventions to detect and eliminate unnecessary or inappropriate antibiotic use	Multidrug redundant antibiotic use Antibiotic use in nonbacterial infections or bacterial colonizations Empirical antibiotic regimens that are inadequate or too broad Antibiotic selections that do not adequately treat culture-confirmed pathogens
Process to measure and monitor antimicrobial use	Internal benchmarking
Periodic distribution of facility-specific antibiogram	Provides rates of relevant antibiotic susceptibilities to key pathogens

Abbreviations: AS, antimicrobial stewardship; IDSA, Infectious Diseases Society of America; PIDS, Pediatric Infectious Diseases Society; SHEA, Society for Healthcare Epidemiology of America,

Role of Regulations to Promote AS

In a 2012 joint policy statement, the IDSA, SHEA, and PIDS recommended that AS programs should be mandated through existing regulatory mechanisms such as the Centers for Medicare & Medicaid Services.[9] They also outlined specific requirements for AS programs (**Table 4**). At present, no regulatory mandates require AS at institutions at the federal level in the United States. In 2008, the California Health and Safety Code[59] mandated that all general acute care hospitals begin evaluating and monitoring the appropriateness of antimicrobial use within each institution—the first regulation of its kind in the United States. However, this bill did not include specific language on how institutions should perform these evaluations and monitor antimicrobial use. As pointed out by the joint policy statement, lessons can be learned from California Senate Bill 739 to help create an effective regulatory policy that leads to widespread presence of AS by providing specific mandates for establishing AS programs within various practice settings and by defining the role of such programs in promoting appropriate antibiotic use.

Future Directions for AS

Further research evaluating the strategies and outcomes of AS programs in pediatrics is needed, especially for pediatric-specific patient populations such as neonatal ICUs and other specialty services. In addition, efforts to expand AS activities in outpatient settings should continue by creating novel and innovative protocols that are effective in addressing the challenges unique to this practice setting wherein access to financial support and infectious diseases expertise may be limited. A similar approach is needed for pediatric AS in community hospitals or pediatric wards that are part of an adult-based medical center. Finally, education and outreach programs need to be further developed to assist practitioners in evidence-based antimicrobial use and increase awareness among patients, families, and communities of the benefits of judicial antimicrobial use.

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