PSAP

PHARMACOTHERAPY SELF-ASSESSMENT PROGRAM

SEVENTH EDITION • BOOK 9

INFECTIOUS DISEASES

AMERICAN COLLEGE OF CLINICAL PHARMACY

Antimicrobial Stewardship

By Marc H. Scheetz, Pharm.D., BCPS (AQ Infectious Diseases);
and Michael Postelnick, BSPharm, BCPS (AQ Infectious Diseases)

Reviewed by Craig A. Martin, Pharm.D., BCPS (AQ Infectious Diseases); and
Anne L. Hume, Pharm.D., FCCP, BCPS

Learning Objectives

1. Identify integral members of a multidisciplinary team for performing antimicrobial stewardship efforts.
2. Devise a strategy to measure outcomes of antimicrobial stewardship.
3. Develop priorities and goals for an antimicrobial stewardship team.
4. Evaluate different strategies of antimicrobial stewardship and justify resource use.
5. Develop a business plan for a sustainable antimicrobial stewardship team using evidence-based practices.

Introduction

Appropriate antimicrobial stewardship remains one of the most important strategies for preserving the efficacy of antimicrobial agents in the treatment of infectious diseases. Pharmacists remain uniquely situated to provide expert guidance on the appropriate agent, dosage, and duration of therapy for antimicrobials at both the patient and policy level. These interactions with the medical team can expedite care, minimize adverse drug reactions, and improve patient outcomes. This chapter highlights strategies to effectively manage antimicrobial stewardship efforts.

History

The dawn of the antimicrobial era heralded tremendous advances in the treatment of patients with infection. Confidence was high that the medical community had all but won the war against microbes. In the late 1960s, U.S. Surgeon General William H. Stuart reportedly said it was "time to close the book on infectious diseases" and "declare the war against pestilence won." Unfortunately, with the growing number of highly resistant pathogens, exactly the opposite has occurred.

The considerable efficacy and relatively low risk of toxicity associated with antimicrobials led to their widespread and inappropriate use. During the early part of the antimicrobial era, little concern existed about the stewardship of these resources because the pharmaceutical industry continuously produced innovative, highly effective agents that filled the void when older agents lost their effectiveness. Furthermore, the competition between pharmaceutical companies in marketing these agents sometimes encouraged their inappropriate use.

In hospitals, expenditures for antimicrobials outpaced those for all other drugs. In the late 1980s, antimicrobial expenditures commonly approached 40% of the hospital pharmacy drug budget. The onset of prospective payment systems such as Medicare reimbursement based on

Baseline Review Resources

The goal of PSAP is to provide only the most recent (past 3–5 years) information or topics. Chapters do not provide an overall review. Suggested resources for background information on this topic include:

- Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis 2007;44:159–77.
- Drew RH, White R, MacDougall C, Hermsen ED, Owens RC Jr; Society of Infectious Diseases Pharmacists. Insights from the Society of Infectious Diseases Pharmacists on antimicrobial stewardship guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Pharmacotherapy 2009;29:593–607.

Abbreviations in This Chapter	
CDSS	Clinical decision support systems
DDD	Defined daily dose
DOT	Day of therapy
QALY	Quality-adjusted life-year

diagnosis-related groups encouraged pharmacy departments to critically evaluate antimicrobial use in their institutions. These early programs set the stage for current antimicrobial stewardship programs.

Goals

Antimicrobial stewardship is a program that supports the appropriate selection, dosing, route, and duration of antimicrobial therapy, with goals to match these functions. The primary goal of these programs is to improve clinical outcomes while minimizing the unintended adverse consequences of antimicrobial use. It may seem intuitive that these programs should also reverse antimicrobial resistance; however, halting or slowing resistance is a more achievable goal because resistance mutations are durable once they are established.

Other important goals include ensuring that only antimicrobials active against the involved pathogen are prescribed and using the most fiscally appropriate approach. The Infectious Diseases Society of America, in conjunction with the Society for Healthcare Epidemiology of America, has published guidelines that serve as a framework for the antimicrobial stewardship programs. Core stewardship strategies with the greatest evidence include prospective audit with intervention and feedback performed by an infectious diseases physician; and a clinical pharmacist with training in infectious diseases or formulary restriction with required preauthorization for selected antimicrobials.

Multidisciplinary Approach

To be effective, an antimicrobial stewardship program should be multidisciplinary. Antimicrobial stewardship should be considered a medical staff function under the auspices of Patient Safety and Quality Assurance. Core members to include on the team are an infectious diseases physician and a clinical pharmacist with training in infectious diseases. The optimal team will also include a clinical microbiologist, an infection control professional, an information systems specialist, and the hospital epidemiologist.

Surveys show that among hospitals with active stewardship teams, clinical pharmacists are the most common members, underscoring the recognition of pharmacists for their competency in this area. In addition, the support of health system administrators is essential for the program to secure necessary resources and authority. Information technology support is also vital in tracking antimicrobial use on an ongoing basis. Infection control and hospital epidemiology can assist the team in focusing efforts to address local antimicrobial resistance issues. Data from the clinical microbiologist allow the evaluation of evolving local trends in antimicrobial resistance and assist in measuring the long-term impact of the program.

Pharmacists can receive antimicrobial stewardship training in several ways. Postdoctoral training is available through PGY2 ID residencies and PGY2/3 ID fellowships. These opportunities can be found at the Society of Infectious Diseases Pharmacists Web site *(www.sidp.org)*. In addition, pharmacists may enroll in a computer-based certification program through the same society or through a separate organization, Making a Difference in Infectious Diseases.Pharmacotherapy This group also offers live training *(www.mad-id.org)*.

Antimicrobial Use in Hospital Systems

Antimicrobial Resistance

The ability of bacteria to develop and maintain antimicrobial resistance has been a hallmark of the antimicrobial era. From the development of staphylococcal resistance to penicillin to current issues with carbapenem-resistant Enterobacteriaceae, bacteria have a remarkable capacity to respond to antimicrobial exposure.

Antimicrobial consumption has been clearly associated with an increased incidence of resistance. Countries with centralized health care systems such as Finland have reduced rates of resistance by limiting prescriptions for particular agents. On a patient level, data support that individuals with the greatest exposure to antimicrobials are likely to be colonized with resistant organisms. In addition, resistant organisms are more likely to be found in the hospital, where antimicrobial use is concentrated, than in the community setting. In the hospital, areas such as intensive care units show a higher incidence of multidrug-resistant organisms than do general care units.

Escalating Costs

Growing antimicrobial expenditures has been one of the primary triggers for examining antimicrobial use in institutions. Antimicrobial formulary committees have worked to limit the use of expensive agents that offered little advantage over other antimicrobials. In addition, other costs associated with the inappropriate use of antimicrobials have become apparent.

The costs associated with antimicrobial resistance, adverse effects, and inappropriate antimicrobial selection likely exceed the costs associated with poor formulary management. For instance, infections caused by resistant organisms result in longer hospital stays, require more resources, and have a higher mortality rate than when the same infection is caused by a susceptible organism. The costs of these differences are estimated at $21,000 per resistant infection. Reducing a single center's rate of resistant infections by 3.5% could save almost $1 million in hospital costs. In addition, the treatment of adverse effects from antimicrobials prescribed when treatment is not indicated, can be viewed as an unnecessary and preventable cost. With patient stay per diem rates of $2000–$5000, these costs quickly dwarf those for antimicrobial acquisition.

As resistant organisms have become more common, clinicians have used more potent agents with broader spectrums to ensure coverage of these pathogens. This practice was supported by data showing that patients who do not receive therapy that is active against the infecting organism at treatment initiation are more likely to suffer adverse consequences from their infection. For example, patients in septic shock show decreased survival of 8% per hour when appropriate therapy is delayed. As such, clinicians must differentiate between critically ill patients, who require broad empiric therapy, and individuals with less acute infections, who can wait for antimicrobial use that is more selective. Broadening therapy unnecessarily increases costs as well as the burden of resistance. This becomes a self-perpetuating cycle and a greater economic burden on the institution.

Although most antimicrobials are relatively safe, the incidence of preventable adverse effects associated with their use is significant. A recent study of emergency department visits for adverse drug reactions showed that antimicrobials led to more such visits than did drug classes considered more toxic (e.g., anticonvulsants, anticoagulants). Hypersensitivity reactions are common adverse events associated with antimicrobials that may not be easily predicted. Antimicrobials are also the most common drugs leading to serious drug-induced liver injury.

Antimicrobial-induced diarrhea is another problem, and *Clostridium difficile* infection is a serious complication. *C. difficile* infections are often difficult to treat, can be recurrent, and may be associated with increased morbidity and mortality. Other antibiotic adverse reactions such as seizures and blood dyscrasias are rare, but they underscore the need for appropriate antimicrobial prescribing. The medical management of patients who develop preventable adverse effects to antimicrobials also contributes to the cost of therapy.

Cost-effectiveness is another issue that the antimicrobial stewardship program should consider. To achieve the desired outcome, clinicians need to use an antimicrobial that is effective against the infecting pathogen. Culture and susceptibility results are often used to help guide therapy. However, clinicians occasionally fail to note discrepancies between the causative organism and the antimicrobial selected. In the authors' organization, therapeutic antimicrobial mismatches (e.g., an antimicrobial used for a pathogen that shows resistance) are monitored using computerized clinical decision support systems (CDSS) with interventions developed by the stewardship team. Despite this consistent presence, about 15 therapeutic-antimicrobial mismatches per quarter are deemed critical. A critical mismatch is one in which, if therapy is not altered, a high probability of significant harm might occur to the patient, with subsequent increased costs from the management of these adverse events. These critical events usually involve untreated or inappropriately treated bloodstream infections. Because the incidence of antimicrobial resistance continues to rise, surveillance to identify and address these mismatches will become increasingly important from both a patient safety and cost standpoint.

Methods of Tracking Stewardship Outcomes

The sustainability of an antimicrobial stewardship program requires the documentation of both clinical and fiscal outcomes. The following provides a framework for documenting interventions in a valid and measurable manner.

Antimicrobial Use Measurements

The measurement of fiscal and clinical outcomes of antimicrobial therapies begins with the appropriate unit of measure for the numerator that defines antimicrobial consumption. Although debate exists on the most appropriate metric for antimicrobial use, two main measures are accepted.

The first is the defined daily dose (DDD) of an antimicrobial. The World Health Organization *(www.who.int/classifications/atcddd/en/)* established the DDD, which represents the average daily dosage of an antimicrobial in a "standard" patient. Pharmacists quickly recognize that this classification disregards patient-specific factors. For example, if patient A has normal kidney function and receives 1000 mg of vancomycin twice daily, the patient would be considered to have received one DDD of vancomycin. Patient B has a creatinine clearance of 60 mL/minute and receives 1000 mg of vancomycin once daily to provide a drug exposure similar to patient A. However, patient B would be classified as having received one-half DDD of vancomycin.

To address the patient-specific factors that are ignored in the DDD system and classify antimicrobial days on the basis of similar exposure profiles, day of therapy (DOT) measurements have been defined. The DOT represents a day in which any amount of the therapy was received. An inherent problem with DOTs is that it assumes the drug was dosed appropriately. Hence, patients who are under- or overdosed could be misclassified with only a single antimicrobial day. Despite these limitations, DOTs better reflect the overall population of antimicrobial exposures.

Efforts are under way to improve the electronic capture of DDDs and DOTs so that systems with electronic medical records may eventually compare their antimicrobial use with that of peer hospitals. A denominator (e.g., hospitalized patient-days) is then established such that the total drug amount (i.e., DDD or DOT) is divided by the number of patients at risk. By doing so, a rate of antimicrobial use per a standardized number of patients (e.g., 40 DDDs/1000 patient-days) can be created.

Fiscal Measurements

Because antimicrobials continue to make up a considerable portion of the drug budget for many hospitals, accurate evaluation of their cost is essential to fiscal stability. Comparing acquisition costs as raw numbers (e.g., $3 million in 2010 vs. $2.5 million in 2009) requires that all other variables remained unchanged. As a result, most facilities choose to compute antimicrobial costs per patient-day. A standard approach is to calculate costs per month or per quarter depending on the hospital volume. Once these numbers are compiled, data are normalized to antimicrobial costs per 1000 patient-days. Data should also be compared using similar calendar months to ensure that seasonal variations in antimicrobial use do not result in spurious conclusions.

Large reductions in cost per patient-day commonly occur in the early years of a stewardship program. However, antimicrobial savings will eventually reach a nadir because these are necessary drugs, and the ultimate goal is to direct therapy to the appropriate patients, not to eliminate their use. Once a program has reached this point, financial outcomes can still be monitored as a function of change in cost over time. Because drug costs will still increase yearly with inflation, these known increases can be modeled to produce projected costs for similar drug use in the following year. The institutional administration and antimicrobial stewardship leadership should establish reasonable goals so that when a targeted value for antimicrobial use is attained, further cost reduction is not expected. Failure to set reasonable goals and apply correction factors may result in requests from administration for reductions in appropriate antimicrobial use and potentially worse patient outcomes (Figure 1-1).

Antimicrobial purchase costs account for less than 10% of the inpatient health care costs for patients with infections; therefore, they are just one of the financial targets for stewardship teams. The cost of improper treatment, which may lead to prolonged hospitalizations and the promotion of resistance, can quickly dwarf the cost of a single antimicrobial treatment course. Other indirect costs such as additional procedures related to nosocomial superinfections and the decreased societal productivity of patients should be considered. Estimates have shown that the attributed cost of antimicrobial-resistant infections at a single institution can be more than $13 million a year. Although a goal of preventing all antimicrobial-resistant infections is likely unachievable, any significant progress in this area can improve hospital finances with paralleled patient outcomes.

Clinical Outcomes

Many studies have confirmed the positive effect of antimicrobial stewardship on financial outcomes, but benefits on clinical outcomes are less common in the literature. Clinical outcome studies are more difficult to conduct, although they are necessary to assess the full value of antimicrobial stewardship. Limited data suggest that when comparing before and after stewardship efforts or trials of stewardship teams with no stewardship team, clinical outcomes range from better to indifferent. Specifically, active antimicrobial stewardship has decreased antimicrobial use for nonbacterial infections, and some studies have shown a decreased incidence of antimicrobial resistance. Benefit has also been shown through the avoidance of preventable adverse drug reactions.

Mathematic modeling has shown that antimicrobial stewardship efforts to ensure proper care for bloodstream infections are justifiable from the hospital perspective, costing only about $2400 per quality-adjusted life year (QALY) gained. Such cost-effectiveness studies allow a calculation of the cost associated with increasing effectiveness, in this case 1 additional life-year gained of quality health. The positive effects from all of these

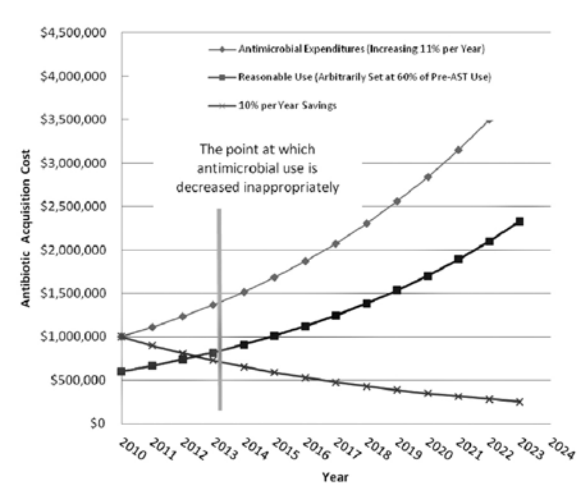

Figure 1-1. Projected yearly increase of an antimicrobial budget with an 11% rate of inflation, theoretical data.

AST = antimicrobial stewardship team.

studies should be considered with the understanding that a bias exists toward a type I error rate (i.e., authors and editors are more likely to publish favorable efforts). Additional studies assessing clinical outcomes are discussed in the following section.

Antimicrobial Stewardship Strategies

The many strategies for the conduct of antimicrobial stewardship fall into two categories: prospective/active antimicrobial management and retrospective/passive efforts. Approaches can be combined to maximize efficiency and intended outcomes. This combined strategy is often referred to as prospective audit and feedback.

Preauthorization/Formulary Restriction

Prospective antimicrobial restriction involving preauthorization and formulary restriction can be employed in several ways. The most common method is to restrict antimicrobial use to a set of criteria. For example, the use of linezolid could be limited to methicillin-resistant *Staphylococcus aureus* pneumonia if this were appropriate, given the other available drugs in the hospital system. Criteria can be based on patient factors (e.g., specific disease states, allergies, antimicrobial history) or on drug-specific criteria (e.g., maximum length of therapy, limitation to combination therapy). Restrictions can either be absolute, such that therapy is never permitted, or conditional after the evaluation of specific criteria.

Restrictive criteria are often placed at the point of prescribing through the use of an antimicrobial order form. When restrictions are placed prospectively, most institutions allow the dispensing of drug when a review cannot be completed in a timely manner. This allows patients to receive active therapy immediately.

Order forms can become less effective if providers intentionally use ambiguous indications to obtain the restricted agent. Pharmacists must be keenly aware of ways to circumvent the system (e.g., fictitious indications, dispensing drug after day-shift hours). In certain cases it is prudent to fully evaluate the indication and require review by a stewardship expert before dispensing. These restrictions are often enacted by an antimicrobial stewardship team, which functions as the gatekeeper of restricted agents. The requesting physician usually contacts the service, and the patient case is compared with hospital guidelines and interpretative criteria for appropriate use. The antimicrobial stewardship team serves as an impartial arbitrator and generally has the authority to allow the use of a restricted antimicrobial for patient-specific situations.

Because disputes can occur between those connected to the patient case and those applying guidelines based on objective criteria, most institutions have an appeals process. This can be a review by an impartial physician not involved in the patient case but with expertise in the subject matter.

Outcomes with Preauthorization/ Formulary Restriction

Restrictive stewardship programs can result in immediate outcomes (primarily financial gains) for hospitals. With appropriate enforceability, cost savings have been reported as high as $800,000 yearly. Several studies have also shown that limiting antimicrobial use to appropriate indications can decrease antimicrobial resistance. These restrictions may limit the horizontal transfer of bacteria (i.e., transfer of a resistant pathogen from one patient to another) by decreasing the favorability of the environment. When several patients receive broad-spectrum antibacterial therapy that alters normal flora, the environment is well adapted for rapid horizontal transfer of bacteria across hosts. This phenomenon was emphasized with the *C. difficile* incidence when changes in clindamycin prescribing were temporally associated with the cessation of disease. Clindamycin use altered the normal microbiota of patients; thus, the transfer of *C. difficile* from one patient to another occurred more readily.

Caution should be taken when applying antimicrobial stewardship to reverse resistance. Many institutions often try to curb antimicrobial use to reverse antimicrobial resistance in response to antimicrobial exposure. Studies on this approach have been less encouraging. For example, cephalosproin restriction resulted in a compensatory decrease in resistance to cephalosporins; however, increased use and increased resistance was seen with carbapenems.

Benefits and Pitfalls

The chief advantage of preauthorization and formulary restriction is that the critical period for antimicrobial selection is the point before the patient receives a drug. Thus, patients are assessed before any outcome can be attributed to a therapy. In doing so, antimicrobials can be stringently managed, and appropriateness of therapy can reach high levels. In addition, this strategy builds education into the process. By interrupting a drug order for a suboptimal antimicrobial before a patient receives it, prescribers can be engaged in a discussion of best practices to ensure optimal therapy for their patient and for the ecology of their hospital. However, education through preauthorization, although effective, is limited because these interventions are often inefficient and improve the care of only one patient at a time. In addition, these efforts are generally unsustainable when the active support is removed.

Several disadvantages also exist with restrictive approaches. First, hiring additional staff to evaluate each antimicrobial can be difficult and expensive. A formulary restriction without an appeals process is problematic and may result in improper patient care.

A second disadvantage is that therapy can be delayed by the additional approvals needed with this process. For some infections, this delay can affect patient outcomes. The literature shows that timely therapy for serious infections is associated with improved patient outcomes, although the data are strongest comparing active treatments that were initiated within less than 1–2 days. In the absence of septic shock, data are unclear regarding whether a delay in therapy of a few hours is significant for individual patient outcomes. Studies assessing the global impact of hurried treatment are emerging, and a slight delay to allow time to solidify the diagnosis may prove beneficial. For example, attempting to hasten the time to antimicrobial therapy for community-acquired pneumonia was associated with more incorrect diagnoses. Preauthorization programs may not delay care when carefully developed.

Finally, this method of antimicrobial stewardship, if not appropriately supported by personnel, can increase tensions between front-line practitioners and administration.

Prospective Audit and Feedback Strategies

Prospective audit and feedback empowers a specialist to interact directly with prescribers to tailor antimicrobial care for patients. In general, these strategies are employed after the drug is initially dispensed. Patient populations that receive a disproportionate amount of care or specific antimicrobials can be targeted. In both cases, antimicrobial use is evaluated against a set of approved guidelines to ensure the optimal use of drug therapy. By targeting a specific population or drug, time efficiency can be maximized.

To identify populations to target, antimicrobial use can be compared according to patient-specific factors such as a cancer diagnosis. The days of therapy can be tracked for the patients on these specific units. Compilation of antimicrobial consumption allows benchmarking to compare current use with that in previous years. Once targets are defined, hospital-specific guidelines can be enforced in real time to improve care and identify opportunities for education.

A common goal of the prospective audit and feedback strategy is to identify and correct situations in which suboptimal care is occurring. In these cases, stewardship may result in additional antimicrobial treatment. For instance, many stewardship teams prospectively review gram-negative bacteremias to ensure that patients are receiving the most active and appropriately narrow therapy. Identification of these cases provides opportunities for practitioner education.

Computerized CDSS are relatively new additions to antimicrobial stewardship. These tools are designed to improve identification of inappropriate antimicrobial care at both the patient and hospital level. These CDSS allow real-time hospital antibiograms; track antimicrobial consumption at the patient level; identify patients to target by disease state, hospital location, or infecting organism; and interface with clinicians to provide feedback.

Clinical Outcomes Data

Studies assessing prospective audit and feedback consistently find decreased antimicrobial use and associated costs. Randomized trials comparing prospective audit and feedback strategies with the standard of care have shown a \$400–\$600 antimicrobial cost decrease per patient, a 37% decrease in antimicrobial use, and trends toward decreased patient length of stay.

A distinct advantage of prospective audit and feedback is that a discussion may occur about the best treatment between the practitioner and stewardship personnel. When feedback has occurred in this manner, acceptance rates of around 90% have been reported. These interventions have led to either improved or similar patient outcomes. Furthermore, these strategies employ education as a function of stewardship duties. One study found that 99% of patients receiving combination therapy initially required streamlining of antimicrobials to narrower therapies. Prospective audit and feedback resulted in practitioners following the advice of the stewardship team in 83% of the cases, and ultimately, nearly all (i.e. 97% of the original 83%) completed the recommended therapy. The practitioner knowledge gained was durable 7 months after program initiation, with only 54% of similar cases requiring intervention.

The goals of prospective audit and feedback are an extension of the traditional oversight process used in the prescription process, a role in which pharmacists are uniquely trained and situated. Prospective audit and feedback is common in academic hospitals, where antimicrobial specialists are most prevalent; however, these strategies may also be employed in the community. Community settings have seen almost a 20% reduction in antimicrobial costs when intermittent stewardship was performed 3 days/week. Even without extensive infectious diseases training, critical pathways and protocols can be created to ensure guideline-consistent care, and following well-accepted guidelines has improved patient outcomes.

Computerized CDSS can expedite prospective audit and feedback. For example, a stewardship team selectively targeted patients with two or more antimicrobials with overlapping spectrum of activity found that CDSS decreased the number of patients requiring review by 84%; of those reviewed, 71% had inappropriate therapy that required intervention, and redundant therapy was successfully discontinued in 98% of these cases. Thus, the use of CDSS can increase the specificity of antimicrobial review. Moreover, stewardship undertaken with the aid of computerized CDSS has been prospectively compared with conventional care delivered by an antimicrobial stewardship team. Notably, the team using computer technology achieved more cost savings in 3 months, with more interventions in a shorter amount of time per day.

Benefits and Pitfalls

Prospective audit and feedback strategies for antimicrobial stewardship facilitate a team approach to patient care, with practitioners focusing on individual patients and global hospital-based outcomes. This open feedback loop can reduce conflict between front-line practitioners and stewardship team members and allow efforts to be focused on broad-spectrum antimicrobials likely to promote resistance. This strategy also allows stewardship team members to intervene in cases of insufficient therapy. Although this may result in increased antimicrobial use, practitioners may be more receptive to the presence of a stewardship team when suggestions are not limited to a reduction in drug therapy.

Comparisons of Strategies

Active antimicrobial stewardship strategies such as prospective audit and feedback have been compared with passive approaches such as the use of order forms, stop orders, and limited formularies. A study that randomized medical teams to prospective audit and feedback support or standard indication-based antimicrobial guidelines found that prospective audit and feedback was associated with a shorter median duration of inappropriate antimicrobial use (2 days vs. 5 days) and a shorter median duration of hospital stay (7 days vs. 8 days).

A multisite study compared five institutions with passive antimicrobial management with nine institutions with active antimicrobial management; results showed better outcomes in the sites using active management. A stronger correlation with decreased cost of programs was also found with active management. In another study, outcomes differed on the basis of the provider performing stewardship, with infectious diseases pharmacists and physicians achieving better results than ID medical fellows, chief resident physicians, or attending physicians.

Recommendations from Professional Organizations

Antimicrobial stewardship is supported by several organizations in the United States and is obligatory in the United Kingdom and the European Union. In the United States, experts from the Society of Infectious Diseases Pharmacists, the Infectious Diseases Society of America, and the Society for Healthcare Epidemiology of America have created comprehensive guidelines for the conduct of antimicrobial stewardship. In addition, Web sites of the Society for Healthcare Epidemiology of America *(www.shea-online.org/news/stewardship.cfm)* and the Centers for Disease Control and Prevention (CDC; *www.cdc.gov/getsmart/healthcare/improve-efforts/index.html,*) have compiled outcomes data from antimicrobial stewardship studies and useful tools for the conduct of antimicrobial stewardship.

Although antimicrobial stewardship has been associated with favorable outcomes, participation in the United States has been largely voluntary to date. California has mandated that acute care hospitals monitor and evaluate antimicrobial use. The legislation also requires a quality improvement committee for the oversight of the judicious use of antimicrobials. Although many of the specifics remain to be defined formally, this initiative might be the first of stricter regulatory requirements for the judicious use of antimicrobials in the United States.

Role of the Pharmacist

Appropriate antimicrobial stewardship continues to gain importance as antimicrobial resistance rises, and only a few new drugs are developed each year. Pharmacists should serve as front-line practitioners in the appropriate stewardship of antimicrobials. Both prospective and retrospective stewardship efforts have shown promise for improving clinical outcomes and reducing costs.

Antimicrobial stewardship programs will likely expand beyond major medical centers and into the community. These programs will be multidisciplinary and will require pharmacy leadership for the achievement of goals based on patient outcomes rather than solely financial objectives. Hospitals will be able to benchmark their antimicrobial use and compare their antimicrobial consumption with similar U.S. hospitals. Sites will be able to participate in the CDC Antimicrobial Use and Resistance Option *(www.cdc.gov/nhsn/PDFs/pscManual/11pscAURcurrent.pdf).*

Annotated Bibliography

1. Camins BC, King MD, Wells JB, Googe HL, Patel M, Kourbatova EV, et al. Impact of an antimicrobial utilization program on antimicrobial use at a large teaching hospital: a randomized controlled trial. Infect Control Hosp Epidemiol 2009;30:931–8.

    This well-designed study randomized stewardship strategy at the level of the medical team, with some teams receiving prospective audit and feedback and some not. A primary strength of the study is that two commonly used strategies for stewardship (i.e., prospective audit and feedback and a passive restrictive

methodology) were compared. This study showed that the prospective audit and feedback group had a shorter patient length of stay (7 days vs. 8 days, p=0.03), lower antimicrobial median DDD (2 vs. 4 DDD, p<0.001), and fewer inappropriate antimicrobial days per patient (2 vs. 5, p<0.001). However, despite randomization, the patients treated by the different approaches might have varied in the severity of their underlying illness, with worse results predicted in the prospective audit and feedback group. The available data in the report suggest that patients who were more critically ill were in the prospective audit and feedback group because they had more bloodstream infections and fewer episodes of asymptomatic bacteriuria.

2. Carling P, Fung T, Killion A, Terrin N, Barza M. Favorable impact of a multidisciplinary antibiotic management program conducted during 7 years. Infect Control Hosp Epidemiol 2003;24:699–706.

This effort was one of the first to document the clinical benefits of antimicrobial stewardship efforts. The authors completed an interrupted time-series analysis in which antimicrobial use and antimicrobial resistance was followed before and after the implementation of an antimicrobial management program. The authors documented a decrease in the use of third-generation cephalosporins and aztreonam after the implementation of the program. In addition, there was a decrease in the associated antimicrobial costs and resistance, although patient severity of illness increased. Rates of *C. difficile* remained stable and rates of ceftazidime-resistant Enterobacteriaceae slightly decreased during the study period. Although this study shows that changes in antimicrobial resistance are possible, caution is urged because other studies have not replicated these findings. Of note, the program resulted in savings of $200,000–$250,000 in yearly acquisition costs after accounting for program costs.

3. Dellit TH, Owens RC, McGowan JE Jr, Gerding DN, Weinstein RA, Burke JP, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. Clin Infect Dis 2007;44:159–77.

These joint guidelines between the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America assess the evidence for the following antimicrobial stewardship strategies: education, guidelines and clinical pathways, antimicrobial cycling, antimicrobial order forms, combination therapy, streamlining or de-escalation of therapy, dose optimization, and parenteral to oral conversion. For instance, the guidelines evaluate the popular contemporary practice of "cycling" antimicrobials. They found that the practice is often unsuccessful for several reasons. First, low-protocol adherence often exists in practice, with "cycled" antibiotics not administered because of drug allergy concerns, conflicts with national guidelines, and prescriber preference. Second, available studies show that benefits are usually transient, and resistance re-emerges rapidly.

The guidelines are comprehensive and are essential reading for anyone considering the initiation of an antimicrobial stewardship program. The guidelines clearly highlight the strength of evidence for each strategy and effectively capture best practice evidence as well as popular opinion through traditional rating schemes (e.g., strength of recommendation B, quality grade III). Suggestions also exist for the appropriate composition of antimicrobial stewardship teams.

4. Drew RH, White R, MacDougall C, Hermsen ED, Owens RC Jr. Insights from the Society of Infectious Diseases Pharmacists on antimicrobial stewardship guidelines from the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. Pharmacotherapy 2009;29:593–607.

As a formal addendum to the Infectious Diseases Society of America/Society for Healthcare Epidemiology of America Stewardship guidelines, the Society of Infectious Diseases Pharmacists provided additional analyses of the programmatic strategies of antimicrobial stewardship. Practical insights into appropriate program goals and outcome measures and known pitfalls to the measurements of each are discussed. The authors also provide recommendations for the proper training of individuals seeking to perform antimicrobial stewardship activities. This guide, together with the compilation of empiric evidence provided in the Infectious Diseases Society of America/Society for Healthcare Epidemiology of America guidelines, can be used to form a business proposal for antimicrobial stewardship. Although these guidelines point clinicians in the proper direction, many of the references need to be evaluated fully to properly implement the stewardship strategies.

5. Evans RS, Pestotnik SL, Classen DC, Clemmer TP, Weaver LK, Orme JF Jr, et al. A computer-assisted management program for antibiotics and other antiinfective agents. N Engl J Med 1998;338:232–8.

A landmark trial in computerized clinical decision support, this study was the first major successful attempt to apply artificial intelligence to antimicrobial stewardship. Computer algorithms were used to formulate recommendations for appropriate antimicrobial treatment (i.e., escalation or de-escalation) at the patient level. This before-and-after study found that antimicrobial susceptibility-antimicrobial choice mismatch reports substantially decreased (from 27% to 3%) after the implementation of computer algorithms. The study also found decreases in excessively dosed antimicrobials, patient length of stay, and adverse drug events (all p<0.05). This study showed that CDSS combined with appropriate oversight of antimicrobial use could lead to improved patient outcomes. Since this trial, many other studies have shown that, in addition to clinical benefits, financial benefits are realized when an open feedback loop is combined with computerized clinical support.

6. Glowacki RC, Schwartz DN, Itokazu GS, Wisniewski MF, Kieszkowski P, Weinstein RA. Antibiotic combinations with redundant antimicrobial spectra: clinical epidemiology and pilot intervention of computer-assisted surveillance. Clin Infect Dis 2003;37:59–64.

Although 10 years old, the study showed the ability of simple computer algorithms to improve patient care. Despite the known benefits of computerized systems, only a small percentage of hospitals have implemented this technology. This retrospective cohort study analyzed the efficiency of a computer system designed to identify redundant antimicrobial therapy. Of patients receiving two or more antimicrobials, the system targeted team interventions by identifying 16% with redundant and unnecessary antimicrobial coverage. Further study showed that 71% of these antimicrobial combinations were inappropriate, and team intervention was successful 98% of the time. Hence, this study shows that computer software using relatively simple decision rules can improve the specificity of antimicrobial stewardship aims and increase time efficiency. These straightforward interventions accounted for almost $50,000 annually in savings (in 2003 dollars).

7. Harbarth S, Nobre V, Pittet D. Does antibiotic selection impact patient outcome? Clin Infect Dis 2007;44:87–93.

Because a cornerstone of antimicrobial stewardship is the correction of inappropriate antimicrobial choices, the clinician should be well versed in the poor outcomes attributable to incorrect selection. This article reviews current literature defining the relationship of inappropriate therapy to patient outcomes. Specifically, literature is presented and interpreted for the direct impact of antimicrobial therapy on cure rates and the utility of combination therapy for gram-negative sepsis. Both are common scenarios likely to be encountered and highlight the importance of the stewardship pharmacist functioning under the auspices of safety initiatives. A potential limitation of this article is that additional data have emerged in the setting of bacterial septic shock, where active therapy and time to active therapy were shown to be more significant.

8. Hoffman JM, Doloresco F, Vermeulen LC, Shah ND, Matusiak L, Hunkler RJ, et al. Projecting future drug expenditures—2010. Am J Health Syst Pharm 2010;67:919–28.

Versions of this article are published annually and describe each year's changes in antimicrobial acquisition costs. Using the values reported, stewardship teams can adjust their cost savings for inflation according to market factors. Antimicrobial agents are reported as a separate drug class. For instance, between 2007 and 2008, antimicrobials increased 7.3% in cost. The data are always limited because future inflation predictions are speculative and cannot be calculated until the year is fully completed. Projecting drug budget costs for future years is never an exact science, but these projections can aid stewardship pharmacists and administrators in preparing for potential changes on the horizon.

9. Lautenbach E, LaRosa LA, Marr AM, Nachamkin I, Bilker WB, Fishman NO. Changes in the prevalence of vancomycin-resistant enterococci in response to antimicrobial formulary interventions: impact of progressive restrictions on use of vancomycin and third-generation cephalosporins. Clin Infect Dis 2003;36:440–6.

This study is an example of an interrupted time-series analysis, a commonly used methodology for antimicrobial stewardship studies. These analyses are popular because they allow the study of patient-level data and do not require patient randomization. In this study, vancomycin and third-generation cephalosporins were sequentially restricted. Despite decreases in vancomycin (24%) and third-generation cephalosporin use (86%), there was no associated decrease in the prevalence of vancomycin-resistant enterococci. Instead, the rates of vancomycin-resistant enterococci rose steadily throughout the 10-year study period ($p<0.001$ for trend). This study showed the prolonged effect of antimicrobial restriction rather than the short-term impact evaluated by other smaller studies. The implication is that horizontal transfer because of poor infection control practices drives most antimicrobial resistance. This article also demonstrates that organisms such as vancomycin-resistant enterococci are less impacted by antibiotic consumption and are most likely to be transmitted by health care workers who do not follow routine infection control standards such as hand hygiene practices after patient contact. Curtailing antimicrobial use has a limited impact on resistance outcomes with these organisms. Proper hand hygiene is important to decrease horizontal transfer, and gowns and gloves alone may not completely decrease transmission.

10. MacDougall C, Polk RE. Antimicrobial stewardship programs in health care systems. Clin Microbiol Rev 2005;18:638–56.

This comprehensive review includes a critical evaluation of the available data on antimicrobial stewardship up to 2005. The authors reviewed each of the antimicrobial stewardship strategies and the advantages/disadvantages associated with each. The appropriate roles for each team member are discussed. The article provides insight into the best methodologies for assessing antimicrobial stewardship outcomes and standardizing data for an individual hospital. In addition, the article provides clinicians with a relatively simple way to calculate changes in antimicrobial consumption at the hospital level and describes the appropriate trending procedures to analyze interrupted time-series data (i.e., pre- and postintervention data). Understanding the appropriate way to quantify a program's benefits is paramount if stewardship teams are to move away from being only cost-minimization teams.

11. McGregor JC, Weekes E, Forrest GN, Standiford HC, Perencevich EN, Furuno JP, et al. Impact of a computerized clinical decision support system on reducing

inappropriate antimicrobial use: a randomized controlled trial. J Am Med Inform Assoc 2006;13:378–84.

This randomized controlled trial was designed to test the efficiency and effectiveness of computerized clinical decision support software. The trial was the first to evaluate commercially available CDSS software. Patients were randomized to a control group of prospective audit and feedback or an intervention group of prospective audit and feedback supplemented with commercially available CDSS software. At baseline, patients were similar in the two groups, with a slightly worse chronic disease score in the intervention arm (median score 6 vs. 5, p=0.06). The study showed that stewardship was more time efficient in the intervention group (3.2 vs. 4.1 person-hours/day) and more cost-effective for antimicrobials in the intervention group ($84,000 savings in 3 months or a savings of $37 per patient); however, hospital mortality and patient length of stay were similar in the two groups. These results are encouraging because commercially available CDSS may provide the functionality required for improved patient care with antimicrobial stewardship.

12. Paladino JA. Economics of antibiotic use policies. Pharmacotherapy 2004;24:232S–238S.

The economics of antimicrobials remain largely unchanged over time. The cost of antimicrobial therapy is often discussed only with respect to acquisition price or average wholesale price for external comparisons; however, other factors should also be considered. The article discusses cost-containment strategies commonly employed by antimicrobial stewardship programs and downstream costs that should be considered. Antimicrobial costs usually account for less than 10% of a patient's hospitalization, with other factors such as duration of hospitalization driving overall costs. A complete understanding of the costs surrounding antimicrobial treatment is vital to setting appropriate program goals and ensuring that program stability is based on outcomes other than nonstandardized antimicrobial purchase costs.

13. Polk RE, Fox C, Mahoney A, Letcavage J, MacDougall C. Measurement of adult antibacterial drug use in 130 US hospitals: comparison of defined daily dose and days of therapy. Clin Infect Dis 2007;44:664–70.

A proper metric for antimicrobial use is necessary to benchmark an antimicrobial stewardship program against itself as well as other programs. Many methodologies have been suggested to estimate antimicrobial use while standardizing for the number of patients. Two popular methodologies, DDDs and DOTs, have been recommended by experts. The DDDs approach represents a standard dose of an antibacterial for a "typical" patient, and DOTs are self-explanatory. This study applied both metrics to a data set and found discordance between the metrics. The authors found that the direction of discordance differed with each antimicrobial reviewed. Understanding the difference between the metrics is important for any stewardship team that wishes to benchmark data.

14. Rahal JJ, Urban C, Horn D, Freeman K, Segal-Maurer S, Maurer J, et al. Class restriction of cephalosporin use to control total cephalosporin resistance in nosocomial *Klebsiella*. JAMA 1998;280:1233–7.

This interrupted time-series analysis is often cited as an example of the "squeezing of the balloon" phenomena. This phenomena suggests that for every antimicrobial action, a somewhat equal and opposite reaction in resistance occurs. If use of antimicrobial A is limited and use of antimicrobial B is favored, resistance can be predicted to shift from antimicrobial A to antimicrobial B. Although a simplification, this phenomenon has been shown several times. Individuals involved in developing antimicrobial policy should be aware that antimicrobial resistance patterns might change. In this study, restricted cephalosporin use (an 80% reduction) was associated with 44% fewer ceftazidime-resistant *Klebsiella* spp. infections (p<0.01). However, a compensatory 41% increase in imipenem use was associated with a 69% increase in imipenem-resistant *Pseudomonas aeruginosa*. These data further suggest that antimicrobial cycling strategies are unlikely to be successful.

15. Roberts RR, Hota B, Ahmad I, Scott RD 2nd, Foster SD, Abbasi F, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital: implications for antibiotic stewardship. Clin Infect Dis 2009;49:1175–84.

Well-performed studies on the costs of antimicrobial resistance are lacking because they are difficult to perform. This study, although limited by the problems of generalizability, carefully controls for confounders through propensity score adjustments and provides evidence of the cost savings achievable with antimicrobial resistance reduction. Using randomly selected data from a tertiary care medical center, the authors analyzed data at the patient level and adjusted for confounders. Such a methodology, although appropriate, is rare in studies of the cost of antimicrobial resistance where ecologic level analyses are preferred for ease of completion. The detailed analysis allowed the capture of full hospital costs including length of stay in all wards, number and type of laboratory and radiologic tests received, specialty consultations, bedside procedures, and minutes of operating room time for surgical procedures. With conservative estimates, the study showed that more than $900,000 could be saved yearly at a single institution through the prevention of antimicrobial-resistant infections. This study supports that targets for antimicrobial stewardship teams need not focus solely on antimicrobial budget cost reductions.

16. Scheetz MH, Bolon MK, Postelnick M, Noskin GA, Lee TA. Cost-effectiveness analysis of an antimicrobial stewardship team on bloodstream infections: a probabilistic analysis. J Antimicrob Chemother 2009;63:816–25.

This mathematic modeling study using Monte Carlo simulation sought to answer whether antimicrobial stewardship teams could be financially justified with clinical outcomes rather than absolute cost reduction. The results of this study showed that antimicrobial stewardship programs could improve patient outcomes for serious bloodstream infections by changing inactive therapy to active therapy. The hospital cost of antimicrobial stewardship for this purpose is about $2400 per QALY gained. In addition, an acceptability curve showed that more than 90% of programs should be cost-effective at a rate of less than $10,000 per QALY. The results are encouraging because the traditional benchmark for the acceptability of medical interventions is $50,000 per QALY. The study suggests that antimicrobial stewardship services designed to improve care can be justified, even in the absence of strategies to reduce antimicrobial acquisition costs.

Self-Assessment Questions

Questions 1 and 2 pertain to the following case.
Your hospital has received funding to start an antimicrobial stewardship team. You have been asked to champion the effort and to jointly establish evidence-based outcomes to monitor and track the team's progress.

1. **Which one of the following is the best metric for this purpose?**
   A. Drug costs per patient-day standardized to inflation and hospital patient mix.
   B. Impact of recommendations on resistance patterns according to the hospital antibiogram.
   C. Risk-adjusted mortality of patients receiving care under the stewardship program.
   D. Rate of transition of patients from intravenous to oral antibiotics.

2. You have agreed on the outcomes to measure with hospital administration and begin assembling the antimicrobial stewardship team. Hospital administration has noted that the budget may expand in future years if outcomes justify the need. Human resources authorizes you to hire one of the following staff combinations. **Which one of the following combinations would best contribute to the stewardship team's intended outcomes?**
   A. An infectious diseases (ID)-trained pharmacist and two interested nurses.
   B. An ID-trained pharmacist, a microbiologist, and a quarter-time epidemiologist.
   C. An ID-trained pharmacist, one nurse, and a half-time data informatics person.
   D. An ID-trained pharmacist and a half-time ID-trained physician.

3. As a clinical manager for a department of pharmacy, you are asked to provide recommendations for the goals of antimicrobial stewardship. Your community hospital has 250 beds, and cannot provide additional financial support. In addition to you, the hospital has three clinical pharmacists who have a full schedule addressing general pharmacotherapy issues. **Which one of the following strategies would result in the best outcomes given the financial constraints?**
   A. Individual case review of all patients daily for infection-antimicrobial drug mismatches.
   B. Development of clinical pathways for common ID in your hospital with retrospective review for pathway adherence.
   C. Implementation of a monthly educational program geared toward hospital-employed physicians and nurses.
   D. Targeting of the five most expensive antibiotics and requiring prospective pharmacy approval before use.

Questions 4–6 pertain to the following case.
You have been hired by a 250-bed community hospital to initiate an antimicrobial stewardship program. Benchmark data provided to you by hospital administration suggest that the organization spends 20% more on antimicrobial purchases than do similar institutions in the area. These data were the catalyst for administrative support for your position. The medical staff consists primarily of generalist physicians. Your pharmacy has the resources to allow one decentralized clinical pharmacist daily. Computerized physician order entry will be implemented late in the current fiscal year. The institution provides cancer care and is affiliated with a tertiary care medical center, which provides the medical staff to care for these patients. Patients with leukemia and lymphoma account for about 20% of the daily census. The tertiary care center has had several outbreaks of extended-spectrum β-lactamase–producing organisms, requiring empiric carbapenem use for neutropenic fever. All protocols for the care of patients with cancer are consistent between the two institutions. One ID-trained physician travels to several institutions and does some consulting in your hospital. The microbiology laboratory is on-site, with automated susceptibility testing done using the Vitek-2 system. The laboratory compiles an institution-wide antibiogram every 2 years; this was done 18 months ago. This antibiogram showed significant issues with fluoroquinolone-resistant *Escherichia coli* and *Pseudomonas aeruginosa,* but all other results were consistent for a rural hospital of its size.

4. **Which one of the following is the best first step in establishing a viable stewardship program?**
   A. Compile an up-to-date antibiogram for the institution.
   B. Enlist the Pharmacy and Therapeutics Committee to restrict fluoroquinolones.
   C. Develop empiric antimicrobial use guidelines for the institution.
   D. Enlist the ID physician to join the stewardship team.

5. As a condition for administrative support, the stewardship program is expected to show at least a 10%

reduction in antimicrobial expenses for the next fiscal year. **Given the limited time and resources, which one of the following would be the best first intervention to undertake?**

A. Implement a pharmacist-driven, hospital-wide antimicrobial de-escalation program.
B. Require preapproval by the stewardship pharmacist for all high-cost antimicrobials.
C. Enlist the oncologists and microbiology director to establish an appropriate neutropenic fever protocol for the institution.
D. Undertake a comprehensive formulary review to ensure that the least expensive antimicrobial drug from each class is exclusively available.

6. You have successfully achieved both the financial and clinical first-year goals of the program. The patient mix and census is projected to remain consistent, and the hospital administration asks you to submit financial goals for the coming year. **Which one of the following goals would best show the impact of your programs?**

A. Improve fluoroquinolone activity against *E. coli* isolates to match benchmark hospitals.
B. Decrease antimicrobial expenditures below current benchmarks.
C. Significantly reduce institutional vancomycin use.
D. Maintain growth of antimicrobial expenditures below the projected national level.

Questions 7–9 pertain to the following case.

You are an ID-trained pharmacist and faculty member at the local college of pharmacy. Your clinical practice site is the adjacent 650-bed university hospital, where you and the chief of ID serve as codirectors of the antimicrobial stewardship program. Another ID-trained pharmacist faculty member shares stewardship responsibilities with you. The hospital completed the implementation of an electronic health record system during the past year. Your current responsibilities include a review of culture reports to identify patients who may benefit from alterations in therapy. About 100 culture and susceptibility results are generated by the microbiology laboratory daily. You or your colleague review about half of these results. An estimated 75% of cases require no intervention; in 23%, an antimicrobial dose de-escalation would be appropriate; and in 2% a mismatch between the causative organism and the prescribed antibiotic is identified, requiring a change in therapy. The acceptance rate of the team's recommendations approaches 90%. As part of the annual review process for the program, you want to expand its impact. Hospital administration is committed to improving the care of patients with ID and has told you to consider all available options.

7. **Based on the available evidence, in which one of the following areas would expanding the review of antimicrobials and culture results be most cost-effective?**

A. De-escalation in bloodstream infections.
B. Mismatches in bloodstream infections.
C. Mismatches in hospital-acquired pneumonia.
D. Mismatches in community-acquired pneumonia.

8. You are asked to propose a plan to improve the impact of antimicrobial stewardship. The budget allows no increase in financial resources for the effort. **Which one of the following would provide the best results with the least need for additional resources?**

A. Embedding ID protocols into the electronic health record.
B. Adding a PGY2 ID pharmacy resident.
C. Developing a preauthorization strategy for antimicrobial restriction.
D. Implementing an antimicrobial cycling program in the intensive care units.

9. Hospital administration is willing to consider adding a third-party clinical decision support tool to the current electronic medical record. After evaluating the available programs, you are preparing a proposal to justify the purchase of this tool, using language that would resonate with hospital administrative and financial officers. **Which one of the following would be the best primary reason for the hospital to approve this tool?**

A. Decrease antimicrobial expenditure for the hospital.
B. Increase effectiveness with no added personnel.
C. Improve data management to facilitate utilization reviews and research.
D. Improve ability to provide point-of-care treatment recommendations.

10. You are codirector of an antimicrobial stewardship program in an academic medical center. You currently employ a program of prospective audit and feedback for designated restricted antimicrobials, which include the carbapenem class. You have recognized an exponential growth in the number of patients initiated on carbapenem therapy. Many of these patients are on general medicine wards and are receiving carbapenem therapy for questionable indications. In most cases, a causative pathogen is never isolated; however, based on clinical improvement, the patients are unable to be successfully

de-escalated from carbapenem therapy. **Which one of the following would most effectively decrease unnecessary carbapenem use without compromising patient care?**

A. Recommend invasive pulmonary sampling for all patients with suspected pneumonia.
B. Require stewardship program preapproval for carbapenem use on general medicine wards.
C. Require stewardship program preapproval for carbapenem use on all wards.
D. Restrict carbapenem use to ID consultation only.

11. Your practice site serves a large transplant population located in a single nursing unit. Random audits of the unit reveal 65% adherence to institutional hand hygiene policy. The antimicrobial stewardship team is asked to evaluate the contribution of antimicrobial use to continued problems with outbreaks of vancomycin-resistant enterococci on this unit. The evaluation shows that vancomycin use on this unit is 30% greater than on similar units, and that piperacillin/tazobactam is the hospital's primary broad-spectrum agent with very little use of other broad-spectrum therapy. **Which one of the following interventions is most likely to quickly control these outbreaks?**

A. Decrease the use of vancomycin.
B. Decrease the use of piperacillin/tazobactam.
C. Implement mask, glove, and gown isolation for all patients in the institution.
D. Enhance enforcement of hand hygiene polices.

12. You are beginning a project to characterize the volume of antimicrobial use in your institution. The institutional information system has provided you with the past 3 years of data on antimicrobial purchases, which reflect 1 year before and 2 years after the start of your stewardship program. The organization wishes to benchmark your data to another local hospital that has similar programs, identical information technology systems, and a comparable patient mix, but that is 100 beds smaller. Nursing units in both institutions are localized by clinical program. Your average occupancy rate is 82% of capacity, and the comparator institution averages a 95% occupancy rate. **Which one of the following would best compare antimicrobial consumption between the institutions?**

A. Grams of antibiotic purchased for each institution adjusted for bed capacity.
B. Inflation-adjusted dollar expenditures for each antimicrobial class for each institution.
C. Calculated defined daily doses (DDDs) per patient-day of each agent for each institution.
D. Calculated total grams of antimicrobial used per nursing unit.

13. An intensivist in your institution has expressed interest in examining the use of antimicrobials in the intensive care unit. Your review finds that most empiric therapy in the unit is carbapenem based. Examination of antibiogram data for the unit suggests equal activity against gram-negative bacteria for carbapenems, piperacillin/tazobactam, and cefepime. The intensivist suggests that a program of cycling between the three classes be implemented in the unit to help maintain activity of all classes of agents. **Which one of the following is the best response to this proposal?**

A. Cycle different antimicrobial classes for 3-month periods.
B. Cycle different antimicrobial classes for 6-month periods.
C. Rotate randomly between the three different classes of antimicrobials.
D. Restrict carbapenem use to situations with documented resistance to other agents.

14. You have been hired to implement an antimicrobial stewardship program on a 1-year contract. Administrators expect to see significant decreases in antimicrobial consumption and antimicrobial expenses before considering renewal of your contract. **Which one of the following would have the best chance of meeting the administration's requirements?**

A. Antibiotic order forms.
B. Preauthorization requirement.
C. Prospective audit and feedback.
D. Empiric antimicrobial use guidelines.

15. You have received approval for the purchase of a clinical decision support system to augment your antimicrobial stewardship program. You would like the software to address greater capture rates of inappropriate antimicrobial therapy, better review of antimicrobial use patterns, increased response to changes in organism susceptibility patterns, and improved empiric use of antimicrobial therapy. **Based on the current capabilities of clinical decision support systems, which one of the following features would most contribute to your improvement goals?**

A. Real-time antibiogram generation capability.
B. Real-time alerting of bug-drug mismatches.
C. Artificial intelligence for selection of empiric therapy.

D. Alerts generated when patients are initiated on a specific antimicrobial.

16. You are evaluating the impact of an antimicrobial stewardship program on institutional antibiotic expenditures. **Which one of the following, if occurring in the previous fiscal year, would be the most significant confounding factor?**

A. 10% average increase in antibiotic prices.
B. Establishment of a bone marrow transplant program.
C. Establishment of a new outpatient surgery program.
D. 10% increase in average daily census.

17. You implemented an antimicrobial stewardship program 1 year ago. At the time, the medical staff supported the initiative. You decided that a preapproval process managed by you and your residents would be the best way to improve antimicrobial therapy in the organization. However, conflicts have arisen regarding the approval of antimicrobials for specific patients. These conflicts have significantly decreased the medical staff support as well as the effectiveness of the stewardship program. **Which one of the following adjustments would best enhance the program's effectiveness?**

A. Stop preapproval; implement antimicrobial order forms.
B. Transfer approval duties to the ID fellow.
C. Stop preapproval; implement a prospective audit and feedback program.
D. Provide more education regarding the program to the medical staff.

18. An antimicrobial stewardship program has been in place in your institution for the past 2 years. Antimicrobial therapy has improved as measured by a 5% decrease in total antimicrobial volume, a 10% decrease in use of carbapenems, a 15% decrease in fluoroquinolones, and a 5% decrease in vancomycin, as well as a decrease in the average length of therapy by 1 day. However, antimicrobial resistance continues to increase, as shown by a larger number of vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus,* and extended-spectrum β-lactamase isolates than at the start of the program. **Which one of the following best explains the lack in improvement of antimicrobial susceptibilities?**

A. Improvements in use must take place across relevant classes of antimicrobials to show decreased resistance.
B. Insufficient time has elapsed to show improved antimicrobial susceptibilities.
C. Changes in use patterns were not significant enough to result in a change in resistance.
D. Continued third-generation cephalosporin use resulted in the increased resistance.

19. In the first year of your institution's antimicrobial stewardship program, antimicrobial expenses declined by 30%. In analyzing the decline, you identified several factors that could have contributed. **Which one of the following is most likely to consistently contribute to this decline in annual antimicrobial expenses?**

A. Price declines in antimicrobials.
B. Prudent formulary management.
C. Decrease in patient census.
D. Prospective audit and feedback program.

20. You have been asked to give a presentation to the medical staff about your antimicrobial stewardship program. You wish to highlight the most important aspect of your program to the organization and to patient care. **Which one of the following goals would be most important to emphasize?**

A. Improved economic and cost-savings benefits.
B. Improved patient safety and quality of care.
C. Decreased use of broad-spectrum antimicrobials.
D. Decreased outbreaks of resistant organisms.