

CONTINUING EDUCATION DISCUSSION GUIDE

AN INTERPROFESSIONAL APPROACH  
TO ANTIMICROBIAL STEWARDSHIP:  
**IMPLEMENTING TEAM-BASED  
STRATEGIES THAT IMPACT  
PATIENT OUTCOMES**

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This continuing education discussion guide is part of an educational initiative designed to provide the antimicrobial stewardship team with timely, relevant, and useful information on issues in the implementation and management of antimicrobial stewardship programs. For additional resources on this topic, including on-demand continuing educational offerings, visit [www.leadstewardship.org](http://www.leadstewardship.org).

The estimated time to complete this activity is 60 minutes. This activity is provided free of charge and is available from June 28, 2013 to April 25, 2015.

### TARGET AUDIENCE

This continuing education (CE) activity is beneficial for physicians, pharmacists, physician assistants, and nurse practitioners practicing in large or small health systems who are interested in learning more about antimicrobial stewardship and implementing antimicrobial stewardship programs.

### LEARNING OBJECTIVES

After participating in this application-based educational activity, participants should be able to

1. Discuss the relationship between inappropriate antimicrobial use, antimicrobial resistance, hospital length of stay, mortality, and health care costs, and explain the impact of antimicrobial stewardship programs (ASPs) on these variables.
2. Describe recent trends in antimicrobial resistance, research, and development of new antimicrobial agents, and efforts to address concerns about these trends.
3. Describe an interprofessional team approach and recommend strategies to achieve the goals of antimicrobial stewardship in health systems.
4. Review the role of care bundles in antimicrobial stewardship, and examine process and outcome metrics used to demonstrate a need for and evaluate the success of ASPs in improving quality of care.
5. Examine challenges and pitfalls in the implementation of ASPs in health systems, especially institutions with limited resources.

### SYSTEM REQUIREMENTS

**Web Browser:** Microsoft Internet Explorer, Mozilla Firefox, Apple Safari or Google Chrome.

**Note:** Please disable any "pop-up blocker" features.

**Software:** Adobe Acrobat Reader version 7 or above to view PDF files (If you do not have Acrobat Reader, you can download it for free from <http://get.adobe.com/reader>).

**Connection Speed:** Cable, DSL, or better of at least 300 kbps.

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## EXECUTIVE SUMMARY

Increases in antimicrobial resistance and the lack of new antimicrobial agents in the research and development pipeline have created a global health crisis because of the threat of a return to a pre-antibiotic era with uncontrollable infectious diseases. Inappropriate use of antimicrobial agents and inadequate infection prevention and control measures contribute to antimicrobial resistance, which increases hospital lengths of stay, mortality, and health care costs. Efforts have been made to address these problems on a local, state, national, and global scale.

Antimicrobial stewardship is a coordinated quality-improvement effort to promote the judicious and effective use of antimicrobial agents that includes but is not limited to the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy. Antimicrobial stewardship programs (ASPs) improve the appropriateness of antimicrobial use and reduce antimicrobial resistance, mortality, hospital length of stay, and health care costs. A variety of strategies, each of which has advantages and disadvantages, may be used for antimicrobial stewardship. A combination of strategies (e.g., care bundle) may be more effective than single interventions.

An interprofessional antimicrobial stewardship team should be established. Education and training is available for team members through various educational programs and informal methods. Lack of funding and personnel are the most common barriers to ASP implementation. A strong business case for implementing an ASP should be prepared to obtain support and authority from health system administration. Process and outcome metrics and data related to antimicrobial use, resistance, and infections can be used to demonstrate a need for and evaluate the success of ASPs in improving quality of care. Focusing ASP efforts initially on readily implemented strategies likely to produce results is recommended to optimize the benefit from limited resources. Problems with lack of staff cooperation with ASP requirements may be avoided or overcome using an interprofessional approach that involves key opinion leaders in ASP development.

## INTRODUCTION

Healthcare-associated infections (HAI) are common in American hospitals and health systems, affecting roughly one of every 20 inpatients.<sup>1</sup> Hospital-acquired infections are among the leading causes of death in the United States.<sup>1</sup> Many HAIs are the result of excessive or inappropriate antibiotic use and the emergence and transmission of antimicrobial-resistant pathogens, especially multidrug-resistant organisms. Up to 50% of antimicrobial use in hospitals is unnecessary or inappropriate.<sup>2</sup> Systemic anti-infective agents are the third most costly items in the pharmacy budgets of U.S. nonfederal hospitals, with expenditures exceeding \$1.9 billion in 2012.<sup>3</sup> Inadequate infection prevention and control measures and the transmission of community-acquired infections caused by resistant pathogens contribute to antimicrobial-resistant infections in hospitals.<sup>4</sup> Increases in hospital length of stay, mortality, and health care costs are associated with antimicrobial resistance.<sup>5,6</sup> Every year hospital-acquired infections account for \$28 billion to \$33 billion in preventable health care costs in the United States.<sup>1</sup>

The majority of hospital-acquired infections in the United States are caused by a small group of bacteria with increasing resistance to currently available antimicrobial agents.<sup>7,8</sup> In the past, the acronym ESKAPE was used for these pathogens (Table 1) because of the high likelihood of their escape from the effects of antimicrobial therapy. These agents are now referred to as ESCAPE pathogens to reflect recent increases in antimicrobial resistance in and the impact of hospital-acquired infections caused by *Clostridium difficile* (*C. difficile*) and Enterobacteriaceae.<sup>9,10</sup>

Infections caused by resistant pathogens (e.g., methicillin-resistant *Staphylococcus aureus* [MRSA], vancomycin-resistant *Enterococcus*, extended-spectrum  $\beta$ -lactamase-producing organisms) have been a cause

for concern for many years.<sup>7</sup> More recently, infections caused by carbapenem-resistant Enterobacteriaceae (CRE), such as *Klebsiella pneumoniae* carbapenemase (KPC)-producing and metallo- $\beta$ -lactamase-producing Enterobacteriaceae, have become increasingly widespread and problematic in U.S. hospitals, with a mortality rate of up to 50%.<sup>11</sup> Carbapenem-resistant Enterobacteriaceae often carry genes that confer a high level of resistance to many other antimicrobial agents.<sup>11</sup>

Nearly a decade ago, the Infectious Diseases Society of America (IDSA) described the growing problem of antimicrobial resistance and the lack of new antimicrobial agents in the research and development pipeline to combat infections caused by these pathogens. Policy makers were urged to take prompt legislative action to address the problem by creating financial incentives for pharmaceutical manufacturers to invest time and resources in research. Subsequent reports demonstrate that the problem of antimicrobial resistance and lack of new antibiotics in the research and development pipeline is a global one that has worsened, with increases in the incidence of multidrug-resistant infections for which currently available antimicrobial agents are ineffective.<sup>9,12,13</sup> The Strategies to Address Antimicrobial Resistance Act (known as STAAR or H.R. 2400) was introduced in 2009 to encourage the development of new antimicrobial agents as well as strengthen federal antimicrobial resistance surveillance, infection prevention and control, and research efforts.<sup>14</sup> No timeline is available for when action might be taken to pass the legislation.

Other groups have been active in efforts to call attention to and mitigate the problem of antimicrobial misuse and resistance. In 2003, the Centers for Disease Control and Prevention (CDC) launched the Get Smart: Know When Antibiotics Work program as part of a national media campaign to reduce the rate

**TABLE 1.**  
Changes in Problematic Resistant Pathogens<sup>9,10</sup>

Previous ESKAPE Pathogens	Current ESCAPE Pathogens
<i>Enterococcus faecium</i>	<i>Enterococcus faecium</i>
<i>Staphylococcus aureus</i>	<i>Staphylococcus aureus</i>
<i>Klebsiella pneumoniae</i>	<i>Clostridium difficile</i>
<i>Acinetobacter baumannii</i>	<i>Acinetobacter baumannii</i>
<i>Pseudomonas aeruginosa</i>	<i>Pseudomonas aeruginosa</i>
<i>Enterobacter</i> species	Enterobacteriaceae (includes <i>Enterobacter</i> species, <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> , and other pathogens)

of rise of antimicrobial resistance by promoting health care provider adherence to antimicrobial prescribing guidelines, decreasing demand for antimicrobial agents for viral upper respiratory infections among healthy adults and parents of young children, and increasing patient adherence to prescribed antibiotics for upper respiratory infections.<sup>15</sup>

In 2010, IDSA launched the “10 x ‘20 initiative,” a call to action to develop 10 new safe and effective antimicrobial agents by the year 2020.<sup>16</sup> The organization has called on global political, scientific, industry, economic, intellectual property, policy, medical, and philanthropic leaders to create incentives that stimulate new antimicrobial research and development.

In 2011, IDSA released a policy paper on combating antimicrobial resistance to save lives.<sup>17</sup> Establishment and support of antimicrobial stewardship programs (ASPs) in all health care settings (e.g., hospitals, long-term care facilities, outpatient clinics, ambulatory surgical centers, private practices) was advocated by IDSA. Specific recommendations for legislative action and funding were made to the U.S. Congress, including strengthening and rapid enactment of STAAR and requiring ASPs as a condition of participation in the federal Medicare and Medicaid programs or through another regulatory mechanism. An antibiotic innovation and conservation fee also was proposed, with 75% of the revenue used to fund new antimicrobial agent development and 25% used to fund antimicrobial stewardship.

The Generating Antibiotic Incentives Now (GAIN) Act was implemented in the United States in October 2012.<sup>18,19</sup> This legislation has provisions to encourage research and development of new antimicrobial agents to treat life-threatening infections (e.g., fidaxomicin, which is used to treat *C. difficile*-associated diarrhea, and other so-called Qualified Infectious Disease Products or QIDPs). An additional 5 years of market exclusivity and priority review and fast track approval by the Food and Drug Administration are among the GAIN Act provisions. The creation of a pathogen-focused antimicrobial drug development pathway is mandated by the legislation.

In 2013, a proposed antibiotic salvage bundle was put forth by IDSA to “preserve the miracle of antibiotics.”<sup>20</sup> Aggressive promotion of antimicrobial stewardship is one of seven elements in this bundle.<sup>20</sup>

Efforts also have been made in countries outside the United States to address antimicrobial resistance and encourage research and development of new antimicrobial agents because of the global nature of these problems.<sup>21,22</sup> The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was established in late 2009 to identify urgent antimicrobial resistance issues that could be better addressed through intensified cooperation between the United States and

the European Union.<sup>23</sup> In 2011, the TATFAR released 17 recommendations for future collaboration focusing on appropriate therapeutic use of antimicrobial agents in the medical and veterinary communities (e.g., campaigns to promote appropriate antimicrobial use in humans), prevention of both healthcare- and community-associated drug-resistant infections (e.g., surveillance of drug resistance), and strategies for improving the pipeline of new antimicrobial agents (e.g., incentives for research and development of new antimicrobial agents, regulatory approaches for antimicrobial products).

### ROLE OF ANTIMICROBIAL STEWARDSHIP

The lack of new antimicrobial agents in the research and development pipeline makes it imperative that currently available agents are used wisely to stem the emergence of resistance to and loss of effectiveness of these agents. Antimicrobial stewardship—a coordinated effort to promote the judicious and effective use of antimicrobial agents that includes but is not limited to the appropriate selection, dosing, route of administration, and duration of antimicrobial therapy—is an important strategy for achieving this goal.<sup>2</sup> When used in conjunction with infection prevention and control, antimicrobial stewardship also prevents the transmission of antimicrobial-resistant pathogens in health systems.

The primary goal of antimicrobial stewardship is to optimize clinical outcomes while minimizing unintended consequences of antimicrobial use (e.g., toxicity, the selection of pathogenic organisms, the emergence of resistance).<sup>2</sup> Reducing health care costs without adversely affecting the quality of care is a secondary goal of antimicrobial stewardship.

Antimicrobial stewardship programs have been shown to improve physician awareness of and adherence to treatment guidelines and appropriateness of antimicrobial use and reduce antimicrobial resistance.<sup>24-29</sup> The programs also reduce mortality, hospital length of stay, and health care costs.<sup>24,29,30</sup> The cost-effectiveness of ASPs is well documented.<sup>31-34</sup>

### STRATEGIES

Guidelines for developing an institutional program to enhance antimicrobial stewardship were published in 2007 by IDSA and the Society for Healthcare Epidemiology of America (SHEA).<sup>2</sup> The IDSA/SHEA guidelines call for two proactive core strategies as the foundation of ASPs: (1) prospective audit with intervention and feedback and (2) formulary restriction and preauthorization.<sup>2</sup> Supplemental elements may be used in conjunction with these core strategies depending on local practice patterns and available resources. Table 2 lists potential advantages and disadvantages of the various types of interventions used in ASPs.

**TABLE 2.**  
Potential Advantages and Disadvantages of IDSA/SHEA Core Strategies and Supplemental Elements of Antimicrobial Stewardship Programs<sup>2,31,35-39</sup>

Core Strategies	Potential Advantages	Potential Disadvantages
Prospective audit with direct intervention and feedback	<ul style="list-style-type: none"> <li>Reduction in inappropriate antimicrobial use</li> <li>Education and modification of future prescribing</li> <li>Preservation of prescriber autonomy</li> </ul>	<ul style="list-style-type: none"> <li>Difficulty identifying patients with inappropriate therapy and communicating with prescribers</li> <li>Legal concerns about failure to follow written recommendations</li> </ul>
Formulary restriction and preauthorization requirements	<ul style="list-style-type: none"> <li>Immediate and substantial reductions in antimicrobial use and costs</li> </ul>	<ul style="list-style-type: none"> <li>Increased staffing requirements</li> <li>Delayed initiation of therapy while awaiting approval from authorized prescriber</li> <li>Increased use of and resistance to alternative antimicrobial agents</li> <li>Prescriber pushback due to perceived loss of autonomy</li> </ul>
Supplemental Elements	Potential Advantages	Potential Disadvantages
Education	<ul style="list-style-type: none"> <li>Improved prescribing behavior and acceptance of ASP strategies</li> </ul>	<ul style="list-style-type: none"> <li>Marginal efficacy for modifying prescribing behavior when used without active intervention</li> <li>Need for repetition</li> </ul>
Guidelines and clinical pathways	<ul style="list-style-type: none"> <li>Improved antimicrobial use and reduced practice variation</li> </ul>	<ul style="list-style-type: none"> <li>Poor adherence</li> </ul>
Antimicrobial order forms	<ul style="list-style-type: none"> <li>Improved antimicrobial use</li> <li>Facilitated implementation of guidelines and clinical pathways</li> </ul>	<ul style="list-style-type: none"> <li>Inappropriate interruption in therapy due to automatic stop orders</li> <li>Time required to fill out paper forms</li> <li>Time required to evaluate appropriateness of orders</li> </ul>
Combination therapy <sup>a</sup>	<ul style="list-style-type: none"> <li>In theory, improved clinical outcomes and prevention of resistance, especially in selected types of patients and situations</li> </ul>	<ul style="list-style-type: none"> <li>Sometimes redundant and unnecessary</li> <li>Lack of extensive data demonstrating improved clinical outcomes and reduced resistance</li> </ul>

**TABLE 2. (CONTINUED)**

Potential Advantages and Disadvantages of IDSA/SHEA Core Strategies and Supplemental Elements of Antimicrobial Stewardship Programs<sup>2,31,35-39</sup>

Supplemental Elements	Potential Advantages	Potential Disadvantages
Streamlining or de-escalation of therapy	<ul style="list-style-type: none"> <li>Reduced antimicrobial exposure, selection of resistant pathogens, and health care costs</li> </ul>	<ul style="list-style-type: none"> <li>Prescriber reluctance to de-escalate therapy when cultures are negative and clinical improvement has been observed</li> <li>Lack of acceptance of assays for biomarkers used to monitor and shorten therapy</li> </ul>
Dose optimization	<ul style="list-style-type: none"> <li>Tailored therapy based on patient characteristics, causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agent</li> </ul>	<ul style="list-style-type: none"> <li>Nursing staff concerns about incompatibilities when prolonged infusions are used</li> </ul>
Parenteral-to-oral conversion	<ul style="list-style-type: none"> <li>Decreased hospital length of stay, workload, and health care costs</li> <li>Reduced risk of complications from intravenous access</li> </ul>	<ul style="list-style-type: none"> <li>Difficulty identifying eligible patients</li> <li>Time required to contact prescriber for authorization to switch to oral therapy</li> </ul>

ASP: antimicrobial stewardship program; IDSA: Infectious Diseases Society of America; SHEA: Society for Healthcare Epidemiology of America  
<sup>a</sup>Not routinely recommended in IDSA/SHEA guidelines

*Prospective audit with intervention and feedback* to the prescriber (i.e., evaluating the appropriateness of orders for antimicrobial agents, contacting the prescriber if the order is inappropriate, and recommending alternative therapy) can reduce inappropriate antimicrobial use and serve an educational purpose to modify future prescribing.<sup>2,36</sup> This strategy allows prescribers to maintain autonomy, which is a concern with some other interventions.<sup>36</sup> Difficulty identifying patients with inappropriate therapy and communicating recommendations to prescribers are potential problems. Computerized systems can be used to screen for and identify patients with inappropriate therapy based on microbiology and pharmacy data. Legal concerns about failure to follow written recommendations may arise; developing policies and procedures for oral communication without permanent documentation may help alleviate these concerns.<sup>35</sup>

*Formulary restriction and preauthorization* involves limiting the use of an antimicrobial agent to certain indications, prescribers, physician services, or patient

populations, often depending on local antimicrobial resistance patterns and patient safety issues.<sup>36,37</sup> Immediate and substantial reductions in antimicrobial use and costs can be achieved through these strategies, although increases in the use of and resistance to an alternative antimicrobial agent may result.<sup>2</sup> Formal written agreements established through the pharmacy and therapeutics (P & T) committee permitting automatic therapeutic substitution of antimicrobial agents without contacting the prescriber facilitate the use of this strategy.<sup>31</sup>

Disadvantages of the use of formulary restriction and preauthorization requirements include increased staffing requirements, prescriber pushback (i.e., opposition) due to a perceived loss of autonomy, and delays in initiation of therapy.<sup>35,36,40</sup> Because of these shortcomings, a combination of core strategies, including order review with feedback, formulary restriction, and preauthorization, tailored to the needs of the institution is now more commonly used instead of formulary restriction alone.<sup>41</sup>

To avoid delays in therapy, which can adversely affect clinical outcomes, policies and procedures that facilitate immediate dispensing of a first dose and applying formulary restrictions and preauthorization requirements only to subsequent doses have been suggested.<sup>38</sup> This approach is designed to strike a balance between preventing the excessive antimicrobial use that promotes resistance and incurring the delays in therapy that adversely affect clinical outcomes. Initial antimicrobial therapy that is later determined to be inappropriate or redundant based on the results of culture and antimicrobial susceptibility tests is discontinued as soon as possible.

*Education* is needed to promote acceptance of ASP strategies and influence prescribing behavior.<sup>2</sup> Education should be provided in conjunction with active intervention (e.g., prospective audit and intervention) because passive education alone (e.g., distribution of written guidelines) is only marginally effective for modifying prescribing behavior.<sup>2</sup> Education in conjunction with prospective feedback to the prescriber about antibiotic choice and duration has been shown to be effective for reducing excessive durations of antibiotic therapy for community-acquired pneumonia.<sup>42</sup>

*Guidelines and clinical pathways* that are evidence based and take into consideration local microbiology and antimicrobial resistance patterns may improve antimicrobial use.<sup>2</sup> These guidelines and clinical pathways should be developed with interprofessional input to improve the likelihood of adherence.

*Antimicrobial order forms* with requirements for the prescriber to justify antibiotic use and automatic stop features to prevent excessively long therapy can reduce inappropriate antimicrobial use.<sup>2</sup> Inappropriate interruption in therapy from the use of automatic stop orders is a potential problem that can be avoided by educating prescribers about order renewal requirements.<sup>2</sup> Completion of paper antimicrobial order forms can be time consuming. Incorporating antimicrobial order forms into computerized physician order entry (CPOE) systems minimizes the time required to complete forms.<sup>36</sup>

*Combination therapy* involves the use of more than one antimicrobial agent instead of monotherapy to provide a more broad spectrum of coverage in certain types of patients and situations. In theory, this approach improves clinical outcomes and prevents antimicrobial resistance, although the data are insufficient. Combination therapy often is redundant and unnecessary. Therefore, it is not routinely recommended in the IDSA/SHEA guidelines.<sup>2</sup>

*Streamlining or de-escalation of therapy* is an intervention designed to decrease the selection pressure that leads to resistance. The most common approach to streamlining involves discontinuing inappropriate

or redundant antimicrobial therapy based on culture and antimicrobial susceptibility data (e.g., discontinuing broad-spectrum therapy and initiating targeted therapy with a more narrow spectrum of activity suited to the isolated pathogen). This intervention reduces antimicrobial exposure, the selection of resistant pathogens, and health care costs by targeting the causative pathogen more effectively.<sup>2</sup> However, cultures are negative in many infected patients, and streamlining of therapy based on antimicrobial susceptibility data is not possible in these patients. Clinicians often are reluctant to de-escalate therapy when cultures are negative and clinical improvement has been observed.<sup>35</sup>

Patients with hospital-acquired, ventilator-associated, or healthcare-associated pneumonia and cultures typically receive a three-drug regimen empirically to minimize mortality from multidrug-resistant pathogens. A possible approach to reducing selection pressure in such patients entails switching to a single antibiotic if cultures are negative for MRSA and *Pseudomonas aeruginosa* (*P. aeruginosa*).<sup>43</sup>

Reducing the duration of antimicrobial therapy is another approach to de-escalation of antimicrobial therapy. The duration of antimicrobial therapy in many clinical practice guidelines is based on expert opinion, not the results of randomized clinical trials. The use of a short duration of therapy (e.g., 8 days vs. 15 days) in patients with ventilator-associated pneumonia (VAP), for example, has been shown to not compromise clinical outcomes in patients with pathogens other than *P. aeruginosa*.<sup>44-46</sup> Colonization with resistant bacteria and VAP recurrence are associated with a longer duration of therapy.<sup>47</sup>

Biomarkers for bacterial infection and sepsis, such as procalcitonin, have been used to shorten antimicrobial therapy without adversely affecting clinical outcomes.<sup>39</sup> However, the rate of acceptance of assays for such biomarkers in U.S. hospitals has been slow.

*Dose optimization* is an intervention to improve drug dosing and administration taking into consideration the patient characteristics (e.g., age, weight), causative pathogen, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agent.<sup>48</sup> Pharmacokinetic and pharmacodynamic studies have demonstrated that reductions in mortality can be achieved through the use of extended (i.e., prolonged) instead of standard infusions of  $\beta$ -lactam antibiotics in patients with *P. aeruginosa* infections.<sup>49</sup> Barriers to use of dose optimization include nursing staff concerns about drug incompatibilities in the intravenous (i.v.) tubing used for drug administration, which can be addressed through antimicrobial use guidelines (e.g., use of prolonged infusions of  $\beta$ -lactam antibiotics, extended dosing intervals for aminoglycosides).



*Parenteral-to-oral conversion* for antimicrobial agents when the patient's condition permits can reduce the risk of complications from i.v. access (e.g., catheter-related infections) and decrease the hospital length of stay, workload, and health care costs without compromising patient safety.<sup>2,31</sup> Identifying suitable patients for conversion can pose a challenge. Guidelines with clinical criteria for conversion should be developed to facilitate use of this intervention. These guidelines might be incorporated into the CPOE system. Collaborating with dietitians to identify patients with new dietary orders also can facilitate identification of patients eligible to convert from parenteral to oral antimicrobial therapy.<sup>31</sup>

In the 2010 ASHP national survey of pharmacy practice in hospital settings, a variety of strategies were used to improve antimicrobial use in hospitals with ASPs, including national or local guidelines (90%), daily review of orders for targeted antimicrobial agents with feedback to prescribers (77%), formulary or prescribing restrictions for targeted antimicrobial agents (74%), education of individuals or groups of prescribers (69%), and use of clinical decision support technology at the time of order entry (31%).<sup>50</sup> Strategies involving education or information technology were more commonly used in large hospitals than in smaller facilities.

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*What strategies do you use to encourage appropriate antibiotic use in your institution? Which strategies have the greatest impact?*

*Is there a proven strategy that you have not yet implemented? What are the barriers to implementation of new strategies, and how might these barriers be overcome?*

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## CARE BUNDLES

Care bundles are groups of evidence-based interventions for a defined patient population and care setting that result in greater improvement in outcomes when implemented together than when each intervention is used alone.<sup>51</sup> The concept of care bundles was developed by the Institute for Healthcare Improvement (IHI) in 2001. Care bundles are developed by an interprofessional team and based on clinician consensus. Each bundle comprises three to five interventions (i.e., elements) for a defined patient population in one location. Each element is relatively independent and should be descriptive rather than prescriptive (i.e., flexible to allow for clinical judgment and adaptable to meet local needs), with provisions to "opt out." Compliance with bundles is readily assessed on an "all-or-none" basis, with a goal of at least 95% compliance.

Care bundles were developed initially by the IHI for patients in intensive care units (ICUs) receiving mechanical ventilation or with central venous lines.<sup>51</sup> Reductions in VAP and central line-associated bloodstream infections

(CLABSIs) were observed with use of the care bundles in the IHI 100,000 Lives Campaign and 5 Million Lives Campaign involving more than 4000 U.S. hospitals and in the Patient Safety First Campaign in the United Kingdom. The use of sepsis care bundles based on guidelines from the 2004 Surviving Sepsis Campaign, an international collaborative effort, also resulted in improved patient outcomes.<sup>51,52</sup> Other care bundles, including insertion and care of peripheral i.v. and urinary catheters, prevention of surgical site infection (SSI), and prevention and management of *C. difficile* diarrhea, have been developed.<sup>51,53</sup>

The use of care bundles has been suggested for antimicrobial stewardship, with the goals of optimizing prescribing behavior and patient outcomes and minimizing adverse effects from and resistance to antimicrobial agents.<sup>53,54</sup> A proposed antimicrobial care bundle for surgical prophylaxis would address choice of antibiotic therapy based on local guidelines (including antimicrobial susceptibilities) and type of surgery, administration of the first dose within a guideline-defined time before the surgical incision, and discontinuation of antimicrobial therapy within a guideline-defined time after the first preoperative dose or surgical end time.<sup>53</sup> An antimicrobial care bundle for treatment of infection in the acute care setting would address the initiation of therapy, including documentation of the clinical rationale, sending appropriate specimens to the microbiology laboratory, choice of antimicrobial therapy based on local policies (e.g., antimicrobial susceptibility) and the patient risk group, and removal of any foreign body and drainage of pus or surgical intervention. Elements of an antimicrobial care bundle for continuation of antimicrobial therapy in the acute care setting would include daily assessment of the appropriateness of de-escalation of therapy, parenteral-to-oral conversion, and discontinuation of antimicrobial therapy based on clinical signs and symptoms and laboratory test results, with monitoring of serum antibiotic concentrations in accordance with local policies. All of these proposed antimicrobial care bundles involve process metrics, not outcome metrics.

Improvement in process metrics (e.g., documentation of treatment rationale, collection of appropriate culture specimens) has been demonstrated with the use of antimicrobial care bundles.<sup>55-59</sup> However, data demonstrating an impact on outcome metrics (e.g., incidence of resistant hospital-acquired infections, infection-related mortality, hospital length of stay) are lacking. Identifying the contribution of a particular element in a care bundle to a clinical outcome probably will not be possible.<sup>60</sup>

## INTERPROFESSIONAL APPROACH

The IDSA/SHEA guidelines for developing an institutional ASP call for an infectious diseases (ID) physician and a clinical pharmacist with ID training to serve as

core members of an interprofessional antimicrobial stewardship team, with compensation provided for their time.<sup>2</sup> According to the ASHP statement on the pharmacist's role in antimicrobial stewardship and infection prevention and control, pharmacists should assume a prominent role in antimicrobial stewardship because of their knowledge of and influence over antimicrobial use and membership on interprofessional committees in the institution.<sup>61</sup> In the 2010 ASHP national survey of pharmacy practice in hospital settings, the pharmacist's primary role in ASPs was one of leadership and accountability in about half of hospitals with ASPs, with pharmacists serving primarily in a clinical support role in another third of hospitals with ASPs.<sup>50</sup> Few hospitals with ASPs reported a lack of pharmacist involvement.

A clinical microbiologist, infection preventionist, hospital epidemiologist, and information system specialist should be included on the ASP team, according to the IDSA/SHEA guidelines.<sup>2</sup> Microbiology is in a state of transition because of the introduction of important new rapid diagnostic microbiology assays.<sup>20,30,62,63</sup> The clinical microbiologist can play an instrumental role in ensuring that the best available assays are used to rapidly and reliably detect pathogens and their antimicrobial susceptibilities for prompt initiation of treatment. This information also is used in the preparation of antibiogram reports with aggregate data on the susceptibility of various pathogens to different antibiotics in the institution during a specific period, which is useful for choosing empiric therapy before the results of culture and susceptibility tests are available.<sup>6,64</sup>

Infection preventionists and health care epidemiologists can play a pivotal role in ASPs through early identification of multidrug-resistant organisms and by promoting adherence to hand hygiene and other infection prevention strategies.<sup>65</sup> Educating staff, patients, and visitors about these infection prevention strategies is another important contribution of these ASP team members.<sup>65</sup>

Information system specialists are critical to the success of ASPs. Computerized physician order entry, electronic medical records, and electronic clinical decision support systems can facilitate the implementation of many of the ASP interventions listed in Table 2.<sup>66</sup> Systems with the capability for managing data on a real-time basis are particularly valuable. Ideally, interfaces between the clinical laboratory and the CPOE system are established to facilitate the use of guidelines and clinical pathways with antibiotic selection based on culture and antimicrobial susceptibility data.

Information technology can be used to efficiently collect and analyze process and outcomes data to yield meaningful insight into the impact of ASP activities.

Antimicrobial drug use data that illustrate problems with prescribing involving specific physician services, types of patients, hospital units, or antimicrobial agents can be generated using information technology.

The use of information technology (particularly CPOE) can minimize the staff time needed for labor-intensive ASP interventions, especially formulary restriction, preauthorization, and antimicrobial order forms. Incorporating guidelines and clinical pathways into CPOE systems also has the potential to improve adherence.<sup>8</sup>

Information technology can be used to educate physicians, other health care professionals, students, and patients about ID and the need for antimicrobial stewardship. Hospital-specific applications (i.e., "apps") posted on the Internet for downloading and use on smart phones, tablets, and other mobile communications devices have been developed to promote antimicrobial stewardship.<sup>67</sup> Some applications can be used to provide access to educational programs, drug information, current literature, and news about ID at the point of care and other convenient locations.<sup>67</sup>

The availability of information technology and information systems specialists often is limited in small community hospitals in rural areas.<sup>68</sup> These limitations must be considered in choosing process and outcome metrics and planning ASP interventions. However, sophisticated information systems are not necessarily required for a successful ASP. The scope of the ASP should take into consideration the available information technology, personnel, and other resources.

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*Who is responsible for antimicrobial stewardship in your institution? What other persons and departments should participate to ensure an interprofessional team approach? What contributions might they make to improving antimicrobial use and reducing resistance?*

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## EDUCATION AND TRAINING

Although the IDSA/SHEA guidelines call for an ID physician and a pharmacist with ID training to serve as core members of the antimicrobial stewardship team, the lack of these personnel should not impede ASP implementation.<sup>68,69</sup> A staff physician or pharmacist, medical or pharmacy resident, physician assistant, or nurse practitioner with a strong interest in ID could serve on the team in institutions that lack an ID physician or pharmacist. Physician and pharmacist members of the P & T committee might serve on the ASP team because this committee is the ideal forum for coordinating ASP activities due to its authority for managing antimicrobial use in the institution.

Basic and advanced antimicrobial stewardship training programs for pharmacists, physicians, physician assistants, nurses, nurse practitioners, and other clinicians are available from MAD-ID Making a Difference in Infectious Diseases Pharmacotherapy ([www.mad-id.org](http://www.mad-id.org)). Educational programming on ID and antimicrobial stewardship also is available through this organization at its annual meeting.

In many institutions, the responsibility for antimicrobial stewardship falls to personnel without advanced ID training. These individuals can contribute to antimicrobial stewardship in substantial ways. For example, staff pharmacists can identify patients receiving i.v. therapy that could be converted to oral therapy, detect therapy that has exceeded the recommended duration, and screen orders for restricted antimicrobial agents that require authorization or are not consistent with guidelines or clinical pathways.<sup>37</sup>

Personnel without advanced ID training can augment their knowledge of ID and antimicrobial stewardship through various informal methods, such as attending rounds with ID physicians. Identifying a pharmacist or physician mentor with ID expertise and discussing patient cases with this mentor is another method. Participating in ID-related continuing education programs also can be helpful. Educational applications on ID topics are available for use with smart phones, tablets, or other devices, allowing for point-of-care education.<sup>67</sup>

### ESTABLISHING AN ASP

In the 2010 ASHP national survey of pharmacy practice in hospital settings, nearly half (44%) of 566 hospitals had an ASP.<sup>50</sup> Such programs were more common in large hospitals with 600 or more beds (83%) than in small hospitals with fewer than 50 beds (32%).

Implementing ASPs can present a challenge because of a lack of funding and personnel, opposition to or reluctance of physicians to accept the ASP, and other barriers. In a 2009 survey of ID physicians in U.S. hospitals, the most common barriers to implementing an ASP were lack of funding and lack of personnel.<sup>41</sup> One in four established ASPs had no paid physician or pharmacist.<sup>41</sup>

Obtaining support and authority from health system administration for initiating an ASP requires preparation of a strong business case based on the potential consequences of inappropriate antimicrobial use and antimicrobial resistance, especially increased mortality and health care costs. The many published reports demonstrating the cost-effectiveness of ASPs in improving antimicrobial use and reducing antimicrobial resistance, mortality, and health care costs should be used to strengthen the business case for an ASP. Cost savings from reductions in antimicrobial use alone are

limited. Increases in pharmacy costs for added personnel may be associated with ASP implementation. However, substantial cost savings can be realized from ASPs through improved efficiency of care and shortened hospital and ICU lengths of stay.<sup>70</sup> The references at the end of this discussion guide and the resources listed at [www.leadstewardship.org/resources.php](http://www.leadstewardship.org/resources.php) are helpful for preparing proposals to justify devoting resources to the ASP.

Current reimbursement policies of the Centers for Medicare & Medicaid Services (CMS) whereby payment is not provided for certain hospital-acquired infections that the agency considers avoidable “never events” can be used to strengthen the financial argument for implementing an ASP.<sup>71,72</sup> The agency discontinued payment for these and other preventable medical errors that result in serious consequences for the patient beginning in 2008. In October 2012, CMS reduced diagnosis-related group payments for excess hospital readmissions for certain conditions, including pneumonia, as a provision of the Affordable Care Act involving the Medicare Inpatient Prospective Payment System.<sup>73</sup> Currently nearly one in five Medicare beneficiaries is readmitted to the hospital within 30 days after discharge.<sup>74</sup>

The CMS Partnership for Patients is an initiative designed to improve the quality, safety, and affordability of health care for Americans, with the goal of reducing hospital readmissions within 30 days by 20% and preventable hospital-acquired conditions by 40% before the end of 2013 compared with 2010.<sup>74</sup> The initiative focuses on several aspects of patient safety related to ID (e.g., catheter-associated urinary tract infections [UTIs], CLABSIs, SSIs, VAP).

Recommendations and requirements of influential groups, such as IDSA, SHEA, the Joint Commission, and CDC, provide support for ASP implementation. The Joint Commission’s National Patient Safety Goal 7 to reduce the risk of HAIs requires the implementation of evidence-based practices to prevent HAIs due to multidrug-resistant organisms, CLABSIs, SSIs, and indwelling catheter-associated UTIs.<sup>75</sup> Failure to meet this NPSG could affect Joint Commission accreditation decisions.

### THE CALIFORNIA EXPERIENCE

A regulatory mandate designed to strengthen and promote optimal antibiotic use in California health care facilities took effect in January 2008.<sup>76,77</sup> The new law requires that all general acute care hospitals develop a process for evaluating the use of antibiotics and monitoring the results as part of quality improvement activities.<sup>6</sup> An ASP is not necessarily required, but the law influenced the establishment of an ASP in nearly one of four California hospitals participating in a recent

survey.<sup>78</sup> The regulatory mandate made it easier to justify to hospital administration investing financial and staff resources in an ASP.<sup>6</sup> A statewide ASP was developed in 2010 in California in response to the regulatory mandate.<sup>77</sup> Elements of this statewide effort include program recommendations based on best practices (e.g., the strategies listed in Table 2), consultation with and education of antimicrobial teams at hospitals, regional collaboration among hospitals, and development of internal and external performance measures.<sup>77</sup> The external performance measures serve as benchmarks to facilitate comparison of antimicrobial use among institutions.

Similar legislation could be adopted by CMS in the future, providing a mandate and justification for ASP implementation nationwide. Experience gained in California could be valuable to health policy makers and administrators planning to implement statewide ASPs in other states. In Massachusetts, a statewide educational program has been shown to facilitate implementation and improvement of ASPs, although there is no regulatory mandate for ASPs in the state.<sup>79</sup>

**DEMONSTRATING NEEDS AND RESULTS**

Process and outcome metrics and data related to antimicrobial use, resistance, and infections can be used to demonstrate a need for the ASP and evaluate its success in improving the quality of care. These data also can be used to validate the usefulness of the ASP, support the need to continue it, identify problems to address in quality improvement activities, and prioritize the use of limited resources. Examples of process metrics include the percentage of recommendations for antibiotic use implemented (Table 3), which reflects ASP acceptance.<sup>68</sup> A low rate of implementation suggests a need for education. The percentage of isolates of a pathogen with antimicrobial resistance is an outcome metric that reflects ASP success.<sup>68</sup> A longer period often is required after an intervention before improvement is observed in outcome metrics than improvement in process metrics.<sup>68</sup>

A combination of process and outcome metrics usually is used in ASPs.<sup>68</sup> In a 2012 survey of physicians and pharmacists at 48 U.S. acute care hospitals, including 41 hospitals with ASPs, process metrics (e.g., antimicrobial use and costs) were more commonly assessed than outcome metrics (e.g., infection-related mortality, antibiotic-associated length of stay).<sup>81</sup>

The use of care bundles ensures that a systematic approach to patient care is used so that care is consistent for all patients based on local evidence-based guidelines.<sup>53</sup> The rate of compliance with antimicrobial care bundles can be assessed as a process metric to identify shortcomings in the delivery of patient care as part of quality improvement efforts.<sup>53</sup>

Antibiograms are reports of the susceptibility of various pathogens to different antibiotics during a specific period (usually 1 year). Susceptibilities often vary among different regions in the country, different hospitals in a city, and even different areas in a hospital (e.g., ICUs).<sup>8</sup> Antibiograms are compiled by the clinical microbiology department for the overall institution and various hospital locations. The information provided in antibiograms is useful in conjunction with data on antimicrobial use and costs for common hospital-acquired infections because antibiograms reflect local microbiology and resistance patterns. The insight obtained from these data can be used to establish guidelines and clinical pathways for empiric antimicrobial therapy that optimize clinical outcomes and minimize health care costs.

Antibiograms typically provide susceptibility data for an isolate to various individual antimicrobial agents, but they are not useful for identifying the most effective combination antimicrobial therapy for the isolate. Combination antibiograms provide information about the susceptibility of isolates to various combinations of antimicrobial agents.<sup>82,83</sup> In ICU patients who are likely to be infected with resistant gram-negative pathogens, combination antibiograms may be useful for selecting empiric antimicrobial therapy.<sup>84</sup>

**TABLE 3.** Examples of Antimicrobial Stewardship Process and Outcome Metrics<sup>68,80</sup>

Process Metrics	Outcome Metrics
<ul style="list-style-type: none"> <li>▪ Percentage of recommendations for antibiotic use implemented</li> <li>▪ Number of full-time equivalents dedicated to ASP activities</li> <li>▪ Amount of time invested in ASP activities</li> </ul>	<ul style="list-style-type: none"> <li>▪ Percentage of isolates of a pathogen with antimicrobial resistance</li> <li>▪ Incidence of <i>Clostridium difficile</i> infection</li> <li>▪ Number of resistant hospital-acquired infections per 1000 patient-days</li> </ul>
ASP = antimicrobial stewardship program	

Data from antibiograms may be useful as outcome metrics of the success of ASP activities, but antimicrobial resistance rates should not be relied on solely to judge the success of an ASP.<sup>85</sup> Resistance rates may also reflect the impact of infection prevention and control measures and the transfer from nursing homes of patients with antimicrobial-resistant infections.<sup>37,86</sup>

Reports of data gathered using process and outcome metrics should be prepared and shared with hospital administrators and other stakeholders.<sup>68</sup> Comparison of data collected before and at appropriate intervals after implementing an ASP can be used to demonstrate the impact of the ASP and detect trends. Comparisons of data gathered using process and outcome metrics may be made with benchmarks established at other hospitals in a region or throughout the nation.<sup>68</sup> Reports should be tailored to the audience, with an emphasis on cost data for administrators and safety data for clinicians.

As with all quality improvement activities, goals for performance should be established for ASPs, and the success of the ASP in meeting these goals should be periodically evaluated. Strategies should be revised as needed to achieve performance goals. The processes for evaluating and improving ASP performance might be coordinated with other quality improvement activities used for earning and maintaining hospital accreditation and physician specialty board certification (e.g., self-evaluation of practice performance using what are referred to as practice improvement modules).<sup>87</sup>

### INITIAL STRATEGIES

Implementing an ASP where none exists can be daunting, especially when resources are limited. Focusing initially on readily implemented strategies likely to produce results has been recommended to optimize the benefit from limited resources.<sup>31</sup> Reducing the 30-day hospital readmission rate has been suggested because of the high rates of readmission of Medicare beneficiaries and large potential economic impact of failure to reduce these rates.<sup>31</sup> Because the ESCAPE pathogens in Table 1 are responsible for most hospital-acquired infections in the United States, the ASP should focus on these organisms.<sup>8,10</sup>

Batch preparation of parenteral antimicrobial doses to reduce waste is a strategy that has been successful in managing the pharmacy budget at a large, academic institution.<sup>31</sup> The challenges in small community hospitals and non-teaching institutions differ from those faced at larger academic facilities, so the approach to implementation of an ASP must be tailored to address the needs of the institution.<sup>68</sup>

Establishing realistic initial goals for the ASP is recommended. Subsequent efforts can be more ambitious, especially if the results of initial efforts are sufficient to obtain additional resources for ASP activities.

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*What goal might you target initially with antimicrobial stewardship activities at your institution?*

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### PUSHBACK

Health-system staff members may oppose ASP implementation and fail to cooperate with program requirements for various reasons, including resistance to change. A diplomatic approach is needed in overcoming this pushback. An interprofessional effort involving key opinion leaders in ASP development to obtain their buy-in before initiating an ASP can facilitate the implementation process. Health-system staff members must respect and trust individuals leading the ASP implementation process. The benefits and requirements of the ASP should be explained to all staff who will be involved in the ASP to promote adherence. A variety of formats may be used for education (e.g., in-service programs, grand rounds, electronic newsletters). Patient safety should be emphasized to dispel the common misperception of ASP as a cost-driven bureaucratic effort that undermines physician autonomy. The educational message should be tailored to the audience, with different content for emergency department physicians who administer first doses of antibiotics and ID physicians who manage subsequent therapy.<sup>8</sup> The design of ASP processes should be user friendly to facilitate adherence.<sup>8</sup>

The assistance of an ID physician champion (i.e., key opinion leader) can be obtained to address problems with uncooperative colleagues, but this remedy may not be feasible in small hospitals without ID physicians. The authority and support of hospital administration may be needed to address problems with uncooperative prescribers.<sup>68</sup>

### CONCLUSION

Antimicrobial resistance is a growing public health problem with a substantial clinical and economic impact. The potential impact and cost-effectiveness of ASPs have been demonstrated, but implementation of these programs can be a challenge. An interprofessional approach is needed to develop an effective ASP that improves patient outcomes. The need for effective ASPs is urgent to prevent a return to a pre-antibiotic era with uncontrollable infectious diseases.

### CONTINUING EDUCATION CREDIT INFORMATION

#### TO RECEIVE CONTINUING EDUCATION CREDIT

Once you have read the discussion guide (an assessment test is provided below as a study aid only), click on the link below to take the online assessment test (minimum score 70%) and complete your evaluation. Participants may print their official statements of continuing education credit immediately.

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## ASSESSMENT TEST STUDY AID

This assessment test is provided here as a study aid only. Follow the instructions above to complete this assessment test and the evaluation online to obtain CE credit for this activity.

1. Which of the following statements about the impact of antimicrobial stewardship programs (ASPs) is correct?
  - a. They improve antimicrobial use but their impact on antimicrobial resistance, hospital length of stay, mortality, and health care costs remains to be demonstrated.
  - b. They improve antimicrobial use and reduce antimicrobial resistance, but their impact on hospital length of stay, mortality, and health care costs remains to be demonstrated.
  - c. They improve antimicrobial use and reduce antimicrobial resistance, hospital length of stay, and mortality, but their impact on health care costs remains to be demonstrated.
  - d. They improve antimicrobial use and reduce antimicrobial resistance, hospital length of stay, mortality, and health care costs.
2. Which of the following pathogens recently became a cause of increasingly widespread and problematic infections in U.S. hospitals?
  - a. Carbapenem-resistant Enterobacteriaceae.
  - b. Extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli*.
  - c. Methicillin-resistant *Staphylococcus aureus*.
  - d. Vancomycin-resistant *Enterococcus*.
3. Which of the following is legislation implemented in the United States in 2012 with provisions to encourage research and development of new antimicrobial agents to treat life-threatening infections?
  - a. Get Smart: Know When Antibiotics Work.
  - b. Generating Antibiotic Incentives Now.
  - c. Strategies to Address Antimicrobial Resistance.
  - d. The 10 x '20 Initiative.
4. For which of the following antibiotics or antibiotic classes have pharmacokinetic and pharmacodynamic studies demonstrated that reductions in mortality can be achieved through the use of extended (i.e., prolonged) instead of standard infusions in patients with *Pseudomonas aeruginosa* infections?
  - a. Aminoglycosides.
  - b.  $\beta$ -lactam antibiotics.
  - c. Linezolid.
  - d. Vancomycin.
5. Which of the following is a potential disadvantage of parenteral-to-oral conversion as a strategy for antimicrobial stewardship?
  - a. Difficulty identifying eligible patients.
  - b. Prescriber pushback.
  - c. Lack of demonstrated impact.
  - d. Legal concerns about failure to follow recommendations.
6. Which of the following is a potential disadvantage of the use of care bundles?
  - a. Difficulty assessing and quantifying compliance.
  - b. Difficulty identifying the contribution of a particular element to a clinical outcome.
  - c. Lack of flexibility to accommodate local needs.
  - d. Prescriptive nature of the elements.
7. Which of the following was the most common barrier to implementation of ASPs in a 2009 survey of infectious disease physicians in U.S. hospitals?
  - a. Inadequate education.
  - b. Lack of administrative support.
  - c. Lack of funding.
  - d. Physician pushback.
8. Which of the following tools is best used to overcome barriers to ASP implementation related to increased staffing requirements for labor-intensive ASP interventions and a lack of personnel?
  - a. Antibigrams.
  - b. Care bundles.
  - c. Computerized physician order entry.
  - d. Education.
9. Which of the following is considered an outcome metric in evaluating an ASP?
  - a. Percentage of recommendations for antibiotic use implemented.
  - b. Rate of compliance with an antimicrobial care bundle for surgical prophylaxis with the agent chosen and timing of the first and last doses.
  - c. Number of resistant hospital-acquired infections per 1000 patient-days.
  - d. Number of hours invested in ASP activities during the fiscal year.
10. Which of the following strategies is best used to prevent a lack of prescriber cooperation with ASP requirements?
  - a. Distribute written policies, procedures, and guidelines for the ASP.
  - b. Obtain support and authority for the ASP from health system administrators.
  - c. Provide an analysis of the cost-effectiveness of the ASP.
  - d. Use an interprofessional approach involving key opinion leaders in ASP development.

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