Antimicrobial Stewardship Programs in Community Hospitals: The Evidence Base and Case Studies

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By controlling and changing how antimicrobial agents are selected and administered, antimicrobial stewardship programs (ASPs) aim to prevent or slow the emergence of antimicrobial resistance; optimize the selection, dosing, and duration of antimicrobial therapy; reduce the incidence of drug-related adverse events; and lower rates of morbidity and mortality, length of hospitalization, and costs. There is an abundant and growing body of evidence demonstrating that ASPs change the quantity and quality of antimicrobial prescriptions; however, measuring whether, when, and how ASPs improve patient outcomes and change patterns of antimicrobial resistance—which is the ultimate goals of ASPs—has been difficult, but the totality of evidence indicates that ASPs are capable of achieving these goals. In this article, we review the existing data on ASPs and their effects on patient care and antimicrobial resistance, as well as strategies for establishing ASPs in different types of hospitals.

The primary goals of antimicrobial stewardship programs (ASPs) are to prevent or slow the emergence of antimicrobial resistance; optimize the selection, dosing, and duration of antimicrobial therapy in individual patients; reduce adverse drug events, including secondary infections (e.g., Clostridium difficile infection [CDI]); and reduce morbidity, mortality, length of hospitalization, and health care–related costs [1–3]. The intent of ASPs is to accomplish these goals by providing a framework for accountability in the use of antimicrobial agents and by improving, modifying, and decreasing such use at the level of the individual patient. There is an abundant and growing body of evidence demonstrating that ASPs decrease the quantity and improve the quality of antimicrobial prescriptions in both academic and community hospitals, but the measurement of their impact on patient outcomes and antimicrobial resistance has been more difficult. The totality of evidence, however, suggests that ASPs are capable of achieving these latter goals [2–5].

BENEFITS OF ANTIMICROBIAL STEWARDSHIP PROGRAMS

Decreased Use of Antimicrobials

Numerous studies that have compared antimicrobial use before and after introduction of an ASP have shown reductions in antimicrobial consumption and related costs, in inappropriate prescribing practices, and in length of hospital stays [6–16]. Moreover, taken together, these studies show that these outcomes are associated with a corresponding financial benefit that is sufficient to justify the resources allocated to develop and maintain such programs. In addition, ASP activities have been associated with improved physician adherence to evidence-based guidelines and processes of care, particularly for patients in critical care units [9, 17, 18].
lists representative studies that have reported reductions in antimicrobial resistance after introduction of different types of ASPs [8, 12, 19, 20].

The process and fiscal benefits of ASPs have been shown in small community hospitals as well as in large academic or regional medical centers. For example, LaRocco et al [10] used a prospective audit and feedback strategy to modify antimicrobial use at a 120-bed community hospital and decreased total antimicrobial costs by $177,000 over a 1-year period. Carling et al [8] showed similar results in a medium-sized community hospital in Boston, Massachusetts. An 80-bed hospital in Switzerland that used elements of an audit and feedback ASP in addition to formulary restrictions reduced antimicrobial use by 36% (P < .001) and reduced antimicrobial-related expenditures by 53% ($100 per patient admitted to the hospital) [21]. Of interest, this program was entirely run by internal medicine physicians, not infectious diseases specialists.

### Clinical Outcomes

Presumably, more-appropriate and decreased antimicrobial use as a result of an ASP should lead to improved patient clinical outcomes. Data are accumulating that show that effective ASPs are associated with increased clinical and microbiologic therapeutic successes for infection and a reduced incidence of bacteremia, Gram-negative infection, antimicrobial drug–related adverse events, and CDI [8, 11, 12, 17, 20]. For example, at the Hospital of the University of Pennsylvania, a comprehensive stewardship program resulted in substantial improvements in appropriate antimicrobial selection and increased cure rates and decreased treatment failure rates for therapy of infection, compared with usual practice (Figure 1) [12]. In addition, there is fairly strong evidence that ASPs will decrease the incidence and prevalence of CDI, although many of these studies involved interventions in response to outbreaks of CDI. One study showed a decrease in CDI incidence from 2.2 cases per 1000 patient-days to 1.4 cases per 1000 patient-days (P = .002) after an ASP was implemented at the Hospital of the University of Pennsylvania, a comprehensive stewardship program resulted in substantial improvements in appropriate antimicrobial selection and increased cure rates and decreased treatment failure rates for therapy of infection, compared with usual practice (Figure 1) [12].

### Table 1 Representative Studies Demonstrating Reductions in Antimicrobial Resistance After Introduction of Different Types of Antimicrobial Stewardship Programs (ASPs)

<table>
<thead>
<tr>
<th>Study, year</th>
<th>Location</th>
<th>Type of ASP introduced</th>
<th>Outcome after introduction of ASP</th>
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<tbody>
<tr>
<td>Carling et al [8], 2003</td>
<td>University-affiliated teaching hospital, Boston, Massachusetts</td>
<td>Audit and feedback from all third-generation cephalosporins, aztreonam, parenteral fluoroquinolones, and imipenem</td>
<td>- 22% reduction in use of parenteral broad-spectrum antimicrobials (P &lt; .001)</td>
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<td>- Clostridium difficile infections decreased from 2.2 to 1.4 cases per 1000 patient-days (P = .002)</td>
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<td>- Significant decrease in resistant Enterobacteriaceae (P = .02)</td>
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<td>Fishman [12], 2006</td>
<td>Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania</td>
<td>Combined audit and feedback and prior authorization</td>
<td>- Appropriate antimicrobial selection increased from 32% to 90%</td>
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<td>- Cure rate increased from 55% to 91%</td>
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<td>- Clinical failure rate decreased from 31% to 5%</td>
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<td>- Prevalence of resistant pathogens decreased from 9% to 1%</td>
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<td>Lipworth et al [19], 2006</td>
<td>625-Bed academic medical center and a 344-bed urban community hospital</td>
<td>Prior authorization: restricted access to ceftazidime and ceftriaxone</td>
<td>- 86%-97% decrease in use of these agents at both hospitals</td>
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<td>- Prevalence of ESBL-EK decreased by 45% at academic medical center (P &lt; .001) and 22% at the community hospital (P = .36)</td>
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<td>Valiquette et al [20], 2007</td>
<td>Secondary/tertiary-care hospital, Quebec, Canada</td>
<td>Audit and feedback strategy focused on appropriate use of second- and third-generation cephalosporins, ciprofloxacin, clindamycin, and macrolides</td>
<td>- Decreased total antimicrobial consumption by 23%</td>
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<td>- Decreased targeted antimicrobial consumption by 54%</td>
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<td></td>
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<td>- Incidence of C. difficile infection decreased by 60% (P = .007)</td>
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</tbody>
</table>

a community hospital [8]. Furthermore, in response to an outbreak of CDI in Quebec, Canada caused by a binary toxin producing strain, implementation of increased infection-control measures failed to have an impact on the outbreak, whereas a subsequent campaign to reduce targeted antimicrobial consumption resulted in a statistically significant decrease in the incidence of C. difficile-associated diarrhea ($P = .007$) [20].

One of the most important measures to demonstrate improved patient care and outcomes would be improved mortality rates. Few studies, however, have demonstrated improved mortality rates or have been designed to do so. Similarly modest reductions in disease-specific mortality rates in a community hospital attributable to an ASP have been reported [21]. To obtain solid evidence supporting a mortality rate reduction attributable to an ASP would require a large, well-controlled, multicenter prospective trial, and this is unlikely to occur in the near future. It is of particular note, however, that, whereas most studies have not reported the positive impact of an ASP on mortality rates, these same studies have failed to show that introduction of an ASP was associated with increased mortality rates or other negative patient outcomes [6, 7, 11, 14].

Preventing and/or Reducing Antimicrobial Resistance

It can be hypothesized that limiting or reducing inappropriate antimicrobial use will result in decreased pressure for development or persistence of drug-resistant bacterial pathogens. Unfortunately, the factors associated with antimicrobial resistance are complex and multifactorial, making it difficult to attribute any change in resistance prevalence or lack thereof to a specific intervention. In addition, other methodologic problems exist for a study designed to link improved antimicrobial susceptibility to an ASP [2].

Despite this, there is a body of evidence suggesting that ASPs do prevent, delay, and/or limit the emergence of drug-resistant pathogens, including Gram-negative bacilli, in particular, and, potentially, vancomycin-resistant enterococci [8, 13, 20, 22–30].

One compelling study examined an ASP in a 500-bed community hospital in Queens, New York, that restricted access to all cephalosporins in an effort to reduce the incidence of cephalosporin-resistant Klebsiella spp. colonization and infection [31]. Over a 1-year period, there was an 80.1% hospital-wide reduction in cephalosporin use, which correlated to a hospital-wide 44% reduction in the incidence of clinical cultures positive for Klebsiella spp. ($P < .01$), including a 70.9% reduction in use of the intensive care unit (ICU; $P < .001$). It should be noted, however, that, because of a concomitant increase in the use of imipenem in the same hospital, there was an inadvertent 68.7% hospital-wide increase in the incidence of imipenem-resistant Pseudomonas aeruginosa infection ($P < .01$). Such unintended consequences should be looked for when intensive restriction interventions are implemented.

A similar study, conducted in 2 hospitals (a 625-bed academic medical center and a 344-bed urban community hospital), restricted access to ceftriaxone and ceftazidime [19]. Over the course of 5 years, the use of ceftriaxone and ceftazidime decreased by 86% and 95%, respectively, at the academic medical center and by 95% and 97%, respectively, at the community hospital. The prevalence of extended-spectrum β-lactamase–producing Escherichia coli and Klebsiella species (ESBL-EK) decreased by 45% at the academic medical center ($P < .001$) and by a nonsignificant 22% at the community hospital ($P = .36$). Patients at the community hospital were more likely to reside in long-term care facilities, were older, and were more likely to have a decubitus ulcer than were those from the academic medical center, which may explain why there was no statistically significant decrease in the prevalence of ESBL-EK infections at that hospital. Another community hospital, however, did demonstrate a significant ($P = .02$) decrease in resistant Enterobacteriaceae infections following ASP implementation [8]. Taken together, and subject to their limitations, these studies do strongly suggest that effective antibiotic stewardship can lead to a decrease in antimicrobial resistance, which is a meaningful achievement. In addition, studies that have looked at therapy of infections such as ventilator-acquired pneumonia have shown that reducing the length of therapy decreases the subsequent risk of acquiring colonization or infection due to antimicrobial-resistant organisms at the level of the individual patient [29]. ASPs that assist clinicians in adhering to guidelines based on evidence from such studies should thus be able to have an impact on antimicrobial resistance at the level of the individual patient.

STEWARDSHIP IN COMMUNITY HOSPITALS: CASE STUDIES

As noted throughout this supplement to Clinical Infectious Diseases, the structure of an ASP must conform to available resources; that is, one type of ASP will not necessarily be the best fit for any one medical facility. Indeed, in the studies cited above that describe the clinical benefits of ASPs, no 2 hospitals used exactly the same ASP structure or core or supplemental interventions. This section describes different potential strategies for developing unique, hospital-specific ASPs and shows how available resources can be molded into an ASP.

Case Study #1: Small Rural Hospital

Hospital 1 is a small, 150-bed rural hospital. The hospital has a single, 4-bed ICU that is mostly used for patients receiving chronic ventilation. Private-practice physicians admit patients to the hospital. There is no hospitalist or infectious diseases specialist on staff, and 2 private practice infectious diseases groups provide consultations and have admitting privileges.
There are 4 full-time pharmacists, and the pharmacy operates from 7 AM to 10 PM daily. The pharmacy and therapeutics committee is chaired by the chief medical officer. Microbiology is outsourced. This small hospital is primarily challenged by its lack of specialized staffing. Support from the local infectious diseases group practices and compensation for their contributions to the ASP will be essential to the success and acceptance of an ASP.

There are at least 2 strategies available to this hospital. First, if the concept of an ASP has support from hospital administrators, the initial step would be to establish a stewardship committee with a financially compensated infectious diseases specialist as medical director. The stewardship committee would report to the P&T committee, essentially becoming a pharmacy and therapeutics subcommittee. From there, the initial stewardship activities would be to establish an antimicrobial formulary, institute daily (or near daily) pharmacist review of antimicrobial prescriptions, and create an antibiogram if one is not available.

In the absence of institutional support, a different strategy is needed. The first step here is to identify an ASP champion (as described elsewhere in this supplement) to advocate for establishing an ASP. In this scenario, no independent antimicrobial committee could be immediately established. Rather, all initiatives, changes, and improvements would be moderated by the existing pharmacy and therapeutics committee, and all initial tasks, such as establishing a formulary and reviewing antimicrobial use, would be done in consultation with an infectious diseases specialist. Once those tasks are accomplished, the ASP, in consultation with the infectious diseases specialist, can begin to implement changes in how antimicrobial agents are used (eg, intravenous to oral switch programs and limitation of duration of therapy). With both strategies, the key to success is securing the commitment of a private-practice infectious diseases specialist and effectively including both community and private-practice infectious diseases groups by ensuring equal opportunity for representation from both groups in stewardship activities.

**Case Study #2: Small Suburban Hospital**

Hospital 2 is an 80-bed suburban institution and part of a larger hospital network with a central pharmacy and therapeutics committee. The hospital has no ICU or infectious diseases specialist on staff. A hospitalist service primarily admits patients from 3 large practices in the area. An infectious diseases consultant visits once per week, and there are 2 full-time pharmacists. Microbiology services are outsourced. This hospital faces 2 unique challenges to establishing an ASP: first, it lacks an infectious diseases specialist; and second, because it is part of a larger hospital system, the pharmacy has no direct control over its formulary.

The strategy for this hospital is dependent on the presence or absence of a local physician champion. In the absence of a local champion, the hospital could collaborate with other hospitals within its network and, through the central pharmacy and therapeutics committee and a remote physician willing to provide support and expertise, implement stewardship activities, such as developing guidelines and/or restrictions for the existing formulary. Although restrictions are often unpopular, in a very small hospital with limited staffing, restrictions may be the most efficient, least time-consuming, and most direct method of controlling antimicrobial use.

Alternatively, a physician champion, possibly a hospitalist or subspecialist, could lead the hospital to establish its own unique ASP. In this scenario, stewardship activities would also be implemented through the pharmacy and therapeutics committee. Initial, easily approved steps would be the development of guidelines for specific agents and pathways for treating common infections. The needed resources for this strategy include dedicated time for a hospitalist and pharmacist to devote to building an ASP and, perhaps, some additional infectious diseases training for each. For systems such as this, the possibility of investment in electronic software programs, which can greatly increase efficiency across the system, should be considered. The key to success for this hospital is finding the right physician champion and garnering support from the local hospital leadership. One important decision when identifying a champion is to consider how a physician without infectious diseases training will be received by administrators, other physicians, allied health care workers, payers, decision makers, and the larger health care system. In some systems, a leader without specific infectious diseases training may be readily accepted and effective, whereas in other systems, a champion with infectious diseases training may be necessary to capture widespread support.

**Case Study #3: Large, University-Affiliated Community Hospital**

Hospital 3 is a 220-bed, university-affiliated community hospital with two 10-bed ICUs. Trainees staff most services, with hospitalists attending. There are 2 dedicated infectious diseases specialists and 10 full-time pharmacists providing service 24 h a day, 7 days a week. One pharmacist is dedicated to clinical pharmacy initiatives but not specifically to ASP activities. The formulary is administered by a pharmacy and therapeutics committee with an antimicrobial subcommittee that is also responsible for the parent university hospital. A microbiology laboratory is available offsite at the academic center. The development and implementation of an ASP specifically for the community hospital is being done at the request of hospital leadership. The hospital has 2 key challenges: there is no infectious diseases–trained pharmacist, and it will likely need to develop an ASP that is different from that of the affiliated, larger academic hospital.
One option for such a situation is to integrate the community hospital’s stewardship activities and initiatives with those of the existing antimicrobial subcommittee at the academic center by having a physician and pharmacist join the subcommittee, if this has not yet occurred. Working through the larger committee may help identify opportunities for intervention and will minimize the amount of new infrastructure needed to develop the ASP. However, the larger committee may slow the implementation of changes at the smaller, individual community hospital because of increased layers of review by individuals not necessarily familiar with the hospital and its medical staff functions. It is also possible that the larger academic center will have different patient populations, challenges, and stewardship priorities than those of the community hospital and will be focused on activities that are unnecessary or already in place in the community hospital. Initially, the community hospital could adopt the policies of the academic center, either as part of the larger committee or independently, and then tailor those strategies to conform to the smaller hospital’s needs.

The alternative to combining efforts with the larger hospital, as in Case Study #2, is for the community hospital to develop its own, independent ASP. This would enable the community hospital to craft its own initiatives but, obviously, may be more labor and resource intensive than joining with an already established program. The initial stewardship activities of the new ASP, as for any program, would be to create a unique antibiogram, if not already in existence, and outline criteria for the use of major drug classes or treatment pathways for common disease. The key to success will be training the pharmacist ASP team leader.

CONCLUSIONS

The preponderance of available data confirms that ASPs, in all types and sizes of hospitals, reduce antimicrobial use, improve patient outcomes, and have the potential to prevent and/or control the emergence of antimicrobial-resistant organisms. For ASPs to be successful, they must address the specific needs of individual institutions and be built on available resources, the limitations and advantages of each institution, and the available staffing and technological infrastructure. With careful strategic planning and commitment from all involved parties, ASPs can become a reality for all community hospitals.

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