

Antimicrobial Stewardship at the Tipping Point

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ABSTRACT

Although the idea for antimicrobial stewardship (AMS) has been around for a long time, it has not reached a tipping point where most hospitals have an effective antimicrobial stewardship program (ASP). The purpose of this manuscript is to report on the present status of AMS. Do ASPs have convincing data on patient survival, patient safety, and cost reduction? Is regulatory pressure converging to drive rapid development of ASPs? Are recent mandates in North America and the United Kingdom propelling ASPs toward a tipping point? If not, what needs to be done?

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In his bestselling book, *The Tipping Point*, Malcolm Gladwell defines the “tipping point” as “the moment of critical mass, the threshold, or the boiling point” when an idea finally catches fire and becomes the norm or the generally accepted thing to do.¹ Antimicrobial stewardship programs (ASPs) have been around for some time, but that tipping point has yet to be achieved at which most hospitals and long-term care facilities have effective programs.

Recent mandates and proposed standards for ASPs in North America and the United Kingdom (UK) are stimulating movement toward a tipping point. But what will it take to reach that point? The purpose of this article is to report on the present status of antimicrobial stewardship (AMS). Do ASPs have convincing data on patient survival, patient safety, and cost reduction? Is regulatory pressure rapidly converging to drive expedited development?

Antimicrobial Stewardship

AMS is often defined as a systematic approach to the use of antimicrobial agents to achieve optimal outcomes, as close to 100% of the time as possible. This means using the correct agent, at the correct dose, with the correct route of administration and for the appropriate duration, to cure or prevent infection, while minimizing toxicity and emerging resistance. However, we think the current state of practice is more like:

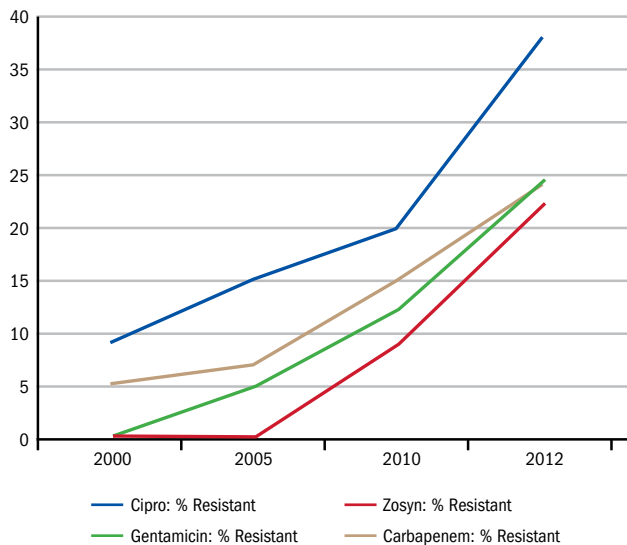
- Optimal agent used: ~80%
- Correct dose used: ~80%
- Narrow-spectrum antibiotic used when cultures are available and patient is stable: ~10% to 20%
- Optimal duration of therapy used: ~30%
- The likelihood that all sequential steps are optimal: ~4.5%

The Urgent Need for Effective ASPs

The increasing frequency of news reports about antimicrobial resistance contribute to a sense of impending doom,



Figure 1. Typically Decreased Sensitivities: Percent Resistant *Pseudomonas Aeruginosa* in Recent Years



Data from 2013 Visante Consult in 350-bed community hospital (with permission)

an “antimicrobial Armageddon.”² Is this Chicken Little speaking or is the threat very real? Bacteria relentlessly reinvent themselves to resist the killing power of antibiotics. The World Bank lists antimicrobial resistance as one of the top 10 threats to global economic progress.³ The CDC says “superbugs” are emerging much more quickly than expected, and the problem is now “very serious.”⁴ Data from an AMS consultation (Figure 1) in a 350-bed community hospital (conducted by the healthcare consulting firm Visante, Inc) show how resistance to antibiotics emerges unless effective ASPs are in place.

In hospitals, infections caused by multidrug-resistant organisms (MDROs) are associated with higher mortality, excess stay, and additional cost.³ Driving antimicrobial resistance is the inappropriate use of antimicrobial agents, estimated by the CDC to be as high as 50% of overall use. Another concern is that the pipeline for developing new antimicrobial agents (Figure 2⁵) is sparse.

A Brief History of AMS

In the early 1970s, clinical pharmacy services were established in North American hospitals, and some clinical pharmacists set about assessing the use of antibiotics due to the increases they were seeing in microorganism resistance. Evidence-based treatment guidelines and regulation of antibiotic use started to surface through hospital pharmacy and therapeutics committees.

In 1996, John McGowan, Jr, MD, and Dale N. Gerding, MD, then infectious disease specialists at Emory University

School of Medicine in Atlanta, coined the term “AMS.”⁶ A decade later, bacterial, antiviral, and antifungal resistance had risen to such a degree that the CDC was alarmed, and in 2007, the Infectious Disease Society of America (IDSA) and the Society for Healthcare Epidemiology of America published guidelines for developing an ASP.⁷

Recent Events

Recent events are driving ASP development in North America and the UK:

California: according to the California Department of Public Health, “California is the first (and remains the only state) to enact AMS legislation. Since 2008, California law has required that general acute care hospitals develop a process for monitoring the judicious use of antibiotics, and the results are monitored by quality improvement committee(s). In September of 2014, California Senate Bill 1311 was signed into law, further requiring hospitals to adopt and implement an AMS policy, under guidelines established by federal government and professional organizations, and to establish a physician-supervised multidisciplinary ASP with at least one physician or pharmacist who has undergone specific training related to stewardship.”⁸

United States: the Presidential Executive Order “Combating Antibiotic-Resistant Bacteria, issued in September 2014 requires federal agencies to review existing regulations and propose new regulations or other actions to require hospitals to implement robust ASPs that adhere to best practices—similar to California’s Senate bill. Agencies will also be required to define, promulgate, and implement ASPs in other settings, such as long-term care facilities and outpatient settings.

CDC: in 2014, the CDC recommended that all US hospitals have an ASP.⁹

Canada: since 2013, Accreditation Canada mandates that all acute care facilities have an ASP.¹⁰

United Kingdom: as part of the 5-year forward initiative to improve care by the National Health Service (NHS), AMS has become a central initiative of NHS England.¹¹

Unfortunately, most mandates are unfunded. However, with further actions outlined below, ASP development is moving forward toward its tipping point.

New Standards and Reporting Requirements

The Joint Commission (TJC) recently developed proposed medication standards, to be implemented beginning this summer, that cover general hospitals, critical access hospitals, ambulatory healthcare, nursing care centers, and office-based surgery.¹² Some proposed standards include:

- having a ASP that is based on evidence-based national guidelines

- the highest-level executives (C-suites) establishing ASPs as an organizational priority
- educating staff members and independent practitioners—any and all involved in ordering, dispensing, administration, and monitoring—about antimicrobial resistance and AMS. The education would begin upon hiring and continue annually
- educating patients and their families, as needed, on the proper use of antimicrobial medications, including antibiotics
- having a multidisciplinary AMS team that includes pharmacists, infectious-disease physicians, and infection preventionists
- core ASP elements: leadership commitment, drug expertise, action, tracking, reporting, and education
- using organization-approved multidisciplinary protocols
- collecting and analyzing data on its ASP, including prescribing and resistance patterns
- taking action on improvement opportunities identified in its ASP.

CMS is now using the following criteria when doing surveys¹³:

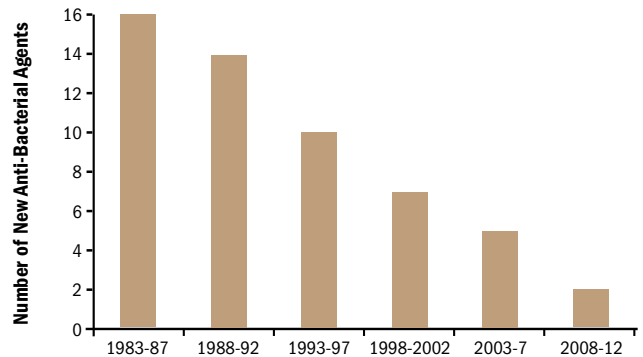
- The hospital has named a leader (eg, physician, pharmacist) responsible for program outcomes of antibiotic stewardship activities at the hospital
- The hospital's antibiotic stewardship policy and procedures require practitioners to document in the medical record, or during order entry, an indication for all antibiotics besides other required elements such as dose and duration
- The hospital has a formal procedure for all practitioners to review the appropriateness of any antibiotics prescribed after 48 hours from the initial orders (eg, antibiotic time-out)
- The hospital monitors antibiotic use (consumption) at the unit and/or hospital level.

The Evidence that AMS Works

Mark R. Chassin, MD, FACP, MPP, MPH, president and CEO of the Joint Commission, has said, “The Joint Commission knows that ASPs are a proven method of reducing the inappropriate use of antibiotics and improving patient safety.”

Although it seems intuitive that ASPs work, the quality of evidence for antimicrobial stewardship is poor. There are only 8 systematic reviews (none just looking at randomized controlled trials [RCTs]) and only 3 RCTs. A definitive, evidence-based study on ASPs has yet to be published. However, the anecdotal information and data are robust. For

Figure 2. Number of New Antibiotics Approved by the FDA, 1983-2012⁵



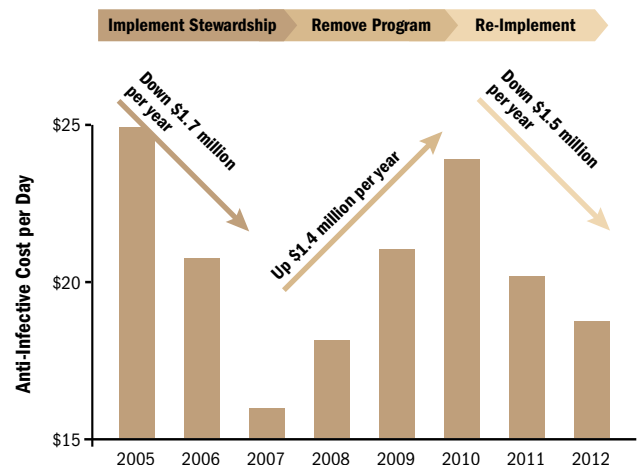
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example, the CDC has authored a helpful document, “Impact of Antibiotic Stewardship Program Interventions and Cost,” that lists findings from 15 published manuscripts.¹⁴

Other revealing data that support ASPs include what happens to total hospital antibiotic cost when an ASP is discontinued (Figure 3).³ Clearly, effective ASPs must be developed then consistently sustained over time.

A 2013 study revealed the impact of the temporary absence of a clinical pharmacist from an ASP.¹⁵ The rates of inappropriate use of imipenem-cilastatin, linezolid, and micafungin during the pharmacist's absence increased by 27%, 39%, and 35%, respectively, with corresponding increases in the average duration of therapy of 0.7, 4.0, and 3.2 days. In addition, the number of cases of *Clostridium difficile* infection increased more than 3-fold (from 8 to 25) during the pharmacist's absence.

Figure 3. “You Can’t Quit After 2 or 3 Years!” The Importance of Consistent, Persistent Antimicrobial Stewardship



Status of AMS in North America

Until a few years ago, AMS in the United States was reaching maturity only in larger, mostly academic hospitals; it had fledging status in midsize hospitals and was almost nonexistent in smaller hospitals. Although most practitioners agree that AMS is needed, it has not been at the top of C-suite concern. However, with the recent mandate from California, and renewed interest at the CDC, Joint Commission, and CMS, interest in ASPs is heating up in the United States.

ASPs are also garnering great interest in Canada, particularly in Ontario.¹⁰ An AMS project for that province includes multiple phases. In the first, a comprehensive survey examined the current state of hospital-based AMS practices in Ontario. In the second phase, the project team convened an international consensus forum to uncover and prioritize interventions considered to be appropriate and effective. The 6 interventions identified (in no particular order) were:

- Implement an ASP at the hospital level
- Use the antimicrobial stewardship self-assessment tool
- Do a prospective audit with intervention and feedback at the individual patient and prescriber level
- Provide education/training to build antimicrobial stewardship capacity
- Collect data and feedback at an institutional or program level
- Tailor antimicrobial therapy, with strategies including de-escalation, streamlining, and intravenous to oral switches.

The third phase, currently under discussion, proposes testing these interventions in a representative sample of pilot hospitals.

Overcoming Barriers to Success

Several organizations offer advice on how to start an ASP and maintain the core elements necessary for success.^{16,17} One such organization, Visante, Inc, which helps hospitals start ASPs and do benchmarking, and makes recommendations on AMS, finds that success rests on a few rate-limiting steps:

1. **Leadership.** A leaderless ASP is ineffective. According to the CDC, a medical staff leader should be responsible for program outcomes, and a pharmacy leader should co-lead the program.¹⁶ The medical staff leader should be an infectious-disease physician, possibly a hospitalist with strong interest in infectious disease; the pharmacist leader, ideally, is a clinical pharmacist with infectious-disease training.¹⁷

2. **Medical staff buy-in and organizational approval.** AMS consultants sometimes see ASPs with stalled progress because the program is solely pharmacy-based. For greatest effect, there must be buy-in by the hospital's medical staff (executive committee) and C-suite. The ASP leadership and the director of pharmacy should negotiate with hospital administration to obtain enough authority, compensation, and administrative support for the necessary infrastructure to be successful.¹⁷
3. **Getting everyone on the same age.** Collaboration must also exist among the antimicrobial stewardship team (physicians, pharmacists, nurses, microbiologists/infection control specialists, epidemiologists), the infection control committee, and the pharmacy and therapeutics committee.¹⁷
4. **Benchmarking.** Developing a baseline of data for the ASP program is critical. What is the status of antimicrobial resistance? Are you playing in the bottom of the sixth inning or the top of the ninth, so to speak? How extensive is your usage of antimicrobial agents? Your antimicrobial cost? Benchmarking against yourself is the best benchmarking.
5. **Implementing best practices.** Some programs have been doing this for a long time, and representatives have shared in the literature what has gone right and wrong. Review the experiences of programs similar to yours, in same type and size of hospital.
6. **Audit and feedback to prescribers.** Data generated on comparing prescribing and prescribers is critical to continuing success. Data systems must be structured correctly to capture this important information.

Getting Started

The important steps in getting an ASP started include:

- Gaining organizational approval. Two challenges must be overcome: convincing the medical staff and convincing the C-suite to support and take action. The program will go nowhere without medical staff support, so convincing the medical staff leadership comes first.
- Making the clinical case for an ASP.** The main components of the clinical case are:
- Dealing with the rising tide of antimicrobial resistance
 - The reality that resistance is developing faster than new antibiotic therapies. Correcting this situation is a major component of the recent presidential initiative to fund new drug development

- Potential therapeutic failure, with an increased mortality risk of 6.5% for each patient who becomes infected with resistant organisms
- Potential malpractice threats associated with not treating patients using evidence-based antibiotic strategies

Making the Business Case for an ASP^{17, 18:}

- Fewer cases of *C. difficile* and MDROs result in:
 - » Reduced antibiotic use and, therefore, total antibiotic cost
 - » Increased hospital reputation
 - » More satisfied patients (who return in the event future hospitalization is needed)
 - » Freed beds for new admissions
 - » Happier physicians, content in their workplace
 - » Value-based purchasing: with better performance, get paid more.
- *Putting the ASP team together.* Who should be on the ASP team? Remember that enthusiasm and commitment are almost as important as expertise, so choose wisely.
- *Establishing your baseline.* The best start is ascertaining the degree of antimicrobial resistance in your facility. Do you have an antibiogram? Does it reach the standards for this tool? How often is it published? How is it distributed? How often is it distributed? To whom? Comparing the oldest with the newest antibiogram provides an opportunity to see the trends for resistance. Other important baseline metrics should include some on usage and cost.
- *Developing the core elements.* The core elements necessary for success are:
 - » Implementing policies that support optimal antibiotic use. For example:
 - document dose, duration, and indication on all orders
 - develop and implement facility-specific treatment recommendations
 - » Implementing interventions that support optimal antibiotic use. For example:
 - antibiotic time-outs
 - prior authorization of restricted antibiotics
 - guidelines and clinical pathways
 - making intravenous to oral switches, when indicated
 - dose optimization
 - streamlining and de-escalation of therapy
- *Providing feedback to prescribers.* Track physician adherence to evidence-based antibiotic use around

variables such as percent of patients treated with guideline-recommended selection, dosing, de-escalation recommendations, duration for antibiotics for common infections, and optimal prophylactic antibiotic use.

Although many physicians instinctively feel that exceptions need to be made for their patients because they are “different” in some way, when regularly scheduled discussions highlight individual discrepancies from the norm of high performers, random variation decreases. The success of these discussions is contingent on having a respected physician champion present the data, with close support of the clinical pharmacist champion and the infection prevention/control and microbiology professionals.

Conclusions

Although AMS has been a well-known concept for quite some time, only now is the tipping point approaching, as effective ASPs are being developed in a rapidly increasing number of hospitals. Recent mandates in Canada and the UK, as detailed above, and the evidence of ASPs successfully reducing total antibiotic costs, hospital stay lengths, mortality, and other key clinical and financial parameters, provide increased pressure on all hospitals to act now to develop effective ASPs.

The fundamental structure, function, and key elements for an effective ASP are readily available from sources such as IDSA.¹⁶ If you have already started an ASP, keep going. If not, don't delay in beginning one. ASPs are now becoming part of the basic fabric of high-quality hospitals and healthcare systems. There are few opportunities as effective as ASPs to simultaneously increase patient care, quality, and safety, and decrease hospital cost and move toward controlling the epidemic of antimicrobial resistance imminent-ly threatening our ability to prevent and treat infection.

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