Communicating with Facility Leadership; Metrics for Successful Antimicrobial Stewardship Programs (ASP) in Acute Care and Long-Term Care Facilities

MAYA BEGANOVIC, PharmD, MPH; KERRY L. LAPLANTE, PharmD, FCCP, FIDSA

ABSTRACT

Up to 50% of hospital-administered and 70% of nursing home-administered antimicrobials are inappropriately prescribed. There is a great need to focus local, national and global efforts on appropriate antibiotic use. Formal programs dedicated to appropriate antibiotic use have been established in most US hospitals. These antimicrobial stewardship programs (ASP) exist to ensure that the correct drug, dose and duration of an antimicrobial is given, and only when there is a true bacterial infection (as opposed to bacterial colonization or a viral infection). These programs increase patient safety and reduce unintended consequences including *Clostridium difficile* infections, medication-related adverse effects, and antimicrobial resistance. Most of these programs are co-lead by an interdisciplinary team consisting of an infectious diseases (ID) pharmacist and an ID physician. However, consistent and meaningful metrics to study the impact of ASPs have not been elucidated. With the Joint Commission Standards for Acute Care facilities, and Centers for Medicare and Medicare (CMS) for long-term care facilities making antimicrobial stewardship (AMS) a condition of participation, both facilities will be scrambling to create appropriate quality care indicators to measure program success. One major theme across all healthcare settings is that ASPs must collaborate with facility leadership and key stakeholders at each institution in order to have an impactful benefit on patient quality of care, and safety. It is the purpose of this review to offer several economic, process, and patient-outcome measurements for ASP to optimally communicate with facility leadership.

KEYWORDS: antimicrobial stewardship, outcome assessment, process assessment, hospitals, long-term care facilities

INTRODUCTION

Antimicrobial stewardship programs (ASP) consistently demonstrate a reduction in antimicrobial utilization, favorable patient outcomes, and cost savings in both large academic medical centers and smaller community hospitals.[1,2] The demand for ASPs follows studies which indicate that up to 50% of hospital-administered antimicrobials, and up to 70% of long-term care facility-administered antimicrobials are prescribed inappropriately.[2,3] Misuse of antimicrobial agents (i.e. incorrect selection of drug, dose, frequency, duration or indication) has led to a rapid rise in antimicrobial-resistant bacteria that are estimated to cause at least 2 million illnesses and 23,000 deaths, annually.[4] The most common antimicrobial-related adverse events are *Clostridium difficile* infection (CDI), hypersensitivity reactions, and general medication-related adverse events.[5]

In acute care facilities, ASPs are ideally comprised of multidisciplinary teams consisting of an infectious diseases physician, an infectious diseases clinical pharmacy specialist, a clinical microbiologist, an infection control professional, an information system specialist, and a hospital epidemiologist.[2] These programs have repeatedly demonstrated a positive influence on patient outcomes (e.g. reduction in adverse drug events, CDI, morbidity and mortality, length of stay, antimicrobial resistance, and inappropriate prescribing), as well as healthcare expenditures.[5] In long-term care facilities, the responsibilities of AMS typically fall on the infection control and prevention nurse, ideally with assistance from consultant pharmacists, the directors of nursing and medical center directors.

Appropriate antimicrobial utilization aims to improve patient outcomes and minimize multi-drug resistance (MDR). Appropriate antibiotic use is a national priority (National Action Plan for Combating Antibiotic-Resistant Bacteria) that calls for establishment of ASPs in accordance with the Centers for Disease Control and Prevention (CDC) "Core Elements of Hospital Antibiotic Stewardship Programs" (**Table 1**).[3,6] The 2017 Joint Commission and Centers for Medicare and Medicaid Services will require hospitals and long-term care facilities to develop ASPs following these elements. Two of these CDC core elements relate to tracking and reporting measures of ASP success. However, selecting metrics to evaluate ASPs, their impact on patient outcomes, and development of resistance is challenging for a variety of reasons, including patient complexity, confounding factors, and metric selection that accurately depicts the program's impact.[7] The purpose of this review is to discuss available metrics and provide guidance for selecting metrics within institutions.

Table 1. Centers for Disease Control and Prevention (CDC) Core Elements of Hospital Antibiotic Stewardship Programs

Element	Description
Leadership commitment	Dedicating personnel, as well as financial and information technology resources
Accountability	Appointing single leader to be responsible for program outcomes
Drug Expertise	Appointing single pharmacist leader to support optimal antimicrobial utilization
Action	Implementing at least one actionable recommendation (e.g. antimicrobial time-out 48 hours post-empiric therapy)
Tracking	Monitoring antimicrobial prescribing and resistance patterns
Reporting	Regular reporting of tracked data to relevant staff
Education	Educating clinicians on optimal prescribing and resistance

Table 2. Metrics and Target Interventions

Measure (Level of Ease)	Conceivable Metrics*	Application of conceivable metrics to sample syndrome-specific targets
Process (Least difficult)	• Days of therapy (DOT) • Unnecessary days of therapy avoided • Provider adherence to syndrome-specific guideline/clinical pathway • Time to effective antimicrobial therapy • Time to optimal antimicrobial therapy after organism identification and sensitivity report • Proportion of patients converted from intravenous to oral medication • Number of urinalyses ordered in the ED	• Optimize therapy for bloodstream infections after implementation of molecular rapid diagnostic testing (e.g. MALDI-TOF MS, Film Array [BioFire], Verigene [Nanosphere], Accelerate Pheno and Accelerate PhenoTest [Accelarate Diagnostics], etc.) • Reduce inappropriate antimicrobial prescribing for respiratory viral infections ruled in via PCR-respiratory panel without signs of bacterial infection • Reduce or eliminate inappropriate antimicrobial prescribing for asymptomatic bacteriuria • Optimize antimicrobial use for infections in immunocompromised hosts • Reduce or eliminate inappropriate antimicrobial prescribing for skin and soft tissue infections • Reduce vancomycin use in low-MRSA risk patient population with pneumonia • Optimize empiric antimicrobial use toward common resistance patterns in nursing home and/or long-term facilities
Outcomes (Moderately difficult)	• Hospital length of stay • Intensive care unit (ICU) length of stay • 30-day mortality • Infection-related mortality • Unplanned 30-day hospital readmission • Proportion of patients with hospital-acquired CDI • Proportion of patients with clinical failure	
Resistance (Most difficult)	• Resistance patterns via annual antibiogram • Pathogen-specific resistance • Patient population-specific resistance	

*Does not represent a complete list;
MALDI-TOF MS= matrix-assisted laser/desorption ionization time of flight mass spectrometry

METRICS

Process and Antimicrobial Use Measures

Tracking and reporting antimicrobial use and outcomes data is critical to not only evaluating the success of the ASP, but also in identifying areas for improvement.[3,8,9] Generally, interventions are implemented to evaluate process and/or outcome measures (**Table 2**).[3,8,10] Process measures are easiest to evaluate as they utilize surrogate indicators to demonstrate whether an ASP successfully changed processes (e.g. guidelines/clinical pathway adherence), prescriber behavior (e.g. accurate diagnosis; appropriate drug-indication pairing, correct antimicrobial dose, frequency, and duration; appropriate and timely therapeutic modifications), resource utilization, or expenditure.[10,11] From the administrative standpoint, process measures, particularly resource utilization and expenditures, are critical to track as they highlight the need for continued support of ASPs. ASPs are associated with substantial cost savings that often stabilize after an initial period.[2,3] However, continued support is warranted as costs increase after program termination.[12]

Antimicrobial consumption can be evaluated using metrics such as days of therapy (DOT) or defined daily doses (DDD). These metrics reflect an aggregate amount of antimicrobial consumption, and are often standardized with patient-days in the denominator to allow for comparison between hospitals, regions, and/or countries.[3] Despite multiple available metrics, the CDC recommends utilizing DOT as the primary antimicrobial consumption metric because it provides more clinically relevant data than other metrics, including DDD.[3] However, calculating DOTs requires patient-level antimicrobial use data, which may not be feasible for all facilities. Under such circumstances, DDD may be utilized as an alternative despite several key disadvantages.[3,8] DDD reflects the amount of drug a typical, adult patient would receive for any given day utilizing World Health Organization (WHO)-approved DDD values, and therefore cannot be used for pediatric patients requiring weight-based dosing, as DDD interpretation is not translatable into meaningful data for that population.[13] This measure was not originally designed as an antimicrobial stewardship (AMS)

Table 3. Days of Therapy (DOT) versus Defined Daily Doses (DDD)

Description	DOT	DDD
	• Summation of days patient receives at least one dose of antimicrobial agent without regard to dose	• Average maintenance dose for main indication in 70kg-adults • Total grams used*/ World Health Organization (WHO)-approved DDD value**
Example	• Patient receives ceftriaxone 2gm Q12h plus ampicillin 2gm Q4h for 42 days • 2 antimicrobials X 42 days = 84 DOT	• Patient receiving ceftriaxone (CRO) 2gm Q12h plus ampicillin (AMP) 2gm Q4h for 42 days • DDD-values for ceftriaxone and ampicillin =2gm • DDD_{CRO}= (4gm dose/ 2gm DDD) x 42 days= 84 DDD; DDD_{AMP}= (12gm dose/ 2gm DDD) x 42 days= 252 DDD; total= 336 DDD
Standardization	• DOT/ patient-days • DOT/ patient-admission	• DDD/ patient-days • DDD/ patient-admission
Advantages	• Clinically relevant data • Expanded utilization in both adult and pediatric patients • Standardizing DOT can be used as benchmark to compare antimicrobial consumption between facilities, and regions	• Easy to obtain and does not require patient-level data • Standardizing DDDs can be used as benchmark to compare antimicrobial consumption between facilities, and regions
Limitations	• Requires patient-level antimicrobial use data • Optimal DOT unknown • Combination therapy yields higher DOT regardless of spectrum of activity	• Assumes all dosing is routine and may overestimate DDD in patients who require appropriately higher dosing (e.g. central nervous system infections, obesity, high-MIC pathogen infections, etc.) • May underestimate DDD in patients that appropriately require lower doses (e.g. renal impairment) • Combination therapy yields higher DDD regardless of spectrum of activity • Institutions must have similar antimicrobial composition/formulary to allow for comparison • Cannot be utilized for pediatric patients

*Obtained from purchased, dispensed, or administered data
** Available at: https://www.whocc.no/atc_ddd_index/

metric, and should not be used as such, when possible, as it has numerous flaws and biases.[3,8] DOT is not without flaws either. Although it provides useful overall antimicrobial consumption data, the optimal DOT number to target remains unknown. Reduction in DOT may not be beneficial for hospitals with already lean numbers. Indication-specific DOT data may be more optimal; however, data is currently unavailable. Comparison between DOT and DDD is further detailed in **Table 3**.

Other metrics, including length of therapy (i.e. sum of day's patient received antimicrobials regardless of drug or dose), grams used (obtained from purchased, dispensed, or administered data) and expenditures (i.e. monetary value spent obtained from purchased, dispensed, or administered data) are available. However, they are not recommended as a consumption measure as these metrics cannot be used to compare specific antimicrobial usage, are inaccurate, and may be affected by changes in cost, respectively.[14]

Outcome measures

Although process measures are substantially easier to collect and provide useful data, particularly during early program design, it is not enough to meet goals of ASPs.[11] The primary goals of ASPs include: 1) minimizing the progression of resistance; 2) optimizing antimicrobial selection (i.e. drug, dose and duration); and 3) reducing adverse drug events (i.e. CDIs, morbidity and mortality, length of stay and healthcare expenditures).[10] These goals cannot be evaluated through process measures alone.[11,15] For example, while improvement in antimicrobial utilization has demonstrated reduction in CDI[16], it cannot be completely explained by this process measure as additional unmeasured factors, including the role of infection control measures, can influence CDI rates.[5] Regardless, data on CDI rates are often collected and may be useful when interventions targeting reduction of highly CDI-associated antimicrobials (e.g. fluoroquinolones) are implemented.

Other helpful metrics evaluating outcomes related to ASPs in acute care facilities include: length of stay, 30-day mortality, unplanned hospital readmission, proportion of patients with clinical failure, days of avoided hospitalization (readmission, emergency room visits), as well as days of avoided central venous access and parenteral therapy administration.[5] Measuring such outcomes is challenging, particularly

for new programs and may become more feasible in the future as clear definitions and guidance is provided.[7] Interventions focused on syndrome-specific outcomes may be more practical.[5] With development and implementation of molecular rapid diagnostic testing (mRDT), measuring patient outcomes in bloodstream infections has demonstrated a reduction in mortality, particularly in institutions with ASPs.[17] Likewise, directing AMS efforts to antimicrobial discontinuation in institutions with high rates of inappropriate prescribing for respiratory tract infections[18], particularly in setting of polymerase chain reaction (PCR)-positive respiratory panels and low procalcitonin levels, is reasonable.[19]

Resistance

Antimicrobial resistance is perhaps the most challenging outcome to measure due to its multi-factorial development and dispersal.[3,5] Implementation of ASPs has been associated with a reduction in both Gram-positive and Gram-negative resistance[20], but similar to CDI rates, these findings may be confounded by other factors that impact antimicrobial resistance, including infection control measures, changes in prevalent organisms within an institution, patient demographics, and other care practices.[5] Tracking resistance of select pathogens, or patient populations that benefit most from AMS intervention may provide additional benefit to solely tracking and reporting overall resistance patterns.[5]

SELECTING AND APPLYING METRICS AT YOUR INSTITUTION

Expert consensus studies focusing on metric selection have been conducted.[7-9] These groups propose six patient-level metrics ready for immediate use in acute care settings and we offer personnel expertise that may best assist in data collection. These six areas include; hospital-onset CDI (infection control and prevention); healthcare-associated CDI (infection control and prevention); incidence of drug resistant infections (microbiology and infection control and prevention); antimicrobial DOT per patient-admission (pharmacy); DOT per patient-days (pharmacy); and redundant therapy events (pharmacy).[7] Clinical outcome measures were not selected due to concerns with accurately associating outcomes to AMS intervention in setting of unmeasured confounding factors (e.g. severity of illness, infection-control activities).[7] Similarly, unmeasured confounding factors including improved infection control measures, may influence CDI rates. Another structured panel used to identify quality-improvement metrics had several similarities to the patient-level expert consensus.[8] However, these panel members chose to include clinical outcome measures (i.e. antimicrobial-related organism mortality, 30-day mortality, conservable days of therapy, and unplanned 30-day hospital readmission).[8] Ideal metrics have yet to be elucidated as no single metric demonstrated superiority to others. Metrics should be individualized for each facility and aimed to satisfy short-term (e.g. reduction in antimicrobial consumption, patient outcomes) and long-term (e.g. resistance) goals.[3]

CONCLUSION

Tracking and reporting measures that ensure ASP success and highlight areas for improvement is challenging as ideal metrics remain unknown. Regardless of metric selection, ensuring accurate and consistent data collection is critical. The CDC assists providers through various resources. Particularly helpful is the National Healthcare Safety Network (NHSN), a widely used tracking system designed to measure antimicrobial utilization with risk adjustment that allows for inter- and intra-facility comparison. NHSN website provides several useful resources including various slide-sets and YouTube videos that assist providers with several components of ASP development. Other helpful resources are outlined in **Table 4**.

Table 4. Helpful Resources

Description	Link
CDC NHSN hospital-acquired infections tracker	https://www.cdc.gov/nhsn/acute-care-hospital/
Joint Commission new antimicrobial stewardship standard	https://www.jointcommission.org/assets/1/6/New_Antimicrobial_Stewardship_Standard.pdf
CDC Long-term Care Facility infections prevention guidance	https://www.cdc.gov/longtermcare/index.html
CMS guidance for long-term care facilities	https://www.cms.gov
University of Rhode Island antimicrobial stewardship treatment pathways	http://web.uri.edu/antimicrobial-stewardship/treatment-pathways/
Rhode Island Department of Health antimicrobial stewardship	http://www.health.ri.gov/healthcare/about/antimicrobialstewardship/

References

1. Ruttimann S, Keck B, Hartmeier C, Maetzel A, Bucher HC. Long-term antibiotic cost savings from a comprehensive intervention program in a medical department of a university-affiliated teaching hospital. *Clin Infect Dis.* 2004;38(3):348-356.
2. Dellit TH, Owens RC, McGowan JE, Jr., et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis.* 2007;44(2):159-177.
3. Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs, 2014 Atlanta, GA: CDC; 2014.
4. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2013 Atlanta, GA: CDC;2013.
5. Barlam TF, Cosgrove SE, Abbo LM, et al. Executive Summary: Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis.* 2016;62(10):1197-1202.
6. The White House. National action plan for combating antibiotic-resistant bacteria, 2015. Available at: https://www.whitehouse.gov/sites/default/files/docs/ national_action_plan_for_combating_antibotic-resistant_bacteria.pdf. Accessed 4 March 2017.
7. Moehring RW, Anderson DJ, Cochran RL, et al. Expert Consensus on Metrics to Assess the Impact of Patient-Level Antimicrobial Stewardship Interventions in Acute-Care Settings. *Clin Infect Dis.* 2017;64(3):377-383.
8. Morris AM, Brener S, Dresser L, et al. Use of a structured panel process to define quality metrics for antimicrobial stewardship programs. *Infect Control Hosp Epidemiol.* 2012;33(5):500-506.
9. van den Bosch CM, Geerlings SE, Natsch S, Prins JM, Hulscher ME. Quality indicators to measure appropriate antibiotic use in hospitalized adults. *Clin Infect Dis.* 2015;60(2):281-291.
10. Ohl CA, Luther VP. Antimicrobial stewardship for inpatient facilities. *J Hosp Med.* 2011;6 Suppl 1:S4-15.
11. McGowan JE. Antimicrobial stewardship--the state of the art in 2011: focus on outcome and methods. *Infect Control Hosp Epidemiol.* 2012;33(4):331-337.
12. Standiford HC, Chan S, Tripoli M, Weekes E, Forrest GN. Antimicrobial stewardship at a large tertiary care academic medical center: cost analysis before, during, and after a 7-year program. *Infect Control Hosp Epidemiol.* 2012;33(4):338-345.
13. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC classification and DDD assignment, 2013. Oslo: WHO Collaborating Centre for Drug Statistics Methodology; 2012.
14. Morris AM. Antimicrobial Stewardship Programs: Appropriate Measures and Metrics to Study their Impact. *Curr Treat Options Infect Dis.* 2014;6(2):101-112.
15. MacDougall C, Polk RE. Antimicrobial stewardship programs in health care systems. *Clin Microbiol Rev.* 2005;18(4):638-656.
16. Feazel LM, Malhotra A, Perencevich EN, Kaboli P, Diekema DJ, Schweizer ML. Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis. *J Antimicrob Chemother.* 2014;69(7):1748-1754.
17. Timbrook TT, Morton JB, McConeghy KW, Caffrey AR, Mylonakis E, LaPlante KL. The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis. *Clin Infect Dis.* 2017;64(1):15-23.
18. Gonzales R, Malone DC, Maselli JH, Sande MA. Excessive antibiotic use for acute respiratory infections in the United States. *Clin Infect Dis.* 2001;33(6):757-762.
19. Timbrook TT, Maxam M, Bosso J. Antibiotic Discontinuation Rates Associated with Positive Respiratory Viral Panel and Low Procalcitonin Results in Proven or Suspected Respiratory Infections. *Infect Dis Ther.* 2015;4(3):297-306.
20. Davey P, Marwick CA, Scott CL, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev.* 2017;2:CD003543.

Authors

Maya Beganovic, PharmD, MPH, Infectious Diseases Research Program, Providence Veterans Affairs Medical Center, Providence, RI; College of Pharmacy, University of Rhode Island, Kingston, RI.

Kerry L. LaPlante, PharmD, FCCP, FIDSA, Infectious Diseases Research Program, Providence Veterans Affairs Medical Center, Providence, RI; College of Pharmacy, University of Rhode Island, Kingston, RI; Center of Innovation in Long-Term Support Services, Providence Veterans Affairs Medical Center, Providence, RI; Warren Alpert Medical School of Brown University, Division of Infectious Diseases, Providence, RI.

Correspondence

Kerry L. LaPlante, PharmD, FCCP, FIDSA
Professor, University of Rhode Island
College of Pharmacy
7 Greenhouse Rd, Suite 295A
Kingston, RI 02881
401-874- 5560
KerryLaPlante@uri.edu