

Association of Inpatient Antimicrobial Utilization Measures with Antimicrobial Stewardship Activities and Facility Characteristics of Veterans Affairs Medical Centers

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BACKGROUND: Antimicrobial stewardship programs (ASPs) have been advocated to improve antimicrobial utilization, but program implementation is variable.

OBJECTIVE: To determine associations between ASPs and facility characteristics, and inpatient antimicrobial utilization measures in the Veterans Affairs (VA) system in 2012.

DESIGN: In 2012, VA administered a survey on antimicrobial stewardship practices to designated ASP contacts at VA acute care hospitals. From the survey, we identified 34 variables across 3 domains (evidence, organizational context, and facilitation) that were assessed using multivariable least absolute shrinkage and selection operator regression against 4 antimicrobial utilization measures from 2012: aggregate acute care antimicrobial use, antimicrobial use in patients with non-infectious primary discharge diagnoses, missed opportunities to convert from parenteral to oral antimicrobial therapy, and double anaerobic coverage.

SETTING: All 130 VA facilities with acute care services.

RESULTS: Variables associated with at least 3 favorable changes in antimicrobial utilization included presence of post-graduate physician/pharmacy training programs, number of antimicrobial-specific order sets, frequency of systematic de-escalation review, presence of pharmacists and/or infectious diseases (ID) attendings on acute care ward teams, and formal ID training of the lead ASP pharmacist. Variables associated with 2 unfavorable measures included bed size, the level of engagement with VA Antimicrobial Stewardship Task Force online resources, and utilization of antimicrobial stop orders.

CONCLUSIONS: Formalization of ASP processes and presence of pharmacy and ID expertise are associated with favorable utilization. Systematic de-escalation review and order set establishment may be high-yield interventions. *Journal of Hospital Medicine* 2017;12:301-309. © 2017 Society of Hospital Medicine

The deleterious impact of inappropriate and/or excessive antimicrobial usage is well recognized. In the United States, the Centers for Disease Control and Prevention (CDC) estimates that at least 2 million people become infected with antimicrobial-resistant bacteria with 23,000 subsequent deaths and at least \$1 billion in excess medical costs per year.¹

In response, many healthcare organizations have developed antimicrobial stewardship programs (ASPs). Guidelines co-sponsored by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America, as well as recent statements from the CDC and the Transatlantic Taskforce on Antimicrobial Resistance, all

recommend core ASP elements.²⁻⁵ The guidelines provide general recommendations on ASP structure, strategies, and activities. The recommended ASP structure is a team of physicians and pharmacists that collaborates with facility governing committees and other stakeholders to optimize antimicrobial use. While personnel with expertise in infectious diseases (ID) often lead ASPs, hospitalists are also recognized as key contributors, especially in quality improvement.^{6,7} Recommended strategies include prospective audit of antimicrobial use with intervention and feedback and formulary restriction with preauthorization. Recommended activities include education, creation of guidelines, clinical pathways, and order forms, and programs to promote de-escalation and conversion from parenteral (IV) to oral (PO) antimicrobial therapy. However, limited evidence exists regarding the effectiveness of these ASP core elements.^{8,9} While Cochrane reviews found clear evidence that particular stewardship strategies (eg, audit and feedback, formulary restriction, guidelines implemented with or without feedback, protocols, computerized decision support) can be effective in reducing antimicrobial usage and improving clinical outcomes over the long term, little evidence exists favoring 1 strategy over

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another.⁸ Furthermore, most individual studies of ASPs are single-center, making their conclusions less generalizable.

In 2012, the VA National Antimicrobial Stewardship Task Force (ASTF), in conjunction with the VA Health-care Analysis and Information Group (HAIG) administered a survey on the characteristics of ASPs at all 130 acute care VA facilities (Appendix A). We used these survey results to build an implementation model and then assess associations between facility-level variables and 4 antimicrobial utilization measures.

METHODS

Survey and Data

In 2011, the ASTF was chartered to develop, deploy, and monitor a strategic plan for optimizing antimicrobial therapy management. Monthly educational webinars and sample policies were offered to all facilities, including a sample business plan for stewardship and policies to encourage de-escalation from broad-spectrum antimicrobials, promote conversion from parenteral to oral antimicrobial therapy, avoid unnecessary double anaerobic coverage, and mitigate unnecessary antimicrobial usage in the context of *Clostridium difficile* infection.¹⁰

At the time that ASTF was chartered, the understanding of how ASP structures across VA facilities operated was limited. Hence, to capture baseline institutional characteristics and stewardship activities, ASTF and HAIG developed an inventory assessment of ASPs that was distributed online in November 2012. All 130 VA facilities providing inpatient acute care services responded.

We derived 57 facility characteristics relevant to antimicrobial utilization and conducted a series of factor analyses to simplify the complex dataset, and identify underlying latent constructs. We categorized resulting factors into domains of evidence, context, or facilitation as guided by the Promoting Action on Research Implementation in Health Services framework.¹¹ Briefly, the evidence domain describes how the facility uses codified and noncodified sources of knowledge (eg, research evidence, clinical experience). Organizational context comprises a facility's characteristics that ensure a more conducive environment to put evidence into practice (eg, supportive leadership, organizational structure, evaluative systems). Facilitation emphasizes a facility personnel's "state of preparedness" and receptivity to implementation.

Using factor analysis to identify facility factors as correlates of the outcomes, we first examined polychoric correlations among facility characteristics to assess multicollinearity. We performed independent component analysis to create latent constructs of variables that were defined by factor loadings (that indicated the proportion of variance accounted for by the construct) and uniqueness factors (that determined how well the variables were interpreted by the construct). Factors retained included variables that had uniqueness values of less than 0.7 and factor loadings greater than 0.3. Those associated with uniqueness values greater than 0.7 were left as single items, as were characteristics deemed a priori to be

particularly important to antimicrobial stewardship. Factor scales that had only 2 items were converted into indices, while factor scores were generated for those factors that contained 3 or more items.¹²⁻¹⁵

Data for facility-level antimicrobial utilization measures were obtained from the VA Corporate Data Warehouse from calendar year 2012. The analysis was conducted within the VA Informatics and Computing Infrastructure. All study procedures were approved by the VA Central Institutional Review Board.

Measures

Four utilization measures were defined as dependent measures: overall antimicrobial use; antimicrobial use in patients with non-infectious discharge diagnoses; missed opportunities to convert from parenteral to oral antimicrobial therapy; and missed opportunities to avoid double anaerobic coverage with metronidazole.

Overall antimicrobial use was defined as total acute care (ie, medical/surgical/intensive care) antibacterial use for each facility aggregated as per CDC National Healthcare Safety Network Antimicrobial Use Option guidelines (antimicrobial days per 1000 patient days present). A subanalysis of overall antimicrobial use was restricted to **antimicrobial use among patients without an infection-related discharge diagnosis**, as we surmised that this measure may capture a greater proportion of potentially unnecessary antimicrobial use. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)¹⁶ codes for infectious processes were identified by a combination of those classified previously in the literature,¹⁷ and those identified by finding the descendants of all infections named in the Systematized Nomenclature of Medicine--Clinical Terms.¹⁸ Next, all remaining codes for principal discharge diagnoses for which antimicrobials were administered were reviewed for potential indications for systemic antibacterial use. Discharges were considered noninfectious if no codes were identified when systemic antimicrobials were or could be indicated. For this measure, antimicrobial days were not counted if administered on or 1 day after the calendar day of surgery warranting antimicrobial prophylaxis.

Missed opportunities for conversion from parenteral to oral (IV to PO) formulations of highly bioavailable oral antimicrobials (ciprofloxacin, levofloxacin, moxifloxacin, azithromycin, clindamycin, linezolid, metronidazole, and fluconazole) were defined as the percentage of days of unnecessary IV therapy that were given when PO therapy could have been used among patients who were not in intensive care units at the time of antimicrobial administration who were receiving other oral medications, using previously described methodology.¹⁹ **Missed opportunities for avoiding redundant anaerobic coverage with metronidazole** were defined as the percentage of days in which patients receiving metronidazole also received antibiotics with activity against anaerobic bacteria, specifically beta-lactam/beta-lactamase inhibitors, carbapenems, cefotetan/cefoxitin, clindamycin, moxifloxacin, or tige-

cycline), using previously described methodology.²⁰ Patients for whom *C. difficile* testing was either ordered or positive within the prior 28 days (indicating potential clinical concern for *C. difficile* infection) were excluded from this endpoint.

Analysis

The variables derived above were entered into a multivariable model for each of the 4 antimicrobial utilization measures. The least absolute shrinkage and selection operator (LASSO) regression was used to determine significant associations between variables and individual utilization measures.²¹ LASSO was chosen because it offers advantages over traditional subset selection approaches in large multivariable analyses by assessing covariates simultaneously rather than sequentially, supporting prediction rather than estimation of effect.²² *P* values were not reported as they are not useful in determining statistical significance in this methodology. A tuning parameter of 0.025 was determined for the model based on a cross-validation approach. Significant variables remaining in the model were reported with the percent change in each utilization measure per unit change in the variable of interest. For binary factors, percent change was reported according to whether the variable was present or not. For ordinal variables, percent change was reported according to incremental increase in ordinal score. For continuous variables or variables represented by factor or index scores, percent change was reported per each 25% increase in the range of the score.

RESULTS

Inpatient Facility Antimicrobial Stewardship Characteristics and Antimicrobial Utilization

Frequencies of key facility characteristics that contributed to variable development are included in Table 1. Full survey results across all facilities are included in Appendix B. Factor analysis reduced the total number of variables to 32; however, we also included hospital size and VA complexity score. Thus, 34 variables were evaluated for association with antimicrobial utilization measures: 4 in the evidence domain, 23 in the context domain, and 7 in the facilitation domain (Table 2).

Median facility antimicrobial use was 619 antimicrobial days per 1000 days present (interquartile range [IQR], 554-700; overall range, 346-974). Median facility noninfectious antimicrobial use was 236 per 1000 days present (IQR, 200-286). Missed opportunities for conversion from IV to PO antimicrobial therapy were common, with a median facility value of 40.4% (391/969) of potentially eligible days of therapy (IQR, 32.2-47.8%). Missed opportunities to avoid double anaerobic coverage were less common (median 15.3% (186/1214) of potentially eligible days of therapy (IQR, 11.8%-20.2%; Figure).

Overall Antimicrobial Use

Four variables were associated with decreased overall antimicrobial use, although with small magnitude of change: presence of postgraduate physician/pharmacy training pro-

grams (0.03% decrease per quarter increase in factor score; on the order of 0.2 antimicrobial days per 1000 patient days present), presence of pharmacists and/or ID attendings on general medicine ward teams (0.02% decrease per quarter increase in index score), frequency of systematic de-escalation review (0.01% decrease per ordinal increase in score), and degree of involvement of ID physicians and/or fellows in antimicrobial approvals (0.007% decrease per quarter increase in index score). No variables were associated with increased overall antimicrobial use.

Antimicrobial Use among Discharges without Infectious Diagnoses

Six variables were associated with decreased antimicrobial use in patients without infectious discharge diagnoses, while 4 variables were associated with increased use. Variables associated with the greatest magnitude of decreased use included facility educational programs for prudent antimicrobial use (1.8% on the order of 4 antimicrobial days per 1000 patient days present), frequency of systematic de-escalation review (1.5% per incremental increase in score), and whether a facility's lead antimicrobial stewardship pharmacist had ID training (1.3%). Also significantly associated with decreased use was a factor summarizing the presence of 4 condition-specific stewardship processes (de-escalation policies, policies for addressing antimicrobial use in the context of *C. difficile* infection, blood culture review, and automatic ID consults for certain conditions) (0.6% per quarter increase in factor score range), the extent to which postgraduate physician/pharmacy training programs were present (0.6% per quarter increase in factor score range), and the number of electronic antimicrobial-specific order sets present (0.4% per order set). The variables associated with increased use of antimicrobials included the presence of antimicrobial stop orders (4.6%), the degree to which non-ID physicians were involved in antimicrobial approvals (0.7% per increase in ordinal score), the level engagement with ASTF online resources (0.6% per quarter increase in factor score range), and hospital size (0.6% per 50-bed increase).

Missed Opportunities for Parenteral to Oral Antimicrobial Conversion

Missed opportunities for IV to PO antimicrobial conversion had the largest number of significant associations with organizational variables: 14 variables were associated with fewer missed opportunities, while 5 were associated with greater missed opportunities. Variables associated with the largest reductions in missed opportunities for IV to PO conversion included having guidelines for antimicrobial duration (12.8%), participating in regional stewardship collaboratives (8.1%), number of antimicrobial-specific order sets (6.0% per order set), ID training of the ASP pharmacist (4.9%), and VA facility complexity designation (4.2% per quarter increase in score indicating greater complexity).²³ Variables associated with more missed opportunities included stop orders (11.7%), overall perceived receptiveness to antimicro-

TABLE 1. Frequencies of Key Facility Antimicrobial Stewardship Characteristics at VA Facilities Contributing to Variable Development (N=130)

Facility Characteristics	Facilities (n)	(%)
Contributors to evidence domain	103	79
Internal inpatient ID consultation available	120	92
Any restriction of antimicrobial use	47	36
Guidelines for antimicrobial duration (any)	96	74
Written clinical pathways/guidelines for specific conditions (any)		
Contributors to context domain		
At least one full-time attending ID physician at facility	78	60
Dedicated clinical pharmacist in ED	20	18
Presence of outpatient parenteral antimicrobial therapy program	85	65
Facility rates helpfulness of VA ASTF SharePoint site as "very helpful" or "helpful"	82	63
Facility rates helpfulness of ASTF sample policy for intravenous to oral antibiotic conversion as "very helpful" or "helpful"	68	52
Facility rates helpfulness of ASTF sample policy for avoidance of double anaerobic coverage as "very helpful" or "helpful"	51	39
Facility rates helpfulness of ASTF sample policy for improving outcomes in patients with <i>Clostridium difficile</i> infection as "very helpful" or "helpful"	51	39
Facility rates helpfulness of ASTF sample business plan as "very helpful" or "helpful"	49	38
Facility identifies more information technology/data tools support as beneficial in achieving optimal antibiotic use	95	73
Facility identifies more support from administration as beneficial in achieving optimal antibiotic use	79	61
Facility identifies more support from pharmacy as beneficial in achieving optimal antibiotic use	75	58
Facility identifies more support from ID physicians as beneficial in achieving optimal antibiotic use	73	56
Facility identifies more prescriber buy-in as beneficial in achieving optimal antibiotic use	77	59
Facility identifies more educational tools support as beneficial in achieving optimal antibiotic use	73	56
Facility identifies more guidelines support as beneficial in achieving optimal antibiotic use	67	52
Surgical residency program	84	65
ID fellowship program	68	52
Pharmacy residency program	102	78
Participation in AS collaborative within geographic region (ie, regional AS conference or committee)	13	10
ID physician approves antibiotics during weekdays	57	44
ID physician approves antibiotics during nights/weekends	39	30
ID pharmacist approves antibiotics during weekdays	44	34
ID pharmacist approves antibiotics during nights/weekends	8	6
Non-ID physician approves antibiotics during weekdays	7	5
Non-ID physician approves antibiotics during nights/weekends	11	8
Formal policy for ASP established	29	22
Policy for de-escalation of antimicrobials	19	15
Policy for intervention on antimicrobial usage in context of <i>C. difficile</i> infection	25	19
Timely review of blood cultures to assure appropriate therapy	56	43
Automatic ID consults for certain conditions	36	28
Automatic stop orders for antimicrobial duration	98	75
Electronic antimicrobial order form(s) for any specific antimicrobial	55	42
General medicine service deemed "very receptive" or "receptive" to ASP	110	85
ICU medicine service deemed "very receptive" or "receptive" to ASP	90	69
Facility has AS team	49	38
ID physician is a part of AS team	45	35
Clinical pharmacist/clinical pharmacy specialist is part of AS team	49	38
Antibiograms disseminated via facility intranet	96	74
Antibiograms disseminated via pocket card reference	56	43
Medication use evaluation performed for any antibiotic in prior 2 y	61	47
Provision of group- or provider-specific feedback on patterns of antibiotic use	55	42

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TABLE 1. Frequencies of Key Facility Antimicrobial Stewardship Characteristics at VA Facilities Contributing to Variable Development (N=130) (continued)

Facility Characteristics	Facilities (n)	(%)
Contributors to context domain		
Reporting of clinical outcomes related to antimicrobial use	71	55
Systematic review for de-escalation performed (always or usually)	39	30
Measurement of antibiotic use in defined daily doses	18	14
Measurement of antibiotic use in days of therapy	19	15
Measurement of antimicrobial expenditures	37	28
Contributors to facilitation domain		
ID physicians attend on medical ward teams	89	68
Clinical pharmacist assigned to acute care teams	118	91
Business plan for ASP approved or in development	41	32
ASP clinical pharmacist/clinical pharmacy specialist with ID training	34	26
Educational programs for prudent antimicrobial use	94	72
Communication to providers on principles of antibiotic use		
E-mail alerts	51	39
Newsletters	37	28
Pharmacy alerts	48	37
Engagement with ASTF outreach efforts:		
Finding ASTF national webinars "very helpful" or "helpful"	70	54
Finding ASTF face-to-face meetings "very helpful" or "helpful"	48	37
Electronic resources used to facilitate ASP activities:		
Basic electronic medical record system	115	88
Proprietary software	14	11
Administrative electronic databases	23	18

NOTE: Abbreviations: AS, antimicrobial stewardship; ASP, antimicrobial stewardship programs; ASTF, antimicrobial stewardship task force; ED, emergency department; ICU, intensive care unit; ID, infectious diseases; VA, Veterans Affairs.

bial stewardship among clinical services (9.4%), the degree of engagement with ASTF online resources (6.9% per quarter increase in factor score range), educational programs for prudent antimicrobial use (4.1%), and hospital size (1.0% per 50-bed increase).

Missed Opportunities for Avoidance of Double Anaerobic Coverage

Four variables were associated with more avoidance of double anaerobic coverage: ID training of the lead ASP pharmacist (8.8%), presence of pharmacists and/or ID attendings on acute care ward teams (6.2% per quarter increase in index score), degree of ID pharmacist involvement in antimicrobial approvals, ranging from not at all (score=0) to both weekdays and nights/weekends (score=2; 4.3% per ordinal increase), and the number of antimicrobial-specific order sets (1.5% per order set). No variables were associated with less avoidance of double anaerobic coverage.

Variables Associated with Multiple Favorable or Unfavorable Antimicrobial Utilization Measures

To better assess the consistency of the relationship between organizational variables and measures of antimicrobial use, we tabulated variables that were associated with at least 3

potentially favorable (ie, reduced overall or noninfectious antimicrobial use or fewer missed opportunities) measures. Altogether, 5 variables satisfied this criterion: the presence of postgraduate physician/pharmacy training programs, the number of antimicrobial-specific order sets, frequency of systematic de-escalation review, the presence of pharmacists and/or ID attendings on acute care ward teams, and formal ID training of the lead ASP pharmacist (Table 3). Three other variables were associated with at least 2 unfavorable measures: hospital size, the degree to which the facility engaged with ASTF online resources, and presence of antimicrobial stop orders.

DISCUSSION

Variability in ASP implementation across VA allowed us to assess the relationship between ASP and facility elements and baseline patterns of antimicrobial utilization. Hospitalists and hospital policy-makers are becoming more and more engaged in inpatient antimicrobial stewardship. While our results suggest that having pharmacists and/or physicians with formal ID training participate in everyday inpatient activities can favorably improve antimicrobial utilization, considerable input into stewardship can be made by hospitalists and policy makers. In particular, based on this work,

TABLE 2. Antimicrobial Stewardship Facility Variables Examined According to PARIHS Domain^a

No.	Factor Name	Variable Type (range)	Contributing Survey Question(s)/ Data Sources ^a
<i>Evidence domain</i>			
E1	Availability of inpatient ID consultation (score 0= non-ID physicians or pharmacists handling ID issues; score 5=internal inpatient ID service)	Ordinal (0-5)	Q12
E2	Presence of policies that restrict certain antimicrobials	Binary (0,1)	Q22
E3	Guidelines for antimicrobial duration	Binary (0,1)	Q33
E4	Number of written clinical pathways/guidelines for specific conditions	Ordinal (0-7)	Q25a
<i>Context domain</i>			
<i>Structural characteristics</i>			
C1	Facility complexity (level 1a, 1b, 1c, 2, or 3)	Continuous	Internal VA data
C2	Hospital beds (no.)	Ordinal (0-433)	Internal VA data
<i>Resources</i>			
C3	Full-time ID attendings on site (no.)	Ordinal (0-10)	Q1a
C4	Dedicated clinical pharmacist in ED	Binary (0,1)	Q13
C5	Presence of outpatient parenteral antimicrobial therapy program	Binary (0,1)	Q14
C6	Degree of engagement with VA ASTF (summary of helpfulness ratings of ASTF SharePoint site and sample policies)	Factor score	Q42-46,
C7	Perceived benefit of types of support in achieving optimal antimicrobial use (number of categories of additional support deemed potentially helpful to AS)	Factor score	Q54
<i>Affiliation/networks</i>			
C8	Presence of postgraduate physician/pharmacy training programs (ID fellowship, surgical residency, pharmacy residency)	Factor score	Q2, Q5, Q7
C9	Participation in stewardship regional collaboratives	Binary (0,1)	Q18
<i>Decision-making</i>			
C10	Degree of involvement of ID physicians and/or fellows in antimicrobial approvals (ie, during weekdays vs. nights/ weekends)	Index	Q23e,f
C11	Degree of ID pharmacist involvement in antimicrobial approvals	Ordinal (0-2)	Q23e,f
C12	Degree of non-ID physician involvement in antimicrobial approvals	Ordinal (0-4)	Q23e,f
<i>Formalization</i>			
C13	Presence of formal stewardship policy	Binary	Q17, Q20a
C14	Presence of condition-specific stewardship interventions (number present of de-escalation policies, policies for addressing antimicrobial use in the context of <i>C difficile</i> infection, blood culture review, automatic ID consults for certain conditions)	Factor score	Q29, Q31, Q32, Q38
C15	Antimicrobial stop orders in place	Binary (0,1)	Q34
C16	Number of antimicrobial-specific order sets in place	Ordinal (0-9)	Q24
<i>Receptiveness to change</i>			
C17	Overall receptiveness to stewardship among clinical services (count of clinical services deemed "receptive" or "very receptive")	Factor Score	Q55
<i>Leadership</i>			
C18	Degree and duration of physician and pharmacy involvement in stewardship (how long ASP has been in place and percentage of time dedicated to ASP by physicians and pharmacists)	Factor Score	Q19, Q19f,g
<i>Evaluation and feedback</i>			
C19	Degree of dissemination and evaluation of antimicrobial outcome data (number of methods of antibiogram dissemination plus whether MUE has been done on any antibiotic within 2 y)	Index	Q16b, Q52
C20	Degree to which antimicrobial usage and outcomes are reported to providers (frequency of group- or provider-specific feedback on patterns of antimicrobial use and whether reports on clinical outcomes related to antibiotic use are generated)	Index	Q49, Q50a
C21	Frequency of systematic de-escalation review (score 0=never; score 4=always)	Ordinal (0-4)	Q30

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TABLE 2. Antimicrobial Stewardship Facility Variables Examined According to PARIHS Domain^a (continued)

No.	Factor Name	Variable Type (range)	Contributing Survey Question(s)/ Data Sources ^a
C22	Measurement of antimicrobial usage in defined daily doses or days of therapy	Binary (0,1)	Q51a,b
C23	Measurement of antimicrobial expenditures	Binary (0,1)	Q51c
Facilitation domain			
F1	Presence of pharmacists and/or ID attendings on acute care ward teams	Index	Q9a, Q11
F2	Business plan for antimicrobial stewardship (in place or in development)	Ordinal (0-2)	Q47
F3	Lead antimicrobial stewardship pharmacist has ID training	Binary (0,1)	Q19f5d
F4	Educational programs for prudent antimicrobial use	Binary (0,1)	Q35
F5	Number of resources utilized to update providers on antimicrobials (email alerts, newsletters, pharmacy alerts, other)	Ordinal (0-4)	Q36
F6	Level of engagement with ASTF educational resources and/or face-to-face ASTF meetings (combined helpfulness rating of ASTF webinars and meetings)	Index	Q39, Q40
F7	Number of electronic resources used to facilitate AS activities (basic electronic medical record system, proprietary software, administrative databases)	Ordinal (0-2)	Q48

^aSee Appendix A for full set of survey questions and Appendix B for the full survey results.

NOTE: Abbreviations: ASP, antimicrobial stewardship programs; ASTF, antimicrobial stewardship task force; ED, emergency department; ID, infectious diseases; MJU, medication use evaluations; PARIHS, Promoting Action on Research Implementation in Health Services; VA, Veterans Affairs.

the highest yield from an organizational standpoint may be in working to develop order sets within the electronic medical record and systematic efforts to promote de-escalation of broad-spectrum therapy, as well as encouraging hospital administration to devote specific physician and pharmacy salary support to stewardship efforts.

While we noted that finding the ASTF online resources helpful was associated with potentially unfavorable antimicrobial utilization, we speculate that this may represent reverse causality due to facilities recognizing that their antimicrobial usage is suboptimal and thus seeking out sample ASTF policies to implement. The association between the presence of automatic stop orders and potentially unfavorable antimicrobial utilization is less clear since the timeframe was not specified in the survey; it may be that setting

stop orders too far in advance may promote an environment in which critical thinking about antimicrobial de-escalation is not encouraged or timely. The larger magnitude of association between ASP characteristics and antimicrobial usage among patients without infectious discharge diagnoses versus overall antimicrobial usage also suggests that clinical situations where infection was of low enough suspicion to not even have the providers eventually list an infectious diagnosis on their discharge summaries may be particularly malleable to ASP interventions, though further exploration is needed in determining how useful this utilization measure may be as a marker for inappropriate antimicrobial use.

Our results complement those of Pakyz et al.²⁴ who surveyed 44 academic medical facilities in March 2013 to develop an ASP intensity score and correlate this score and

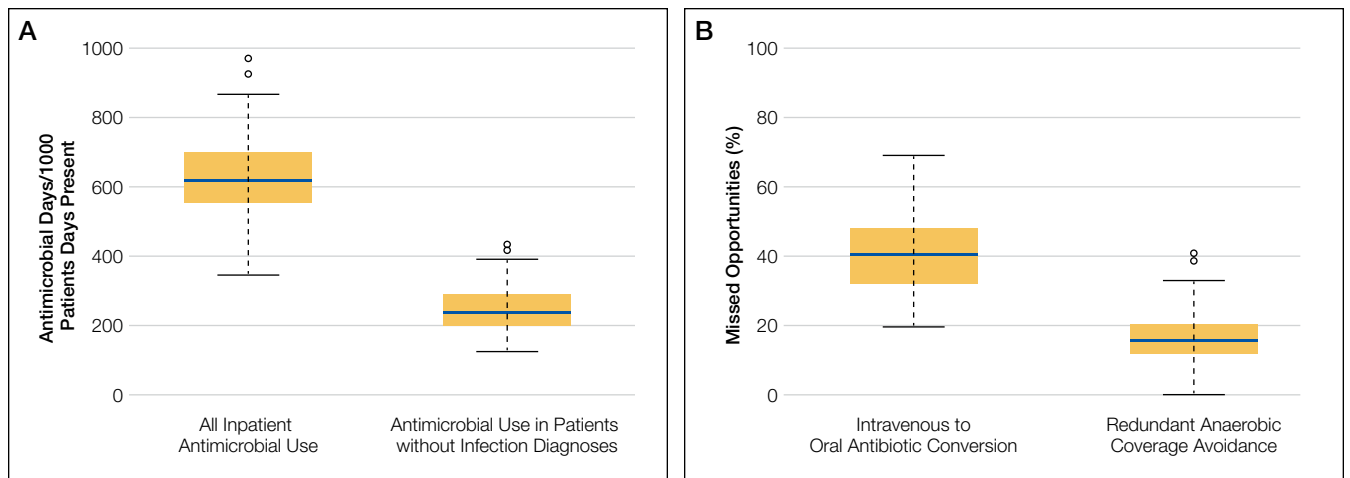


FIG. (A) Overall antimicrobial use and antimicrobial use among patients discharged with no infectious diagnoses. (B) Missed opportunities for parenteral to oral antimicrobial conversion and to avoid potentially unnecessary double anaerobic coverage

NOTE: Box shows median and 25-75 percentiles; whiskers show 5%-95% range; circles represent individual outlier VA facilities.

TABLE 3. Variables Associated with Multiple Antimicrobial Utilization Measures^{a,b}

No.	Factor Name	All antimicrobial use	Antimicrobial use in patients with noninfectious primary diagnoses	Parenteral to oral missed opportunities	Avoiding double anaerobic coverage missed opportunities
Associated with multiple potentially favorable utilization					
C8	Presence of postgraduate physician/pharmacy training programs (ID fellowship, surgical residency, pharmacy residency; factor score)	-0.034%	-0.60%	-1.2%	
C16	Number of antimicrobial-specific order sets in place (ordinal, range 0-9)		-0.40%	-6.0%	-1.5%
C21	Frequency of systematic de-escalation review (ordinal, range 0-4)	-0.011%	-1.5%	-0.060%	
F1	Presence of pharmacists and/or ID attendings on acute care ward teams (factor score)	-0.022%		-1.6%	-6.2%
F3	Lead antimicrobial stewardship pharmacist has ID training (binary)		-1.3%	-5.0%	-8.8%
Associated with multiple potentially unfavorable utilization					
C2	Hospital beds (ordinal, range 0-433; percentage change reported for 50-bed increase)		0.62%	1.0%	
C6	Degree to which an individual facility found ASTF sample policies to be helpful (factor score)		0.59%	6.9%	
C15	Antimicrobial stop orders in place (binary)		4.6%	11.7%	

^aAll reported associations with antimicrobial utilization measures are statistically significant using a LASSO (least absolute shrinkage and selection operator)-tuning parameter of 0.025. The magnitude of association is reported as percentage change in the utilization measure according to presence of the factor or not (for binary variables), incremental change in ordinal score (for ordinal factors), and quarter increase in factor score range (for factors for which factor score was reported).

^b≥3 potentially favorable or ≥2 potentially unfavorable antimicrobial utilization measures.

NOTE: Abbreviations: ASTF, antimicrobial stewardship task force; ID, infectious diseases.

its specific components to overall and targeted antimicrobial use. This study found that the overall ASP intensity score was not significantly associated with total or targeted antimicrobial use. However, ASP strategies were more associated with decreased total and targeted antimicrobial use than were specific ASP resources. In particular, the presence of a preauthorization strategy was associated with decreased targeted antimicrobial use. Our particular findings that order set establishment and de-escalation efforts are associated with multiple antibiotic outcomes also line up with the findings of Schuts et al, who performed a meta-analysis of the effects of meeting antimicrobial stewardship objectives and found that achieving guideline concordance (such as through establishment of order sets) and successfully de-escalating antimicrobial therapy was associated with reduced mortality.^{25,26} This meta-analysis, however, was limited by low rigor of its studies and potential for reverse causality. While our study has the advantages of capturing an entire national network of 130 acute care facilities with a 100% response rate, it, too, is limited by a number of issues, most notably by the fact that the survey was not specifically designed for the analysis of antimicrobial utilization measures, patient-level risk stratification was not available, the VA population does not reflect the U.S. population at-large, recall bias, and that antimicrobial prescribing and stewardship practices have evolved in VA since 2012. Furthermore, all of the antimicrobial utilization measures studied are imperfect at capturing inappropriate antibiotic use; in particular, our reliance on principal ICD-9 codes for noninfectious outcomes requires prospective validation. Many survey questions were subjective and subject to misinterpretation; other unmeasured confounders may also be present. Causality cannot be inferred from association. Nevertheless, our findings support many core indicators for hospital ASP rec-

ommended by the CDC and the Transatlantic Taskforce on Antimicrobial Resistance,^{3,4} most notably, having personnel with ID training involved in stewardship and establishing a formal procedure for ASP review for the appropriateness of an antimicrobial at or after 48 hours from the initial order.

In summary, the VA has made efforts to advance the practice of antimicrobial stewardship system-wide, including a 2014 directive that all VA facilities have an ASP,²⁷ since the 2012 HAIG assessment reported considerable variability in antimicrobial utilization and antimicrobial stewardship activities. Our study identifies areas of stewardship that may correlate with, positively or negatively, antimicrobial utilization measures that will require further investigation. A repeat and more detailed antimicrobial stewardship survey was recently completed and will help VA gauge ongoing effects of ASTF activities. We hope to re-evaluate our model with newer data when available.

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