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1A Report of the Efforts of the Veterans Health Administration National Antimicrobial 2Stewardship Initiative

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47 ABSTRACT :	

48<u>Objective</u>: To detail the activities of the Veterans Health Administration (VHA) Antimicrobial 49Stewardship Initiative and evaluate outcomes of the program.

50<u>Design</u>: Observational analysis

51<u>Setting:</u> The VHA is a large integrated healthcare system serving approximately 6 million 52individuals annually at over 140 medical facilities.

53Methods: Utilization of nationally developed resources, proportional distribution of antibiotics, 54changes in stewardship practices and patient safety measures were reported. In addition, inpatient 55antimicrobial use was evaluated before and after inception of national stewardship activities. 56Results: Nationally developed stewardship resources were well utilized and many stewardship 57practices significantly increased, including development of written stewardship policies at 92% 58of facilities by 2015 (p < 0.05). While the proportional distribution of antibiotics did not change, 59inpatient antibiotic use significantly decreased after the start of activities by the VHA 60Antimicrobial Stewardship Initiative (p < 0.0001). A 12% decrease in antibiotic use was noted 61overall. VHA has also noted significantly declining use of antimicrobials prescribed for resistant 62Gram-negative organisms including carbapenems and declining hospital readmission and 63mortality rates. Concurrently VHA experienced decreasing rates of *Clostridium difficile* 64infection.

65<u>Conclusions:</u> The VHA has implemented a national antimicrobial stewardship program with 66continued education, disease-specific guideline and example policy development in addition to 67other highly utilized resources. While no specific ideal level of antimicrobial utilization is 68known, VHA has shown that improving antimicrobial usage in a large healthcare system may be 69achieved through national guidance and resources with local implementation of antimicrobial 70stewardship programs.

92INTRODUCTION:

93The Centers for Disease Control and Prevention (CDC) estimates that two million people
94annually acquire infections due to antimicrobial-resistant organisms in the United States.
95Increasing resistance and a decrease in development of effective therapeutics create challenges in
96the management of infectious diseases. Antimicrobial use is one of the strongest risk factors for
97the development of antimicrobial-resistant infections and may also lead to unintended
98consequences such as adverse drug events and infection due to *Clostridium difficile*.^{2,3,4,5}
99Antimicrobial stewardship programs (ASPs) strive to optimize antimicrobial use to avoid
100unintended consequences and improve clinical outcomes.

101

102The Department of Veterans Affairs (VA), Veterans Health Administration (VHA) recognized the 103importance of antimicrobial stewardship programs and began the VHA Antimicrobial 104Stewardship Initiative in mid-2010 with the goal of providing national guidance and resources 105for implementation of ASPs at local VHA medical centers (VAMCs). This initiative is 106coordinated through the VHA National Antimicrobial Stewardship Taskforce (ASTF) chartered 107in May 2011. The ASTF, co-chaired by representatives from the VHA National Infectious 108Diseases Service and the National Pharmacy Benefits Management Services, is comprised of a 109twenty-five member multidisciplinary team selected based on their areas of expertise. In January 1102014, with the publication of VHA Directive 1031 which requires all VHA medical facilities to 111implement, maintain and annually evaluate ASPs, the VA solidified its commitment to optimize 112antimicrobial usage and improve the care of Veterans.⁶

113

114The purpose of this report is to detail the activities of the VHA Antimicrobial Stewardship 115Initiative and evaluate national process and outcome measures of the program.

117METHODS:

118Setting:

119The VHA is a large, federal, integrated healthcare system serving approximately 6 million 120individual patients annually at over 140 medical facilities distributed throughout the country. 121VHA medical facilities offer a wide range of acute care, long term care, outpatient and 122rehabilitation services to enrolled Veterans across the United States. (Veteran population 123demographics and VHA medical facility characteristics in Supplemental Tables 1 and 2) 124

125Engagement: Education and Information Gathering:

126The VHA Antimicrobial Stewardship Initiative began with a series of educational conferences to 127discuss the concept of stewardship with interested VHA field practitioners. This series consisted 128of a face-to-face conference repeated in three separate geographic regions to ensure system-wide 129representation from May through July of 2010 and a follow-up conference, in November 2011, 130focused more specifically on implementation of stewardship activities and development of ASP 131networks.

132

133A number of additional stewardship activities were undertaken in 2011. A nationwide group of 134approximately 250 volunteer field stewardship champions, representing diverse disciplines 135including clinical pharmacists and infectious diseases physicians, was identified to serve as a 136resource for communication and dissemination of stewardship topics and from whom multiple 137stewardship "best-practices" documents were collected. To aid in antimicrobial optimization the 138on-line version of The Sanford Guide® To Antimicrobial Therapy, an authoritative reference on

139antimicrobial therapy, was provided for use at all VHA medical facilities beginning in October 1402011. Also in October 2011, the ASTF administered a voluntary self-reported survey of 141stewardship practices across the VA to gain an understanding of existing ASPs and determine 142which ASTF activities and resources might be most useful.

143

144In January 2012, the ASTF implemented two additional key activities. An internal VHA 145Antimicrobial Stewardship Microsoft SharePoint® site was launched to serve as a robust 146repository of stewardship documents, resources and tools for facilities to utilize in development 147and expansion of local stewardship programs. The ASTF also launched an ongoing monthly 148series of educational web-based teleconferences (e.g. webinars) which covered a range of 149infectious diseases clinical topics and implementation strategies pertinent to stewardship.

150

151To follow up on the 2011 voluntary survey of stewardship practices, a required comprehensive 152systematic survey, performed with the assistance of the VHA Healthcare Analysis and 153Informatics Group, was administered to each VHA facility in November 2012. This survey was 154revised and performed again in December 2015 to evaluate uptake and progress of stewardship 155activities in the field.

156

157Encouragement: Policy Development and Dissemination:

158Beginning in 2012, a series of stewardship-related example policies and intervention tools,
159itemized in Table 1, were developed by the ASTF. The general approach to drafting these
160documents involved conducting a literature search of existing evidence and, when possible,
161performing a retrospective review of VHA practice patterns in areas targeted for intervention.
162Many of these policies were created within a framework that utilized antimicrobial stewardship

163champions, particularly clinical pharmacists, to identify appropriate patients and make
164recommendations to optimize therapy. These example policies and intervention tools were
165subsequently "launched" through the monthly webinar series and posted to the VHA
166Antimicrobial Stewardship Microsoft SharePoint[®] site for elective adaptation and
167implementation as facilities deemed appropriate.

168

169The ASTF coordinated with VA Central Office to encourage local facility institutional support 170for stewardship. Leadership support for ASPs was demonstrated at the highest levels with the VA 171Under Secretary for Health's Information Letter on Antimicrobial Stewardship published in July 17220127. This Letter, distributed to all VAMCs, described the importance and encouraged 173development of ASPs in the VA. Additionally, a memorandum was distributed through the VA 174operational hierarchy in September 2013 encouraging local administration at each VAMC to 175provide funding for clinical pharmacists to complete antimicrobial stewardship certificate 176programs dependent upon need. Clinical pharmacists were to be selected locally for certificate 177programs based on training, background and job requirements. VA Central Office leadership 178confirmed its commitment to stewardship with the publication of VHA Directive 1031: 179Antimicrobial Stewardship Programs in January 2014. This Directive required all VAMCs to 180implement, maintain and evaluate ASPs designed to optimize available local resources including 181identification of local stewardship provider and pharmacist champions.

182

183 Data sources:

184Resource Utilization Data

185Attendance at face-to-face educational meetings and "attendee lines" used for webinars were 186tallied at the time of the events. Attendee lines represents the minimal number of attendees as

187multiple individuals may have viewed a presentation together using a single line. Utilization of 188computerized stewardship resources was obtained through each individual website's totaled log-189in data per month. Individual VAMC stewardship activities were identified through the three 190distinct national surveys conducted in 2011, 2012 and 2015.

191

192Antimicrobial Use Data

193The VA's Office of Information and Technology built the Corporate Data Warehouse (CDW) to 194standardize and consolidate VA clinical data including Bar Code Medication Administration Data 195(BCMA) for administered medications incorporated in the VA's electronic medical record. The 196CDW was used to obtain BCMA data for the calculation of inpatient antimicrobial days of 197therapy (DOT). DOT was defined as a single dose of an antimicrobial given intravenously or 1980rally to a patient on a single day regardless of the strength or frequency of the drug. 8 For 199example, administration of vancomycin as a single 1-gm dose or as two 1-gm doses given 12 200hours apart both constitute one DOT. DOT for an antibiotic with possible intravenous and oral 201 forms combined both formulations in the usage data for that agent. Nationwide VAMC inpatient 202bed days of care (BDOC) were obtained from the VA's Austin Information Technology Center 203data center. BDOC were defined as day during which a person is confined to a bed in which the 204patient stays overnight. Inpatient status was defined as an admission to an acute care bed 205including an intensive care unit, step down unit, medical or surgical unit and observational bed 206status. The antimicrobial use calculations excluded hemodialysis, psychiatric, rehabilitation or 207long-term care nursing units. DOT/1000 BDOC by quarter were evaluated for all antibiotics 208 from 2007 through 2015. All antibiotic use data were analyzed in an aggregated de-identified

209manner. Of note, at no time during the analysis period did the VHA experience any significant 210national formulary changes or prolonged shortages of antibiotics.

211

212For dissemination of these data beyond programmatic needs, the analysis was evaluated by the 213institutional review board at the Cincinnati VA Medical Center.

214

215Statistics:

216Using SAS version 9.3 (SAS Institute), linear regression analysis was used to examine the 217progression of the DOT/1000 BDOC by quarter for the time periods before and after inception of 218the VHA Antimicrobial Stewardship Initiative. A comparison of the linear regression slopes was 219performed to determine any significance in the difference of the slopes for the two time periods. 220Chi-square analyses were used to examine the proportional distribution of antibiotic use for 221specific antibiotics, antibiotic classes or groups from 2007 to 2015. Chi-square analyses were 222also used to determine the differences in selected stewardship activities and reported challenges 223from the 2011, 2012 and 2015 surveys.

224

225RESULTS:

226Process Measures - Utilization of Resources and Stewardship Practices Nationwide:

228hosted nearly 450 participants from VHA facilities evenly distributed throughout the country.

229The on-line version of the Sanford Guide[®] and the VHA Antimicrobial Stewardship Microsoft

230SharePoint[®] site experienced consistently increasing utilization with an average number of

231monthly visits of more than 5000 and 2400, respectively. In addition, the ASTF monthly

232webinars were well attended with an average of more than 175 attendee lines used per month.
233(Figure 1) As shown in Table 1, the ASTF example policies were utilized as varying rates with a
234high of fifty-one percent of facilities with intravenous to oral conversion interventions reporting
235use of that ASTF example policy in development of local processes.

237The initial 2011 ASTF Inventory of Stewardship Practices indicated that each of the 126 238respondent acute care VAMCs performed at least one stewardship activity with over 70% of 239facilities performing the following activities: generation of annual antibiograms, imposed 240formulary restrictions, policies for criteria for use of certain antimicrobials, utilization of 241inpatient clinical pathways/guidelines, selective microbiology results reporting and dose 242optimization of selected antimicrobials. The subsequent 2012 and 2015 surveys, completed by 243130 and 140 VAMCs respectively, demonstrated progressive increases in numerous additional 244stewardship practices and decreases in reported challenges to ASPs. By the time of the 2015 245Stewardship Survey, eighty-nine percent of facilities had defined a stewardship team, up from 24641% in 2011 (p < 0.05), and ninety-two percent of facilities had a written policy for stewardship, 247up from 17% in 2011 (p < 0.05). The results of selected stewardship practices and challenges 248with improvements from the 2011, 2012 and 2015 surveys are summarized in Figures 2 and 3.

Outcome Measures - Nationwide VHA Antimicrobial Use, Resistance and Patient Safety:251Aggregated quarterly inpatient antibiotic use, shown in Figure 4, significantly decreased after the
252start of activities by the VHA Antimicrobial Stewardship Initiative in the second quarter of 2010
253(p < 0.0001). A 12% decrease in antibiotic use was noted overall from a quarterly high of 761.2

254DOT/1000 BDOC prior to the Initiative in the first quarter of 2008 to 673.3 DOT/1000 BDOC in 255the final quarter of 2015.

257Use of broad spectrum antimicrobials for highly resistant organisms, such as carbapenems, 258polymyxins and tigecycline, are potential surrogates for resistance given their role in the 259treatment of such resistant organisms. All three of these antimicrobial classes/agents 260demonstrated significantly increased use prior to inception of the VHA Antimicrobial 261Stewardship Initiative, with a decreasing trend in the use of carbapenems and significantly 262decreased use of polymyxins and tigecycline noted after the Initiative began. (Figure 5) A 263comparison of the linear regression slopes determined significant decreases in use of each of the 264antimicrobial classes/agents (P < 0.05 for each).

266Vancomycin, fluoroquinolones, piperacillin-tazobactam and cephalosporins were consistently the 267most frequently administered antibiotics or antibiotic classes from January 2007 through 268December 2015 with vancomycin and piperacillin-tazobactam alone consistently totaling nearly 269one-third of all antibiotic use. The proportion of fluoroquinolone use dropped from 18% in 2007 270to 13% in 2015 and the proportion of cephalosporin use increased from 16% in 2007 to 22% in 2712015 but neither trend was significant (p = 0.95 and 0.97 respectively). Percentage distributions 272of the remainder of the antibiotic agents, classes and groupings remained stable throughout the 273time period with no significant differences seen across the years (p = 0.99). (Supplemental 274Figure 1)

276The VHA Multidrug Resistant Organism Prevention Initiative, a highly active complementary 277national program, maintains a specific prevention initiative for *Clostridium difficile* infection, 278implemented July 2012, incorporating a bundled approach of infection control and 279environmental management practices with cultural transformation. This parallel program has 280published decreasing rates of *C. difficile* infection in both acute and long term care VHA 281facilities in the same time period as concomitant activity by the VHA Antimicrobial Stewardship 282Initiative. 9,10

283

284Hospital acute and intensive care length of stays have remained stable while readmission and 285mortality rates have decreased since inception of the VHA Antimicrobial Stewardship Initiative. 286(Supplemental Table 3) Total hospital discharges related to infectious diseases as determined by 287diagnosis related group have increased from 2012 to 2014 and the percentage distribution of 288those discharges by infectious diseases diagnosis group have remained stable. (Supplemental 289Figure 3)

290

291DISCUSSION:

293global antibiotic consumption rising by 36% from 2000-2011.¹¹ With as much as half of all 294antibiotic use potentially unnecessary, antimicrobial stewardship programs with methods to 295optimize antimicrobial use have become essential. ^{12,13,14} To this end, the VHA has instituted a 296successful National Antimicrobial Stewardship Initiative coordinated through its National 297Antimicrobial Stewardship Taskforce. The Taskforce has developed effective, highly utilized 298educational programs, tools and resources to support implementation and augmentation of local

299VHA ASPs and spearheaded publication of VHA national policies regarding stewardship. VHA 300national stewardship policies allow VAMCs to utilize local experts and resources to optimize and 301individualize their ASPs. After the start of the VHA National Antimicrobial Stewardship 302Initiative's activities, inpatient antimicrobial use declined significantly by 12% overall with 303673.3 DOT/1000 BDOC noted in the final quarter of 2015. No change was noted in the yearly 304proportional distribution of specific antimicrobial agents, classes and groups which intimates that 305the decrease in antimicrobial use was not related specifically to one agent or class but a more 306global overall decline in use across antimicrobial classes. Additionally, from 2012 to 2015 VA 307has noted decreasing rates of *C. difficile* infection and significant declining use of antimicrobial 308agents prescribed for highly resistant Gram-negative organism including carbapenems. ^{9,10} 309During this same period of time, improvements in VHA medical facility readmission and 310mortality rates were observed.

312There are few reports in the literature describing antimicrobial use in a large diverse healthcare 313system such as the VA. Polk et al, working with the University HealthSystem Consortium, 314reported on antibiotic use in 2009 from seventy academic medical centers in the United States. 15 315These researchers found a mean hospital-wide use of 839.0 DOT/1000 patient-days while 316inpatient VHA antimicrobial usage for that calendar year was considerably lower at 718.1 317DOT/1000 BDOC. Also, more recently, Baggs et al published an analysis of inpatient antibiotic 318use from 2006 to 2012 demonstrating an overall national DOT of 755 per 1000 patient-days 319which is higher than VHA's average quarterly use from 2007 to 2012, 718.6 DOT/1000 BDOC. 16 320In addition, these researchers estimated significant increases in several antibiotic classes 321including carbapenems with 32.3 DOT/1000 patient-days noted in 2012. Carbapenem use in

322VHA initially increased prior to the inception of the VHA Antimicrobial Stewardship Initiative 323but subsequently decreased with an average quarterly use of 28.3 DOT/1000 BDOC noted in 3242012.

325

326There are some limitations of this report. At the time of this report validated national 327microbiologic data extraction tools for VHA were not available, therefore use of broad spectrum 328antimicrobials for highly resistant organisms were employed as surrogates for resistance. 329Additionally, the concomitant successful VHA MDRO C. difficile Prevention Initiative limits 330interpretation of the impact of the VHA Antimicrobial Stewardship Program on *C. difficile* rates. 331The VHA Antimicrobial Stewardship Initiative provides national support and resources for local 332implementation of stewardship interventions but does not require implementation of specific 333stewardship policies or define appropriateness of use. VHA facilities are encouraged to design 334ASPs around their unique needs and available resources. This approach and the diverse nature of 335VAMCs with varying levels of facility capabilities and patient complexities do not allow for 336analysis of the impact of specific stewardship interventions from a national perspective nor can 337we conclude which interventions may be most effective at optimizing antimicrobial use to 338appropriate levels. VA researchers, however, are utilizing the VHA Stewardship Surveys to 339overlay stewardship activities with antimicrobial use to define key characteristics of effective 340ASPs. From information provided on the 2012 VHA Stewardship Survey, Chou et al concluded 341that decreased antimicrobial use was associated with having infectious diseases physicians and 342pharmacists present, as well as the frequency of patient-level reviews of antimicrobial use, and 343having a policy to address antimicrobial use in patients with *C. difficile* infection .¹⁷ A similar 344analysis from data reported on the 2015 VHA Stewardship Survey is in process.

346Over the course of several years with dedicated national and local volunteers, the VA has
347established stewardship programs nationwide. Through continued education, disease-specific
348guideline reviews, sample policy development and other resources, along with leadership
349engagement and support, the VHA Antimicrobial Stewardship Initiative has ongoing efforts to
350optimize antimicrobial use and attain the goal of a 20% reduction in inpatient antibiotic use by
3512020 set forth in the National Action Plan for Combatting Antibiotic-Resistant Bacteria. While
352no specific ideal level of antimicrobial utilization is known, the VA has shown that decreasing
353antimicrobial usage in a large healthcare system may be achieved through national guidance and
354resources with local implementation of ASPs. The VHA Antimicrobial Stewardship Initiative
355will continue to lead in the development of stewardship programs with expansion of stewardship
356activities to other areas of patient care, particularly long-term and outpatient care, hopefully
357serving as a model for other large healthcare systems.

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481Table 1: Antimicrobial Stewardship Taskforce Example Policies and Interventions

482¹Facilities that reported performing the specified interventions on the 2015 Stewardship Survey
483²Percentage of facilities performing the specified intervention that reported utilizing the ASTF
484example policies to develop the intervention

	Example Policy	Launch	Percent of	Percent	
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	Date	Facilities¹ (n = 140)	Facilities that Utilized ASTF Examples ²
Intravenous to Oral Conversion Tool	May 2012	116 (83%)	51%
Avoidance of Double Anaerobic Coverage	Jun 2012	99 (71%)	42%
Intervention to Improve Outcome for Patients with <i>C</i> . <i>difficile</i> Infection	Aug 2012	90 (64%)	21%
Stewardship Monitoring of Outpatient Parenteral Antimicrobial Therapy	Nov 2012	85 (61%)	22%
Vancomycin De-escalation	Jan 2013	97 (69%)	32%
Workload Documentation Guidance	May 2013	64 (46%)	27%
Broad-Spectrum Gram-Negative De-escalation	Oct 2013	98 (70%)	24%
Pneumonia Duration of Therapy	Sep 2014	63 (45%)	21%
S. aureus Bacteremia Intervention	Jul 2015	83 (59%)	20%

489Figure 1: Monthly Use of Nationally Provided Resources

490Total monthly log in usage data for electronic resources provided by the VHA Antimicrobial 491Stewardship Initiative and attendee lines used for stewardship educational webinars. *Note* – 492usage data for the VHA Antimicrobial Stewardship SharePoint® site became unavailable after 493March 2015 due to a website platform change.

495Figure 2: Comparison of Selected Stewardship Practices

496Percentage of reported activities at VHA medical centers from surveys completed in 2011, 2012 497and 2015 compared by Chi-square analyses. Abbreviations: IV, intravenous; PO, oral; NS, non-498significant.

499

500Figure 3: Comparison of Reported Challenges to Stewardship Programs

501Percentage of reported challenges to stewardship programs incurred at VHA medical centers 502from surveys completed in 2012 and 2015 compared by Chi-square analyses. Abbreviations: IT, 503information technology; ID, infectious diseases.

504

505Figure 4: Veterans Health Administration (VHA) Inpatient Antibiotic Use: Days of 506Therapy (DOT) per 1000 Bed Days of Care (BDOC)

507Inpatient antibiotic use before and after inception activities for the VHA Antimicrobial 508Stewardship Initiative in the 2nd quarter of calendar year 2010 (denoted by the vertical black 509line) by simple linear regression with comparison of slopes. An overall 12% decline in use was 510noted. Abbreviations: DOT, days of therapy; BDOC, bed days of care.

511

512Figure 5: Inpatient Use of Selected Antibiotics Targeting Resistant Organisms

513Carbapenems, polymyxins and tigecycline use before and after inception of activities for the 514VHA Antimicrobial Stewardship Initiative in the 2nd quarter of calendar year 2010 (denoted by 515the vertical black line) by simple linear regression with comparison of slopes. Abbreviations: 516DOT, days of therapy; BDOC, bed days of care.

517

518