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Potential Impact of Antibiotic Stewardship Programs on Overall Antibiotic Use in Adult Acute-Care Hospitals in the United States

To the Editor—We sought to characterize the expected decline in US acute-care antibiotic prescribing resulting from new accreditation standards requiring antibiotic stewardship programs.[1] We conducted a narrative review of published literature assessing the impact of antibiotic stewardship program implementation on total antibiotic prescribing in acute-care hospitals in the United States.

A PubMed search was performed using the following search strategy: antimicrobial OR antibiotic AND stewardship from January 1996 to December 2016. Finally, 12 articles and 1 abstract that reported the effect of antimicrobial stewardship programs on total antibiotic use in adult US acute-care hospitals were included. The median and interquartile range (IQR) of decline in antibiotic use observed with implementation of antibiotic stewardship programs were calculated (Table 1). If no significant decline in antibiotic use was noted, percentage decline was considered to be zero. To quantify the expected national decline in antibiotic use following the implementation of antibiotic stewardship programs, the calculated median and IQR were applied to the 2012 national estimate of adult antibiotic use in acute care hospitals obtained from the Truven Health MarketScan Hospital Drug Database (HDD).[2]

Most studies reported the implementation of "audit and feedback," with or without antibiotic restriction; 2 studies evaluated the effect of computerized decision support; and 1 study implemented an educational intervention pertaining to the electronic health record. The median decline in antibiotic use was 15.8% (IQR, 0–27.3%). The national estimate of total adult antibiotic use in 2012 in US acute-care hospitals was 103 million days of therapy (DOT) or 817.8 DOT per 1,000 patient days (PD) as reported by the HDD. Widespread implementation of antibiotic stewardship programs would therefore be expected to lead to an estimated median decline of 16 million DOT (IQR, 0–28 million) in total systemic antibiotic use, or a median national target of 688.6 DOT per 1,000 PD in US adult acute-care hospitals.

None of the studies reviewed showed worsening outcomes, such as increased mortality or readmissions, consistent with a recent Cochrane review.[3] Reporting clinical outcomes provides an opportunity to assess the safety and potential benefits of reducing unnecessary antibiotic use. A few studies showed no change or a decrease in *Clostridium difficile* infection and antibiotic-resistant pathogens, which are important metrics for assessing the patient-level impact of antibiotic stewardship.[4]

A publication bias toward positive results may lead to the overestimation of the effect of antibiotic stewardship programs. Hospital characteristics and types of interventions varied, as did the approaches to measurement and to reported outcomes. However, with the implementation of antibiotic stewardship programs in adult US acute-care hospitals, an estimated 15.8% (~16 million DOT) of total antibiotic prescribing might be avoided. This number does not include other important improvements that could be made, such as narrowing the spectrum of therapy and shortening postdischarge courses. Hospital stewardship programs should be supported in their efforts to protect patients from preventable harms caused by unnecessary antibiotic exposure.

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TABLE 1. Published Papers and Abstracts Evaluating Antibiotic Use Changes in Adult Acute Care Hospitals in the United States

Reference	Time	Setting	Design	ASP Description	Result	Decline in Antibiotic Use,
Cook PP, et al. Reduction in broad-spectrum antimicrobial use associated with no improvement in hospital antibiogram. *J Antimicrob Chemother* 2004.	1999–2003	Tertiary-care teaching hospital	Prospective observational pre–post intervention	Antimicrobial management program provided prospective audit and feedback on all patients on controlled antibiotics; restricted antibiotics required approval by infectious disease staff.	Average quarterly total antibiotic use decreased from 1,461 to 1,069 DDD/1,000 PD ($P = .0007$).	26.8%
Cook PP, et al. Sustained reduction in antimicrobial use and decrease in methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile* infections following implementation of an electronic medical record at a tertiary-care teaching hospital. *J Antimicrob Chemother* 2011.	2005–2009	Tertiary-care teaching hospital	Retrospective observational interrupted time series analysis	Evaluation of antibacterial use after electronic medical record implementation, with recommended dosing of antibiotics; reports generated for antibiotic stewardship pharmacists; and targeted education efforts	Antibacterial agent use declined from 775.3 to 552.2 DDD/1,000 PD ($P < .0001$).	28.8%
Cook PP, Gooch M. Long-term effects of an antimicrobial stewardship programme at a tertiary-care teaching hospital. *Int J Antimicrob Agents* 2015.	2001–2013	Tertiary-care teaching hospital	Retrospective observational pre–post intervention	Antibiotic stewardship program performed prospective audit and feedback; restricted antimicrobials required infectious disease approval; electronic health records were introduced in 2007.	Total antimicrobial use decreased from 14,443.5 to 536.6 DDD/1,000 PD ($P < .0001$).	62.8%
Cosgrove SE, et al. Evaluation of postprescription review and feedback as a method of promoting rational antimicrobial use: a multicenter intervention. *Infect Control Hosp Epidemiol* 2012.	2003–2004	5 tertiary-care hospitals	Quasi-experimental pre–post intervention	Postprescription review and feedback during 6-mo intervention period in addition to antimicrobial stewardship programs already in place	Comparing baseline total antimicrobial days/1,000 PD to intervention period. Hosp A, 395.63 to 443.30 Hosp B, 548.02 to 484.01 Hosp C, 474.07 to 460.80 Hosp D, 522.25 to 421.42 Hosp E, 473.46 to 560.87	Hosp A, 0 Hosp B, 11.7% Hosp C, 0 Hosp D, 19.3% Hosp E, 0
Danaher PJ, et al. The antibiotic support team—a successful educational approach to antibiotic stewardship. *Military Med* 2009.	2006	Medium-sized military hospital	Randomized controlled trial	Educational intervention	DDD/patient treatment course significantly lower in intervention group 6.7 vs 12.9 ($P = .05$).	48.1%
Evans RS, et al. A computer-assisted management program for antibiotics and other antiinfective agents. *N Engl J Med* 1998.	1992–1995	Intensive care unit in a community acute-care referral hospital	Prospective observational pre–post intervention	Computerized decision support program for anti-infectives management implemented in 1994	Mean no. of days of excessive anti-infective dosage decreased from 5.9 to 2.7 ($P < .01$).	54.2%
Fraser GL, et al. Antibiotic optimization. An evaluation of patient safety and economic outcomes. *Arch Intern Med* 1997.	1994	Tertiary-care hospital	Randomized controlled trial	Infectious disease fellow performed prospective audit on charts of patients receiving ≥3 d of antibiotic and provided feedback; study compared intervention and nonintervention group.	Similar clinical and microbiologic responses, in-hospital mortality, and a trend toward a shorter length of stay in intervention group. Antibiotic use was 10.16 DDD/1,000 PD in intervention group and 13.59 DDD/1,000 PD in nonintervention group.	25.2%
Morrill HJ, et al. Impact of a prospective audit and feedback antimicrobial stewardship program at a Veterans Affairs medical center: a six-point assessment. *PLoS One* 2016.	2010–2013	Veterans Affairs teaching hospital	Quasi-experimental interrupted time series	Antibiotic stewardship program with infectious disease pharmacist fellow who performed prospective audit and feedback for all patients on antibiotics for appropriateness using decision support template	No change in mortality, and a decrease in median length of stay. No difference in overall mean DOT/1,000 PD.	0
Rimawi RH, et al. Impact of regular collaboration between infectious diseases and critical care practitioners on antimicrobial utilization and patient outcome. *Crit Care Med* 2013.	2011–2012	Medical intensive care unit in a tertiary-care hospital	Prospective observational pre–post intervention	Infectious disease fellow reviewed the charts of patients on antibiotics daily and communicated with critical care team for a 3-mo intervention period.	A reduction in length of stay, mortality and days of mechanical ventilation. Antibiotic use decreased from 1,590 to 1,420 DOT/1,000 PD ($P = .03274$).	10.7%

Standiford HC, et al. 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.	2001–2008	Tertiary-care teaching hospital	Retrospective observational pre–post intervention	An antimicrobial monitoring team was developed in 2001 and integrated into infectious disease consults after 7 y; team reviewed antimicrobial orders and provided recommendations, developed guidelines and policies, ASP cost analysis for 7 y during and after intervention.	Decrease in total antibacterial use from 2004 to 2008 by 323 DDD/1,000 PD ($P = .03$).	27.5%
Stenehjem et al, Stewardship in Community Hospitals—Optimizing Outcomes and Resources (SCORE): a cluster-randomized controlled trial investigating the impact of antibiotic stewardship in 15 small, community hospitals *Open Forum Infect Dis*, IDweek 2016 Abstract.	2011–2013	15 small community hospitals	Cluster randomized controlled trial	Hospitals were randomized to 3 groups and compared adjusted antibiotic use ratio before and during the 15-mo intervention period, with increasing levels of intensity of infectious disease review of data, consultation; antibiotic use data were obtained from NHSN AU option reporting.	Compared adjusted antibiotic use ratio. Compared to program 1, program 3 reduced antibiotic use by 17%. Program 2 did not significantly reduce antibiotic use.	Program 1, 17% Program 2, 0
Storey DF, et al. Implementation of an antimicrobial stewardship program on the medical-surgical service of a 100-bed community hospital. *Antimicrob Resist Infect Control* 2012.	2009–2010	Community hospital	Retrospective observational pre–post intervention	Antimicrobial stewardship team 16-mo intervention; education, audit and feedback of charts, vancomycin dosing, order sets for pneumonia; severe sepsis and parenteral to oral conversion protocol	Reduction in mean monthly antibacterial use decreased from 1,028 to 878.7 DDD/1,000 PD ($P = .011$).	14.5%
Timbrook TT, Hurst JM, Bosso JA. Impact of an antimicrobial stewardship program on antimicrobial utilization, bacterial susceptibilities, and financial expenditures at an academic medical center. *Hosp Pharm* 2016.	2008–2013	Adult academic hospital	Retrospective quasi-experimental pre–post intervention	Antibiotic stewardship program implemented 2009–2013 included prospective audit and feedback, preauthorization, dose optimization, guideline development, and clinical pathways.	Antibiotic utilization measured as DDD/1,000 PD decreased by 2% from 2008 to 2013 ($P = .46$).	0

NOTE. DDD, defined daily dose; DOT, days of therapy; PD, patient days.

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Comments on: A Model to Predict Central-Line-Associated Bloodstream Infection Among Patients With Peripherally Inserted Central Catheters: The MPC Score

To the Editor—We read the article by Herc et al[1] with great interest. Although the methodology and results of the study were very interesting, we think some methodological issues should be noted.

The results demonstrate that area under the curve (AUC) for peripherally inserted central catheter (PICC) dwell times at 6, 10, 14 and 21 days were 0.70, 0.75, 0.77, and 0.80, respectively.[1] The authors point out that the central-line-associated bloodstream infections (CLABSI) risk model at dwell time of 21 days has good prediction performance because the AUC value at 21 days wasat its maximum.[1] To us the most important concern is that the difference between the AUC at 14 and 21 days is negligible (0.77 vs 0.80). In other words, the CLABSI risk model at dwell times of 14 and 21 days may have the same prediction performance. We recommend that the authors try to test the statistical comparison of AUCs with available statistical methods[2,3] because empirical comparisons of AUCs may be misleading.

Although AUC analysis can produce all possible discriminative thresholds, the results of AUC analyses can be hardly translated into clinical practice.[4] Net benefit methods are alternative approaches of receiver operating characteristic curve (ROC) analysis; these methods can better clarify the prediction performance of a PICC-CLABSI risk-prediction tool.

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