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Major Article

Syndrome-specific versus prospective audit and feedback interventions for reducing use of broad-spectrum antimicrobial agents

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Background: Antimicrobial use (AU) of antipseudomonal β-lactams (APBL) has significantly increased over the past decade in US hospitals. This retrospective cohort study compares 2 common antimicrobial stewardship strategies, syndrome-specific interventions and antimicrobial postprescription prospective audit and feedback (PAF), in reducing AU of APBL at a large community-teaching hospital.

Methods: Four antimicrobial stewardship interventions targeting APBL were serially introduced, including 2 syndrome-specific interventions (bloodstream and intra-abdominal infections) and 2 PAF interventions (carbapenems and piperacillin/tazobactam). Multivariable linear regression was used to examine overall AU of APBL and audited antimicrobial agents.

Results: Overall AU of APBL declined from 92.4-69.1 days of therapy (DOT) per 1,000 patient-days between February 2013 and July 2017 ($P < .001$). Both syndrome-specific interventions were associated with significant reduction in AU of APBL (−7.7 [95% confidence interval (CI): −11.5, −4.0] and −6.0 [95% CI: −9.7, −2.3] DOT per 1,000 patient-days) for bloodstream and intra-abdominal infections, respectively). No significant change in overall AU of APBL was observed after implementation of PAF interventions for carbapenems (−1.4 [95% CI: −7.4, 4.6] DOT per 1,000 patient-days) or piperacillin/tazobactam (0.9 [95% CI: −3.7, 5.4] DOT per 1,000 patient-days).

Conclusions: Implementation of syndrome-specific interventions was followed by significant reduction in AU of APBL in this population. Despite reducing AU of targeted agents, neither PAF intervention contributed to overall observed decline in APBL use, likely due to compensatory increase in using other APBL.

It is estimated that 20%-50% of all antimicrobials prescribed in US acute care hospitals are unnecessary.[1] The use of broad-spectrum antimicrobial agents, particularly antipseudomonal β-lactams (APBL), has significantly increased over the past decade.[2] This has been temporally associated with an increase in the proportion of multidrug-resistant (MDR) and carbapenem-resistant *Pseudomonas aeruginosa*.[3]

Measurement and optimization of antimicrobial use (AU) in hospitals are common goals of antimicrobial stewardship programs. Multiple antimicrobial stewardship strategies have been used to reduce unnecessary use of broad-spectrum antimicrobial agents. These include antimicrobial preauthorization, postprescription prospective audit and feedback (PAF), and syndrome-specific interventions.[4]

A recent study demonstrated PAF interventions were more effective than antimicrobial preauthorization in reducing use of broad-spectrum agents.[5] However, there are limited data comparing the effect of PAF and syndrome-specific interventions on AU. This retrospective cohort study examines the impact of the 2 different

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antimicrobial stewardship strategies, syndrome-specific interventions, and antimicrobial PAF on institutional use of APBL.

METHODS

Settings

The study describes antimicrobial stewardship interventions conducted at a large community-teaching hospital in Southeastern United States from February 2013 through July 2017. This hospital cares for adults with various medical and surgical conditions, including a level-1 trauma center and multiple medical and surgical intensive care units. The antimicrobial stewardship team (AST) provides antimicrobial stewardship services to this hospital, Monday through Friday from 7:30 AM to 4:30 PM. At the time of study, this multidisciplinary team consisted of a core group of an infectious diseases physician and 3 rotating pharmacists (2 trained in infectious diseases and 1 in critical care), and a large group of microbiologists, physicians, pharmacists, and nurses of various disciplines. One pharmacist was assigned to antimicrobial stewardship service every month, and the infectious diseases physician provided clinical support and oversight. Pharmacy students, residents, and infectious diseases medical fellows rotated with the AST intermittently. The following APBL were included in the hospital formulary throughout the study period: piperacillin/tazobactam, ceftazidime, cefepime, imipenem/cilastatin, and meropenem.

Antimicrobial stewardship interventions

During the preimplementation phase, no antimicrobial stewardship interventions targeting APBL occurred. Four antimicrobial stewardship interventions targeting APBL were serially implemented later during the 4.5-year study period, that is, 2 syndrome-specific interventions and 2 antimicrobial PAF.

The 2 syndrome-specific interventions primarily targeting APBL consisted of 1 for bloodstream infections (BSI) in January 2014 and another for intra-abdominal infections (IAI) in May 2016. BSI intervention included institutional management guidelines, implementation of rapid diagnostic testing for identification of bloodstream isolates, and real-time antimicrobial stewardship alerts for positive blood cultures for gram-negative bacilli.[6,7] This allowed for timely streamlining of antimicrobial therapy based on bacterial identification and in vitro antimicrobial susceptibility testing results.[7] The IAI intervention consisted primarily of institutional management guidelines encouraging the use of antimicrobial agents without *P aeruginosa* coverage as empirical therapy in the majority of patients with community-onset IAI. Both institutional management guidelines were developed in collaboration with respective subspecialty teams (eg, critical care, general surgery, internal medicine). Educational campaigns accompanied syndrome-specific interventions to ensure health care providers in multiple disciplines were familiar with new management guidelines and interpretation of rapid diagnostic testing results.

PAF of antipseudomonal carbapenems (imipenem/cilastatin and meropenem) was implemented in July 2013. All inpatient carbapenem orders were audited after 48 hours of use. After reviewing patients' electronic medical and microbiological records, recommendations to discontinue antimicrobials were made in patients with low suspicion of bacterial infections. AST recommended de-escalation of carbapenems to narrower spectrum agents based on microbiological results. However, in patients without meaningful microbiological data, alternative antimicrobial options were recommended in the absence of risk factors for infections due to extended-spectrum β-lactamase-producing Enterobacteriaceae or MDR bacteria, for example *P aeruginosa*.[8-10] If treatment with carbapenems was considered appropriate, a stop date was suggested whenever possible.

A second PAF intervention was implemented in November 2016 to monitor piperacillin/tazobactam use for >72 hours after concerns for nephrotoxicity secondary to vancomycin and piperacillin/tazobactam combinations were raised.[11,12] AST recommended discontinuation of piperacillin/tazobactam in patients without evidence of bacterial infections and a stop date, whenever possible, if treatment was considered appropriate. De-escalation of therapy to agents without *P aeruginosa* coverage was recommended in patients without positive cultures or clinical risk factors for *P aeruginosa*.[9,13] Alternative antipseudomonal agents were suggested in patients who had microbiological documentation or clinical risk factors for *P aeruginosa* infections, but for whom risk of nephrotoxicity from continuation of piperacillin/tazobactam was considered high due to concomitant vancomycin use.

Study outcomes

The primary outcome of this study was the overall institutional AU of APBL. Secondary outcomes included AU of targeted APBL by PAF interventions (antipseudomonal carbapenems and piperacillin/tazobactam). Post hoc analyses examined for a potential compensatory increase in ceftriaxone use during the study period and the impact of change in AU of APBL on incidence rate of hospital-onset *Clostridioides difficile* infection (HO-CDI).

AU was calculated using monthly mean days of therapy (DOT) per 1,000 patient-days. AU of APBL included total AU of piperacillin/tazobactam, ceftazidime, cefepime, imipenem/cilastatin, and meropenem. AU of antipseudomonal carbapenems included total AU of imipenem/cilastatin and meropenem. Institutional AU data were collected through SafetySurveillor® (Premier Inc., Charlotte, NC) from February 2013 to October 2014, and TheraDoc® (Premier Inc., Charlotte, NC) from November 2014 to July 2017. Internal validation of AU data were performed during the month of October 2014, when data were available through both programs. Monthly incidence rates of HO-CDI per 10,000 patient-days were obtained from institutional infection prevention surveillance data.

Statistical analysis

First, examination for a potential change in overall AU of APBL throughout the study period was performed. To minimize the impact of monthly fluctuations in AU, the 4.5-year study period was divided into 6-month intervals. The first 6 months of study period represented the preimplementation phase. Analysis of variance was used to compare mean AU across the 9 intervals in the study.

Second, multivariable linear regression was used to evaluate the impact of each intervention on overall AU of APBL while taking other coexisting interventions into account. A 1-month lag was applied to the model to allow assessment of the effect of each intervention from the first full month of implementation. Considering that the 4 interventions in this study were introduced serially and continued throughout the study without interruption, the duration of each intervention in the analysis was from the first full month of implementation until the end of the study. The analysis also adjusted for a potential seasonal variation in AU throughout the study period. The multivariable analysis included the winter months (December through March) as an additional variable in the model to account for a potential increase in AU during the winter season. Similarly, multivariable linear regression models were used to examine secondary outcomes: AU of antipseudomonal carbapenems and piperacillin/tazobactam.

Analysis of variance was used to examine for change in mean ceftriaxone use during the study period. Linear regression was used to

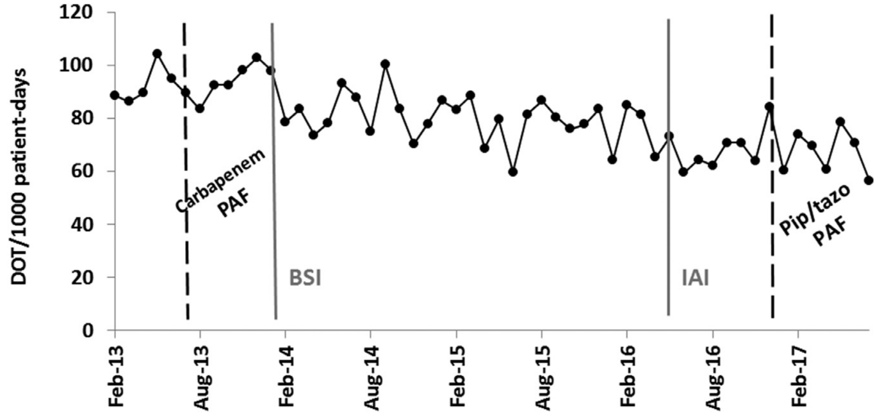

Fig 1. Antimicrobial use of antipseudomonal β-lactams during the study period. Black dashed lines indicate the months PAF interventions were implemented; grey solid lines indicate the months syndrome-specific interventions were implemented. *BSI*, bloodstream infections; *DOT*, days of therapy; *IAI*, intra-abdominal infections; *PAF*, prospective audit and feedback; *pip/tazo*, piperacillin/tazobactam.

examine the association between incidence rate of HO-CDI and AU of APBL.

JMP Pro version 13.0 (SAS Institute Inc, Cary, NC) was used for statistical analysis. The level of significance for statistical testing was defined as P <.05 (2-sided).

RESULTS

The overall AU of APBL declined from 92.4 (95% confidence interval [CI]: 85.3, 99.5) in the preimplementation phase to 69.1 (95% CI: 61.9, 76.2) DOT per 1,000 patient-days in the last 6 months of the study (P < .001; Fig 1). When accounting for seasonal variation in AU and the presence of various interventions in the multivariable model, both syndrome-specific interventions were associated with significant reduction in AU of APBL (−7.7 [95% CI: −11.5, −4.0] and −6.0 [95% CI: −9.7, −2.3] DOT per 1,000 patient-days for BSI and IAI, respectively). No significant change in overall AU of APBL was observed after implementation of PAF interventions for carbapenems or piperacillin/tazobactam (Table 1).

There was a considerable decline in AU of antipseudomonal carbapenems from 27.7 (95% CI: 25.5, 29.8) in the preimplementation phase to 2.1 (95% CI: 0, 4.3) DOT per 1,000 patient-days during the last 6 months of the study (P < .001). PAF of carbapenems was associated with reduction in carbapenem use (−6.8 [95% CI: −9.0, −4.7] DOT per 1,000 patient-days; Table 1). However, this decline in carbapenems use was temporally associated with an increase in AU of other APBL, namely piperacillin/tazobactam and cefepime (Fig 2).

AU of piperacillin/tazobactam also declined from 54.5 (95% CI: 45.8, 63.2) in the preimplementation phase to 35.5 (95% CI: 26.8, 44.2) DOT per 1,000 patient-days toward the end of study (P < .001). PAF of piperacillin/tazobactam was associated with a significant reduction in AU of piperacillin/tazobactam (−7.9 [95% CI: −14.6, −1.1] DOT per 1,000 patient-days; Table 1). This decline in piperacillin/tazobactam use was accompanied by an increase in cefepime use, nearly canceling the net effect of the intervention on overall AU of APBL (Fig 3).

The reduction in AU of APBLs was not associated with a compensatory increase in ceftriaxone use. To the contrary, the analysis demonstrated a 22% decline in ceftriaxone use from 58.5-45.4 DOT per 1,000 patient-days during the study period (P < .001).

Incidence rate of HO-CDI declined from 3.7 during the peak of AU of APBL in the preimplementation phase to 2.4 per 10,000 patient-days during the nadir of APBL use in the study. There was a significant association between the incidence rate of HO-CDI and AU of APBL (P = .001). Incidence rate of HO-CDI declined by 0.47 per 10,000 patient-days (95% CI: 0.20, 0.74) for each interval decline in APBL use of 10 DOT per 1,000 patient-days.

DISCUSSION

To our knowledge, this is the first study to compare the impact of antimicrobial PAF and syndrome-specific interventions on AU of broad-spectrum agents in a large community hospital with consistent antimicrobial stewardship service. Implementation of a series of antimicrobial stewardship interventions was associated with a 25% overall reduction in AU of APBL. Syndrome-specific interventions were more successful than antimicrobial PAF in reducing APBL use in this patient population.

Each PAF intervention was associated with decrease in AU of the respective antimicrobial agent or class but did not significantly contribute to the overall decline in AU of APBL. The reduction in carbapenem use after implementation of carbapenem PAF was associated with a temporal increase in AU of both piperacillin/tazobactam and cefepime (Fig 2). Similarly, the decline in piperacillin/tazobactam use

Table 1
Multivariable linear regression models demonstrating impact of each intervention on use of APBL, carbapenems, and piperacillin/tazobactam

Intervention/variable	Change in antimicrobial use (95% confidence intervals); *P* value		
	APBL	Carbapenems	Piperacillin/tazobactam
Carbapenems PAF	−1.4 (−7.4, 4.6); .64	−6.8 (−9.0, −4.7); <.001	1.4 (−7.5, 10.4); .75
Bloodstream infections	−7.7 (−11.5, −4.0); <.001	−4.8 (−6.1, −3.4); <.001	−7.0 (−12.6, −1.3); .02
Intra-abdominal infections	−6.0 (−9.7, −2.3); .002	−1.3 (−2.7, 0); .05	−1.3 (−6.8, 4.2); .64
Piperacillin/tazobactam PAF	0.9 (−3.7, 5.4); .70	−1.0 (−2.7, 0.6); .22	−7.9 (−14.6, −1.1); .02
Winter season*	2.0 (−0.7, 4.6); .15	−0.2 (−1.2, 0.8); .69	4.7 (0.7, 8.8); .02

APBL, antipseudomonal β-lactams; *PAF*, prospective audit and feedback.
*Winter season represents the months of December through March.

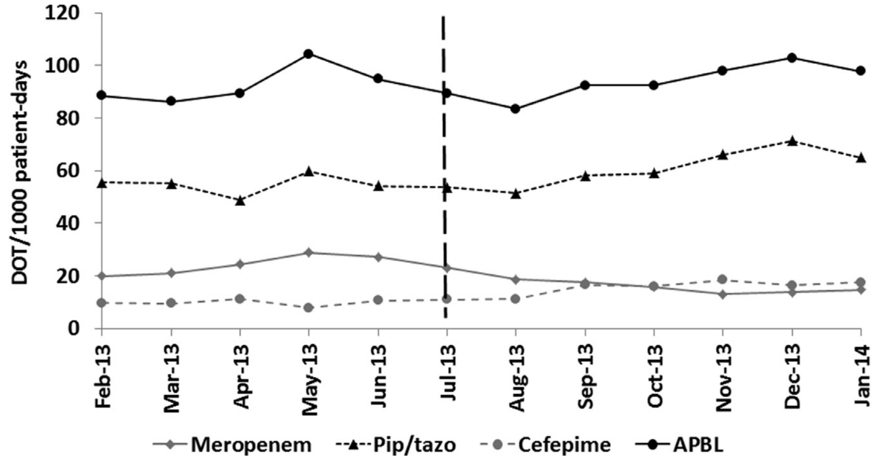

Fig 2. Antimicrobial use of APBL before and after carbapenem prospective audit and feedback intervention. Antimicrobial agents with use <5 DOT per 1,000 patient-days are not shown but are accounted for in overall antimicrobial use of APBL. Black dashed line indicates the month the intervention was implemented. *APBL*, antipseudomonal β-lactams; *DOT*, days of therapy; *pip/tazo*, piperacillin/tazobactam.

after PAF was almost completely compensated for by an increase in cefepime use (Fig 3). This demonstrated phenomenon of "squeezing the balloon" emphasizes the need to restructure and repackage antimicrobial stewardship interventions to fit within the scope of primary health care providers' clinical practice interests. Antimicrobial PAF likely created a feeling among clinicians that the use of audited antimicrobial agents was not preferred at this hospital. These data suggest the easiest solution, on their part, was replacement of these agents with ones closest in spectrum of activity. Such action was likely taken to avoid a pending telephone call from the AST. The educational message of reducing AU of broad-spectrum agents to minimize antimicrobial resistance rates and other antimicrobial adverse events such as HO-CDI was likely lost between the AST and primary health care providers. However, this does not imply that antimicrobial PAF interventions are completely void of any benefits to the health care system. Reducing carbapenem use after implementation of PAF was temporally associated with a decline in incidence rates of infections due to carbapenem-resistant Enterobacteriaceae.[14] Second, AST review of carbapenem use allowed identification of another antimicrobial stewardship opportunity given high frequency of carbapenem prescription in patients with penicillin allergy. This was followed by system-wide interventions, including preapproved indications for carbapenems, reconciliation of penicillin allergy, and improved antimicrobial management in this patient population.[15] It is also encouraging that the effects of carbapenem interventions were sustained for 4 years in this study. Of note, carbapenem use remained low after implementation of piperacillin/tazobactam PAF. The decline in piperacillin/tazobactam use was compensated for by an increase in cefepime use, but not meropenem or imipenem/cilastatin. This paved the way for a third PAF intervention for cefepime, which was launched after the conclusion of this study. To avoid a repeat "squeezing of the balloon," ceftazidime was removed from the hospital formulary at the same time. Auditing the use of all APBL creates the perception in the hospital that any APBL use is discouraged in the absence of risk factors or microbiological evidence of infections due to *P aeruginosa* and other MDR gram-negative bacteria.[9,13]

It is possible that timely optimization of antimicrobial therapy in syndrome-specific interventions provided an advantage over PAF after 48-72 hours of AU. Application of institutional management guidelines recommendations at the time of clinical presentation with suspected infections and live alerts for Gram stain results (usually within 24 hours of hospital admission in patients with BSI) allowed

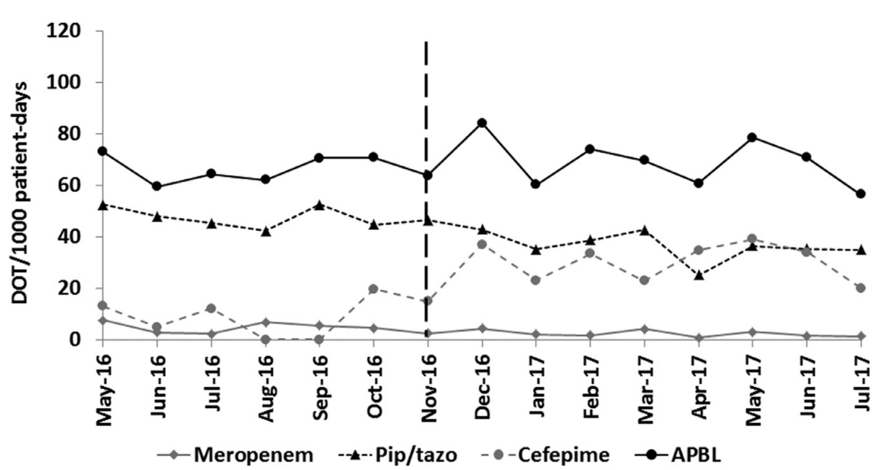

Fig 3. Antimicrobial use of APBL before and after pip/tazo prospective audit and feedback intervention. Antimicrobial agents with use <5 DOT per 1,000 patient-days are not shown but are accounted for in overall antimicrobial use of APBL. Black dashed line indicates the month the intervention was implemented. *APBL*, antipseudomonal β-lactams; *DOT*, days of therapy; *pip/tazo*, piperacillin/tazobactam.

early assessment of antimicrobial regimens. However, antimicrobial recommendations were often delayed by design for 48-72 hours in PAF interventions. However, the significant reduction in AU of audited agents suggests this time lag is likely not a major factor in determining impact of PAF interventions. Moreover, this hypothesized time difference in initiation of interventions from starting antimicrobial therapy did not necessarily provide an advantage for antimicrobial preauthorization over PAF interventions as demonstrated in a previous study.[5]

The current study demonstrates that antimicrobial stewardship interventions focusing on facilitation of appropriate use of antimicrobials for specific infections through multidisciplinary educational and advisory efforts are successful in reducing AU of broad-spectrum agents. Syndrome-specific interventions likely enhance the image of AST in hospitals as facilitators and optimizers of patient care.[16] The local guidelines were published electronically on the hospital's formulary website and printed in the annual antimicrobial guidebook, which was disseminated to existing and new health care providers. These syndrome-specific management guidelines have a clearly visible and understandable educational message of discouraging the nonstratified use of APBL in hospitalized patients with suspected infections and the importance of de-escalation of antimicrobial therapy based on bacterial identification and in vitro antimicrobial susceptibility testing results. It is also likely that the positive, collegial, and informative message in syndrome-specific interventions in advising primary clinicians which antimicrobials to prescribe in a particular clinical situation has more resonance by creating a sense of ownership for these interventions. Additionally, administrative approval of the management guidelines by the hospital's pharmacy and therapeutics committee provides opportunities for local peer-review and dissemination. Considering that the majority of gram-negative BSI were secondary to urinary source of infection, primary health care providers and clinical pharmacists were encouraged to use recommended antimicrobial regimens in gram-negative BSI guidelines for empirical therapy of hospitalized patients with acute pyelonephritis until specific local management guidelines were developed for this clinical syndrome.[6]

It is reassuring that the decline in AU of APBL was not associated with a compensatory increase in ceftriaxone use. The 22% decline in ceftriaxone use in the post hoc analysis emphasizes the strategy of de-escalation of antimicrobial therapy to the narrowest-spectrum effective agent in patients with BSI and IAI. Extension of this practice to hospitalized patients with acute pyelonephritis as encouraged by the AST likely contributed to this process as well. It is also encouraging that the decline in APBL use was temporally associated with a significant reduction in the incidence rate of HO-CDI. This is conceivable given that APBL were associated with the highest odds of HO-CDI among all antimicrobials used in hospitalized patients in a recent large cohort study.[17] Moreover, early de-escalation of APBL was associated with a lower risk of HO-CDI in patients with Enterobacteriaceae BSI as demonstrated recently.[18]

This study has strengths and certain limitations. Multiple interventions were introduced serially in one hospital. Using multivariable linear regression analysis allowed examination of AU before and after each intervention while considering the impact of other coexisting interventions. The relatively long study duration allowed for a baseline period of 6 months before full implementation of the first intervention (after accounting for a 1-month lag) and at least 6 months between each intervention and the next one. The long study duration also allowed adjustments for potential seasonal variation in AU. However, this may not control for provider preferences, changes in antimicrobial prescription practices between providers, and other interpersonal biases. Multicenter cluster randomized trials provide the ultimate clinical research design for such studies. In addition, AU is a quantitative measure that does not directly measure antimicrobial appropriateness. It is reassuring that the reduction in AU of APBL did not compromise appropriateness of antimicrobial therapy or patients' clinical outcomes.[7,15]

CONCLUSIONS

The current study demonstrated that syndrome-specific interventions were associated with significant decline in AU of APBL. Antimicrobial PAF interventions reduced use of the audited agents but did not impact overall AU of APBL likely due to compensatory increase in using other APBL. In an era of encouraged and increased reporting of AU to the Centers for Disease Control and Prevention's National Healthcare Safety Network, many hospitals are looking for ideas and methods to reduce AU relative to comparator institutions. The current study provides AST at community hospitals with a framework of suggested interventions to reduce standardized antimicrobial administration ratio, particularly for the category of broad-spectrum antimicrobial agents predominantly used for hospital-onset and MDR bacterial infections.[19] Additionally, it highlights the successful implementation of an "all-hands on" stewardship approach—unified vision, leadership support, technological resources, proactive education, and collaborative interventions—to optimize AU in community hospitals.

References

1. Centers for Disease Control and Prevention. National strategy for combating antibiotic-resistant bacteria. 2014. Available from: www.cdc.gov/drugresistance/pdf/carb_national_strategy.pdf. Accessed June 15, 2018.
2. Baggs J, Fridkin SK, Pollack LA, Srinivasan A, Jernigan JA. Estimating national trends in inpatient antibiotic use among US hospitals from 2006 to 2012. JAMA Intern Med 2016;176:1639-48.
3. Logan LK, Gandra S, Mandal S, Klein EY, Levinson J, Weinstein RA, et al. Multidrug- and carbapenem-resistant *Pseudomonas aeruginosa* in children, United States, 1999-2012. J Pediatric Infect Dis Society 2017;6:352-9.
4. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. 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:e51-77.
5. Tamma PD, Avdic E, Keenan JF, Zhao Y, Anand G, Cooper J, et al. What is the more effective antibiotic stewardship intervention: preprescription authorization or postprescription review with feedback? Clin Infect Dis 2017;64:537-43.
6. Nimmich EB, Bookstaver PB, Kohn J, Justo JA, Hammer KL, Albrecht H, et al. Development of institutional guidelines for management of gram-negative bloodstream infections: incorporating local evidence. Hosp Pharm 2017;52:691-7.
7. Bookstaver PB, Nimmich EB, Smith TJ 3rd, Justo JA, Kohn J, Hammer, KL, et al. Cumulative effect of an antimicrobial stewardship and rapid diagnostic testing bundle on early streamlining of antimicrobial therapy in gram-negative bloodstream infections. Antimicrob Agents Chemother 2017;61, e00189-17.
8. Augustine MR, Testerman TL, Justo JA, Bookstaver PB, Kohn J, Albrecht H, et al. Clinical risk score for prediction of extended-spectrum beta-lactamase-producing Enterobacteriaceae in bloodstream isolates. Infect Control Hosp Epidemiol 2017;38:266-72.
9. Al-Jaghbeer MJ, Justo JA, Owens W, Kohn J, Bookstaver PB, Hucks, J, et al. Risk factors for pneumonia due to beta-lactam-susceptible and beta-lactam-resistant *Pseudomonas aeruginosa*: a case-case-control study. Infection 2018;46:487-94.
10. Foster RA, Troficanto C, Bookstaver PB, Kohn J, Justo JA, Al-Hasan MN. Utility of combination antimicrobial therapy in adults with bloodstream infections due to Enterobacteriaceae and non-fermenting Gram-negative bacilli based on in vitro analysis at two community hospitals. Antibiotics (Basel) 2019;8:e15.
11. Justo J, Dickert EL, Kohn J, Bookstaver PB. Comparative risk of acute kidney injury in patients receiving vancomycin monotherapy or vancomycin and beta-lactam combination therapy [abstract]. 54th Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington DC: 5-9 September 2014; Abstract #2544.
12. Karino S, Kaye KS, Navalkele B, Nishan B, Salim M, Solanki S, et al. Epidemiology of acute kidney injury among patients receiving concomitant vancomycin and piperacillin-tazobactam: opportunities for antimicrobial stewardship. Antimicrob Agents Chemother 2016;60:3743-50.
13. Hammer KL, Justo JA, Bookstaver PB, Kohn J, Albrecht H, Al-Hasan MN. Differential effect of prior beta-lactams and fluoroquinolones on risk of bloodstream infections secondary to *Pseudomonas aeruginosa*. Diagn Microbiol Infect Dis 2017;87:87-91.
14. Tucker K, Lashkova L, Flemming T, Justo J, Kohn J, Al-Hasan MN, et al. Impact of antimicrobial stewardship initiatives on carbapenem utilization and

antimicrobial resistance [abstract]. 55th Interscience Conference on Antimicrobial Agents and Chemotherapy. San Diego, CA: 17-21 September 2015; Abstract #2243.
15. Al-Hasan MN, Acker EC, Kohn JE, Bookstaver PB, Justo JA. Impact of penicillin allergy on empirical carbapenem use in gram-negative bloodstream infections: an antimicrobial stewardship opportunity. Pharmacotherapy 2018; 38:42-50.
16. Martin CA, Armitstead JA, Mynatt RP, Hoven AD. Moving antimicrobial stewardship from restriction to facilitation. Am J Health Syst Pharm 2011;68: 109-10.
17. Harris AD, Sbarra AN, Leekha S, Jackson SS, Johnson JK, Pineles L, et al. Electronically available comorbid conditions for risk prediction of healthcare-associated *Clostridium difficile* infection. Infect Control Hosp Epidemiol 2018;39:297-301.
18. Seddon MM, Bookstaver PB, Justo JA, Kohn J, Rac H, Haggard E, et al. Role of early de-escalation of antimicrobial therapy on risk of *Clostridioides difficile* infection following Enterobacteriaceae bloodstream infections. Clin Infect Dis 2018 Oct 12. [Epub ahead of print].
19. van Santen KL, Edwards JR, Webb AK, Pollack LA, O'Leary E, Neuhauser MM, et al. The standardized antimicrobial administration ratio: a new metric for measuring and comparing antibiotic use. Clin Infect Dis 2018;67:179-85.