Implementation and Impact of an Antimicrobial Stewardship Program at a Non-freestanding Children's Hospital

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OBJECTIVES Pediatric Antimicrobial Stewardship Programs (ASP) have been associated with improvements in antibiotic utilization and patient outcomes; however, ASP studies originating from non-freestanding children's hospitals are lacking. In this study, we present the implementation and impact of a multidisciplinary ASP that employs a collaborative physician and pharmacist driven thrice-weekly prospective audit-with-feedback approach at a non-freestanding children's hospital.

METHODS Implementation was assessed via descriptive design. Pediatric inpatients maintained on predefined targeted antibiotics of interest for 48 to 72 hours preceding ASP review were eligible for inclusion. Outcomes evaluated included ASP recommendation and provider acceptance rates (overall and by antibiotic and provider specialty). Impact was examined using an interrupted time series design (with a preimplementation period of August 1, 2013, to July 31, 2014 and postimplementation period of December 1, 2014 to May 31, 2016). Eligibility included all targeted antibiotic usage among pediatric inpatients, with a control group comprising those who received antibiotics requiring preauthorization. Outcomes analyzed included days of antibiotic therapy per 1000 patient days (DOT/1000 PD) and 30-day hospital readmission rates over time.

RESULTS Postimplementation, 882 antibiotic reviews were performed on 637 patients, with 327 recommendations generated. Reviews of patients maintained on vancomycin and clindamycin, and of those under care of intensivist and hospitalist physicians, were most likely to prompt recommendations. A mean targeted antibiotic usage decrease of 24.8 DOT/1000 PD (95% confidence interval, -62 to 14) was observed postimplementation, with no change in 30-day readmissions (0.64% during both periods).

CONCLUSIONS ASP implementation at a non-freestanding children's hospital was feasible and allowed for identification of areas for targeted quality improvement, while demonstrating modest antibiotic use reduction without adversely impacting patient care.

ABBREVIATIONS ASPs, antimicrobial stewardship programs; DOT/1000 PD, days of antibiotic therapy per 1000 patient days

KEYWORDS antimicrobial stewardship; non-freestanding hospital

J Pediatr Pharmacol Ther 2018;23(2):84-91

DOI: 10.5863/1551-6776-23.2.84

Introduction

Antimicrobial stewardship programs (ASPs) have as their primary objectives promotion of appropriate antimicrobial usage and improvement of patient care outcomes.¹ Though the basic principles of ASPs are constant regardless of the hospital environment in which stewardship is practiced, a "one size fits all" mentality is frequently suboptimal for those who plan to successfully establish a pediatric ASP at their respective institutions. The framework for successful ASP implementation requires understanding institutional expectations, limitations likely to be encountered, and awareness of available resources that can facilitate successful program establishment and maintenance.^{2,3}

In contrast to multiple studies in the medical literature describing successful outcomes associated with formal ASP implementation at large freestanding US children's hospitals,⁴⁻⁹ to the best of our knowledge only one prior study describes outcomes associated with ASP establishment at a non-freestanding pediatric institution,¹⁰ and implementation of a non-freestanding pediatric hospital ASP has yet to be described in detail. Patient populations and antibiotic prescribing practices at such institutions often differ from those at freestanding children's hospitals, and resources for successful program implementation and monitoring may be more limited.^{10,11} Our aims were twofold. First, we planned to describe the implementation of an ASP utilizing a

prospective audit-with-feedback methodology at a non-freestanding children's hospital. Second, we planned to assess this program's impact upon patient care.

Materials and Methods

Setting. Baystate Children's Hospital (BCH) is a 110-bed and 57-bassinette non-freestanding children's hospital affiliated with the University of Massachusetts Medical School-Baystate and located within Baystate Medical Center (BMC), a 716-bed independent academic medical center. A 55-bed level III neonatal intensive care unit (NICU) and a 7-bed level II pediatric intensive care unit (PICU) exist within BCH, and BCH averages approximately 4500 inpatient admissions per year. A total of 68 individuals are enrolled in residency training programs in categorical pediatrics and internal medicine/pediatrics during any given academic year. BMC has a pharmacy residency program with an enrollment of 5 post-graduate year one residents and one post-graduate year two (critical care) resident per year. Inpatient and outpatient infectious diseases (ID) consultations at BCH are performed by the 3 physician members of the BCH ID Division. One of the ID physicians (JMK) has a training background that included extensive exposure to ASP management principles. The BMC Department of Pharmacy utilizes unit-based clinical pharmacy specialists, with 3 individuals delegated to BCH. All of the clinical pharmacists at BCH have graduated from an American Society of Health System Pharmacists-accredited pharmacy residency program, and one (KK) also serves as the BMC pharmacy residency program director. Institutional practice guidelines exist for management of children with acute abdominal pain and suspected appendicitis, for empiric management of febrile infants ≤ 3 months, and for initial dosing of intravenous (IV) vancomycin for adult and pediatric patients. BCH does not perform bone marrow transplantation, solid organ transplantation, or pediatric cardiovascular surgical procedures.

BMC has an adult ASP (established in January 2011 by the Departments of Medicine and Pharmacy) that instituted preauthorization requirements for a number of broad-spectrum antimicrobial agents across the entirety of the hospital system, including BCH. That program does not regularly review usage of the most frequently prescribed pediatric antimicrobials, and prospective-audit-with-feedback on antibiotic orders for adult patients is limited to agents primarily targeting *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus*. Pediatric providers seeking to prescribe one of the preauthorized antimicrobials are required to contact the BCH ID physician on-call prior to pharmacy dispensation.

The BMC Institutional Review Board reviewed and approved all facets of this project.

ASP Implementation. A draft of ASP objectives and methods of operation was developed between

members of the BCH ID Division and BMC's Clinical Pharmacy specialists over the course of 3 months prior to initiation of ASP activities. Approval for implementation was obtained from the BCH Chair of Pediatrics and BMC Director of Acute Care Pharmacy Services. ID physicians met individually with division chiefs in the Department of Pediatrics and surgical subspecialists to inform them of pending program implementation and address questions or concerns regarding program objectives. As a limited number of private pediatricians' offices in the community also serve as primary inpatient providers for their practices' children at BCH, those providers were informed via e-mail, mailing of a formal letter to each practice location, and in-person notification whenever possible. All potential inpatient primary providers were provided with copies of the ASP objectives and proposed methods of operation. No resources (full-time equivalent [FTE] support or otherwise) were allocated to either the ID physicians or clinical pharmacists responsible for ASP establishment and maintenance.

Formal implementation occurred in a stepwise fashion, with new units being added approximately every 6 weeks starting in August 2014—beginning with the general pediatrics wards, followed by the PICU and finally the NICU and newborn nursery.

Patient eligibility criteria for ASP review included: 1) hospitalization on a BCH ward, 2) maintenance on ≥ 1 targeted antibiotic(s) for 48 to 72 hours preceding list generation, and 3) having a primary inpatient provider (regardless of specialty) who predominantly provides care for neonates, children, and/or adolescents. Targeted antibiotics for review included: amoxicillin/clavulanate, ampicillin/sulbactam, cefepime, cefotaxime (when prescribed for patients < 1 month), ceftriaxone, IV and oral (PO) clindamycin, gentamicin, IV and PO levofloxacin, IV and PO metronidazole, piperacillin/tazobactam, tobramycin, and IV vancomycin. Patients excluded from review included those with a formal ID consultation preceding list generation, and those on antibiotics requiring ID preauthorization prior to pharmacy dispensation (except when such patients were concurrently receiving a targeted antibiotic). Individuals with formal ID consults were excluded from review to minimize redundancy (as 2 of the 3 BCH ID physicians were active in establishing and subsequently performing ASP duties) and to mitigate any future possibilities of having conflicting recommendations being provided by 2 separate ID subspecialists (which in turn could lead to provider confusion and suboptimal patient care). Patients on antibiotics requiring ID preauthorization were excluded from review as historically a majority of those individuals had formal ID consultations. Antibiotics requiring ID preauthorization included: ceftazidime, ciprofloxacin, PO vancomycin, IV colistimethate, daptomycin, ertapenem, meropenem, linezolid, and cefotaxime (when given to children ≥ 1 month).

Patients were originally screened using an electronic data-mining software program (initially Safety Surveillance and subsequently TheraDoc [both from Premier, Inc., Charlotte, NC]) already being utilized by the BMC Pharmacy for multiple purposes (including adult stewardship). Once eligibility was confirmed, antibiotic review was conducted during standing meeting times every Monday, Wednesday, and Friday. All meetings were attended by at least 1 ID physician and 1 Clinical Pharmacy specialist, with active participation by pharmacy residents as incorporated into their Pediatrics and Pediatric Critical Care learning experiences. Pharmacy students rotating at BMC as part of their advanced pharmacy practice experience activities in pediatrics were also frequently invited to attend and participate. Representatives from ID and Pharmacy discussed preliminary recommendations for all reviewed patients and established consensus on suggestions requiring formal presentation to primary providers. For situations of ASP concurrence with providers' antibiotic management plans, no intervention was deemed necessary. When consensus opinion determined that a recommendation was warranted, team members would jointly present the advice to providers immediately following conclusion of the standing meeting, while also concurrently discussing with providers the team's rationale underlying the proposed recommendations—consistent with the successful “prospective audit-with-feedback” approach as described elsewhere.^{2–10,12–15} In the event of a recommendation's verbal acceptance by a provider, documentation (in the form of a progress note indicating the mutually agreed upon recommendation) would be placed in the patient's electronic medical record.

In order to evaluate the ASP's implementation, a database was created to capture the following information: review date, antibiotic, primary provider specialty, inpatient location, recommendation(s) made (if any), type of recommendation, and recommendation acceptance/declination by the primary provider. Recommendation types were categorized as: formal ID consult, dosing adjustment, coverage modification (i.e., broaden, narrow, discontinue, or eliminate redundant coverage), toxicity monitoring (for which pharmacokinetic calculations pertaining to aminoglycoside and vancomycin dosing optimization were frequently employed), and transition from IV to PO. Coverage modification recommendations were based on culture and susceptibility data when available. When not available, such recommendations were formulated in accordance with guidelines and policy statements published by the Infectious Diseases Society of America (IDSA), American Academy of Pediatrics, and various other subspecialty organizations. In the absence of culture/susceptibility information and applicable national guidelines, coverage modification suggestions were developed based upon typical bacterial pathogens observed with the various clinical illness scripts encountered. Provider compliance with

implementation of accepted recommendations was determined via retrospective review of patients' electronic medical records.

ASP Impact. Our secondary aim was to assess the ASP impact on patient care. We utilized an interrupted time series design with a preimplementation period from August 1, 2013, to July 31, 2014, and the postimplementation period from December 1, 2014, to May 31, 2016. We chose to exclude the 4 months of the rollout period *a priori* as we were primarily interested in the intercept shift and slope change in the pre- vs. postimplementation periods. Two patient care measures were analyzed: days of therapy (DOT) per 1000 patient days (i.e., DOT/1000 PD)^{2,4,5,16} and 30-day readmissions due to antibiotic usage. Readmission due to antibiotic usage was defined as one occurring secondary to either a direct or indirect antibiotic adverse effect (including clindamycin suspension intolerance by children due to palatability issues and PICC line malfunctions in those discharged to home on IV antibiotic therapy via PICC line), or one involving recurrence/persistence of the infectious condition for which a patient was originally admitted following suboptimal antibiotic management either as an inpatient and/or upon hospital discharge. Examples of the latter included premature transition from IV to PO therapy and inappropriate narrowing of the spectrum of antibiotic coverage for a known bacterial pathogen isolated in culture media.

Eligibility criteria for this portion of the study were similar to criteria for ASP review, with the following exceptions: 1) both targeted and preauthorization antibiotic usage was analyzed, regardless of total durations of therapy or hospitalization, and 2) usage by individuals with formal ID consultation was included. DOT/1000 PD were assessed separately for preauthorization and targeted antibiotic use, with preauthorization usage chosen as the comparator (control) group given exclusion from ASP review. Eligible subjects and their usage were identified from a hospital administrative billing database. Severity index (with an APR-DRG severity score ranging from 1 [mild] to 4 [extreme]) was queried from the billing database and assessed for all subjects who received a targeted or preauthorization antibiotic in the pre and post time periods to evaluate differences in case mix over time. Using subject medical record numbers and month of admission, we queried the electronic data-mining software programs for individual DOT during that month. As DOT was ultimately aggregated by month, subjects whose admission overlapped months had their DOT parsed accordingly. These same databases were also queried for use of nonformulary antibiotics on our targeted or restricted lists. Additional manual review was conducted to remove duplicate values and verify a random sample for accuracy. Following data extraction, DOT was summarized across each month, divided by the total patient days in each month (obtained from the BMC Finance Office), and then

multiplied by 1000 to get the DOT/1000 PD per month.

Using the billing database, we queried our sample for 30-day all-cause readmissions amongst eligible subjects between August 1, 2013, to July 31, 2014, and December 1, 2014, to May 31, 2016. The PI (JMK) then reviewed all readmissions to determine association with antibiotic usage. Readmissions were aggregated into pre- and postimplementation time periods, given their infrequent monthly occurrence.

All new inpatient ID consultations are recorded in an internal BCH Pediatric ID Division database, which was accessed to ascertain whether monthly frequencies of new consultations were affected by ASP implementation. The same pre and post study windows as listed above were used to assess the program's impact on new ID consultations.

Statistical Analysis. Implementation was assessed by aggregating frequencies and percentages from the ASP database; namely, frequency of reviews performed, percentages of recommendations suggested and accepted, and percentage of provider compliance with implementation of accepted recommendations. Results were evaluated in subgroups according to the 5 antibiotics most frequently reviewed and also assessed when analyzed according to provider specialty. In order to evaluate which antibiotics or provider specialties resulted in a greater likelihood of recommendation generation, relative risks (RRs) and 95% confidence intervals (CIs) were calculated separately (using log-binomial models) for each antibiotic or primary team category compared to all others. Acceptance rates for each type of recommendation were also evaluated.

ASP impact was evaluated using the pre-post interrupted time series design described above. DOT /1000 PD were aggregated monthly and modeled using Prais-Winsten regression to account for autoregressive features of the data. Modeling was done in a piecewise fashion (e.g., segmented regression), creating separate slopes and intercepts for both pre and post time periods for both the targeted and preauthorization antibiotic groups. Intercept shifts and slopes were calculated and presented with 95% CIs. Readmission rates in the pre- and postimplementation time periods were assessed via Fisher's exact test. Statistical significance was set at an alpha of 0.05. Student's *t* test was used to compare mean monthly frequency of new ID consultations in the pre and post time periods. Analysis was conducted using Stata v14.1 (StataCorp, LP, College Station, TX).

In terms of power, preliminary data suggested that our autocorrelation was approximately -0.45 . Based upon simulation estimates provided by Zang et al¹⁷ (i.e., to detect either a difference in slopes or an intercept shift assuming an autocorrelation between -0.4 and -0.5 and a two-sided alpha of 0.05), we anticipated sufficient power to detect an effect size of 1 given a sample of 12 months pre and 18 months post.

Results

ASP Implementation. From December 1, 2014, to May 31, 2016, 882 ASP reviews were performed on 637 individual patients. Overall recommendation frequency was 37.1% ($n = 327$), with acceptance of 74.6% ($n = 244$). Of those, compliance was observed for 93.9% ($n = 229$). Reviews were performed most frequently for gentamicin (35%), ceftriaxone (21%), metronidazole (10%), vancomycin (8.2%), and clindamycin (7.6%) (Figure 1). Vancomycin review was most likely to generate a recommendation (RR, 2.08; 95% CI, 1.74–2.48) compared to all other antibiotics reviewed. Clindamycin review was approximately 40% more likely to prompt ASP recommendation (RR, 1.37; 95% CI, 1.05–1.77) relative to all other antibiotics. Conversely, metronidazole review was approximately 50% less likely to lead to recommendation development (RR, 0.46; 95% CI, 0.30–0.73), while gentamicin review was nearly 20% less likely to result in ASP recommendation formulation (RR, 0.81; 95% CI, 0.67–0.97). Recommendation acceptance rates by antibiotic ranged from 72% to 82%.

Reviews were performed most frequently on patients of neonatologists (34%), hospitalists (24%), and surgeons (13%) (Figure 1). Reviews on patients of PICU providers were nearly 60% more likely to result in recommendation formulation (RR, 1.58; 95% CI, 1.26–1.97), compared to patients of all other specialty providers. Additionally, ASP review of an individual under hospitalist care was approximately 40% more likely to trigger a recommendation (RR, 1.37; 95% CI, 1.14–1.65). In contrast, review of targeted antibiotics administered to patients of surgical providers was ~60% less likely to generate a recommendation (RR, 0.43; 95% CI, 0.29–0.65). Acceptance rates across provider specialties ranged from 58% to 100%.

Of 327 ASP recommendations generated for antibiotics reviewed, providers received recommendations for 316 patients (11 patients received multiple concurrent recommendations for formal ID consultation due to maintenance on >1 targeted antibiotic at the time of ASP review). Antibiotic discontinuation was recommended most frequently ($n = 143$ [45%], with 64% accepted), followed by dosing adjustment ($n = 37$ [11.7%], 100% accepted, with ceftriaxone and clindamycin accounting for 46% of recommendations), narrowing of coverage ($n = 33$ [10.4%], 70% accepted), formal ID consultation ($n = 29$ [9.2%], 72% accepted), transitioning from an IV to PO agent ($n = 27$ [8.5%], 89% accepted), broadening of coverage ($n = 21$ [6.6%], 62% accepted), toxicity monitoring ($n = 18$ [5.7%], 94% accepted) and finally eliminating of redundant coverage ($n = 8$ [2.5%], 100% accepted). Recommendations for toxicity monitoring were ~30% more likely to be accepted (RR, 1.29; 95% CI, 1.13–1.47) relative to all other recommendation types, while suggestions pertaining to transitioning from IV to PO therapy were approximately 20% more likely to

Figure 1. Antibiotic stewardship program reviews, recommendations, and acceptance by antibiotic and team.

* Out of total reviews performed.

† RR for likelihood of a recommendation being suggested, compared to all other categories.

‡ Out of total recommendations suggested.

be accepted (RR, 1.22; 95% CI, 1.05–1.42). Conversely, an ASP proposal to discontinue therapy was approximately 20% less likely to gain acceptance (RR, 0.78; 95% CI, 0.68–0.90) than all other recommendation types. Provider compliance with implementation of accepted recommendations ranged from 75% (i.e., for elimination of redundant coverage) to 100% (for formal ID consultation, broadening of coverage, and toxicity monitoring, respectively).

ASP Impact. A total of 5767 discrete courses of therapy administered to 3584 subjects were eligible for analysis. Among the targeted group, 2216 courses (40.6%) were dispensed in the preimplementation time period and 3248 (59.4%) in the postimplementation period. For the preauthorization group, 140 courses of therapy (46.2%) were administered in the pre period and 163 (53.8%) in the post period.

The mean DOT/1000 PD for the targeted antibiotic group immediately prior to ASP implementation was 247.3 (95% CI, 217–277), compared to 222.5 DOT/1000 PD (95% CI, 201–244) immediately following implementation (Figure 2), with a resultant 24.8 DOT/1000 PD decrease observed (95% CI, –62 to 14). Comparatively, the preauthorization group estimates were 19 DOT/1000 PD (95% CI, –11 to 49) pre to 22 (95% CI, 1–44) post, with an absolute increase of 3 DOT/1000 PD (95% CI, –36 to 41).

When evaluating slopes over time, the targeted group was increasing by almost 1.7 DOT/1000 PD (95%

CI, –2.5 to 5.9) in the pre period compared to 0.4 per month (95% CI, –1.8 to 2.7) in the post period, for a difference in slopes of 1.3 DOT per month (95% CI, –6.0 to 3.4). In contrast, the slope for the preauthorization group was 0.1 DOT per month (95% CI, –4.1 to 4.3) in the pre period to –0.6 DOT per month (95% CI, –2.9 to 1.7) in the post period for a difference in slopes of 0.7 DOT (95% CI, –5.5 to 4.0).

There were 22 readmissions of eligible study subjects who had initially received ≥ 1 targeted antibiotic during the study period (9 preintervention and 13 postintervention). The 30-day readmission rate for those who initially received a targeted antibiotic was determined to be 0.64% for both time periods. Only 1 subject who had initially received a preauthorization antibiotic was readmitted within 30 days (post period).

Severity index assessment for both the targeted and restricted groups revealed a median score of 2.0 for both groups in both the pre and post time periods, implying that case mix did not have a strong influence on our findings.

The frequencies of new inpatient ID consults per month were similar across both time periods (mean 31.8 ± 5.7 pre vs. 30.4 ± 3.9 post; $p = 0.4$).

Discussion

In this study, evaluation of the implementation and impact of our non-freestanding children's hospital ASP

Figure 2. Patient days of therapy per 1000 patient days by month.

revealed multiple findings that our ASP has in common with those of large freestanding institutions, while concurrently highlighting certain differences specific to our institution and perhaps to non-freestanding children's hospital stewardship in general.

Implementation analysis revealed that our frequencies of recommendation generation (37.1%), provider acceptance (74.6%), and provider compliance with implementation of accepted recommendations (93.9%) were comparable to those of freestanding children's hospital ASPs (in which reported recommendation generation frequencies ranged between 19% and 45%, provider acceptance from 80% to 84%, and provider compliance with implementation of accepted recommendations between 83% and 92%).^{1,4,5,7} Similarly, antibiotics including ceftriaxone, gentamicin, and vancomycin were reviewed most often.^{4,5,8} Vancomycin review prompted recommendation generation more frequently than other antibiotics, a finding consistent with multiple studies from freestanding institutions.^{6–9,18} Conversely, reviews of gentamicin and metronidazole usage infrequently led to formulation of recommendations. Such findings (plus the observation that reviews performed on targeted therapy prescribed by surgical providers were also less likely to yield ASP recommendations) can be attributed at least in part to the presence of institutional practice guidelines for management of pediatric appendicitis (advising empiric use of ceftriaxone and IV metronidazole for gangrenous and/or perforated appendicitis) and for management of febrile infants

≤3 months (which suggests empiric prescription of ampicillin and gentamicin). Similar to Turner et al,¹⁰ our results underscore the cumulative importance of evidence-based guideline development plus prospective audit-with-feedback methodology in non-freestanding pediatric hospitals with limited stewardship resources. Our finding that recommendations were suggested more frequently for patients of PICU providers (relative to all other provider specialties) highlights the potential need for protocol development for that BCH ward, as guideline establishment with concurrent prospective audit-with-feedback has been shown to be a particularly effective method for maximizing PICU ASP efforts in various settings.^{19,20}

Suggestions for toxicity monitoring and conversion from IV to PO therapy were most frequently accepted relative to all other recommendations. Perhaps not surprisingly, recommendations to discontinue therapy were accepted least frequently. Such findings most likely stem from perceived loss of physician autonomy with discontinuation recommendations, as opposed to implicit confirmation of "correct" prescribing behavior with suggested toxicity monitoring and conversion from IV to PO therapy.³

With respect to ASP impact, an absolute decrease in targeted antibiotic use of 24.8 DOT/1000 PD was observed between the immediate pre- and post-implementation periods. There were no statistically significant trends over time; visually, however, there is a suggestion that the postintervention slope for

the targeted group was flatter than the preintervention slope (Figure 2). Regardless, a visual change in slope was also observed for the preauthorization group, suggesting that some other unidentified system level intervention(s) besides the ASP may have had a spill-over effect in regards to reductions in DOT/1000 PD. One potential explanation for the absence of an observed statistically significant difference could be that mean baseline targeted antibiotic utilization at our institution (247.3 DOT/1000 PD) prior to ASP implementation was already low. As a comparison, Turner et al¹⁰ reported a baseline mean DOT/1000 PD of 367 ± 23 (when excluding cefazolin, cefoxitin, and cefotetan use) prior to ASP implementation at their non-freestanding children's hospital.

No statistically significant difference in readmission rates within 30 days of initial hospital discharge was detected following ASP implementation, with identical frequencies (0.64%) observed during the pre- and postintervention time periods. The absence of an observed difference serves to emphasize both the safety and reliability of ASP recommendations ultimately implemented by providers.

Comparison of mean frequencies of new formal ID consultations per month in the pre- and postimplementation periods revealed no clinically meaningful or statistically significant differences. The most plausible explanation for this finding is that ASP activities generated some inpatient ID consultations while concurrently eliminating the need for others. Such a finding may also allay concerns of those who fear that conflicts of interest (i.e., with regard to formal consultation generation) between an ASP team and an ID Division could be present to a greater extent at institutions with a small number of ID physicians on staff than otherwise might be present at large freestanding children's hospitals.

This study has multiple limitations. First, specific/presumptive diagnoses of patients reviewed by the ASP were not directly recorded; thus, influence of existing institutional practice guidelines on appropriate use of antibiotics as suggested by our results may be overestimated. Regardless, development of such guidelines is advised by the IDSA, and is one of the recommendations as set forth in the Centers for Disease Control and Prevention's *Core Elements of Hospital Antibiotic Stewardship Programs*—thus lending credence to the likelihood of beneficial association.^{14,15} Additionally, procedures typically associated with an elevated degree of antibiotic usage, including bone marrow transplantation, solid organ transplantation, and cardiovascular surgeries, are not performed at BCH. Observed changes in targeted antibiotic utilization over time may therefore be less pronounced than in large freestanding children's hospitals, given that a lower patient acuity level (relative to large freestanding institutions where such procedures are frequently performed) could have

been responsible for our rather low baseline rates of targeted antibiotic usage prior to ASP implementation. Comparison of our utilization rates against institutions of similar size and scope of practice would have been ideal; however, currently available data from such institutions are extremely limited.¹⁰ Our ASP impact analysis was limited to 12 months in the preimplementation period and 18 months in the postimplementation period, which could have constrained additional evaluation for potential confounding variables such as seasonal variation and primary provider turnover.

Despite the above limitations, and despite the lack of institutional resource allocation to any of the physician or pediatric pharmacy ASP members, this study serves to highlight effective implementation and measurement of the impact associated with ASP establishment at a non-freestanding children's hospital—thereby fulfilling a need expressed by multiple studies and commentaries on the subject of pediatric antimicrobial stewardship.^{10,11,21–23} The results of this study reinforce the notion that measurement of ASP impact should not be limited merely to antibiotic consumption, but must also assess outcome measures more difficult to quantify (i.e., ones not readily amenable to traditional statistical analysis).^{14,24} Such future evaluations could include, among others, evaluation of ASP learning effects on prescribing providers.

Opportunities for future ASP-guided quality improvement efforts at BCH identified by our study include creation of measures aimed at provider education, protocol development, and optimal utilization of clindamycin and vancomycin, as well as the need for closer collaboration and institutional guideline development with our hospitalist and intensivist colleagues. Areas for future research include identification of diagnostic conditions at non-freestanding children's hospitals most likely to prompt ASP review and recommendations. Future expansion of our ASP's clinical and educational efforts will require continuous program monitoring of established process and outcome measures, greater administrative support, and establishment of ASPs at additional non-freestanding pediatric institutions similar in size to BCH, in order to allow for optimal data comparison.

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Disclosure The authors declare no conflicts or financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employment, gifts, and honoraria. The authors had full access to all the data and take responsibility for the integrity and accuracy of the data analysis.

Acknowledgment Presented in part at the *Society for Healthcare Epidemiology of America* (SHEA) Spring 2015 Meeting, Orlando, FL, May 14–17, 2015.

Accepted August 28, 2017

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