

Identification of High-Yield Targets for Antimicrobial Stewardship Program Efforts Within a Nonfreestanding Children's Hospital

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ABSTRACT

OBJECTIVES: Identify diagnoses with the highest likelihood of prompting antimicrobial stewardship program (ASP) recommendations and lowest probability of recommendation acceptance, investigate the impact of provider years in practice on recommendation receipt and acceptance, and simultaneously assess the influence of patient and provider-level variables associated with recommendations within a nonfreestanding children's hospital.

METHODS: Retrospective cohort study of antibiotic courses reviewed by the ASP staff from December 1, 2014 to November 30, 2016. Poisson regression was used to detect associations between diagnoses, provider years in practice, and the probability of recommendation receipt and acceptance. Multivariable logistic regression was used to simultaneously examine the influence of patient and provider-level characteristics on recommendation probability.

RESULTS: A total of 938 inpatient encounters and 1170 antibiotic courses were included. Diagnoses were associated with provider receipt ($P < .001$) and acceptance ($P < .001$) of recommendations, with ear, nose, and throat and/or sinopulmonary diagnoses most likely to prompt recommendations (56%; 95% confidence interval [CI], 48–64) and recommendations for neonatal and/or infant diagnoses accepted least often (67%; 95% CI, 58–76). No associations were initially found between provider experience and recommendation receipt or acceptance, although multivariable analysis revealed a trend between increasing years in practice and recommendation likelihood ($P = .001$). Vancomycin usage (64%; 95% CI, 56–72) and ear, nose, and throat and/or sinopulmonary diagnoses (56%; 95% CI, 47–65) had the highest probability of a recommendation. Sensitivity analyses revealed that use of diagnosis-related clinical practice guidelines decreased recommendations and increased acceptance rates, especially for the surgery diagnosis category.

CONCLUSIONS: High-yield targets for ASP activities at our nonfreestanding children's hospital were identified. Clinical practice guidelines have the potential to decrease ASP workload, and their development should be particularly encouraged for ASPs with limited resources.

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The number of inpatient pediatric antimicrobial stewardship programs (ASPs) throughout the United States continues to increase, secondary to factors including the Centers for Disease Control and Prevention 2014 recommendation for all hospitals to implement ASPs and the Joint Commission's 2017 stewardship standard requirement for all critical access hospitals.¹⁻⁴ Despite this growth, there remains a paucity of published literature from nonfreestanding children's hospitals used to identify ideal targets for concerted ASP efforts at such institutions.⁵⁻⁷ Both case mix and patient illness severity at nonfreestanding hospitals differ relative to their freestanding counterparts.⁸ A greater incidence of patients at freestanding centers undergoes cardiac surgery, chest tube placement, and arterial catheter placement and receives mechanical ventilation.⁸ Greater relative percentages of patients at freestanding hospitals carry infectious, oncologic, and cardiovascular diagnoses, whereas endocrinologic, gastrointestinal (GI), and injury-related diagnoses account for greater relative percentages at nonfreestanding institutions.⁸ Clinical and professional responsibilities of physicians in specialties such as hospital medicine can vary between those employed at freestanding versus nonfreestanding facilities.⁹

Our previous analysis of a nonfreestanding children's hospital ASP revealed that reviews of intravenous (IV) vancomycin were most likely to trigger recommendations.⁷ Patient diagnoses were not assessed during that study, however. Given the known differences between freestanding and nonfreestanding hospitals with regard to patient-level characteristics, variations in patient volume, and provider responsibilities,^{5,8-10} our primary objectives of this study were to identify patient diagnoses associated with the highest likelihood of prompting ASP recommendations and lowest likelihood of providers accepting recommendations at our nonfreestanding children's hospital. We hypothesized that certain diagnoses would be associated with greater probabilities of provider recommendation receipt and lesser likelihoods of acceptance relative to others. Secondary aims included evaluating

the impact of provider years in clinical practice on recommendation receipt and acceptance. Similar to Bio et al,¹¹ we anticipated that clinically experienced physicians were most likely to have received recommendations and least likely to have accepted recommendations. In addition, we sought to simultaneously assess patient-level (diagnosis) and provider-level (antibiotic choice, provider team specialty, and years in practice) variables to determine which factors were most predictive of ASP recommendations.

METHODS

Setting

Baystate Children's Hospital (BCH) is a 110-bed and 57-bassinet nonfreestanding children's hospital located within Baystate Medical Center (BMC), a 716-bed independent academic medical center in Springfield, Massachusetts. BCH is administratively nonfreestanding because the executive leadership for BMC and BCH is one and the same. BCH contains a 55-bed level III NICU and 7-bed level II PICU, is affiliated with the University of Massachusetts Medical School—Baystate, and serves as the primary teaching facility for 59 resident physicians in categorical pediatrics and internal medicine and/or pediatrics training programs. The University of Massachusetts Medical School—Baystate Department of Pediatrics at BCH is composed of >100 clinical faculty members representing general pediatrics and multiple pediatric subspecialties. In addition to inpatients on the general pediatrics ward managed by an active pediatric hospitalist service, pediatricians from 5 private practices throughout the metropolitan area serve as primary inpatient providers for hospitalized children from their practices. Residents care for patients with hospitalist and private practice providers and place most orders for antibiotics throughout BCH. In general, however, resident antimicrobial prescribing autonomy is tightly restricted for patients with hospitalist attending physicians and for those in the ICUs (although less so for children with private practice providers). A single advanced practitioner is employed part-time for the surgery service, whereas multiple advanced

practitioners care for neonates under the close supervision of an attending neonatologist. No bone marrow transplants, solid organ transplants, or pediatric cardiovascular surgical procedures are performed at BCH. Institutional clinical practice guidelines (CPGs) exist for management of (1) febrile infants ≤ 3 months (which recommend empirical use of ampicillin and gentamicin), (2) children with acute abdominal pain and suspected appendicitis (within which ceftriaxone and metronidazole are advised for complicated appendicitis), and (3) initial dosing of IV vancomycin. No CPGs exist for empirical antibiotic management of inpatients with any other infectious diagnoses such as community-acquired pneumonia (CAP), osteoarticular infections, or skin and/or soft tissue infections.

Established in 2014, the BCH ASP is staffed jointly by infectious diseases physicians and clinical pharmacy specialists. The physician director has 0.1 full-time equivalent salary support dedicated to stewardship, whereas the unit-based pediatric clinical pharmacy specialists have no dedicated full-time equivalent salary support for stewardship. The ASP staff reviews usage of certain predefined antibiotics 48 to 72 hours after initiation (Table 1) for all inpatients with primary inpatient providers (regardless of specialty) who predominantly care for neonates, children, and/or adolescents. The program uses a thrice-weekly prospective audit-with-feedback methodology, a strategy successfully employed at freestanding institutions and nonfreestanding children's hospitals within larger medical centers.^{5-7,12-15} ASP recommendations include 8 discrete types (Table 1). All data regarding antibiotics reviewed, recommendations suggested, primary team specialty, provider acceptance of recommendations, and provider implementation of accepted recommendations are collected and recorded in an internal ASP quality improvement database as previously described elsewhere.⁷ For each date on which stewardship activities occur, all reviews performed are recorded on detailed rounding sheets shared among ASP team members.

TABLE 1 Characteristics of ASP Reviews by Antibiotic, *N* = 1170

	Antibiotic Reviews, <i>n</i> (%)
Antibiotic reviewed ^a	
Gentamicin	405 (34.6)
Ceftriaxone	237 (20.3)
Metronidazole (IV and PO)	120 (10.3)
Vancomycin (IV)	96 (8.2)
Clindamycin (IV and PO)	86 (7.4)
Piperacillin-tazobactam	63 (5.4)
Cefepime	62 (5.3)
Ampicillin-sulbactam	34 (2.9)
Levofloxacin (IV and PO)	32 (2.7)
Amoxicillin-clavulanate	22 (1.9)
Tobramycin (IV)	7 (0.6)
Cefotaxime	6 (0.5)
Recommendation type	
No recommendation suggested ^b	756 (64.6)
Discontinue antibiotic	183 (15.6)
Recommend formal infectious diseases service consultation	51 (4.4)
Dosing adjustment	49 (4.2)
Narrow coverage	39 (3.3)
Transition from IV to PO	34 (2.9)
Broaden coverage	27 (2.3)
Toxicity monitoring	22 (1.9)
Eliminate redundant antibiotic coverage	9 (0.8)
Primary inpatient care team	
NICU	384 (32.8)
Hospitalist	264 (22.6)
Surgery	180 (15.4)
PICU	112 (9.6)
Private patient	97 (8.3)
Hematology and/or oncology	78 (6.7)
Newborn nursery	37 (3.2)
Gastroenterology	18 (1.5)
Diagnosis category	
Neonatal and/or infant	427 (36.5)
Surgery	210 (17.9)
ENT and/or sinopulmonary	199 (17.0)
Hematologic and/or CNS	139 (11.9)
GI and/or genitourinary	111 (9.5)
Skin and/or soft tissue	44 (3.8)
2 diagnoses	40 (3.4)
Provider years in clinical practice, <i>y</i>	
<5	199 (17.0)
5–15	534 (45.6)
>15	437 (37.4)

Study Design and Data Collection

A retrospective cohort study was performed for all BCH inpatients from December 1, 2014 to November 30, 2016, whose antibiotic courses of therapy underwent review as per the internal ASP database. The BMC Institutional Review Board reviewed and approved all facets of this project.

Working Diagnosis Categories

Copies of the detailed rounding sheets were reviewed to ascertain patient working diagnoses at the time of ASP review. A patient's working diagnosis was defined as the presumptive clinical condition (per the patient's primary provider) that necessitated antibiotic use at the time ASP review occurred. For reviews performed for which no working diagnoses were recorded on the rounding sheets, chart reviews of provider documentation on the dates of ASP reviews were used to establish diagnoses. After identification of all working diagnoses, the diagnoses were condensed into 7 categories by using an approach similar to that used by Goldman et al¹⁶ (Table 1). Included among these was a category for patients for whom >1 working diagnosis category was applicable (ie, 2 diagnoses).

Provider Years in Clinical Practice

A list was generated of all potential BCH inpatient primary providers from December 1, 2014 to November 30, 2016. Board examination certification websites (www.abp.org and www.absurgery.org) were reviewed to obtain initial certification dates for potential providers, which were then used to calculate years in clinical practice. For subspecialists actively practicing in their certified subspecialty during the study period, initial dates of subspecialty certification were used to determine years in clinical practice. Providers were categorized into 1 of 3 groups based on corresponding length of time between initial certification date and December 1, 2014 (i.e., <5, 5–15, and >15 years). Providers on the dates on which ASP reviews occurred were determined via chart review.

Statistical Analysis

Descriptive statistics were used to summarize characteristics at the patient

TABLE 1 Continued

	Antibiotic Reviews, <i>n</i> (%)
CPG ^c	
No	984 (84.1)
Yes	186 (15.9)

CNS, central nervous system; PO, oral.

^a IV amikacin was also eligible for review; however, no amikacin reviews were performed during the study time period.

^b Because of ASP agreement with primary inpatient care team management plan.

^c Febrile infants ≤ 3 mo and gangrenous or perforated appendicitis.

review level (ie, characteristics of the patient at the time of the ASP review) and the antibiotic level (ie, characteristics of the antibiotic prompting the review). Study outcomes included the probability of ASP recommendation and, among those with a recommendation, the probability of acceptance. By using separate models, we estimated these probabilities for 2 primary predictor variables of interest: diagnosis category and provider years in clinical practice. An overall Wald test was used to test the significance of these predictors in the model, and linear contrasts were used to test the trend of increasing years in practice. All tests used a 2-sided α of .05. One of the features of this data set is that providers were repeatedly observed over the study duration. If providers either prescribed a certain way (eg, in a manner prompting more ASP reviews relative to their peers) and/or consistently accepted or rejected ASP recommendations over time, they could unduly weight our estimates. To account for those possibilities, separate generalized estimating equation Poisson regression models clustering on provider were used to generate population-averaged estimates and 95% confidence intervals (CIs). To estimate probabilities (ie, average marginal effects), we used Stata's (Stata Corp, College Station, TX) `margins` command. In terms of power, for an overall χ^2 -type analysis on a 7×2 table (eg, 7 diagnostic categories by presence or absence of a recommendation) with 6 degrees of freedom, we had sufficient power to detect a small effect size (Cohen's w)¹⁷ of 0.125 for an anticipated sample size of 882 reviews.

To address which patient-level and/or provider-level variables were most predictive of ASP recommendations, we

created a multivariable generalized estimating equation logistic regression model (also clustering on provider) to simultaneously estimate adjusted recommendation probabilities and 95% CIs for each diagnosis category, provider years in clinical practice, primary team specialty, and antibiotic reviewed.

We also performed multiple sensitivity analyses. Because the presence of CPGs could impact the probability of a recommendation and/or acceptance, we restricted all of the models (unadjusted and multivariable) to ASP reviews without a CPG and assessed the results for clinically important differences. For the sensitivity analyses, we chose to exclude only the 2 diagnosis-related CPGs (ie, gangrenous and/or perforated appendicitis and febrile infants ≤ 3 months) given the incomplete overlap of the CPG with the diagnosis categories, whereas vancomycin estimates represent the initial dosing CPG in all cases. All analysis was conducted by using Stata MP, version 15.1.

RESULTS

From December 1, 2014 to November 30, 2016, the ASP staff reviewed 1170 discrete antibiotic courses prescribed during 938 individual patient encounters (Table 1). Overall, 414 (35%) reviews prompted ASP recommendations. Providers accepted 307 of 414 (74%) recommendations, with 287 of 307 (93%) ultimately implemented.

Working Diagnosis Categories

Specific diagnoses within each category are listed in Table 2. There was a significant association found between working diagnosis category and probability of recommendation ($P < .001$) (Fig 1). The

ear, nose, and throat (ENT) and/or sinopulmonary category was associated with the greatest likelihood of triggering recommendations (56%; 95% CI, 48–64), with antibiotic discontinuation ($n = 41$; 35% of all ENT and/or sinopulmonary recommendations) and narrowing coverage ($n = 21$; 18%) advised most often. The surgery category was least likely to receive recommendations (23%; 95% CI, 14–32), with all remaining probabilities ranging between 28% and 37%. Of note, a total of 31 of 427 antibiotic courses reviewed for neonatal and/or infant diagnoses involved a CPG for febrile infants ≤ 3 months. Of those, 12 (39%) resulted in a recommendation. Additionally, 155 of 210 antibiotic courses reviewed for surgery diagnoses involved a CPG for gangrenous and/or perforated appendicitis, with 16 (10%) resulting in a recommendation. After restricting the analysis to ASP reviews without a CPG, ASP recommendations for surgery diagnoses increased from 23% to 38%, whereas the rest remained relatively stable. ENT and/or sinopulmonary diagnoses continued to have the highest probability (58%), whereas neonatal and/or infant diagnoses had the lowest probability (30%).

Among 414 recommendations proposed, a significant association was found between the working diagnosis category and probability of provider recommendation acceptance ($P < .001$) (Fig 1). Acceptance was 100% for patients with skin and/or soft tissue infectious diagnoses; however, only 15 total interventions were suggested for that category. Acceptance was also high for the GI and/or genitourinary category (89%; 95% CI, 80–98), with 38 of 43 recommendations accepted. The neonatal and/or infant category had the lowest acceptance rate (67%; 95% CI, 58–76), with 94 of 140 suggestions accepted. Of the 46 rejected neonatal and/or infant category recommendations, 34 (74%) advised antibiotic discontinuation. Diagnoses for 32 of 34 (94%) included ≥ 1 of the following: suspected and/or confirmed early-onset neonatal sepsis, neonatal pneumonia, and/or necrotizing enterocolitis. For all remaining diagnosis categories, acceptance ranged from 71% to 76%. After restricting the analysis to ASP reviews

TABLE 2 Working Diagnoses and Their Categories by Patient, *N* = 938

Diagnosis Category and Diagnosis	<i>n</i>	%
GI and/or genitourinary		
Overall	93	—
Urinary tract infection	41	44.1
Pyelonephritis	20	21.5
Inflammatory bowel disease exacerbation	10	10.8
Abscess(es) due to inflammatory bowel disease	7	7.5
<i>Clostridium difficile</i> infection	6	6.5
Other	9	9.7
ENT and/or sinopulmonary		
Overall	159	—
CAP	46	28.9
Aspiration pneumonia	28	17.6
2 ENT and/or sinopulmonary diagnoses	17	10.7
Tracheitis	14	8.8
CF exacerbation	11	6.9
Peritonsillar and/or retropharyngeal abscess	8	5.0
Hospital-acquired pneumonia	7	4.4
Dental abscess	6	3.8
Ventilator-associated pneumonia	6	3.8
Adenitis ± abscess	5	3.1
Other	11	6.9
Neonatal and/or infant		
Overall	388	—
Suspected or confirmed early-onset neonatal sepsis	244	62.9
Meconium aspiration	33	8.5
Febrile infant ≤3 mo	30	7.7
Early-onset neonatal sepsis plus neonatal pneumonia	27	7.0
Necrotizing enterocolitis	25	6.4
Suspected or confirmed late-onset neonatal sepsis	15	3.9
Neonatal pneumonia	12	3.1
Other	2	0.5
Surgery		
Overall	123	—
Gangrenous and/or perforated appendicitis	82	66.7
Intraabdominal process unrelated to perforated appendicitis	17	13.8
Postoperative management	11	8.9
Surgical site infection	9	7.3
Other	4	3.3
Skin and/or soft tissue		
Overall	38	—
Skin and/or soft tissue infection	37	97.4
Omphalitis	1	2.6

without a CPG, acceptance remained highest for GI and/or genitourinary (89%) and skin and/or soft tissue diagnoses (100%). Acceptance probabilities for neonatal and/or infant diagnoses decreased slightly (to 64%), whereas acceptance for surgery diagnoses decreased from 71% to 60% (making surgery the category with the lowest acceptance rate).

Provider Years in Clinical Practice

Of the 92 providers whose patients underwent ASP review, 15 (16%) were in clinical practice <5 years, with 31 (34%) between 5 and 15 years and 46 (50%) for >15 years. Although likelihood of a recommendation was lowest among those with <5 years' experience (24% vs 39% [5–15] and 35% [>15]), this was not statistically significant ($P = .24$) and no trend was observed ($P_{\text{trend}} = .18$). Acceptance was slightly higher among those with 5 to 15 years of experience (78% vs ~70% in the other 2 groups); however, this also was not statistically significant ($P = .36$) and no trend was observed ($P_{\text{trend}} = .94$) (Fig 2). Inferences for both likelihood of a recommendation and acceptance remained the same after restricting to ASP reviews without a CPG.

Multivariable Assessment

When simultaneously taking into consideration patient-level (diagnosis) and provider-level (antibiotic choice, provider team specialty, and years in practice) factors, the variable with the highest adjusted probability of ASP recommendation was IV vancomycin use (64%; 95% CI, 56–72) (Fig 3). Of the 63 vancomycin recommendations, 9 (14%) suggested dosing adjustment or toxicity monitoring, whereas 42 (67%) advised narrowing coverage or discontinuation. The ENT and/or sinopulmonary diagnosis category was also strongly predictive of ASP intervention (56%; 95% CI, 47–65). Although having a gastroenterologist primary team provider was associated with a 53% probability of ASP recommendation, gastroenterologists prescribed only 18 courses of reviewed antibiotics (during 11 individual patient encounters), resulting in a wide CI and therefore unstable estimate. A significant trend across all provider years in

TABLE 2 Continued

Diagnosis Category and Diagnosis	<i>n</i>	%
Hematologic and/or CNS		
Overall	113	—
Fever and/or neutropenia in oncology patient	48	42.5
Sickle cell anemia exacerbation or suspected acute chest syndrome	27	23.9
Bacteremia	26	23.0
Hypothermia	5	4.4
Other	7	6.2
2 distinct diagnoses	24	—

CF, cystic fibrosis; CNS, central nervous system; —, not applicable.

practice groups was identified, with recommendation probabilities increasing according to the duration of clinical experience (26% [<5 years] to 35% [5–15 years] and finally 39% [>15 years]) ($P_{\text{trend}} = .001$). After restricting the multivariable model to ASP reviews without a diagnosis-related CPG, we continued to observe that IV vancomycin had the highest probability of a recommendation (increased to 66%) followed by ENT and/or sinopulmonary diagnoses (increased to 61%).

DISCUSSION

Patient working diagnosis categories at the time of ASP review significantly influenced

probabilities of provider receipt and acceptance of ASP recommendations at our nonfreestanding children's hospital. No significant associations were initially detected between provider years in clinical practice and recommendation receipt or acceptance, although the multivariable assessment revealed a trend that providers with >15 years in practice were most likely to receive a recommendation. Despite this observed trend, we also found through multivariable analysis that provider years in practice was not among those variables most likely to prompt a recommendation. Our multivariable assessment results strongly emphasize the need for measures to assist

providers with the selection of ideal empirical antibiotic therapy for ENT and/or sinopulmonary infections and reinforce the conclusion from previous studies that IV vancomycin usage optimization should serve as a high-yield target for stewardship programs regardless of institutional size or breadth of clinical practice.^{6,7,13,18–21} The restricted analyses revealed that the presence of institutional CPGs may have an important effect in curbing the need for certain ASP recommendations.

Of all the working diagnosis categories, the ENT and/or sinopulmonary category had the strongest association with ASP recommendations (with 53% advising antibiotic discontinuation or narrowing coverage). This finding is consistent with published data from freestanding children's hospitals used to assert that diagnoses like CAP are likely to trigger recommendations to discontinue and/or modify antibiotic therapy.^{16,22,23} We support the previously stated claim that ASP optimization of antibiotic therapy for diagnoses including sinopulmonary infections like CAP at nonfreestanding children's hospitals is necessary at a relative frequency equal to or perhaps even greater than that encountered at freestanding institutions.¹⁰ Our findings are particularly relevant because pneumonia is known to be the most costly diagnosis for pediatric hospitals that are not freestanding (in contrast to freestanding centers, where costs are greatest for respiratory distress syndrome in newborns and chemotherapy admissions).²⁴ Recommendation acceptance was high for patients in the GI and/or genitourinary category (nearly 66% of which had a urinary tract infection or pyelonephritis), likely because those recommendations were based primarily on urine culture isolate susceptibility testing results that typically returned 48 to 72 hours after being obtained (ie, a duration of time coinciding closely with ASP antimicrobial review).

Providers of patients with neonatal and/or infant category diagnoses had the lowest likelihood of recommendation acceptance in the unrestricted analysis. Most were neonatologists, and obstacles to successful

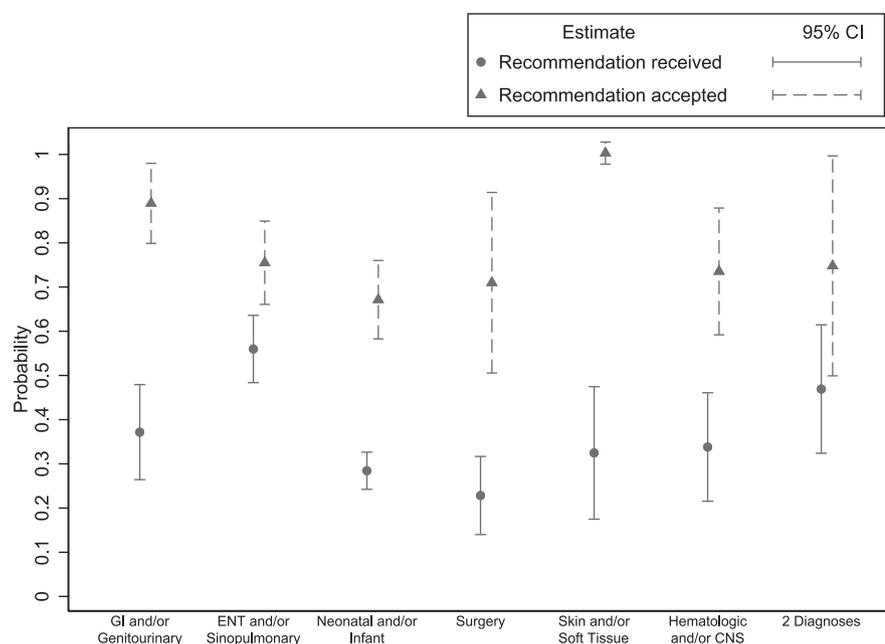


FIGURE 1 Probabilities of provider receipt and acceptance of ASP recommendations by working diagnosis category. CNS, central nervous system.

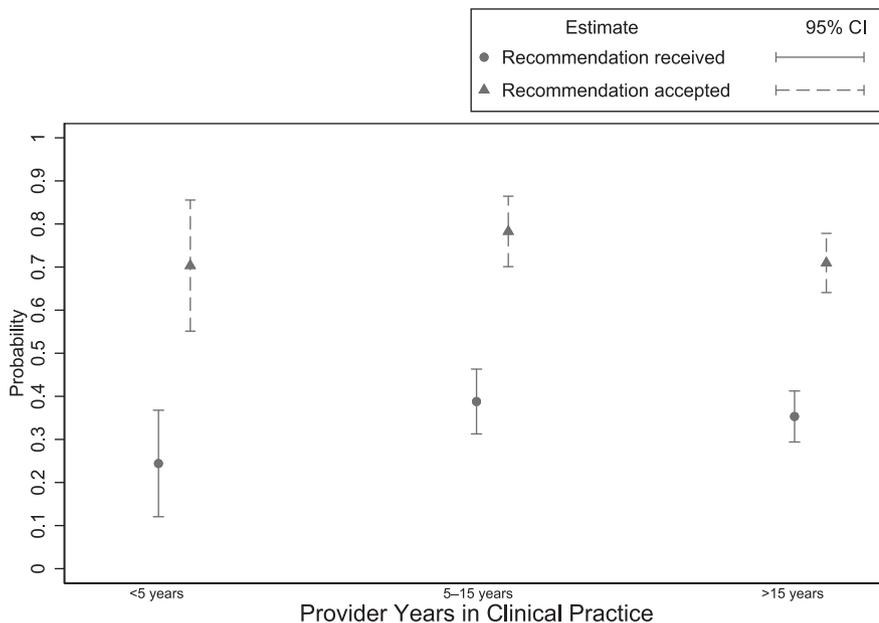


FIGURE 2 Probabilities of provider receipt and acceptance of ASP recommendations by provider years in clinical practice.

antimicrobial stewardship in the NICU have been well documented in the medical literature.²⁵⁻²⁷ The majority of providers who rejected neonatal and/or infant category recommendations advised discontinuation of antibiotics initiated empirically for conditions including early-onset neonatal sepsis and necrotizing enterocolitis. Standardization of the management approaches to such conditions is likely to provide significant benefit.

Rejection of ASP recommendations has previously been linked to behaviors of experienced clinicians relying on past practices that may have resulted in positive outcomes, and such physicians may be more skeptical of new stewardship interventions relative to their less experienced colleagues.^{28,29} Bio et al¹¹ did not initially observe any differences between the duration of provider experience and ASP recommendation acceptance after univariate analysis, although they found a small but statistically significant difference between those variables in their adjusted multivariate model. Similarly, our study did not initially reveal any associations between provider years in clinical practice and likelihood of ASP recommendation receipt. However, when exploring the relationship

between those variables within the context of the multivariable analysis, a significant trend between provider years in practice and recommendations emerged, which reveals that ASP recommendations were most common among experienced providers. Although this finding could be an anomaly unique to BCH, the observed similarities between our results and those of Bio et al¹¹ suggest that the impact of provider clinical experience on ASP recommendations is closely tied to additional factors, including patient diagnosis and primary team specialty. Although provider years in practice was not among the factors most predictive of recommendations in our multivariable analysis, the observed trend between increasing provider years in practice and recommendations reveals that the most effective stewardship educational strategies will account for multiple patient-level and provider-level factors.

The multivariable assessment also revealed that IV vancomycin use had the greatest association with ASP recommendation receipt. A substantial majority of vancomycin recommendations made during the study period were for de-escalation or discontinuation, whereas only a small

number were for vancomycin dosing adjustment and/or toxicity monitoring. Such results reflect the need for provider education regarding appropriate indications for vancomycin initiation and discontinuation at BCH. The multivariable results likewise reveal the conclusion that BCH patients with ENT and/or sinopulmonary diagnoses frequently trigger ASP recommendations.

The impact of diagnosis-related CPGs on BCH stewardship activities was varied. Among neonatal and/or infant diagnoses, the probability of a recommendation for febrile infants ≤ 3 months (39%) was actually higher than the probability for the overall diagnosis category (28%). However, that specific diagnosis accounted for only a small percentage of all ASP reviews performed for patients with neonatal or infant diagnoses. When restricting our analyses to no CPGs, we observed no substantive differences in the probability of a recommendation or acceptance for that diagnosis category. In contrast, reviews of gangrenous and/or perforated appendicitis comprised a large percentage of all surgery category reviews performed, and the probability of a recommendation for that diagnosis (10%) was much lower than for the overall diagnosis category (23%). Furthermore, when restricting our analyses to no CPGs, we observed not only that surgery category recommendations increased by 15% but also that recommendation acceptance decreased by 11%. We believe that these findings reveal the importance of CPGs for the management of pediatric appendicitis, as previously stated by Willis et al.^{30,31} Because the BCH CPG for management of patients with appendicitis predated ASP establishment, we, on the basis of our finding, could also imply that CPGs for select diagnoses at nonfreestanding children's hospitals are equally as important as (or perhaps even more important than) the performance of regular prospective audit with feedback for patients with those same diagnoses.

This study has multiple limitations. The study was performed at a single nonfreestanding children's hospital. The

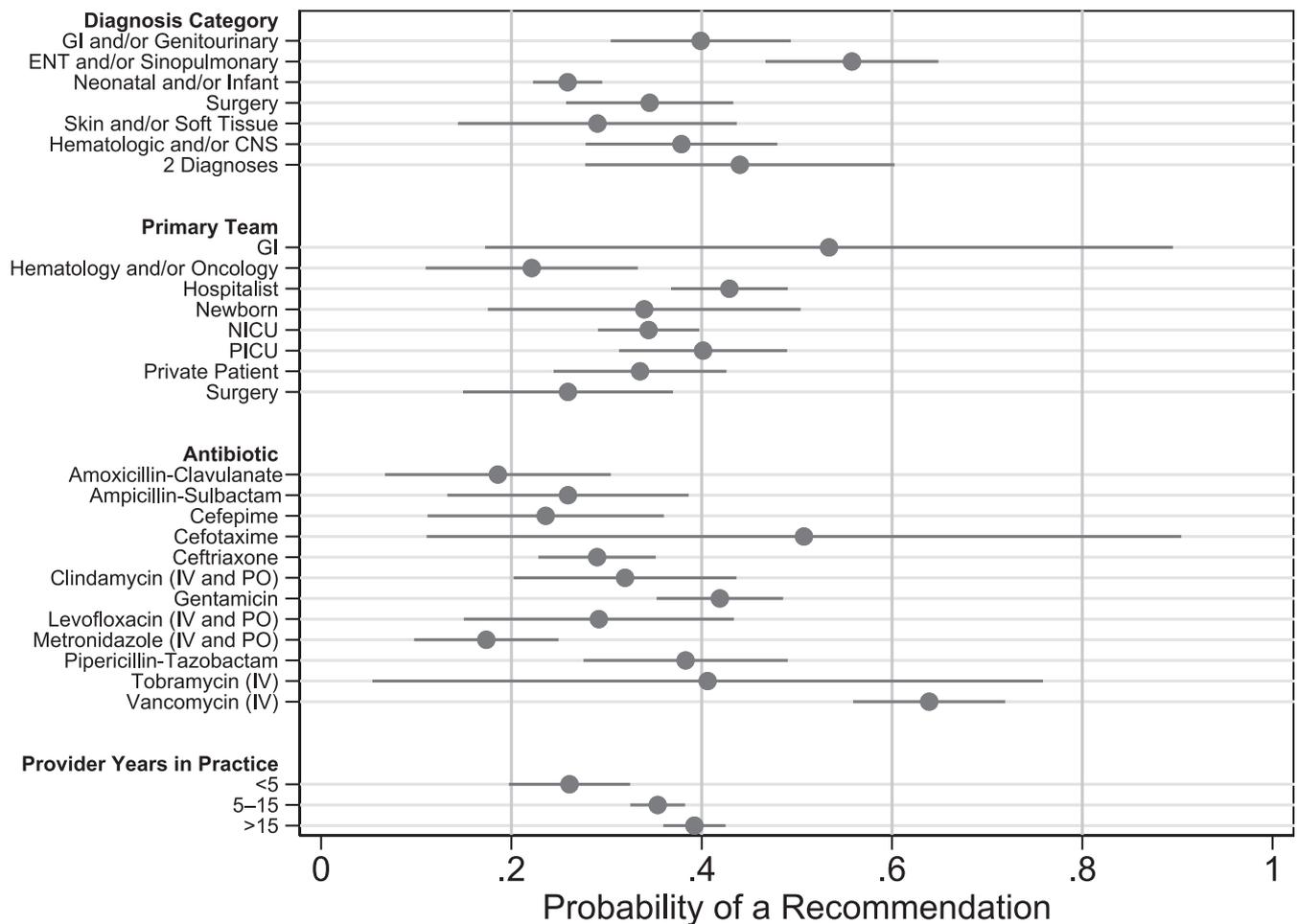


FIGURE 3 Results of a multivariable assessment of provider, patient, and antimicrobial characteristics and their relative probabilities of prompting ASP recommendations. CNS, central nervous system; PO, oral.

case mix of children and frequencies with which certain diagnoses are seen at BCH could differ from other nonfreestanding facilities that offer varying ranges of clinical services. The precise impact of CPGs on ASP recommendations may be under- or overestimated given the provider and case mix at BCH. Despite participation during the study period in a multicenter collaborative aimed at optimizing antibiotic use for CAP,³² BCH does not have a CPG for management of that condition. Such guidelines have previously been shown to decrease broad-spectrum antimicrobial usage at freestanding children's hospitals, and their development is encouraged by the Infectious Diseases Society of America.^{12,32-34} The influence of initial dosing CPGs for vancomycin may be underestimated by us in this study because most of the

recommendations for vancomycin were for de-escalation or discontinuation (whereas the BCH CPG is focused on optimal initial dosing of vancomycin). Regular ASP monitoring of a predefined list of antibiotics could lead to repeated review of specific diagnoses to the possible exclusion of conditions for which reviewed antibiotics are not prescribed. However, our list composition closely resembles that of the only other nonfreestanding US children's hospital besides ours for which such information is currently available in the published medical literature.⁶ The total number of providers whose patients underwent ASP review was low, and therefore the impact of provider years in practice may be highly variable and dependent on practice patterns of a few physicians. However, one would expect that

institutions with a size and scope of practice similar to BCH would have comparable numbers of clinical faculty members. The extent of providers' exposure to ASPs before interaction with ours (eg, at previous places of employment or during residency and/or fellowship training) was not assessed for this study, and such experiences may have influenced provider decision-making.

CONCLUSIONS

The information gleaned from this study reveals an emphasis on patient diagnoses toward which stewardship efforts should be focused at nonfreestanding children's hospitals similar to BCH. On a broader scale, the procedural analyses of this study can be used by any ASP that performs prospective audit with feedback to inform priority areas regardless of institutional

size, setting, or scope of clinical practice. Areas for future emphasis as identified in this study include development of institutional CPGs that dovetail with patient diagnoses and usage of specific antimicrobial agents regularly prompting ASP recommendations. The importance of well-crafted CPGs in decreasing ASP workload cannot be overemphasized. This is particularly relevant for nonfreestanding children's hospitals similar to ours, within which resources for dedicated ASP support can be lacking relative to programs at freestanding centers (and also when compared with proposed minimum standards necessary to demonstrate ASP effectiveness).^{4,5,7,35} Finally, ASP team members should be aware that providers' previous clinical experiences may influence their current clinical practice patterns.

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