ORIGINAL ARTICLE

# Sustained Savings from a Longitudinal Cost Analysis of an Internet-Based Preapproval Antimicrobial Stewardship Program

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OBJECTIVE. To evaluate an internet-based preapproval antimicrobial stewardship program for sustained reduction in antimicrobial prescribing and resulting cost savings.

DESIGN. Retrospective cohort study and cost analysis.

METHODS. Review of all doses and charges of antimicrobials dispensed to patients over 6 years (July 1, 2005–June 30, 2011) at a tertiary care pediatric hospital.

RESULTS. Restricted antimicrobials account for 26% of total doses but 81% of total antimicrobial charges. Winter months (November–February) and the oncology and infant and toddler units were associated with the highest antimicrobial charges. Five restricted drugs accounted for the majority (54%) of charges but only 6% of doses. With an average approval rate of 91.5% (95% confidence interval [CI], 91.1%–91.9%), the preapproval antibiotic stewardship program saved $103,787 (95% CI, $98,583–$109,172) per year, or $14,156 (95% CI, $13,446–$14,890) per 1,000 patient-days.

CONCLUSIONS. A preapproval antimicrobial stewardship program effectively reduces the number of doses and subsequent charges due to restricted antimicrobials years after implementation. Hospitals with reduced resources for implementing postprescription review may benefit from a preapproval antimicrobial stewardship program. Targeting specific units, drugs, and seasons may optimize preapproval programs for additional cost savings.

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The Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society of America (PIDS) recommend implementation of mandatory antimicrobial stewardship programs (ASPs) in healthcare institutions.[1] ASPs are interventions that provide evidence-based approaches for appropriate antimicrobial use.[2,3] Although there are many types of ASPs, two common and well-evaluated strategies are (1) prior authorization for specific antimicrobials, or "preapproval," and (2) postprescription audit with intervention and feedback.[4] These programs effectively reduce the use of antimicrobials and the number of adverse drug reactions and *Clostridium difficile* infections, may reduce the spread of antimicrobial resistance, and reduce costs associated with antimicrobial use.[4-7] Postprescription programs have the best evidence of clinical benefit, according to IDSA.[4] However, they require extensive resources, as compared to preapproval systems, and thus may not be feasible for many hospitals. As an alternative, preapproval ASPs have good evidence of clinical benefit to support their use,[4] require fewer resources, and have resulted in short-term cost savings of $100,000–$900,000 per year.[8-15]

Currently, 61% of adult and 33% of pediatric infectious disease physicians report that their institutions already have an ASP, and a growing number of institutions are planning to start one.[16,17] The two leading barriers to ASP development are insufficient funding and lack of personnel.[16,17] Although optimizing patient outcomes and decreasing antibiotic-related adverse events are arguably the most important benefits of an ASP, demonstration of cost savings is essential to obtain support from hospital administration. Available cost data are limited to short-term evaluations of savings over periods of 4 months to 2 years,[8-10,12-14,18] and evidence of sustained cost savings from a preapproval ASP has not yet been shown. IDSA and SHEA have recommended research into the long-term impacts of formulary restriction and preapproval requirements.[4]

The Johns Hopkins Children's Center (JHCC), a 188-bed

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tertiary care pediatric center, upgraded the preapproval ASP initiated in 1983 to an internet-based system on July 1, 2005. A detailed description of this program has been published.[15] Physicians enter requests for approval of restricted antimicrobials on an online form, and the on-call pediatric infectious disease fellow automatically receives notification of the request and submits a response. Approved requests receive a designated duration of treatment, and the prescription is dispensed by the pharmacy. Antimicrobials are not dispensed if the request is denied, and providers may discuss with the infectious diseases team to optimize treatment. The initial evaluation of the internet-based ASP showed an 11.6% reduction in the number of dispensed doses without an increase in patient length of stay, improved provider satisfaction, a reduction in the number of delayed doses, and estimated cost savings of $370,000 in the first year.[15] In this study, we conducted a retrospective cohort study to determine whether a preapproval antimicrobial stewardship system led to sustained cost savings in the years following implementation.

## METHODS

### Study Design, Setting, and Patient Population

This was a retrospective cohort and cost analysis including all children who received antimicrobials at the JHCC from July 1, 2005 through June 30, 2011. The year of analysis aligned with fiscal year, from July 1 through June 30 of the following year. Records from the pediatric intensive care unit (PICU) and the emergency department were excluded because these units became exempt from preapproval of first doses of restricted antimicrobials. There were no other changes to the ASP. This study was approved by the Johns Hopkins Institutional Review Board.

### Variables and Data Sources

*Antimicrobial doses and charges.* We obtained records of prescribed doses of antimicrobials and their respective charges in US dollars from the inpatient financial database. The charges reflect not drug administration costs but purchase costs and hospital processing charges, as dictated by the state of Maryland's Health Services Cost Review Commission.[19] To account for inflation and changes in prices over time, we calculated an adjusted charge per dose as the average charge per dose over the entire study period for each antimicrobial. Total charges were calculated as the total doses of a drug multiplied by the that drug's adjusted charge per dose.

*Restriction classification.* Restricted antimicrobials in this study are those mandated by the Pharmacology and Therapeutics Committee at the Johns Hopkins Hospital (Appendix A), which is guided by the pediatric infectious disease department and the pediatric pharmacy. The list of restricted drugs remained constant during the study period.

*Duration of patient stay and patient complexity score.* The length of stay (LOS) in days and the patient complexity score for each included patient were obtained from JHCC's case-mix database and linked to financial data. Patient complexity score per visit was derived using the All-Patient Refined Diagnosis Related Group method and is expressed on a 4-point scale with 1 being least and 4 being most complex.[20]

*Approval rates.* The number of restricted antimicrobial prescription requests and the approval status were obtained from the JHCC online preapproval ASP database. Approval rates were calculated as the number of approved requests divided by the number of requests for each year, expressed as a percentage.

*Imputation of December 2008.* The month of December 2008 was an extreme outlier in which the total charges and the number of doses for both unrestricted and restricted antimicrobials were 3 times those of any other month, including other months of December. While this finding was correlated with unusually high numbers of respiratory syncytial virus infections and aggressive use of palivizumab, this correlation did not explain why use of all antimicrobials was elevated. The data from December 2008 skewed results. Therefore, we substituted the average values of the total charges, total doses, average charge per dose, and median LOS and patient complexity score from the other Decembers for the respective values of December 2008. All analyses incorporate this imputation.

### Statistical Analysis

The original database listed each observation as dispensed doses with the unique visit number, patient identification number, and other patient and drug information. Patients with extended stays tended to receive more antimicrobials. So as to not inflate the median LOS and complexity for these patients, the data were collapsed first into individual visits within each month and then into months stratified by restriction status. Total doses and charges were compared using Pearson's $\chi^2$ test, mean patient complexity score using $t$ tests with equal variance, mean charge per dose using $t$ tests with unequal variance, and median LOS using Wilcoxon rank-sum tests.

We computed multivariable linear regression models to examine which variables affected total monthly charges. Covariates included fiscal year (July 1–June 30), restriction status (1 for restricted, 0 for unrestricted), total doses in the month (continuous), average charge per dose (continuous), median LOS (continuous), patient complexity score (continuous), and winter, defined as November through February (1 for winter, 0 for nonwinter). The number of doses and the LOS reflect patient volume. In the final adjusted regression model, all of the above variables were included, as well as an interaction term between winter and restriction status. Data from the same month were clustered to account for similarities in prescribing practices in a given month. The final model considered data normality and linearity, colinearity, distribution of residuals, and the Akaike information criteria. All analyses were performed using Stata, release 12.0.[21]

*Cost savings.* The cost savings were calculated as follows:

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$$\text{cost savings} = (\text{cost if 100\% approval}) - (\text{actual charge})$$
$$= \frac{\text{restricted doses} \times \text{average charge per restricted dose}}{\text{average approval rate}} - (\text{restricted doses} \times \text{average charge per restricted dose}).$$

To provide a cost savings value standardized for patient volume, we calculated cost savings per 1,000 patient-days.

The implementation cost of our program was considered to be the cost of hiring an informatician for 3 weeks at a rate of $100 per hour, plus 33% fringe benefits, and 0.15 full-time equivalents (FTE) of an infectious disease physician or pharmacist with a salary of $120,000 per year, plus 33% fringe benefits. The annual maintenance costs were considered to be 0.01 FTE of an informatician with an annual salary of $100,000, plus 33% fringe benefits, and 0.10 FTE of an infectious disease physician or pharmacist with an annual salary of $120,000, plus 33% fringe benefits.

## RESULTS

### Charges and Doses

A total of 512,287 doses of antimicrobials were dispensed to 18,345 patients during 28,909 unique inpatient hospital visits from July 1, 2005 to June 30, 2011. Table 1 displays a summary and comparison between unrestricted and restricted antimicrobials for the entire study period. Restricted antimicrobials accounted for 81% of total charges and 26% of total doses. The average charge per dose of a restricted antimicrobial was 11 times that of an unrestricted antimicrobial ($49.11 vs $4.33, $P < .001$).

### Charges across Units

The total charges, charge per dose, and charge per 1,000 patient-days across pediatric units for the study period are presented in Table 2. The oncology, infant and toddler, and adolescent units incurred the highest total charges per 1,000 patient-days. This ranking remained after accounting for volume of doses or patient-days. The infant and toddler, oncology, and adolescent units prescribed the most expensive restricted antimicrobials, with average charges of $94.05, $51.08, and $44.93 per dose, respectively.

### Trends of Charges and Doses

The total monthly restricted charges exhibited a seasonal pattern, with higher charges in the winter months than in the summer months (Figure 1). This pattern was not seen for unrestricted charges, which remained steady across seasons.

Characteristics influencing charges were examined using linear regression (Table 3). The unadjusted results showed a decrease in monthly charge of $1,226 each year; however, this was not a significant trend ($P = .35$). Individually, the restriction status, the number of doses, median LOS, patient complexity, and the winter months affected total monthly charges ($P < .001$).

In a multiple linear regression of charges accounting for restriction status, doses, LOS, patient complexity, and winter, average monthly charges did not change over the 6 years ($P = .60$; Table 3). For each increase of 1 dose per month, the monthly charge increased approximately $16 ($P < .001$), similar to the average charge per dose of $16.48 for any antimicrobial, presented in Table 1. LOS and patient complexity no longer had a significant impact, because their effect on charge was mediated through restriction status and the number of doses. Finally, charges varied significantly between winter and nonwinter months and between the two restriction groups. In the winter, the monthly charges of unrestricted antimicrobials were $2,977 greater ($P = .20$) and the monthly charges of restricted antimicrobials were $48,198 greater ($2,977 + $45,221, $P < .001$) than the respective monthly charges during the rest of the year. Comparing restricted to unrestricted antimicrobials, the total charges of the restricted antimicrobials were an additional $131,677 in winter months ($86,456 + $45,221, $P < .001$) and $86,456 in nonwinter months ($P < .001$).

Five restricted antimicrobials accounted for the majority (54%) of total charges: palivizumab (21%), liposomal amphotericin B (18%), meropenem (10%), voriconazole (6%), and tobramycin (5%). Together these drugs accounted for

TABLE 1. Comparison of Costs and Recipient Characteristics for Unrestricted and Restricted Antimicrobials, July 1, 2005–June 30, 2011

| | Unrestricted | Restricted | Overall | *P* |
|---|---|---|---|---|
| Total charges, US$ (%) | 1,626,147 (19.44) | 6,737,590 (80.56) | 8,363,737 | <.001[a] |
| Total doses (%) | 375,083 (73.92) | 137,204 (26.08) | 512,287 | <.001[a] |
| Mean cost/dose, US$ (SD) | 4.33 (0.75) | 49.11 (16.95) | 16.48 (4.96) | <.001[b] |
| Median LOS, days (IQR) | 4 (4–4) | 8 (7–8) | 4 (4–4) | <.001[c] |
| Mean patient complexity score (SD) | 2.48 (0.66) | 3.01 (0.09) | 2.49 (0.07) | <.001[d] |

NOTE. IQR, interquartile range; LOS, length of stay; SD, standard deviation. Analysis after imputation of December 2008 data.
[a] From Pearson's $\chi^2$ test.
[b] From *t* test with unequal variance.
[c] From Wilcoxson rank-sum test.
[d] From *t* test with equal variance.

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TABLE 2. Total Charges, Average Charges per Dose, and Charges per 1000 Patient-Days by Pediatric Unit from July 1, 2005 to June 30, 2011

| | Total charges | | | Average charge/dose | | | Charges per 1,000 patient-days | | |
|---|---|---|---|---|---|---|---|---|---|
| Unit | U | R | Total | U | R | Total | U | R | Total |
| Oncology | 155,865 | 2,670,008 | 2,825,873 | 4.27 | 51.08 | 31.85 | 11,608 | 177,327 | 132,075 |
| Infant/toddler | 439,435 | 1,707,546 | 2,146,981 | 4.41 | 94.05 | 18.22 | 13,903 | 256,196 | 60,560 |
| Adolescent | 404,156 | 1,041,649 | 1,445,805 | 6.90 | 44.93 | 17.69 | 18,999 | 131,355 | 56,663 |
| School-age | 227,514 | 499,587 | 727,101 | 5.29 | 35.72 | 12.75 | 14,875 | 109,655 | 40,056 |
| Research | 50,700 | 90,862 | 141,562 | 6.48 | 28.47 | 12.85 | 15,548 | 88,819 | 36,655 |
| NICU | 332,276 | 1,010,768 | 1,343,044 | 2.62 | 43.80 | 8.95 | 7,861 | 121,647 | 29,868 |
| Psychiatry | 9,020 | 3,595 | 12,615 | 4.55 | 24.96 | 5.93 | 9,923 | 43,310 | 12,899 |
| Nurseries | 37,780 | 2,838 | 40,618 | 3.86 | 0.89 | 3.13 | 8,833 | 3,088 | 7,996 |

NOTE. Charges are in US dollars. Table sorted by unit with highest total charges per 1,000 patient-days. Analysis was performed on original data set without imputation of December 2008. NICU, neonatal intensive care unit; R, restricted; U, unrestricted.

only 6% of total doses prescribed. Again, there is evidence of seasonality, as palivizumab, a respiratory syncytial virus prophylactic agent given to high-risk infants, ranged from 10% of nonwinter charges to 30% of winter charges. When the adjusted charges regression was repeated excluding palivizumab (data not shown), winter months remained significantly more expensive than the remainder of the year ($P = .005$). The same antimicrobials accounted for the most charges regardless of the season (Appendix B).

There was a decrease in the number of unrestricted doses but not in that of restricted doses over the study period (Figure 1). Multiple linear regressions were conducted for doses, adjusting for year, charges, LOS, patient complexity, and winter months (data not shown). With each passing year, we found that the average monthly unrestricted antimicrobial use decreased by 162 doses ($P < .001$); however, there was no change in the average monthly number of doses of restricted antimicrobials ($P = .448$). We did not detect a significant change

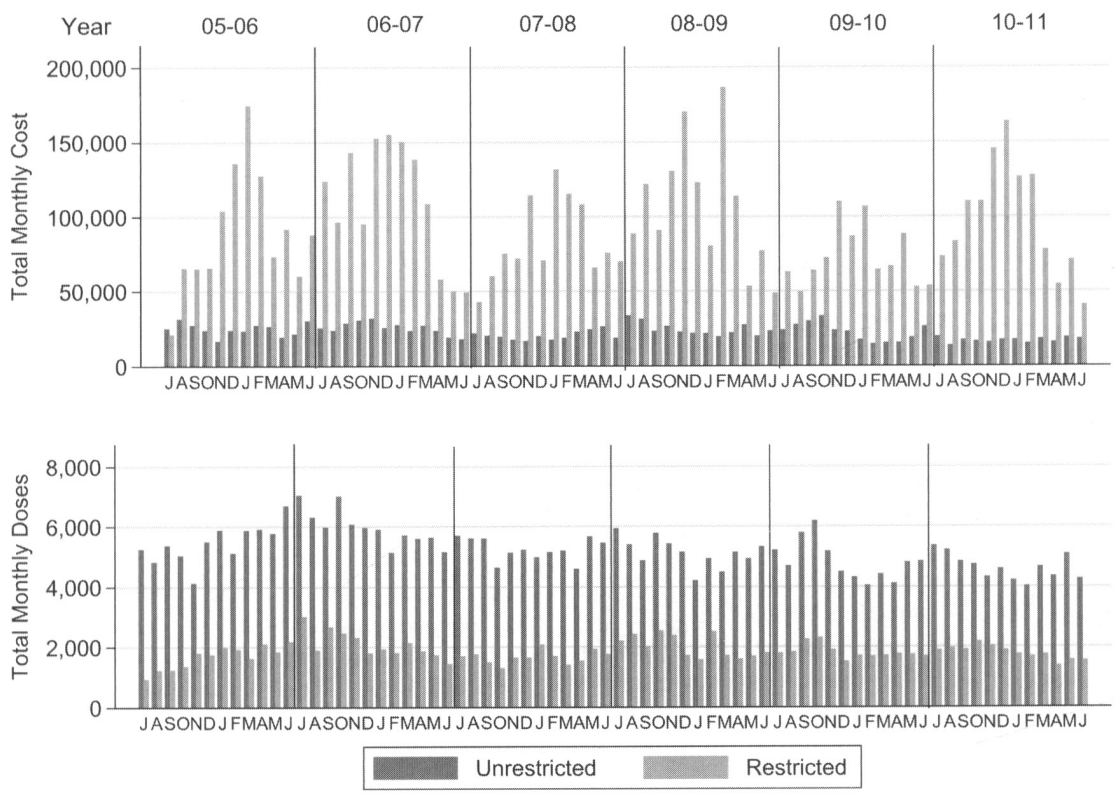



FIGURE 1. Total monthly charges and doses stratified by restriction status and displayed by month, over the 6-year study period, July 2005–June 2011. Vertical lines demarcate fiscal years.

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TABLE 3. Results of Linear Regressions of Average Total Monthly Charges

| Variable | Unadjusted[a] Additional monthly charge (95% CI) | P | Adjusted[b] Additional monthly charge (95% CI) | P |
|---|---|---|---|---|
| Year[c] | −1,226 (−3,826 to 1,373) | .35 | 438 (−1,321 to 2,197) | .62 |
| Restricted | 70,992 (62,241–79,744) | <.001 | 86,456 (58,298–114,614) | <.001 |
| Doses | −18 (−20 to −15) | <.001 | 16 (11–21) | <.001 |
| Median length of stay | 17,111 (14,768–19,455) | <.001 | 3,601 (−880 to 8,082) | .11 |
| Mean patient complexity | 129,037 (110,878–147,196) | <.001 | 21,334 (−27,392 to 70,059) | .39 |
| Winter[d] | 24,325 (16,453–32,196) | <.001 | 2,977 (−1,594 to 7,548)[g] | .20 |
| Winter × restricted[e] | ... | ... | 45,221 (29,550–60,893)[h] | <.001 |

NOTE. Charges are in US dollars. All models are clustered on individual months. Analysis was done after December 2008 imputation. CI, confidence interval.

[a] Single linear regressions.

[b] Multiple linear regression adjusted for all variables presented in table.

[c] Years are defined as July 1–June 30; a continuous variable.

[d] Winter months defined as November–February; a dichotomous variable.

[e] Interaction term of winter months and restriction status.

[g] Additional monthly cost for unrestricted antimicrobials between winter and nonwinter.

[h] Additional monthly cost of restricted antimicrobials between winter and nonwinter equals $45,221 + $2,977.

in LOS ($P = .08$), and there was a marginal decrease in patient complexity score in the study period (−0.01; $P = .008$).

### Cost Savings

Analysis of the antimicrobial stewardship database showed an average annual approval rate of 91.5% (range, 90.7%–93.1%; 95% CI, 91.1%–91.9%). Based on this approval rate, the average savings from the ASP was $103,787 (95% CI, $98,583–$109,172) per year, or $14,156 (95% CI, $13,446–$14,890) per 1,000 patient-days (Table 4). Initiation and annual maintenance costs were estimated to be $39,900 and $17,290, respectively (Table 4). On the basis of these estimates, the program would save $46,597 in the first year and $86,497 in each subsequent year.

## DISCUSSION

In this first longitudinal cost analysis of a preapproval ASP, we found a sustained annual savings of approximately $104,000, or $14,000 per 1,000 patient-days. After costs of implementation are considered, the program is cost saving (Table 4). As there was no significant change in charges over the 6 years, it is anticipated that the estimated annual savings can be projected into the foreseeable future.

Previous studies examining preapproval ASPs found a range of yearly cost savings from $100,000 to $900,000 in adult hospitals[8-10,12-14,18] and from $150,000 to $400,000 in pediatric hospitals.[11,15,22] These were all short-term studies comparing the 3–24 months before and after implementation of the ASP. Our estimated yearly cost savings were lower than those reported in previous studies.[11,15,22] Differences in patient volume, patient populations, time periods, and drug costs make comparisons of cost savings across studies problematic. Exclusion of the PICU in this study is an important difference when comparing our $104,000 annual savings estimate to the initial $370,000 estimate found by Agwu et al[15] after the introduction of JHCC's internet-based ASP.

Recently, two studies assessed long-term savings of adult postprescription ASPs.[23,24] Both studies demonstrated greater annual or per-patient-day savings than ours; however, there are differences in program type, patient volume, and patient populations. It is important to remember that these postprescription programs are also more resource and personnel intensive than preapproval programs and, although preferred, may not be feasible for the majority of healthcare facilities in the United States.

As healthcare institutions begin to develop new ASPs, focusing on high cost factors may be a particularly useful strategy for those with limited resources. The results of this study provide evidence of 3 characteristics associated with higher antimicrobial costs. The winter season incurred significantly higher charges, after patient volume and complexity were considered, because more of the expensive antimicrobials were prescribed. Winter charges remained significantly higher even after palivizumab, which accounted for 30% of winter charges, was excluded. This may be due to increased empiric broad-spectrum antimicrobial use for respiratory infections before culture results are available. Second, a small number of high-cost drugs (palivizumab, meropenem, liposomal amphotericin B, voriconazole, and tobramycin; 6% of all drugs dispensed) accounted for the majority of antimicrobial charges (54%). Third, the oncology, infant and toddler, and adolescent units had the highest charges per patient-day for all antimicrobials. Again, the ranking remained unchanged after palivizumab was excluded. If an institution cannot afford to have an ASP encompassing the entire hospital, it could target the winter, certain broad-spectrum or particularly high-

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TABLE 4. Estimated Cost Savings

| | Formula | Total | Annual | Per 1,000 patient-days[b] | First year | Each subsequent year |
|---|---|---|---|---|---|---|
| A. Total restricted doses | | 137,204 | 22,867 | 3,119 | | |
| B. Total restricted cost[a] | $A \times 49.26$ | 6,738,088 | 1,123,015 | 153,170 | | |
| C. Restricted cost if 100% approval | | | | | | |
| Average | $B/0.9154$ | 7,360,813 | 1,226,802 | 167,325 | | |
| LL 95% CI | $B/0.9193$ | 7,329,586 | 1,221,598 | 166,616 | | |
| UL 95% CI | $B/0.9114$ | 7,393,119 | 1,232,186 | 168,060 | | |
| D. Savings | | | | | | |
| Average[c] | $C - B$ | 622,725 | 103,787 | 14,156 | | |
| LL 95% CI | $C$ (LL) $- B$ | 591,498 | 98,583 | 13,446 | | |
| UL 95% CI | $C$ (UL) $- B$ | 655,030 | 109,172 | 14,890 | | |
| Savings accounting for cost of program | | | | | | |
| Estimated annual savings | | | | | 103,787 | 103,787 |
| Start-up cost | | | | | 39,900[d] | NA |
| Cost of maintenance | | | | | 17,290[e] | 17,290 |
| Total savings | | | | | 46,597 | 86,497 |

NOTE. Except for A, data are in US dollars. Analysis done after December 2008 imputation. Based on approval rate of 91.54% (95% CI, 91.14%–91.93%). CI, confidence interval; LL, lower limit; NA, not applicable; UL, upper limit.

[a] Restricted cost = number of restricted doses × average price per dose for restricted antimicrobials.

[b] There were a total of 43,991 days on which a patient received a restricted antimicrobial.

[c] Average savings = cost of denied restricted doses = cost if all restricted doses were approved − cost of restricted doses approved.

[d] Cost of hiring an informatician for 3 weeks paid $100/h with 33% fringe benefits plus 15% full-time equivalent (FTE) of an infectious disease physician or pharmacist paid $120,000 with 33% fringe benefits.

[e] Cost of 1% FTE of an informatician paid $100,000 salary with 33% benefits and 10% FTE of an infectious disease physician or pharmacist paid $120,000 with 33% fringe benefits.

cost drugs, and the individual units that may account for the majority of antimicrobial costs. As costs are directly related to the number of doses prescribed, this strategy could potentially offer the greatest impact on inappropriate prescriptions averted, in addition to providing the most savings. Further studies examining interventions targeted to these characteristics may be warranted.

There are several limitations to this study. First, we have focused on cost and not appropriateness of antimicrobial prescribing. Even if we have shown a reduction in costs, high costs do not necessarily reflect inappropriate prescribing practices. Although outcomes were not directly measured, we did not see evidence of worse outcomes, as patient LOS did not change and patient complexity decreased marginally across the study period. In addition, as the reduction of costs in this study is directly related to a decrease in the number of antimicrobial doses, we can expect the benefits of reduced antimicrobial usage, such as a likely reduction in adverse reactions due to inappropriate antimicrobial prescriptions and potentially decreased rates of *C. difficile* infection and subsequent antimicrobial resistance.[4-7] However, we did not specifically study these effects.

Second, our cost savings are an estimate. We could not monitor replacement of denied restricted antimicrobial requests with unrestricted prescriptions. However, unrestricted antimicrobials are less than a tenth as expensive as restricted ones, so they are unlikely to negate the cost savings. It is more likely that the savings are a conservative estimate, as they do not account for the costs of drug administration, conversion of intravenous to oral dose, [25] or cost savings from averted adverse medication events.[26] In addition, they do not include drug costs and resulting potential savings from the PICU and the emergency department, which likely have high use of broad-spectrum restricted antimicrobials. Finally, we imputed values for December 2008 because it was an extreme outlier. Performing a sensitivity analysis and excluding this month rather than imputing its values would have led to a substantial underestimate of total costs. By imputing the values rather than including the original data, we have further underestimated the potential costs and cost savings.

Third, because we saw a decrease in unrestricted antibiotic use during the study period, one may wonder whether an external factor independent of the ASP led to decreases in the prescription of unrestricted antibiotics. It is possible that increasing awareness of the detriments of unnecessary antibiotic use led physicians to be more vigilant about prescribing antibiotics for nonbacterial infections; however, this was not specifically studied. The ASP leads to conversations between infectious disease physicians and prescribing doctors. The education provided during these discussions, a strength of a preapproval ASP, may have also contributed to the overall decrease in antibiotic prescriptions and sustained savings.

Finally, because this study was conducted at a pediatric academic hospital, the results may not be generalizable to

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institutions that are nonacademic, nonpediatric, or have differently structured ASPs. We attempted to make the cost savings more applicable to nonacademic settings by using salary estimates of fully trained professionals.

The IDSA, SHEA, and PIDS recommend ASPs in all healthcare institutions and prefer that a postprescription review program be implemented.[1] Indeed, postprescription strategies show the most evidence of improved clinical outcomes in addition to cost savings.[4] Because postprescription ASPs require full-time active surveillance by a clinician or pharmacist, which is time-consuming and resource intensive, they may not be a viable option for many healthcare institutions.[2,3,27] Since only 18%–58% of physicians report receiving compensation for their ASP activities,[17,28] the cost saving from a preapproval ASP potentially could be used to compensate providers and pharmacists who staff the program. Our results demonstrate that a preapproval ASP can lead to sustained savings and is a reasonable first step for institutions looking to establish an ASP.

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## APPENDIX A

## LIST OF RESTRICTED ANTIMICROBIALS

Acyclovir, amikacin, liposomal amphotericin B, azithromycin IV, ampicillin/sulbactam, aztreonam, cefepime, cefotaxime, cefoxitin, ceftazidime, ciprofloxacin, colistimethate, cytomegalovirus intravenous immunoglobulin (IVIG), dalfopristin/quinupristin, daptomycin, ertapenem, fluconazole, foscarnet, ganciclovir, gatifloxacin, itraconazole, linezolid, meropenem, moxifloxacin, micafungin, oseltamivir, palivizumab, piperacillin/tazobactam, posaconazole, ribavirin, valacyclovir, vancomycin, voriconazole, all nonformulary.

## APPENDIX B

## CHARGES FOR THE MOST EXPENSIVE DRUGS

TABLE B1. The Most Expensive Drugs

| | Overall | | Winter | | Nonwinter | |
|---|---|---|---|---|---|---|
| Drug | Charges, % | Rank | Charges, % | Rank | Charges, % | Rank |
| Palivizumab | 20.93 | 1 | 34.18 | 1 | 19.81 | 3 |
| Liposomal amphotericin B | 17.45 | 2 | 14.53 | 2 | 10.48 | 1 |
| Meropenem | 9.59 | 3 | 8.50 | 3 | 10.20 | 2 |
| Voriconazole | 5.57 | 4 | 5.11 | 5 | 6.64 | 5 |
| Tobramycin | 5.19 | 5 | 3.38 | 8 | 5.95 | 4 |
| Cytomegalovirus–intravenous immunoglobulin | 4.82 | 6 | 5.35 | 4 | 5.62 | 8 |
| Linezolid | 4.62 | 7 | 3.39 | 7 | 5.40 | 6 |
| Ampicillin | 4.57 | 8 | 3.54 | 6 | 4.39 | 7 |
| Caspofungin | 3.16 | 9 | 3.36 | 9 | 3.00 | 9 |
| Cefepime | 2.04 | 10 | 1.23 | 11 | 2.70 | 10 |
| Micafungin | 1.86 | 11 | 1.47 | 10 | 2.17 | 11 |

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