Original Article

Evaluation of different antimicrobial stewardship models at a rehabilitation hospital: An interrupted time series (ITS) study

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Abstract

Objective: To evaluate different prospective audit-and-feedback models on antimicrobial prescribing at a rehabilitation hospital.

Design: Retrospective interrupted time series (ITS) and qualitative methods.

Setting: A 178-bed rehabilitation hospital within an academic health sciences center.

Methods: ITS analysis was used to analyze monthly days of therapy (DOT) per 1,000 patient days (PD) and monthly urine cultures ordered per 1,000 PD. We compared 2 sequential intervention periods to the baseline: (1) a period when a dedicated antimicrobial stewardship (AMS) pharmacist performed prospective audit and feedback and provided urine culture education followed by (2) a period when ward pharmacists performing audit and feedback. We conducted an electronic survey with physicians and semistructured interviews with pharmacists, respectively.

Results: Audit and feedback conducted by an AMS pharmacist resulted in a 24.3% relative reduction in total DOT per 1,000 PD (incidence rate ratio [IRR], 0.76; 95% confidence interval [CI], 0.58–0.99; *P* = .04), whereas we detected no difference between ward pharmacist audit and feedback and the baseline (IRR, 1.20; 95% CI, 0.53–2.70; *P* = .65). We detected no statistically significant change in monthly urine-culture orders between the AMS pharmacist period and the baseline (level coefficient, 0.81; 95% CI, 0.65–1.01; *P* = .07). Compared to baseline, the ward pharmacist period showed a statistically significant increase in urine-culture ordering over time (slope coefficient, 1.04; 95% CI, 1.01–1.08; *P* = .02). The barrier most identified by pharmacists was insufficient time.

Conclusions: Audit and feedback conducted by an AMS pharmacist in a rehabilitation hospital was associated with decreased antimicrobial use.

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Antimicrobial resistance is recognized as one of the 10 biggest threats to public health by the World Health Organization.[1] Antimicrobial stewardship programs (ASPs) have been developed to reduce unnecessary use of antimicrobials and to promote the judicious prescribing of antimicrobials.[1–4] The greatest attention has been paid to hospital ASPs where prospective audit and feedback and other multifaceted interventions have reduced antimicrobial use and antimicrobial resistance without increasing patient harm.[5]

Rehabilitation hospitals have comparatively fewer ASP resources, yet opportunities to optimize antimicrobial prescribing have been identified in this setting. In one study, 19% of antibiotic prescriptions in a rehabilitation hospital were unnecessary, and 50% were deemed inappropriate based on organism-drug mismatch or duration of therapy.[6] Despite this recognized need,[6,7] the most effective model of delivery in the inpatient rehabilitation setting is not known.

One of the core strategies of ASPs is prospective audit and feedback, which involves routine assessment of antimicrobial prescriptions and providing feedback to prescribers, most often by dedicated ASP pharmacists in consultation with infectious disease (ID) physicians.[2–4] Despite the extensive evidence supporting this model of ASP within acute-care hospitals, whether or not these results translate into rehabilitation settings is not known.[6,8–11]

We evaluated 2 sequential models of prospective audit and feedback performed at a rehabilitation hospital that included (1) prospective audit and feedback provided by a dedicated antimicrobial stewardship (AMS) pharmacist who consulted with an ID physician and (2) audit and feedback provided by ward pharmacists at the rehabilitation hospital in addition to their existing clinical duties. We evaluated the impact of these different models on antimicrobial prescribing. Additionally, we assessed pharmacist and physician experiences and perceived barriers to antimicrobial stewardship in the inpatient rehabilitation setting.

Methods

Ethics

This study was conducted in accordance with national and institutional standards, as well as the Declaration of Helsinki. This study received institutional approval by the Sunnybrook Research Ethics Board. Written informed consent from study participants was obtained at the beginning of the participant surveys.

Study design and setting

This study was conducted at St. John's Rehab (SJR) Hospital, a 178-bed rehabilitation program within Sunnybrook Health Sciences Centre, a multisite, tertiary-care, academic institution. Models of prospective audit and feedback were evaluated over 3 periods using both quantitative and qualitative methods. The baseline period spanned January 1, 2017, through December 31, 2017. The first intervention period consisted of a dedicated AMS pharmacist conducting prospective audit and feedback from January 1, 2018, to January 31, 2019. No audit and feedback occurred between February 1, 2019, and April 30, 2019. The second intervention period consisted of ward pharmacists conducting prospective audit and feedback from May 1, 2019, until April 30, 2020.

Interventions

Prior to 2017, prospective audit-and-feedback services were not provided within the rehabilitation hospital. In 2018, formal audit and feedback was provided by a trained AMS pharmacist. The pharmacist had previously worked as a full-time AMS pharmacist at the acute-care site, conducting audit and feedback among a variety of patient populations for 14 months. Twice weekly, the AMS pharmacist reviewed all patients on systemic antimicrobial therapy and reviewed cases identified as challenging with the on-call ID physician at a prearranged time, prior to recommendations being provided. Suggestions were documented in the electronic medical record, and verbal feedback was provided to prescribers by the AMS pharmacist. In addition, the AMS pharmacist delivered 4 educational sessions to nurses and prescribers on appropriate urine-culture ordering practices.

When the AMS pharmacist period ended in January of 2019 due to reductions in hospital funding, the ward pharmacists remained committed to providing ongoing antimicrobial stewardship services in addition to their regular clinical duties. This model of stewardship represents a second intervention that was implemented in February 2019. During the transition between the 2 models (February–April 2019), there was no prospective audit and feedback.

During the ward pharmacist period, 7 ward pharmacists assessed new antibiotic orders for patients under their usual clinical coverage. No formal stewardship training was provided to ward pharmacists prior to the initiation of the intervention, due limitations in resources. Throughout the entire study period, pharmacists and prescribers had access to the institution antimicrobial stewardship application, which was launched in November 2015 and included local antibiograms and dosing and treatment guidelines. Pharmacists documented their reviews in the electronic patient record, and suggestions for optimization were provided to prescribers using verbal feedback. There was no prearranged review time with an ID physician during the ward pharmacist period, but a dedicated AMS pharmacist from the acute-care hospital and an ID physician were available for consultation on an as-needed basis. Throughout both intervention periods, 13 prescribers (staff physicians) were practicing at the rehabilitation hospital.

Study outcomes

The primary outcome was the monthly total antimicrobial consumption measured by days of therapy (DOT) per 1,000 patient days (PD). Secondary outcomes included the number of urine cultures ordered monthly, the total number of suggestions, and suggestion acceptance rates. Antimicrobial stewardship suggestions included antibiotic discontinuation, optimization of dose, shortening or extending duration, and changing agent. Urine cultures were included as a diagnostic test of interest given their recognized role in driving unnecessary antibiotic prescribing, which are frequently the focus of ASP feedback.[12] Additional qualitative outcomes, such as the perceived successes and challenges of the ward pharmacist AMS model, were collected from the ward pharmacists using semistructured interviews. Staff physicians were surveyed to assess their perceptions of differences in audit and feedback among the models.

Data collection

Antibiotic days of therapy were extracted from the electronic patient record (MediTech). The numbers of urine cultures ordered per month were provided by the microbiology department. Bed occupancy and patient days were provided by the health records department. Patient diagnostic groups were obtained from data submitted to the National Rehabilitation Reporting System (NRS), within the Canadian Institute for Health Information (CIHI). For qualitative data collection, pharmacist interviews were conducted in person using a 5-item interview questionnaire (Appendix A). One investigator (J.C.) performed all interviews, and all answers were transcribed in written format. Physicians' perceptions and experiences with the different models of pharmacist audit and feedback were collected anonymously through the online survey platform Qualtrics CoreXM. The survey consisted of 6 multiple-choice questions and 1 open-ended question (Appendix B). It was developed by 4 study investigators (J.C., M.E., P.L., and J.L.). Survey questions were tested by 3 of the investigators (J.L., P.L., and M.W.). Surveys were distributed to participants on July 6, 2020. A follow-up e-mail was sent on August 19, 2020, and the survey closed on August 21, 2020. No incentives were offered for participation.

Statistical analysis

An interrupted time series (ITS) analysis was conducted to analyze the outcomes of monthly DOT per 1,000 PD and monthly urine cultures ordered per 1,000 PD. In this analysis, we performed a segmented regression analysis for both measures. A level and slope-change impact model was chosen, and monthly data were modeled using a Poisson regression with the total number of patient days and urine cultures set as the offset variable in their respective models. Testing for autocorrelation and seasonality were carried out by inspecting the residuals from the autocorrelation and partial autocorrelation plots. No evidence of autocorrelation or seasonality was detected. To account for overdispersion and heteroscedasticity, robust sandwich variance estimators were used.

The proportion of pharmacist-reviewed cases for which suggestions were made and accepted during the 2 intervention periods were compared using the χ^2 test. Survey and interview results were analyzed descriptively. Transcribed responses from the pharmacist interview were reviewed and categorized into common themes through the identification of recurring words. All statistical analyses were performed using R version 3.4.3 statistical software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics

During the 12-month baseline period, 2,569 patients were admitted to St. John's Rehab Hospital. During the 13-month AMS pharmacist period, 2,836 patients were admitted to this hospital and during the 12-month ward pharmacist period, 2,525 patients were admitted. Orthopedic conditions were the most common diagnosis on admission across all 3 periods (Table 1).

Antimicrobial use

Implementation of prospective audit and feedback conducted by a trained AMS pharmacist was associated with a statistically significant reduction in total DOT per 1,000 PD when compared to the baseline period (incidence rate ratio [IRR], 0.76; 95% confidence interval [CI], 0.58–0.99; $P = .04$). We detected no significant change in the trend of antimicrobial use for this period (slope coefficient 1.01; 95% CI, 0.96–1.06; $P = .69$) (Table 2 and Fig. 1). Conversely, no statistically significant difference in total DOT per 1,000 PD was detected when comparing prospective audit and feedback completed by ward pharmacists, to baseline with respect to level (IRR, 1.20; 95% CI, 0.53–2.70; $P = .65$) or trend (slope coefficient, 0.96; 95% CI, 0.91–1.01; $P = .11$).

Urine culture ordering

During the baseline period, we detected a trend toward decreased urine-culture ordering (slope coefficient, 0.98; 95% CI, 0.97–1.00; $P = .04$) (Table 2 and Fig. 2). Implementation of prospective audit and feedback conducted by a trained AMS pharmacist did not result in a significant change in level (IRR, 0.81; 95% CI, 0.65–1.02; $P = .07$) or slope (IRR, 0.99; 95% CI, 0.96–1.01; $P = .27$) when compared to the baseline period. Similarly, prospective audit and feedback completed by ward pharmacists resulted in no significant differences in level compared to the baseline period (IRR, 0.85; 95% CI, 0.53–1.34; $P = .47$); however, an increase in the slope of monthly urine cultures ordered was noted (slope coefficient, 1.04; 95% CI, 1.01–1.08; $P = .02$).

Suggestions and acceptance rates

The total number of cases reviewed and suggestions made during the 2 intervention periods are summarized in Table 3. Suggestions were made on a greater proportion of cases reviewed during the AMS pharmacist period compared to the ward pharmacist period (24% vs 13%, $P < .001$). Suggestion acceptance rates were similar throughout both intervention periods (86% vs 88%; $P = .56$). Moreover, 30 suggestions (14%) made by the AMS pharmacist were reviewed with an ID physician. Notably, the recommendation to discontinue antibiotics was made more frequently during the AMS pharmacist period than during the ward pharmacist period (32% vs 17%; $P < .001$).

Physician survey and pharmacist interviews

In total, 8 responses were generated following the dissemination of the online survey to 13 physicians. Of these 8 responses, 6 (75%) of the physicians had been practicing at SJR throughout all 3 periods. Most physicians (75%) felt that they had interacted with a pharmacist, had received suggestions, and had changed their antimicrobial therapy more often during the AMS pharmacist period than during the ward pharmacist period. When asked to provide their experience with audit and feedback, 50% of physicians felt that they had interacted less, 50% of physicians felt that they had received fewer suggestions, and 43% felt that they had changed their antibiotic plan less often when ward pharmacists conducted prospective audit and feedback (Fig. 3).

In total, 7 ward pharmacists (100% of pharmacists at SJR) were interviewed in person to gather insight into the factors contributing to success and challenges to the provision of prospective audit and feedback in their practice. The dedicated AMS pharmacist was not interviewed. All 7 ward pharmacists were experienced practitioners (practicing >5 years), and 6 (86%) practiced at SJR through all 3 periods. The participants subjectively estimated that stewardship activities required an individual mean of 2 hours weekly (15 hours weekly among 7 pharmacists). We identified 3 common themes that participants felt contributed to success and 6 common barriers faced in providing prospective audit and feedback (Fig. 4). The most common barrier identified by participants was insufficient time (N = 6, 86%). All participants noted that collaboration among the pharmacists or rapport with prescribers contributed to success in provision of prospective audit and feedback. The institution-developed Antimicrobial Stewardship Application was also commonly mentioned (N = 3, 43%) as a helpful resource for the participants in lieu of direct access to ID expertise.

Discussion

In this ITS study, introduction of a dedicated AMS pharmacist was associated with a significant reduction in antimicrobial use compared to the baseline, which was not sustained when relying on the existing ward pharmacists alone. This difference was likely explained by the higher number of suggestions provided by the AMS pharmacist and highlights the value of having dedicated antimicrobial stewardship resources within the rehabilitation hospital setting.

Previous studies have demonstrated that resource intensive stewardship programs can reduce unnecessary antimicrobial use in rehabilitation hospital settings. In 2012, Lewis et al[10] evaluated the impact of implementing a multidisciplinary antimicrobial stewardship team with ID expertise and senior administration involvement and reported a 37.3% reduction in days of therapy

Table 1. Patient Population Admitted by Diagnosis

Admission Diagnosis	Baseline Period, No. (%)	Antimicrobial Stewardship Pharmacist Period, No. (%)	Ward Pharmacist Period, No. (%)
Total patients, no.	2,569	2,836	2,525
Orthopedic conditions	879 (34.2)	977 (34.5)	789 (31.3)
Debility	307 (12.0)	399 (14.1)	335 (13.3)
Cardiac conditions	364 (14.2)	381 (13.4)	262 (10.4)
Major multiple trauma	228 (8.9)	280 (9.9)	251 (9.9)
Stroke	254 (9.9)	253 (8.9)	268 (10.6)
Medically complex	258 (10.0)	235 (8.3)	218 (8.6)
Amputation of limb	96 (3.7)	116 (4.1)	126 (5.0)
Burns	50 (2.0)	54 (1.9)	64 (2.5)
Brain dysfunction	65 (2.5)	53 (1.9)	78 (3.1)
Spinal cord dysfunction	30 (1.2)	44 (1.6)	71 (2.8)
Neurological conditions	22 (0.9)	23 (0.8)	33 (1.3)
Pulmonary conditions	16 (0.6)	21 (0.7)	30 (1.2)

Table 2. Segmented Regression Analysis Results

Variable	Level, Rate Ratio (95% CI)	P Value	Trend, Slope (95% CI)	P Value
Total antimicrobial DOT per 1000 PD				
Baseline (Jan 1–Dec 31, 2017)			1.00 (0.96–1.04)	.95
Antimicrobial stewardship pharmacist period compared to baseline (Jan 1, 2018–Jan 1, 2019)	0.76 (0.58–0.99)	.04	1.01 (0.96–1.06)	.69
Ward pharmacists period compared to baseline (May 1–April 30, 2020)	1.20 (0.53–2.70)	.65	0.96 (0.91–1.01)	.11
Urine cultures performed per 1,000 PD				
Baseline (January 1–December 31, 2017)			0.98 (0.97–1.00)	.04
Antimicrobial stewardship pharmacist period compared to baseline (Jan 1, 2018–Jan 1, 2019)	0.81 (0.65–1.02)	.07	0.99 (0.96–1.01)	.27
Ward pharmacists period compared to baseline (May 1–Apr 30, 2020)	0.85 (0.53–1.34)	.47	1.04 (1.01–1.08)	.02

Note. CI, confidence interval; DOT, days of therapy; PD, patient days.

(DOT) per 1,000 patient days (PD). More recently, Tedeschi et al[11] demonstrated a significant reduction in *C. difficile* infections and antimicrobial consumption following the implementation of ID physician bedside consultation and ID-led education program aimed at appropriate prescribing. Relying on an ID physician alone is resource intensive and may not be as sustainable as a model that incorporates a multidisciplinary team including a dedicated ASP pharmacist. Our acute-care hospital and many others have successfully implemented such programs in acute care,[13–16] and our findings suggest that their extension to rehabilitation settings has significant impact on reducing antimicrobial use.

Multiple factors might have contributed to the differences noted between the 2 models evaluated. First, there were systemic process differences between the AMS pharmacist model and the ward pharmacist model. Ward pharmacists conducted assessments and provided feedback in addition to managing all nonstewardship patient care tasks. Time dedicated to prospective audit and feedback was therefore dependent on existing nonstewardship workload and created significant audit-and-feedback process

variation among ward pharmacists which were reflected in semistructured interview results. Because prospective audit and feedback was the primary focus for the AMS pharmacist, a streamlined process for clinical assessment and prescriber feedback was more feasible.

Second, specialized training in antimicrobial stewardship combined with increased accessibility to an ID specialist may have contributed to increased comfort in patient assessments and increased confidence in approaching prescribers by the AMS pharmacist. Similar findings were noted in the study by Tedeschi et al,[11] in which integrating an ID physician into the rehabilitation team with the provision of education and bedside consultation resulted in decreased antimicrobial use and reduced antimicrobial associated harms such as *Clostridioides difficile* infections.

Although a statistically significant decrease in total DOT was not observed in the ward pharmacist period, 5 data points showed decreases in succession (Fig. 1). Although the reasons for this observation are unknown, it is logical to speculate that, over time, ward pharmacists became more comfortable with ID content and
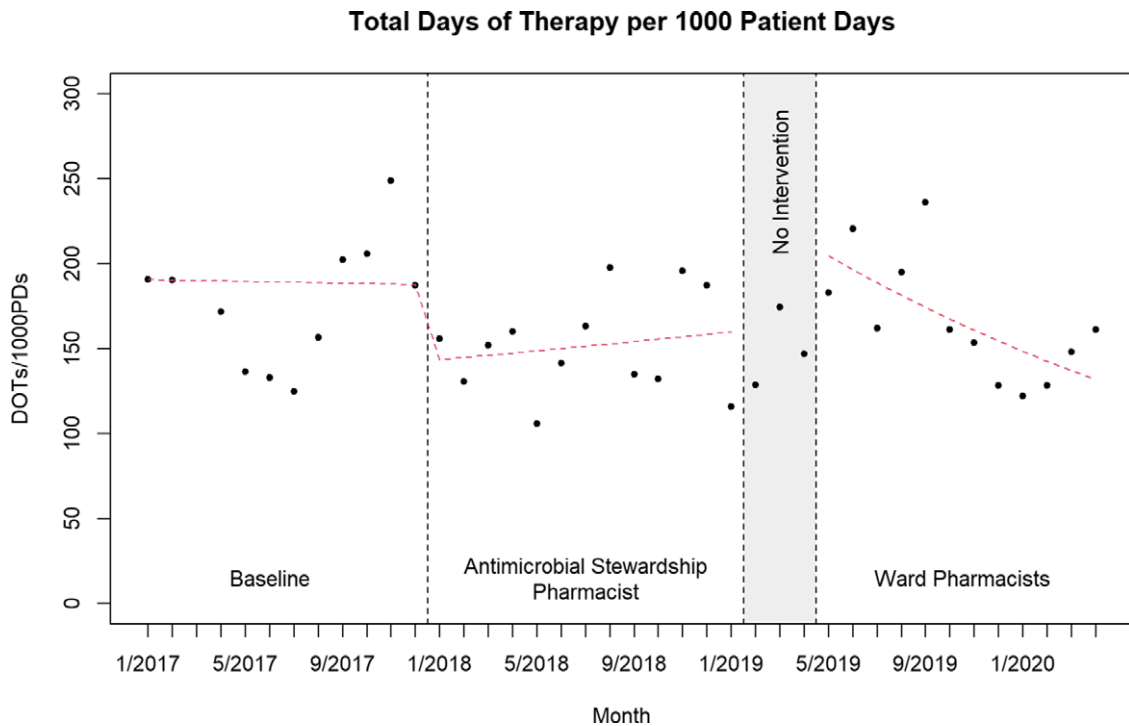
Total Days of Therapy per 1000 Patient Days

Fig. 1. Monthly antimicrobial consumption in days of therapy (DOTs) per 1,000 patient days (PD) during the baseline period (January 1 to December 31, 2017), the antimicrobial stewardship pharmacist period (January 1, 2018, to January 1, 2019), and the ward pharmacist period (May 1 to April 30, 2020).
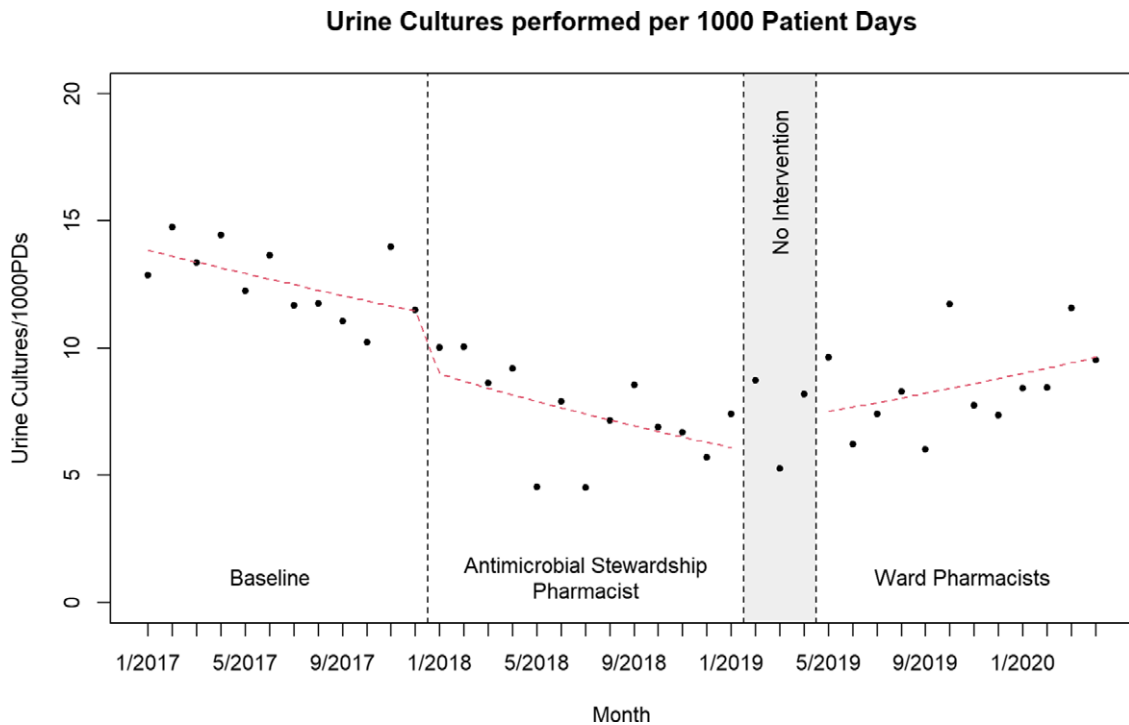
Urine Cultures performed per 1000 Patient Days

Fig. 2. Monthly urine cultures ordered per 1,000 patient days (PD) over the baseline period (January 1 to December 31, 2017), the antimicrobial stewardship pharmacist period (January 1, 2018, to January 1, 2019), and the ward pharmacists period (May 1 to April 30, 2020).

stewardship intervention, in addition to adjusting to new workload pressures. We were unable to evaluate the ward pharmacist model beyond April 2020 due to the coronavirus disease 2019 (COVID-19) pandemic, which affected patient flow, bed occupancy, and reasons for admission. Although a ward pharmacist model may be appealing to institutions with limited stewardship resources, further studies are required to determine whether such a model can achieve improvements in antimicrobial prescribing.

Asymptomatic bacteriuria remains a frequent indication for inappropriate antimicrobial use; thus, we aimed to minimize

Table 3. Suggestions Provided to Prescribers Within Prospective Audit and Feedback Conducted by Antimicrobial Stewardship Pharmacist Compared to Ward Pharmacists

Variable	Antimicrobial Stewardship Pharmacist Period (N = 905), No. (%)	Ward Pharmacists Period (N = 1074), No. (%)	P Value
Total suggestions	218 (24)	141 (13)	<.001
Suggestion details	Antimicrobial Stewardship Pharmacist Suggestions (N = 218), No. (%)	Ward Pharmacists Suggestions (N = 141), No. (%)	P Value
Suggestions accepted	187 (86)	124 (88)	.56
Suggestions reviewed with ID physician	30 (14)	Not applicable[a]	. . .
Discontinue	70 (32)	17 (12)	<.001
Other interventions	148 (68)	124 (88)	<.001

Note. ID, infectious disease.
[a]Total number of reviews with ID physicians not documented; there was no pre-arranged review time between the ward pharmacists and an ID physician.
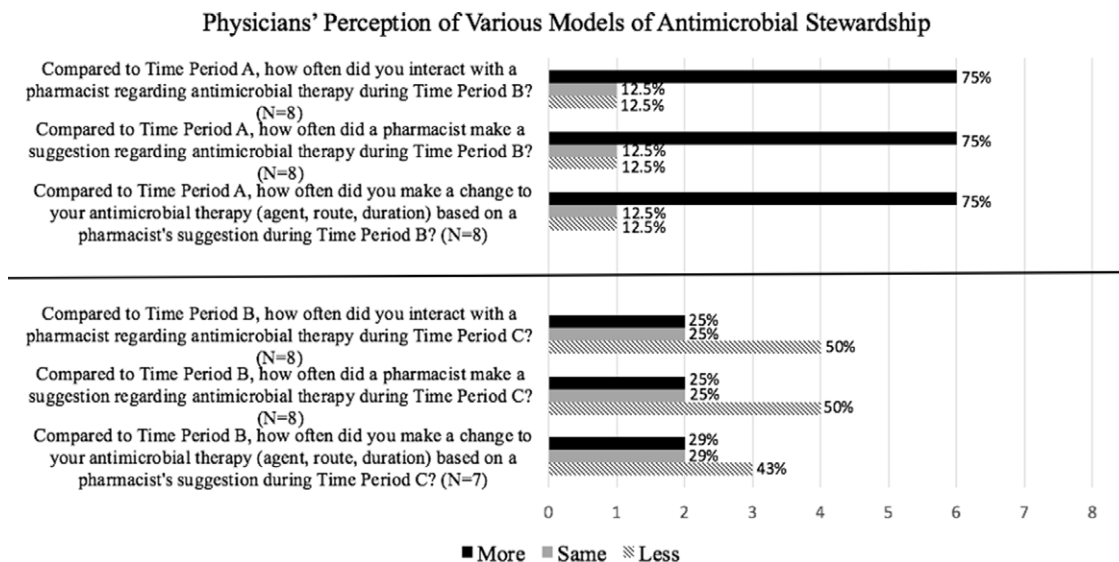

Fig. 3. Physicians' perceptions toward varying models of antimicrobial stewardship in a rehabilitation setting. Time period A: before January 2018, the baseline period. Time period B: January 2018–January 2019, audit and feedback provided by antimicrobial stewardship pharmacist. Time period C: January 2018–January 2019, audit and feedback provided by Ward pharmacists.

unnecessary urine-culture ordering through the provision of education to have downstream effects of reduced antimicrobial prescribing. We detected no significant change in monthly urine cultures when comparing the AMS pharmacist period to baseline; however, the initial baseline period already exhibited a significant slope decrease. The lack of difference is likely related to urine-culture ordering practices that occurred in advance of audit and feedback by multiple different providers.[12] Conversely, a trend toward increased urine-culture prescribing was noted during the ward pharmacist period. This finding may simply represent the waning effects of education over time. Educational initiatives surrounding inappropriate urine culture ordering were implemented exclusively during the AMS pharmacist period. Interestingly, this increasing trend was perceived by the ward pharmacists; this theme emerged as a barrier in the semistructured interviews.

This study had several limitations. First, the main outcome of this study were aggregate measures of antimicrobial use, which may not fully capture changes in antibiotic prescribing behavior.

For instance, clinical indications for antimicrobial use were not collected, and as a result, further analyses evaluating appropriateness could not be carried out. However, secondary outcomes evaluating types of interventions being suggested in both stewardship models provides some insight into appropriateness. Secondly, unmeasured confounding factors may have affected our results, such as concurrent antimicrobial stewardship interventions or changes in the patient population or prescribers over a 3-year time span. The ITS does provide the ability to overcome some internal threats to validity because it evaluates the impacts longitudinally.[17] Thirdly, the qualitative assessment had significant limitations because recall bias may have had a profound impact. Specifically, physicians' recollection of their practice 2 years prior, during the AMS pharmacist period, might have been heavily influenced by the memory of each pharmacist interaction related to antimicrobial therapy. The ward pharmacists interacted with physicians consistently to provide various patient care recommendations, which may have affected the ability to recall all
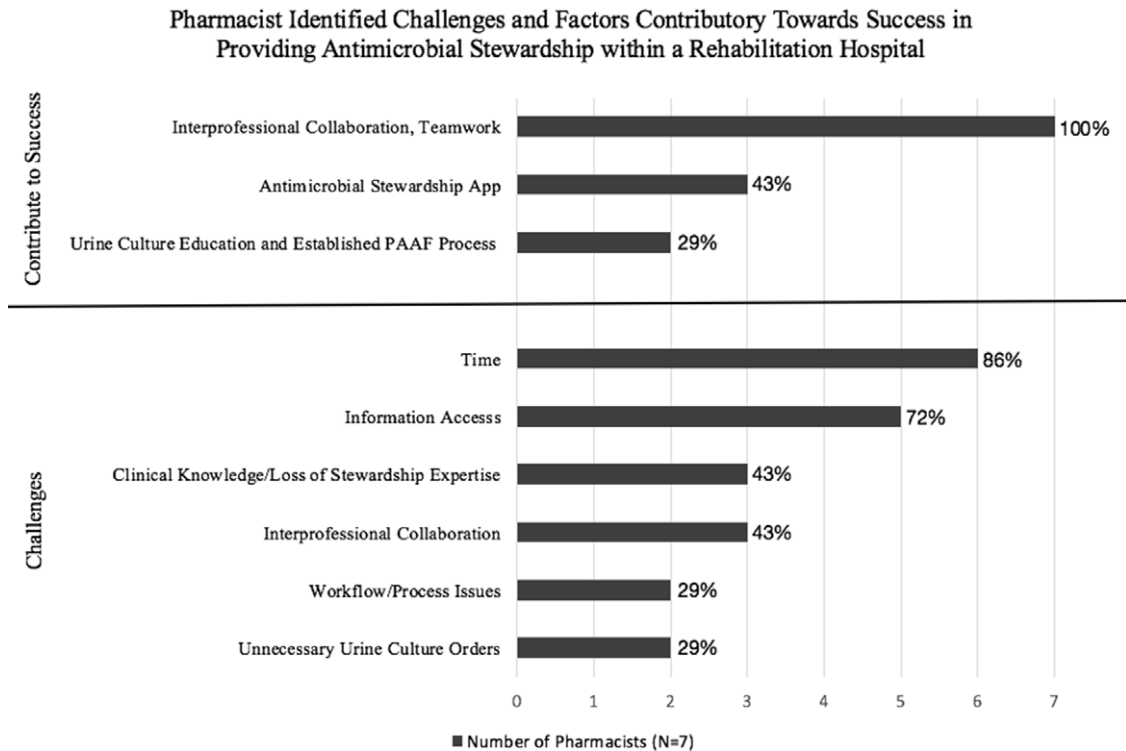
Fig. 4. Ward pharmacist perceptions toward ward pharmacist–led antimicrobial stewardship model in a rehabilitation setting.

antimicrobial-related feedback. Finally, the generalizability of this study is limited because it was a single-center study involving a limited number of prescribers.

In this ITS study, prospective audit and feedback conducted by a trained antimicrobial stewardship pharmacist significantly reduced antimicrobial use compared to the baseline and ward-pharmacist led audit-and-feedback periods. Insufficient time and confidence in subject matter were barriers to the provision of prospective audit and feedback by ward pharmacists in a rehabilitation setting. These findings support the need for antimicrobial stewardship resources in rehabilitation settings, and further research is necessary to determine the most resource efficient model.

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