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MAJOR ARTICLE

Barriers to Adherence to Antimicrobial Stewardship Postprescription Review and Feedback For Broad-Spectrum Antimicrobial Agents: A Nested Case-Control Study

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Background. Postprescription review and feedback (PPRF) is one of the most common strategies in antimicrobial stewardship program (ASP) intervention. However, disagreements between the prescribers and ASP personnel can occur. The aim of the present study was to identify the factors associated with nonadherence to PPRF intervention.

Methods. The present retrospective nested case-control study was performed at a tertiary care center, which has been conducting a once-weekly PPRF for carbapenems and piperacillin/tazobactam since 2014. Nonadherence to ASP recommendations was defined as the failure of the primary care team to modify or stop antimicrobial therapy 72 hours after the issuance of PPRF recommendations. Factors associated with nonadherence to PPRF intervention were identified using multivariate logistic regression analysis.

Results. In total, 2466 instances of PPRF in 1714 cases between April 2014 and September 2019 were found. The nonadherence rate was 5.9%, and 44 cases were found in which carbapenems or piperacillin/tazobactam continued to be used against PPRF recommendations. Factors associated with nonadherence to PPRF recommendations were a previous history of hospitalization within 90 days (adjusted odds ratio [aOR], 2.62; 95% confidence interval [CI], 1.18–5.81) and a rapidly fatal McCabe score at the time of PPRF intervention (aOR, 2.87; 95% CI, 1.18–6.98). A review of the narrative comments in the electronic medical records indicated that common reasons for nonadherence were "the patient was sick" (n = 12; 27.3%) and "the antimicrobial seemed to be clinically effective" (n = 9; 20.5%).

Conclusions. Nonadherence to PPRF recommendations was relatively uncommon at the study institution. However, patients with a severe disease condition frequently continued to receive broad-spectrum antimicrobials against PPRF recommendations. Understanding physicians' cognitive process in nonadherence to ASP recommendations and ASP interventions targeting medical subspecialties caring for severely ill patients is needed to improve ASP.

Keywords. adherence; antimicrobial stewardship program; audit and feedback; broad-spectrum antimicrobials; postprescription review and feedback.

Antimicrobials are commonly used in the acute care setting. Recent studies found that approximately 30% of patients received antimicrobials during hospitalization [1, 2], and 33% of antimicrobial prescriptions were considered inappropriate [3]. A multicenter study in Japan revealed an inappropriate antimicrobial use rate of approximately 40% for the inpatient population at acute care hospitals [4]. The overuse of antimicrobials has contributed to the development of resistant organisms, hampering infection control and treatment [5]. The antimicrobial stewardship program (ASP) in healthcare settings is essential for optimizing antimicrobial therapy to improve individual patient care, reduce hospital costs, and prevent the emergence of antimicrobial resistance (AMR).

Two core strategies are recommended for the healthcare setting: preauthorization and postprescription review and feedback (PPRF) [6]. Postprescription review and feedback alone or limited PPRF also showed effectiveness in decreasing inappropriate antimicrobial prescription and reducing AMR [7–10]. However, these strategies are labor-intensive, and institutions with limited sources may encounter difficulties in implementing them.

Although PPRF may generally be considered to be effective, disagreements between the prescribers and ASP personnel can arise. Previous studies evaluating the efficacy of PPRF showed that nonadherence to ASP recommendations ranged from 15% to 33% [11–13]. The barrier to appropriate antimicrobial prescription is likely to be multifactorial [12, 13]. Although prescriber-related factors (eg, knowledge and attitude) and patient-related factors (eg, underlying conditions

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and disease severity) were associated with nonadherence in previous studies [12–14], factors may differ among healthcare systems. The aim of the present study was to investigate the frequency of nonadherence to PPRF intervention and to identify the factors associated with nonadherence to recommendations against the use of broad-spectrum antimicrobials at a Japanese tertiary care center.

METHODS

Ethical Statement

The institutional review board at Tokyo Metropolitan Tama Medical Center approved this study.

Study Design and Setting

The present retrospective nested case-control study was conducted at Tokyo Metropolitan Tama Medical Center, a 790-bed tertiary care center with 29 subspecialties, including a division of infectious diseases and an ASP. All of the physicians in the division of infectious diseases were also actively involved in antimicrobial stewardship activities.

An ASP run by a multidisciplinary team was implemented in April 2014. The team consisted of 2 infectious disease physicians, 2 infectious disease fellows, 1 clinical pharmacist, 1 microbiology laboratory technician, and an infection control nurse. Before its implementation, there was no form of antimicrobial stewardship except for an infectious disease (ID) consultation service, which was begun in July 2013 by a physician with American Board of Internal Medicine Infectious Diseases certification [15]. Details of the PPRF intervention at the study institution have been described elsewhere [9]. A clinical pharmacist routinely monitored all inpatient antimicrobial consumption, and all hospital wards were included in the PPRF intervention. All the members attended a once-weekly PPRF meeting. Once the appropriateness of broad-spectrum antimicrobials (ie, carbapenems and piperacillin/tazobactam) was determined, their use was documented in each patient's electronic medical records (EMRs). Carbapenem use was considered appropriate for the treatment of febrile neutropenia, infections only susceptible to carbapenem antimicrobials, and infections for which carbapenems were conventionally considered to be first-line agents, whereas piperacillin/tazobactam use was considered appropriate for the following: treatment of febrile neutropenia, empiric therapy for healthcare-associated infections (HAIs), definitive therapy for HAIs for which piperacillin/tazobactam was considered the best choice based on clinical conditions and culture results, and polymicrobial infections for which piperacillin/tazobactam was the preferred therapy [9].

For all patients with inappropriate antimicrobial use, our recommendations on antimicrobial use were issued by the designated ID physician directly contacting the primary care providers by telephone and through documentation in the EMR. Nonadherence to ASP recommendations was defined as the failure of the primary care team to modify or stop antimicrobial therapy 72 hours or more after the issuance of the PPRF recommendations.

Participants

Patients older than 18 years who received a once-weekly PPRF were included. From our PPRF database, cases of nonadherence to PPRF recommendations between April 2014 and September 2019 were first identified, then 3 controls per case consisting of patients for whom the prescribers accepted the PPRF recommendations were randomly selected from the cohort in the same period to minimize selection bias. Cases in which ID consultation was performed within 72 hours after PPRF and cases in which an ID physician recommended continuing broad-spectrum antimicrobial administration were excluded. The relevant patients in the case group were excluded before selecting the controls. If patients received multiple PPRF in 1 episode, only the first was included. Multiple episodes in the same patient were counted individually. Patient consent was waived because the study was retrospective, involved no interaction with patients, and PPRF was one of the ASP interventions routinely performed as part of a hospital-wide quality improvement project. The institutional review board at the study institution approved this study.

Data Collection

All data on ASP intervention were prospectively collected, whereas individual data on cases of nonadherence to ASP were retrospectively collected by a manual review of the EMR. Data on patient demographics, preexisting medical conditions, medical exposures, colonization of multidrug-resistant organisms (MDROs), source of infections, antimicrobial treatment information, laboratory information, patients' condition at the time of PPRF, including their McCabe score [16], prescriber information (ie, department, postgraduate year, decision-maker), length of stay, in-hospital mortality, readmission, and adverse events after PPRF were collected. The reasons for nonadherence were also collected by reviewing each patient's EMR. Multidrug-resistant organisms in the study institution included methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococci*, carbapenem-resistant *Enterobacteriaceae*, multidrug-resistant (MDR) *Acinetobacter* spp, MDR *Pseudomonas* spp, and extended-spectrum cephalosporin-resistant organisms based on the definition of the US Centers for Disease Control and Prevention [17]. Each patient had a representative primary care provider (PCP) except patients in the department of critical care medicine and some medical or surgical departments (eg, general internal medicine and general surgery) in which care was administered by multiple team members. A prescriber was defined as the patient's

PCP or a physician who prescribed broad-spectrum antimicrobial agents at the time of a PPRF. Adverse events after a PPRF included *Clostridioides difficile* infection (CDI) developing within 3 months of antimicrobial administration, acute kidney injury (AKI) developing within 1 month of antimicrobial administration, and MDRO acquisition confirmed by clinical culture specimens during index hospitalization. The definition of CDI and AKI was based on the clinical practice guidelines of the Infectious Diseases Society of America, the Society for Healthcare Epidemiology of America [18], and Kidney Disease: Improving Global Outcomes [19].

Statistical Analysis

In univariate analyses, categorical variables were compared using the χ^2 test or Fisher's exact test as appropriate, and continuous variables were compared using the Mann-Whitney *U* test. All tests for significance were 2-tailed, with $P < .05$ considered significant.

Multivariate logistic regression was done to predict the factors associated with nonadherence to PPRF intervention. Factors related to nonadherence in previous studies, including patients' underlying illness (eg, diabetes mellitus) [12], and prescriber-related factors, including surgeons [14] and senior physicians [13], were forced into the final model. In addition, for factors with $P < .1$ on univariate analysis with clinical plausibility, we assessed multicollinearity by examining the variance inflation factors and 2-by-2 tables to ensure the independence of the explanatory variables. Variables were retained in the final model if $P < .05$. The Hosmer-Lemeshow test was used to assess goodness of fit for the logistic regression model. All analyses were performed using Stata version 15 (StataCorp, College Station, TX).

RESULTS

In total, 2466 PPRF interventions in 1714 cases were found in the cohort between April 2014 and September 2019. Of the 2466 PPRF interventions, 854 involved inappropriate use and 50 involved nonadherence (5.9%). The nonadherence rate by year was 12.3% (2014), 6.8% (2015), 7.9% (2016), 4.2% (2017), 4.6% (2018), and 3.7% (2019). After excluding 2 PPRF interventions with ID consultation obtained within 72 hours after a PPRF recommendation to continue using broad-spectrum antimicrobial agents and 4 PPRF interventions within the same episode, 44 cases of continued carbapenem or piperacillin/tazobactam use against PPRF recommendations were subsequently identified. In addition, 132 controls were selected. The median day of carbapenem or piperacillin/tazobactam use between the initial antimicrobial administration date and the PPRF date was 5 days (interquartile range, 4–7 days). The demographic, clinical, and laboratory characteristics of the patients at the time of PPRF in both the case and control groups are shown in Table 1. In the nonadherence group, the percentage of patients with a history of hospitalization, chemotherapy, and steroid use before index hospitalization was greater (68.2% vs 39.4%, 18.2% vs 5.3%, 45.5% vs 15.9%), and more patients had a rapidly fatal McCabe score at the time of PPRF intervention (47.7% vs 27.7%). Hematology/oncology (n = 41; 23.3%), gastroenterology (n = 29; 16.5%), general surgery (n = 26; 14.8%), and critical care medicine (n = 25; 14.2%) accounted for more than 60% of all departments. Intra-abdominal infections were the most common (n = 38; 21.6%), followed by febrile neutropenia (n = 23; 13.1%). The details of the infection sources are shown in Supplementary Figure 1.

Hematology/oncology (n = 16; 36.4%), critical care medicine (n = 9; 20.5%), and gastroenterology (n = 8; 18.2%) accounted for more than 70% of the nonadherence group. Of the 44 nonadherence cases, 11 (25%) involved care given by 3 hematology/oncology physicians. In the multivariate model, the factors independently associated with nonadherence to PPRF intervention were a previous history of hospitalization within 90 days (adjusted odds ratio [aOR], 2.62; 95% confidence interval [CI], 1.18–5.81) and a rapidly fatal McCabe score at the time of PPRF intervention (aOR, 2.87; 95% CI, 1.18–6.98) (Table 2). There was no statistical difference in the incidence of adverse events and key clinical outcomes related to antimicrobial practice between the 2 groups (Table 3). In the 44 cases with nonadherence to PPRF recommendations, the main reasons documented in the EMR were "the patient was sick" (n = 12; 27.3%), "the antimicrobial seemed to be clinically effective" (n = 9; 20.5%), "the patient was immunocompromised" (n = 7; 15.9%), "the patient was colonized with an MDRO" (n = 4; 9.1%), and "the patient was scheduled to be transferred or discharged soon" (n = 4; 9.1%) (Table 4).

DISCUSSION

The present study described the frequency of nonadherence to PPRF recommendations for broad-spectrum antimicrobial use at a tertiary care center and demonstrated that patient-related factors, including a previous history of hospitalization and higher severity of illness at the time of PPRF intervention, were independently associated with nonadherence even after adjusting for previously reported factors associated with nonadherence. Although the overall nonadherence rate was low at the study institution, some unique findings related to continuing broad-spectrum antimicrobial use against PPRF recommendations provided a better understanding of prescribing behaviors in the treating physicians.

As seen in Table 2, a previous history of hospitalization within 90 days and a rapidly fatal McCabe score at the time of PPRF intervention were independent factors in nonadherence. A previous history of hospitalization was thought to be a risk factor for acquiring MDRO [20]. One possible explanation for

Table 1. Clinical Characteristics

Characteristics	Nonadherence (n = 44)	Adherence (n = 132)	*P* Value
Patient Demographics			
Age, median (IQR), years	68 (59–79)	71 (59–80)	.546
Male sex, n (%)	26 (59.1)	74 (56.1)	.861
Charlson Comorbidity Index Score, n (%)			.128
<2	5 (11.4)	34 (35.8)	
2–5	30 (68.2)	78 (59.1)	
>5	9 (20.5)	20 (15.2)	
Diabetes mellitus, n (%)	8 (18.2)	30 (22.7)	.673
Liver disease, n (%)	5 (11.4)	27 (20.5)	.258
Residential status before admission, n (%)			.362
Home	36 (81.8)	109 (82.6)	
Nursing home or long-term care facility	2 (4.6)	3 (2.3)	
Chronic care hospital	2 (4.6)	2 (1.5)	
Acute care hospital	4 (9.1)	18 (13.6)	
Healthcare exposure within 30 days, n (%)	42 (95.5)	115 (87.1)	.164
History of hospitalization within 90 days, n (%)	30 (68.2)	52 (39.4)	.002
History of chemotherapy within 28 days, n (%)	8 (18.2)	7 (5.3)	.013
History of steroid use within 28 days, n (%)	20 (45.5)	21 (15.9)	<.001
Any antimicrobial allergy, n (%)	5 (11.4)	17 (12.9)	1.000
Surgery performed before PPRF during index hospitalization, n (%)	1 (2.3)	36 (27.3)	<.001
Chemotherapy performed before PPRF during index hospitalization, n (%)	8 (18.2)	23 (17.4)	1.000
Steroid use before PPRF during index hospitalization, n (%)	19 (43.2)	39 (29.6)	.100
HSCT performed before PPRF during index hospitalization, n (%)	5 (11.4)	6 (4.6)	.145
History of MDRO acquisition within 1 year before PPRF, n (%)	9 (20.5)	23 (17.4)	.656
Clinical and Laboratory Characteristics at the Time of PPRF			
Onset, n (%)			.141
Community, nonhealthcare-associated	14 (31.8)	23 (17.4)	
Community, healthcare-associated	5 (11.4)	18 (13.6)	
Nosocomial	25 (56.8)	91 (68.9)	
Antimicrobial use before initiation of PPRF antimicrobials, n (%)	34 (77.3)	87 (65.9)	.191
Department, n (%)			.007
Medicine	29 (65.9)	66 (50.0)	
Critical care medicine	9 (20.5)	16 (12.1)	
Surgery	6 (13.6)	50 (37.9)	
ICU stay, n (%)	9 (20.5)	19 (14.4)	.348
Rapidly fatal McCabe score, n (%)	21 (47.7)	30 (22.7)	.002
ANC <500 /μL, n (%)	2 (4.6)	6 (4.6)	1.000
WBC, median (IQR) $\times 10^3/\mu L$	7.9 (5.5–11.0)	6.9 (4.2–10.8)	.474
CRP, median (IQR) mg/dL	4.6 (1.9–9.4)	4.4 (1.5–8.9)	.709
Mechanical ventilation use, n (%)	4 (9.1)	11 (8.3)	1.000
Vasopressor use, n (%)	4 (9.1)	7 (5.3)	.471
Central venous catheter use, n (%)	16 (36.4)	41 (31.1)	.578
ECMO, n (%)	2 (4.6)	3 (2.3)	.600
Prescribers' PGY, n (%)			.043
1–3	2 (4.6)	25 (18.9)	
4–7	26 (59.1)	72 (54.6)	
>7	16 (36.4)	35 (26.5)	
Male prescribers, n (%)	34 (77.3)	97 (73.5)	.693
Prescribing decision made by, n (%)			.053
Single physician	32 (72.7)	74 (56.1)	
Team	12 (27.3)	58 (43.9)	

Abbreviations: ANC, absolute neutrophil count; CRP, C-reactive protein; ECMO, extra-corporeal membrane oxygenation; HSCT, hematopoietic stem cell transplantation; ICU, intensive care unit; IQR, interquartile range; MDRO, multidrug-resistant organism; PPRF, postprescription review with feedback; PGY, postgraduate year; WBC, white blood cell.

Table 2. Factors Associated With Nonadherence to PPRF Intervention[a]

Variables	Univariate Analyses, OR (95% CI)	*P* Value	Multivariate Analyses, aOR (95% CI)	*P* Value
Charlson Comorbidity Index Score				
<2		Ref.		
2–5	2.62 (0.93–7.32)	.067		
>5	3.06 (0.90–10.41)	.074		
History of hospitalization within 90 days	3.30 (1.52–7.36)	.002	2.62 (1.18–5.81)	.018
Surgery performed before PPRF during index hospitalization	0.06 (0.01–0.47)	<.001		
Department at the Time of PPRF				
Medicine		Ref.		
Critical care medicine	1.28 (0.51–3.23)	.601		
Surgery	0.27 (0.11–0.71)	.008		
Rapidly fatal McCabe score at the time of PPRF	3.10 (1.42–6.75)	.002	2.87 (1.18–6.98)	.020
Prescribers' PGY				
1–3		Ref.		
4–7	4.5 (0.99–20.40)	.050		
>7	5.71 (1.20–27.11)	.028		
Prescribing decision made by single physician	2.10 (0.94–4.85)	.053		

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; PGY, postgraduate year; PPRF, postprescription review with feedback; Ref., reference.

[a]The Hosmer-Lemeshow test was used for goodness-of-fit for logistic regression with a *P* value of .38. Variables considered but not included in the multivariate analysis due to multicollinearity, and limited events were a history of chemotherapy within 28 days, history of steroid use within 28 days, and past medical history of diabetes mellitus or liver disease.

the history of hospitalization as a factor in nonadherence is that physicians tend to continue prescribing broad-spectrum antimicrobial agents out of concern to prevent HAIs caused by MDROs. Moreover, physicians may have taken patients' previous history of MDRO colonization into account when deciding on the type of antimicrobial therapy because MDRO colonization persists for more than 1 year in some patients [21]. Even though our ASP personnel reviewed the EMR carefully to decide the appropriateness of antimicrobial use based on predetermined criteria, there may have been a discrepancy with regard to antimicrobial treatment between the ASP personnel and prescribers who cared for patients at their bedside.

The rapidly fatal McCabe score at the time of PPRF intervention is likely to be an indicator of greater disease severity. The McCabe score is normally used to estimate the likelihood of survival in patients with Gram-negative bacteremia [16] and was also shown to be an even better predictor of survival in other infections [22]. Critically ill patients tend to receive prolonged broad-spectrum antimicrobials, which are often unnecessary or inappropriate, and antimicrobial overtreatment is a frequent phenomenon in critical care settings [23]. In the current study, more than one fourth of the nonadherence cases involved the continued use of broad-spectrum antimicrobials due to the severity of the patients' condition.

Previous studies have revealed that physicians caring for critically ill patients perceived AMR to be a substantial problem, and their perception of ASP seemed favorable [24, 25], but fear of treatment failure or a worse clinical outcome in critically ill patients may discourage physicians from de-escalating or discontinuing antimicrobial therapy despite inappropriate use. Hence, ASP in critical care settings is particularly important. Although these situations differed from those in the present

Table 3. Adverse Events and Outcomes

Variables	Nonadherence (n = 44)	Adherence (n = 132)	*P* Value
Total duration of antimicrobial therapy during index hospitalization, median (IQR) days	16 (10–42)	14 (10–28)	.302
Total duration of PPRF antimicrobial therapy during index hospitalization, median (IQR) days	12 (10–19)	11 (6–16)	.063
CDI developing within 3 months after PPRF, n (%)	2 (4.6)	3 (2.3)	.600
AKI developing within 1 month after PPRF, n (%)	12 (29.3)	20 (16.8)	.112
MDRO acquisition after PPRF during index hospitalization, n (%)	2 (4.6)	11 (8.3)	.522
LOS from the date of PPRF to discharge, median (IQR) days	21 (10–54)	21 (8–43)	.637
LOS from the date of admission to PPRF, median (IQR) days	16 (8–36)	15 (7–26)	.421
In-hospital mortality, n (%)	8 (18.2)	19 (14.4)	.629
Readmission within 1 month after discharge, n (%)	7 (15.9)	15 (11.4)	.436

Abbreviations: AKI, acute kidney injury; IQR, interquartile range; CDI, *Clostridioides difficile* infection; LOS, length of stay; MDRO, multidrug-resistant organism; PPRF, postprescription review with feedback.

Table 4. Reasons for Nonadherence to Postprescription Review and Feedback Intervention

Reasons	% (n = 44)
Patient-Related Factors	
"The patient was sick."	27.3% (n = 12)
"The patient was immunocompromised."	15.9% (n = 7)
"The patient was colonized with an MDRO."	9.1% (n = 4)
"The patient was scheduled to be transferred or discharged soon."	9.1% (n = 4)
"The patient had neutropenia."	2.3% (n = 1)
"The patient's CRP level was high."	2.3% (n = 1)
"The patient was allergic to multiple antimicrobials."	2.3% (n = 1)
Prescriber-Related Factors	
"The antimicrobial seemed to be clinically effective."	20.5% (n = 9)
"I would like to continue giving antimicrobials, just in case."	2.3% (n = 1)
"The primary care provider was unavailable."	2.3% (n = 1)
Unknown	6.8% (n = 3)

Abbreviations: CRP, C-reactive protein; MDRO, multidrug-resistant organism.

study, rational antimicrobial use may not worsen clinical outcomes in these contexts, and PPRF can be safely implemented in the intensive care unit [8, 26]. In addition, handshake stewardship, characterized by a rounding-based, in-person approach to feedback, was effective in reducing antimicrobial use [27]. Multifaceted approaches, including education, direct communication, timely ID consultation, sharing of surveillance data, and PPRF, may be the key to promoting ASP further among physicians caring for severely ill patients [8, 27–29].

In this study, a relatively low rate of nonadherence was observed from the start of PPRF. Previous studies revealed that the nonadherence rate ranged from 15% to 33% [11–13]. The main possible explanation for the lower nonadherence rate in the present study compared with previous studies was that the authors telephoned the prescribing physicians directly whenever they detected inappropriate use, thus improving understanding of the importance of appropriate antimicrobial prescription among treating physicians [30]. It is ironic that the ID physicians' act of telephoning the prescribing physicians may have contributed to the relatively high adherence rate due to the cultural background of paternalistic leadership common in Asia, including Japan [31]. In addition, we had already embarked on other ASP, such as reviewing and monitoring sterile site cultures and surveilling antimicrobial consumption before initiating PPRF. A study conducted in 5 academic centers concluded that PPRF was more effective when performed in a hospital with an established ASP [11]. In the current study, nonadherence to PPRF intervention slowly decreased from 12.3% in 2014 to 3.7% in 2019, suggesting the value of maintaining ASP and establishing PPRF as a part of a hospital-wide initiative.

With regard to the characteristics of individual prescribers in the nonadherence group, physicians in hematology/oncology and critical care medicine who may have treated critically ill patients accounted for more than half the cases of nonadherence. Fear of possible, future complications and anxiety about overlooking an infection were reported as prescriber-related factors of inappropriate antimicrobial use [32–36] and may explain why more than 40% of nonadherence cases in our study showed continued use of broad-spectrum antimicrobials against PPRF recommendations due to the severity of the patients' condition or their immunocompromised status. Moreover, it is noteworthy that the prescribing physicians in one fourth of the nonadherence cases were frequently the same hematology/oncology physicians. Antimicrobial stewardship intervention for patients with hematologic malignancies is indeed challenging due to the complexity of the cases, the patients' immunocompromised status, and high mortality related to invasive infections [37]. One possible reason for nonadherence in such cases is that these physicians in hematology/oncology might have had a strong opinion about their antimicrobial prescription policy and believed PPRF to be an unwelcome intrusion. One reason for a number of nonadherence cases (ie, continuing broad-spectrum antimicrobial use against PPRF recommendations) was the perceived clinical effectiveness of the agents. This subjective assessment may have derived from prescribers' past clinical experience. In fact, the inertia of current practices was thought to reflect a lack of provider motivation to change inappropriate antimicrobial use [33]. Such "outlier" physicians may have had legitimate reasons for nonadherence, which may not always have been recorded in the EMR [38]. However, it is equally possible that these physicians were more conservative in their views and thus less inclined to adopt innovative strategies, as seen in the diffusion of innovation theory discussed by Rogers [39]. Although the prescribers in the present study were not directly interviewed because the study was retrospective, their knowledge (eg, familiarity, insight, and ignorance) and attitudes (eg, fear, anxiety, and inertia) may be considered to be potentially modifiable factors [32–36, 40]. Indeed, changing the behavior of such individuals is challenging, but direct face-to-face communication with evidence-based recommendations may facilitate understanding the prescribers' thought processes and open the way for possible educational resolution of differences in opinion [38]. Showing an effort to understand physicians' thought processes via nudge psychology and emphasizing that the goal of ASP is to maximize benefits both to the prescribing physicians and the patients may also be useful [41]. In addition, involving a colleague from the same department as the outlier physicians to help advocate antimicrobial stewardship initiatives can lead to the successful promotion of ASP [42, 43].

Adverse events and outcome measures between the 2 groups in this study did not differ statistically, presumably due to the small sample size. Although the rapidly fatal McCabe score at the time of PPRF intervention was independently associated with nonadherence, no statistical difference in the overall mortality rate or readmission rate was observed between the groups,

indicating that PPRF intervention did not cause any harmful events in the patients and can be safely implemented.

This study has some limitations. First, because it was a single-center, retrospective study, the findings may have limited generalizability, and the collected data may be limited despite the use of standardized definitions and data collection forms. Moreover, some cases may not have been recorded in the EMR, and several potentially modifiable prescriber-related factors described in the previous studies may have been overlooked. Also, even after adjusting for known predisposing factors, other unmeasured factors may have contributed to nonadherence to PPRF intervention.

CONCLUSIONS

In general, nonadherence to PPRF recommendations is relatively common, and the reasons for it are generally multifactorial across institutions; however, nonadherence to PPRF recommendations was relatively uncommon at the study institution, suggesting the importance of the robustness of the existing ASP infrastructure in enhancing the effectiveness of PPRF. Severely ill patients and those with a recent history of hospitalization frequently continued to receive broad-spectrum antimicrobials against PPRF recommendations. Understanding physicians' psychology and individual interventions by targeting medical subspecialties caring for severely ill patients using nudge psychology along with hospital-wide ASP is warranted to promote ASP further.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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