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# Evaluation of a Hospital-Based Post-Prescription Review and Feedback Pilot in Kathmandu, Nepal

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*Abstract.* Capacity building is needed in low- and middle-income countries (LMICs) to combat antimicrobial resistance (AMR). Stewardship programs such as post-prescription review and feedback (PPRF) are important components in addressing AMR. Little data are available regarding effectiveness of PPRF programs in LMIC settings. An adapted PPRF program was implemented in the medicine, surgery, and obstetrics/gynecology wards in a 125-bed hospital in Kathmandu. Seven "physician champions" were trained. Baseline and post-intervention patient chart data were analyzed for changes in days of therapy (DOT) and mean number of course days for intravenous and oral antibiotics, and for specific study antibiotics. Charts were independently reviewed to determine justification for prescribed antibiotics. Physician champions documented recommendations. Days of therapy per 1,000 patient-days for courses of aminoglycoside ($P < 0.001$) and cephalosporin ($P < 0.001$) decreased. In the medicine ward, data indicate increased justified use of antibiotics ($P = 0.02$), de-escalation ($P < 0.001$), rational use of antibiotics ($P < 0.01$), and conforming to guidelines in the first 72 hours ($P = 0.02$), and for definitive therapy ($P < 0.001$). Physician champions documented 437 patient chart reviews and made 138 recommendations; 78.3% of recommendations were followed by the attending physician. Post-prescription review and feedback can be successfully implemented in LMIC hospitals, which often lack infectious disease specialists. Future program adaptation and training will focus on identifying additional stewardship programming and support mechanisms to optimize antibiotic use in LMICs.

## INTRODUCTION

Broad-spectrum antimicrobial use in hospital settings is common. However, research indicates that up to one-third of antimicrobial use in U.S. hospital settings is inappropriate or suboptimal.[1,2] For many low- and middle-income countries (LMIC), data are scarce regarding hospital-based prescribing practices and associated outcomes including antimicrobial resistance (AMR) patterns. The WHO has addressed the need to prioritize AMR as a global health issue and established five strategic objectives including "improvement in the awareness and understanding of AMR through effective communication, education, and training."[3]

Evidence from Nepal suggests that many bacterial pathogens are highly resistant to first-line and some second-line antibiotics. Surveillance data from the Ministry of Health and Population indicate that more than 50% of *Escherichia coli*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae* isolates and 30% of certain *Shigella* spp. and *Vibrio cholera* isolates are resistant to first-line antibiotics.[4] In a previous study of uropathogens among children at the research hospital, more than 54% of 252 samples were multidrug resistant and 25 isolates were extended spectrum beta-lactamase (ESBL) producers.[5] Available data suggest overprescribing of pharmaceuticals within Nepali hospital settings including unjustified use of antibiotics, which encompasses inappropriate or unnecessary indication of use, duration, and antibiotic choice.[6,7] However, to date, there have been very limited efforts to provide antimicrobial stewardship training and resources for hospital-based physicians in Nepal and many other LMICs. The post-prescription review and feedback (PPRF) program has been shown to be effective in U.S. hospitals.[8,9] The approach includes a review of antimicrobial use 48–72 hours after initiation, when additional clinical data are available, coupled with feedback as to whether treatment should be modified or stopped.

The objectives of the current project were to (1) document current antibiotic resistance patterns in the study hospital, (2) adapt existing Nepali and international antibiotic prescribing guidelines based on antibiograms and availability of antibiotics, (3) adapt and implement the PPRF program to address specific conditions within Nepali hospital settings, and (4) conduct a longitudinal outcome evaluation using patient chart reviews and physician logbooks.

## MATERIALS AND METHODS

**Research sites.** The program was a collaboration between the Henry Ford Division of Infectious Disease and Global Health Initiative (Detroit, MI), the Group for Technical Assistance (Kathmandu), and the Public Health Concern Trust (Kathmandu). Public Health Concern Trust is a nongovernmental institution including two hospitals, Kathmandu Model and Kirtipur hospitals. The primary study site was Kathmandu Model Hospital (KMH). Kathmandu Model Hospital is a 125-bed hospital centrally located in the Kathmandu Valley. Opened in 1993, KMH provides a range of in- and outpatient services. For the present study, the PPRF program was piloted in the medicine, surgery, and obstetric/gynecology (ob/gyn) inpatient wards.

**Research population.** Kathmandu Model Hospital serves a broad catchment area within the Kathmandu Valley and the surrounding districts of Dolakha, Sindhupalchowk, Dhading, and Nurwakot. Kathmandu Model Hospital serves a diverse patient population inclusive of a range of economic and ethnic

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groups, as well as rural-to-urban migrants. Eligibility criteria for the patient chart review portion of the evaluation included (1) inpatients within the study wards, (2) inpatients aged 15+ years, and (3) inpatients prescribed antibiotics for at least 72 hours.

**Laboratory surveillance.** Before project implementation, the lead microbiologist at the KMH diagnostics laboratory was trained at the Henry Ford Health System Division of Infectious Disease to support documentation of organisms cultured, susceptibility patterns, and development of antibiograms. Bacterial identification was performed by standard microbiological techniques as described by the American Society of Microbiology.[10] In addition, antibiotic susceptibilities were determined by the Kirby–Bauer disk diffusion method, and results were interpreted according to the guidelines of the Clinical Laboratory Standard Institute.[11] Antibiograms were developed on an annual basis.

**Development of prescribing guidelines.** In 2014, the Nepali Ministry of Health and Population established antimicrobial prescribing guidelines based on international standards. However, translation of these guidelines into a usable document for practicing physicians was needed to support implementation of the PPRF program. The U.S. and Nepali research team and Scientific Advisory Board members collaborated to create a set of guidelines that were responsive to the most common infections seen within the study wards and accounted for the availability of pharmaceuticals. The guidelines are a "working document" and adjustments were made on an as-needed basis throughout the intervention. Guidelines included (1) empiric antibiotic therapies, (2) definitive antibiotic therapies, (3) intravenous to oral conversion, (4) renal dosing, and (5) suggest duration of therapies.

**Post-prescription review and feedback adaptation, physician champions, and stewardship training.** In the United States, PPRF programs are usually supported by hospital infectious disease departments and/or infection specialists. However, in Nepal, there are few infectious disease specialists and a vast majority of hospitals do not include infectious disease departments. Therefore, the PPRF program was led by identified "physician champions" within each of the study wards. The physician champions were selected by the local project principal investigator, who also holds an administrative position at KMH. A total of seven physician champions were selected and trained; six physician champions (86%) stayed at KMH throughout the study period. The six physician champions represented two of four physicians in internal medicine and two of five physicians in both surgery and ob/gyn wards.

Physician champions' responsibilities included (1) attendance at the training and subsequent videoconferencing training sessions, (2) review of eligible patients' charts within their wards (aged 15+ years and on study antibiotics for 72 hours), (3) identification and communication with attending physicians of possible need to modify/de-escalate/stop treatment based on the guidelines. All final treatment decisions were made by the attending physicians, and (4) completion of physician logs to indicate charts reviewed, recommendations made, and if recommendations were implemented.

In February 2017, physician champions, the KMH lead microbiologist, and local coinvestigators participated in a 1-day training. The training included a review of antibiotic resistance, the prescribing guidelines, and implementation procedures for the PPRF program. In addition, the physician champions attended videoconferencing sessions over the intervention period to address any issues or concerns and obtain additional training in topics related to infectious disease. Training was conducted by U.S. and Nepali physicians and scientists.

**Post-prescription review and feedback evaluation: patient chart review and physician champion logbooks.** Eligible patient chart data were collected for 6 months before the PPRF training (August 1, 2016 to January 31, 2017) and 6 months post-PPRF training (March 1, 2017 to August 31, 2017). Individuals with a background in health sciences/public health from a nonprofit local nongovernmental agency (Group for Technical Assistance) were trained to collect patient chart data and physician champion logbooks on a monthly basis in each department.

Eligible charts in each of the three study wards were randomly selected to reach the target number for each hospital ward per month. In internal medicine and surgery, the monthly goals were 15 charts per ward. In ob/gyn, the monthly goal was five to six charts. Before data collection, the total eligible number of charts per ward was identified and that number was divided by the targeted monthly goal. The resulting quotient was used to count and select charts in a chronological order (e.g., every third chart from the beginning to the end of the month). Because the patient charts were randomly selected, the overlap between patient chart data and the physician champion logbook entries is less than 100%.

The sample size was based on published data regarding use of medications among inpatients in a Nepali hospital and an estimated duration of use (7.9 days and SD 6.3).[6] Using a two-sided comparison of a continuous variable (days of therapy (DOT) per 1,000 study patient days [PD]), a sample size of 211 per group (baseline and post-intervention) was determined to detect a difference of 20% with 90% confidence and $\alpha = 0.05$.

Data collected from patient charts included (1) demographics (gender and age), (2) hospital/ward, (3) length of stay, (4) source of infection, (5) patient height/weight, (6) conditions present at study enrollment, (7) systemic antibiotic use (prior 72 hours), (8) origin of onset of infection (hospital, health setting, and community), (9) working and final diagnosis, (10) systemic antibiotic use throughout the hospital stay, (11) therapy prescribed at discharge, (12) infection-related complicating factors, (13) factors associated with persistent infection, and, (14) disposition at the end of hospital stay (if deceased, date, and cause). In addition, laboratory data were documented, including organisms cultured and susceptibilities.

At the end of the study, patient chart data were reviewed by Henry Ford Health System infectious disease specialists to determine whether the prescribed antibiotics were justified. Justified use included initial therapy and therapy changes after recommendations made by physician champions. Appropriateness of duration, de-escalation, antibiotic class, route of administration, and indication for use were considered in the review.

Physician champions were provided with the prescribing guideline books with log pages attached in the back. In the logbooks, physicians documented charts reviewed, recommendations made, and acceptance of recommendations by the attending physicians. Physician champions reviewed charts during their time on the ward and recommendations

were communicated verbally (face-to-face) and/or as written notes.

The physician champion logbooks provided data in terms of how often the physician champions reviewed and provided feedback and whether the attending physician did or did not make changes based on the feedback. Logbook data were entered by physicians on a daily basis. Logbook entries were also reviewed by infectious disease physicians at Henry Ford Health System. Questions and issues related to the logbooks were discussed during the training videoconferences over the course of the post-intervention period.

**Data management and analysis.** Patient chart data were entered into RedCAP (Vanderbilt University, Nashville, TN). RedCAP is a secure web application for building and managing online surveys and databases. RedCAP provides immediate access to data at both the data entry site and off-site (Henry Ford Health System Global Health Initiative). All continuous data were described using means and SDs, whereas categorical data were described using counts and column percentages. Univariate two-group comparisons were conducted using independent two-group *t*-tests for continuous variables and chi-square tests for categorical variables. Total DOT per 1,000 PD was calculated at baseline and intervention periods for each antibiotic. The proportion of DOT per 1,000 PD was compared between baseline and intervention time points using tests of proportion. Statistical significance is set at $P < 0.05$. All analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).[12]

**Ethics.** The study was approved by the Institutional Review Board at Henry Ford Health System, Detroit, MI, and by the National Human Research Council, Kathmandu, Nepal.

## RESULTS

**Organisms cultured and susceptibilities.** Among adult inpatients at KMH in 2017, 355 isolates were identified. The primary organisms were *E. coli* (42%) and *Klebsiella* spp. (16%). Other pathogens included coagulase-negative staphylococci (9%), *Pseudomonas* (9%), *Enterococcus faecalis* (8%), *Staphylococcus aureus* (7%), and *Acinetobactor* spp. (5%).

An antibiogram was developed for 2017 data, accounting for more than 90% of identified specimens at KMH. *Klebsiella* spp. were 100% susceptible to polymyxins and *E. coli* to polymyxins and tigecycline. Both *Klebsiella* spp. and *E. coli* showed low rates of susceptibility to pencillins, 3rd-generation cephalosporins, and fluoroquinolones (Figure 1). These data are consistent with recent surveillance data from the Nepal National Public Health Laboratory. (J. Acharya, National Public Health Laboratory. Unpublished data presented at 2017 and 2018 physician champion training workshops, Kirtipur Hospital, Kathmandu, Nepal.)

**Patient chart data: demographics.** A total of 221 baseline and 230 post-intervention patient chart data were collected and analyzed ($N = 451$). Overall, 54% (244) of patients were female, with a mean age of 50 (SD 19.7 years). A majority of respondents were from medicine (43%; 192) and surgery (41%; 186). There were no significant differences in gender, age, or department between baseline and post-intervention. The mean number of hospitalization days was 6.5 (SD 3.5 days.). Although there was a drop in the number of days of hospitalization between baseline and post-intervention, this difference was not significant (Table 1).

**Patient chart data: antibiotic use at baseline and post-intervention.** Throughout all study wards, DOT per 1,000 PD increased from 761 to 823 ($P < 0.001$) for IV and from 302 to 390 ($P < 0.001$ for oral therapy). Between baseline and post-intervention, cephalosporin use decreased from 420 DOT/1,000 PD to 344 ($P < 0.0001$) and aminoglycoside decreased from 138 DOT/1,000 PD to 95 ($P < 0.001$). There were increases in DOT/1,000 PD for all other study antibiotics, except metronidazole (Table 2).

In the medicine ward, there was an increase in the mean number of days for both (intravenous $P = 0.03$) and oral antibiotics ($P = 0.01$). There were also increases in the mean number of days for doxycycline ($P = 0.04$), carbapenem ($P = 0.02$), and quinolone ($P < 0.001$). However, the mean number of days for aminoglycoside decreased ($P = 0.03$). In addition, review of the data indicates an increase in justified use of antibiotics ($P = 0.02$), de-escalation ($P < 0.001$), documentation of rational use of antibiotics ($P = 0.01$), and following guidelines for antibiotic use both in the first 72 hours ($P = 0.02$) and for definitive therapy ($P < 0.001$).

In the surgery ward, there were no significant changes, except for a decrease in de-escalation of antibiotics at

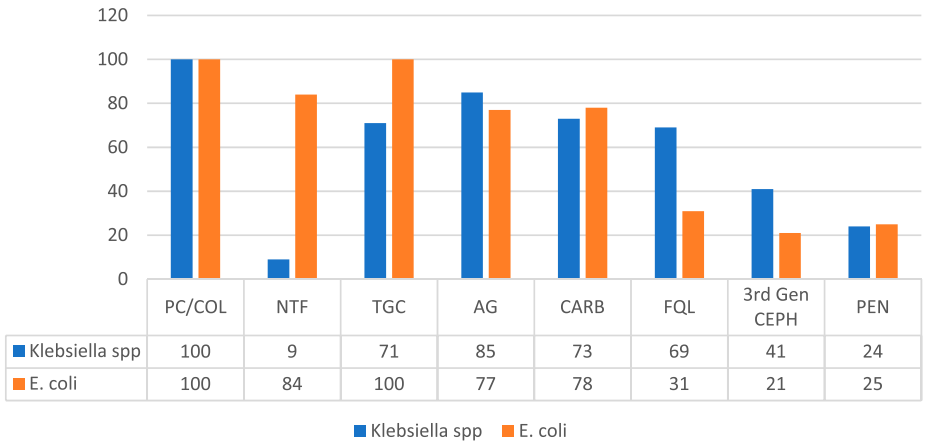


FIGURE 1. Susceptibility of *Klebsiella* spp. and *Escherichia coli* from Kathmandu Model Hospital in-patients (2017). AG = aminoglycoside; CARB = carbapenems; COL = colisten; FQL = fluoroquinolones; NTF = nitrofurantoin; PC = polymyxins; PEN = penicillins; TGC = tigecycline; 3rd-Gen Ceph = 3rd-generation cephalosporins. This figure appears in color at www.ajtmh.org.

TABLE 1
Demographics of baseline and post-intervention patient chart data, Kathmandu Model Hospital

| Variable | Response | All ($N$ = 451) | Baseline ($N$ = 221) | Intervention ($N$ = 230) | $P$-value |
|---|---|---|---|---|---|
| Age (years) | – | 50.0 ± 19.7 | 50.9 ± 20.3 | 49.2 ± 19.1 | 0.38 |
| Gender | Female | 244 (54%) | 118 (53%) | 126 (55%) | 0.77 |
| Department | Medicine | 192 (43%) | 97 (44%) | 95 (41%) | 0.83 |
| | Surgery | 186 (41%) | 90 (41%) | 96 (42%) | – |
| | Obstetric/gynecology | 73 (16%) | 34 (15%) | 39 (17%) | – |
| Length of stay | Days | 6.5 ± 3.5 | 6.7 ± 4.0 | 6.3 ± 3.1 | 0.27 |

post-intervention ($P$ = 0.03). In the ob/gyn ward, at post-intervention, prescribers were less adherent to the guidelines than at baseline ($P$ = 0.04) and there was an increase in the mean number of days on penicillin ($P$ < 0.001). However, there was a decrease in the mean number of days for cephalosporin ($P$ < 0.001). Also, in the ob/gyn ward, there was a trend for decrease in the mean number of days for intravenous administration of antibiotics, (2.5 ± 3.2 versus 1.4 ± 1.4; $P$ = 0.08; Table 3).

**Physician champion logbook data.** Over the 6-month post-intervention period, physician champions in the three wards reviewed and logged a total of 437 charts and determined that 31.6% (138) prescribed antibiotics were unjustified. Recommendations included modify course (83.3%; 115), stop the use of antibiotics (13.0%; 18), and de-escalate (3.7%; 5). Overall, 78.3% (108) of recommendations were followed by the prescribing physician. Recommendations varied by wards (Table 4).

## DISCUSSION

Antimicrobial resistance is a complex global issue that requires a "One Health" approach inclusive of governmental ministries (e.g., health, agriculture, and environment), non-governmental organizations, academic institutions, professional organizations, public and private health systems, and regional, national, and local leaders.[13] In LMICs, there is a need to identify locally salient solutions—which may or may not differ from programs and policies that have been shown to be effective in higher income settings.[14]

At the national level, Nepal has established an AMR technical working group and is developing policies and programs designed to improve laboratory capacity and support surveillance, decrease access to antimicrobials, establish stewardship programming, and advocate for responsible use of antimicrobials among health-care providers, pharmacists, veterinarians, those engaged in animal husbandry, and consumers. However, challenges remain in terms of technical capacity (e.g., laboratory surveillance) and governance to support coordination of program and policy implementation across a broad spectrum of organizations.[15]

Important steps in the development, piloting, and implementation of AMR programs and policies include (1) adapting content and delivery to meet local contexts while simultaneously maintaining essential "core" elements of the intervention and (2) using scientifically validated evaluation strategies to determine effectiveness within specific settings.[16] The PPRF pilot program at KMH was modified to address the lack of infectious disease specialists at KMH and the majority of hospitals in Nepal. Antibiotic guidelines were adapted to address primary pathogens at KMH, current prescribing practices, international and local recommendations, and availability of antibiotics.

Post-prescription review and feedback is one of several hospital-based stewardship audit programs. There is also an ongoing need to find opportunities to enhance AMR education through Continuing Medical Education seminars, video- and web-based modules, case studies and real-time training during clinical rounds. In addition, auditing and education programs can be integrated with restrictive and structural

TABLE 2
Days of therapy (DOT) and DOT per 1,000 patient-days (PD) of prescribed antibiotics at baseline and post-intervention in the medicine, surgery, and obstetric/gynecology wards, Kathmandu Model Hospital

| | Baseline (PD = 1,483) | | Intervention (PD = 1,458) | | |
|---|---|---|---|---|---|
| Treatment | DOT | DOT/1,000 PD | DOT | DOT/1,000 PD | $P$-value |
| Total days of intravenous antibiotics | 1,129 | 761 | 1,201 | 823 | **< 0.001** |
| Total days of oral antibiotics | 448 | 302 | 569 | 390 | **< 0.001** |
| Vancomycin | 0 | 0 | 15 | 10 | **< 0.001** |
| Linezolid | 0 | 0 | 13 | 9 | **< 0.001** |
| Doxycycline | 5 | 4 | 21 | 14 | **0.001** |
| Penicillin | 98 | 66 | 153 | 105 | **< 0.001** |
| Beta-lactam | 190 | 128 | 228 | 157 | **0.03** |
| Cephalosporin | 622 | 420 | 501 | 344 | **< 0.001** |
| Carbapenem | 12 | 8 | 66 | 45 | **< 0.001** |
| Metronidazole | 41 | 28 | 52 | 35 | 0.21 |
| Azithromycin | 217 | 146 | 258 | 177 | **0.02** |
| Clindamycin | 13 | 9 | 36 | 25 | **< 0.001** |
| Quinolone | 129 | 87 | 262 | 180 | **< 0.001** |
| Colistin | 0 | 0 | 11 | 8 | **< 0.001** |
| Aminoglycoside | 205 | 138 | 138 | 95 | **< 0.001** |
| Other course | 46 | 31 | 21 | 14 | **0.01** |

Bolded data $P$ < 0.05.

TABLE 3

Days of prescribed antibiotics, justification, de-escalation, treatment rationale, and fidelity to guidelines at baseline and post-intervention in the medicine, surgery, and obstetric/gynecology (ob/gyn) wards, Kathmandu Model Hospital

| | Medicine | | | Surgery | | | Ob/gyn | | |
|---|---|---|---|---|---|---|---|---|---|
| | Baseline (*N* = 97) | Post-intervention (*N* = 95) | | Baseline (*N* = 90) | Post- intervention (*N* = 96) | | Baseline (*N* = 34) | Post-intervention (*N* = 39) | |
| Mean days of intravenous antibiotics: | **4.4 ± 3.7** | **6.0 ± 6.2** | **0.03** | 6.9 ± 6.2 | 6.1 ± 4.7 | 0.31 | 2.5 ± 3.2 | 1.4 ± 1.4 | 0.08 |
| Mean days of oral antibiotics: | **3.0 ± 2.6** | **4.3 ± 3.9** | **0.01** | 0.9 ± 2.8 | 1.0 ± 1.7 | 0.78 | 2.4 ± 2.3 | 1.9 ± 1.0 | 0.25 |
| Mean days of vancomycin: | 0.0 ± 0.0 | 0.2 ± 1.1 | 0.16 | 0 | 0 | n/a | 0 | 0 | n/a |
| Mean days of linezolid: | 0.0 ± 0.0 | 0.1 ± 0.7 | 0.06 | 0 | 0 | n/a | 0 | 0 | n/a |
| Mean days of doxycycline: | **0.0 ± 0.0** | **0.2 ± 1.0** | **0.04** | 0.1 ± 0.6 | 0.0 ± 0.0 | 0.32 | 0 | 0 | n/a |
| Mean days of penicillin: | 0.6 ± 1.6 | 0.7 ± 1.6 | 0.67 | 0.3 ± 1.2 | 0.3 ± 1.0 | 0.81 | **0.1 ± 0.8** | **1.4 ± 1.1** | **< 0.001** |
| Mean days of beta-lactam: | 0.9 ± 2.2 | 1.3 ± 2.7 | 0.23 | 1.2 ± 2.7 | 1.1 ± 2.6 | 0.82 | 0.0 ± 0.0 | 0.0 ± 0.3 | 0.32 |
| Mean days of cephalosporin: | 2.4 ± 2.8 | 2.0 ± 2.7 | 0.24 | 3.1 ± 4.2 | 2.7 ± 2.9 | 0.46 | **3.2 ± 2.5** | **1.4 ± 1.4** | **< 0.001** |
| Mean days of carbapenem: | **0.1 ± 0.7** | **0.7 ± 2.0** | **0.02** | 0.0 ± 0.0 | 0.0 ± 0.4 | 0.32 | 0 | 0 | n/a |
| Mean days of metronidazole: | 0.0 ± 0.5 | 0.2 ± 1.2 | 0.38 | 0.1 ± 0.8 | 0.2 ± 0.8 | 0.41 | 0.9 ± 1.5 | 0.5 ± 0.7 | 0.16 |
| Mean days of azithromycin: | 2.2 ± 2.2 | 2.7 ± 2.0 | 0.09 | 0.1 ± 0.5 | 0.1 ± 0.5 | 0.86 | 0.0 ± 0.3 | 0.0 ± 0.0 | 0.33 |
| Mean days of clindamycin: | 0.1 ± 1.0 | 0.3 ± 1.7 | 0.48 | 0.0 ± 0.0 | 0.1 ± 0.7 | 0.18 | 0 | 0 | n/a |
| Mean days of quinolone: | **0.5 ± 1.4** | **1.6 ± 2.9** | **< 0.001** | 0.9 ± 1.9 | 1.1 ± 2.3 | 0.42 | 0.0 ± 0.1 | 0.0 ± 0.0 | 0.26 |
| Mean days of colistin: | 0.0 ± 0.0 | 0.1 ± 0.9 | 0.20 | 0 | 0 | n/a | 0 | 0 | n/a |
| Mean days of aminoglycoside: | **0.4 ± 1.3** | **0.0 ± 0.5** | **0.03** | 1.7 ± 3.8 | 1.4 ± 2.3 | 0.52 | 0.5 ± 1.6 | 0.0 ± 0.0 | 0.08 |
| Mean days of other courses: | 0.1 ± 0.6 | 0.2 ± 0.9 | 0.47 | 0.4 ± 2.3 | 0.0 ± 0.4 | 0.18 | 0.1 ± 0.5 | 0.0 ± 0.0 | 0.33 |
| Was the antibiotics course justified? | **50 (52%)** | **65 (68%)** | **0.02** | 61 (68%) | 62 (65%) | 0.72 | 11 (32%) | 9 (23%) | 0.38 |
| Were the antibiotics de-escalated? | **11 (12%)** | **46 (48%)** | **< 0.001** | **56 (62%)** | **44 (46%)** | **0.03** | 15 (44%) | 10 (26%) | 0.11 |
| Was the treatment rational documented accurately? | **61 (64%)** | **79 (83%)** | **0.01** | 58 (66%) | 64 (67%) | 0.83 | 12 (36%) | 20 (51%) | 0.20 |
| Were guidelines followed within the first 72 h of therapy? | **45 (49%)** | **63 (67%)** | **0.02** | 55 (61%) | 64 (67%) | 0.38 | **17 (50%)** | **10 (26%)** | **0.04** |
| Were recommendations followed for definitive therapy? | **38 (41%)** | **66 (69%)** | **< 0.001** | 58 (64%) | 62 (65%) | 0.91 | 11 (32%) | 9 (23%) | 0.38 |

Note: Daptomycin, trim-sulfa, and tigecycline courses were not prescribed in the three wards over the 12-month study period. Bolded data $P < 0.05$.

interventions, for example, automatic stop-orders, and access to rapid diagnostics. In Nepal and other LMICs, the present study team continues to pilot and evaluate auditing and educational activities, as well as alternative means of program delivery (e.g., training of trainers and centers of excellence), to optimize antibiotic use, improve patient outcomes, and increase program sustainability.

Laboratory surveillance data suggest significant resistance to several groups of antibiotics within pathogens most frequently identified at KMH (*Klebsiella* spp. and *E. coli*). These data emphasize the urgent need to adapt and implement stewardship programs in Nepal. The evaluation of the PPRF program followed similar procedures used in the United States and more recently in a pilot program in Vellore, India.[17]

The evaluation provided both evidence of positive changes and need for further development of stewardship training to optimize antibiotic use in low-resource hospital settings. Data indicate that the program was most effective in the medicine ward. And even with increases in mean days of antibiotic use, independent evaluation of the prescribed antibiotics suggests increased justification and evidence of de-escalation at post-intervention. One limitation of the study was that the baseline and post-intervention periods were during different seasons, and variability could be expected in terms of infectious disease risks. Little change was noted in the surgery ward. Prophylactic use of antibiotics tends to be of longer duration in Nepal than in U.S. hospitals. Recommendations related to surgical antibiotic prophylactic use were not adequately emphasized in the initial PPRF training. To further address this issue, a PPRF program is presently being implemented with a focus on wound and burn care in three surgical wards and a burn ICU in Kathmandu and Pokhara (Western Nepal).

There was trend indicating a decrease in the mean number of days for intravenous antibiotics in the ob/gyn ward. Future evaluations may need to increase sample sizes to ensure that significant changes can be detected at both the hospital and the ward levels. In addition, the current evaluation used a quasi-experimental pre- and post-intervention design. There is a need

TABLE 4

Physician champion logbook data and recommendations by Ward, Kathmandu Model Hospital

| | All wards | Medicine | Surgery | Obstetric/gynecology |
|---|---|---|---|---|
| Total charts reviewed | 437 | 216 | 125 | 96 |
| Unjustified courses | | | | |
| Total (% of total reviewed) | 138 (31.6) | 98 (45.4) | 23 (18.4) | 17 (17.7) |
| Stop antibiotics (% of unjustified courses) | 18 (13.0) | 13 (13.3) | 3 (13.0) | 2 (11.8) |
| Modify antibiotic use (% of unjustified courses) | 115 (83.3) | 80 (81.6%) | 20 (87.0) | 15 (88.2) |
| De-escalation (% of unjustified courses) | 5 (3.7) | 5 (5.1) | 0 | 0 |
| Recommendations followed by prescribing physicians | 108 (78.3) | 89 (90.8%) | 17 (73.9) | 2 (11.8) |

in LMICs for randomized control trials to support causality between the PPRC stewardship program and changes in physician prescribing practices (internal validity) and generalizability to support expansion of PPRC to other types of hospitals and other regions of Nepal (external validity).

Whereas total antibiotic days increased and penicillins, azithromycin, and quinolones had significant increases in use, cephalosporin use decreased in compliance with guidelines. Cephalosporins are commonly used in Southeast Asia and contribute as a driving force for ESBL. Reduction in cephalosporin use was a major focus of the intervention, owing to its status as a high-priority issue in Asia and Nepal.[18]

Overall, the physician champion logbook data indicate that the program was successfully implemented. Physician champions reviewed patient charts, physician champions made recommendations based on available guidelines, and a majority of those recommendations were implemented. This is an important first step—the acceptance of advice from colleagues in relation to prescribing practices within a LMIC hospital setting. It should also be noted that the program was fully supported by the hospital administration and leadership and that the published guidelines were recognized as a valuable resource by administrators, physician champions, and prescribing physicians. In an Australian study, facilitating factors related to implementation of a hospital-based stewardship program were acknowledgment of the need for support in prescribing antibiotics and readiness to consult prescribing guidelines.[19]

Hospital-based stewardship is one key defense in relation to AMR. Stewardship programs have been shown to be successful in reducing antimicrobial use in higher income settings. However, the use of antimicrobials in LMIC hospitals continues to be a significant contributor to resistance. These pilot data indicate success with an adapted PPRF training and implementation strategy, development of practice guidelines, and general acceptance of the key premise of PPRF—a collegial team approach to prescribing antibiotics. Outcomes in terms of changes in documented prescribing practices varied by ward and there is clear room for improvement as PPRF and other stewardship programs are implemented and disseminated in hospitals in Nepal and the region.

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