

Antibiotic Use in Medical–Surgical Intensive Care Units and General Wards in Latin American Hospitals

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Background. The objective of this study was to identify antibiotic stewardship (AS) opportunities in Latin American medical–surgical intensive care units (MS-ICUs) and general wards (Gral-wards).

Methods. We conducted serial cross-sectional point prevalence surveys in MS-ICUs and Gral-wards in 41 Latin American hospitals between March 2022 and February 2023. Patients >18 years of age in the units of interest were evaluated for antimicrobial use (AU) monthly (MS-ICUs) or quarterly (Gral-wards). Antimicrobial data were collected using a standardized form by the local AS teams and submitted to the coordinating team for analysis.

Results. We evaluated AU in 5780 MS-ICU and 7726 Gral-ward patients. The hospitals’ median bed size (interquartile range) was 179 (125–330), and 52% were nonprofit. The aggregate AU prevalence was 53.5% in MS-ICUs and 25.5% in Gral-wards. Most (88%) antimicrobials were prescribed to treat infections, 7% for surgical prophylaxis and 5% for medical prophylaxis. Health care–associated infections led to 63% of MS-ICU and 38% of Gral-ward AU. Carbapenems, piperacillin-tazobactam, intravenous (IV) vancomycin, and ampicillin-sulbactam represented 50% of all AU to treat infections. A minority of IV vancomycin targeted therapy was associated with documented methicillin-resistant *Staphylococcus aureus* infection or therapeutic drug monitoring. In both units, 17% of antibiotics prescribed as targeted therapy represented de-escalation, while 24% and 15% in MS-ICUs and Gral-wards, respectively, represented an escalation of therapy. In Gral-wards, 32% of antibiotics were used without a microbiologic culture ordered. Half of surgical prophylaxis antibiotics were prescribed after the first 24 hours.

Conclusions. Based on this cohort, areas to improve AU in Latin American hospitals include antibiotic selection, de-escalation, duration of therapy, and dosing strategies.

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Improving antibiotic use (AU) is considered a core strategy to reduce and control antimicrobial resistance (AMR) [1, 2]. Understanding how antibiotics are prescribed is essential to designing and implementing interventions to optimize their use. Latin America has seen a rise in AMR in recent decades (eg, carbapenem nonsusceptibility among gram-negative organisms has increased from 0.3% in 2002 to 20%–50% in 2016 depending on the country according to the Latin American Network for Antimicrobial Resistance Surveillance) [3]; however, our knowledge of antibiotic stewardship (AS) priorities in the hospital setting remains limited due to scarce studies evaluating current AU patterns [4, 5].

A recent 1-day point prevalence survey (PPS) that evaluated AU in 33 Latin American hospitals from Cuba, Peru, Mexico, El Salvador, and Paraguay reported a wide range of AU prevalence (~44% to 84% depending on the country) as well as low proportions of microbiologic studies before antibiotic initiation (as low as 20%) and of antibiotics prescribed for targeted therapy (7%–27%) [6]. Similarly, a PPS conducted in 43 intensive care units (ICUs) from Latin America reported that 30% of patients did not undergo a microbiologic culture before antibiotic initiation and 57% of antibiotics were prescribed to treat health care–associated infections (HAIs) [7]. Another study that evaluated AU in 84 ICUs from 9 Latin American countries reported high rates of AU for empiric therapy (73%–61%) and guideline compliance (59%–92%) [8]. According to a national PPS study of AU in Argentina, small hospitals had similar AU prevalence as large hospitals [9]. Limitations to published reports include data acquired at a single point in time, data from ICUs alone, and limited information on other important parameters of AU such as therapeutic drug monitoring, appropriateness of indication/dose/duration, and pharmacist involvement in antibiotic prescriptions. To address these knowledge gaps, we conducted serial PPS in medical–surgical ICUs (MS-ICUs) and general wards (Gral-wards) in 41 Latin American hospitals.

METHODS

Study Setting and Survey Methodology

Serial PPS were conducted by the local AS team in 41 hospitals from 5 countries in Latin America (Argentina, Colombia, Ecuador, Guatemala, and Panama) over 12 months (March 2022–February 2023) as part of a larger study to evaluate antibiotic stewardship program (ASP) implementation in the region. We used an adapted version of the global PPS survey. Serial 1-day PPS were performed monthly in the MS-ICUs and quarterly in the Gral-wards. All adult patients (>18 years of age) hospitalized according to the daily census in an MS-ICU or Gral-ward at 8:00 a.m. on the day of the study

were evaluated for AU. Two investigators (R.E.Q. and V.F.) held virtual training webinars with local AS teams to review the data collection form and PPS methodology to ensure consistency across sites. Only patients on a systemically administered antibiotic, antimycobacterial, or antimycotic agent (J01, J02, and J04 using the World Health Organization [WHO] Anatomical Therapeutic Chemical Classification System) were evaluated for AU (ie, topical antibiotics, any antivirals, and antiparasitic agents were excluded). Specialty units (eg, psychiatric ward) and pediatric and neonatal units were excluded.

Patient Consent

The study was approved as exempt by the Johns Hopkins Medicine Institutions Review Board. Additionally, local institutional review board approvals were obtained by participating hospitals. This activity was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy (see, eg, 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.).

Data Collection and Definitions

De-identified information included basic patient characteristics and characteristics related to the antimicrobial prescription (eg, therapeutic indication, administration route, pharmacist validation, dose adjustments, and therapeutic drug monitoring). Prescriptions were categorized as treatment for community-acquired infections, treatment for HAIs, medical prophylaxis, or surgical prophylaxis. Additionally, prescriptions were adjudicated for guideline compliance based on local or international guidelines. Antibiotics for treatment of infections were further categorized as empiric or targeted (ie, based on culture results). Whether a microbiologic culture had been ordered was also recorded. Data collected by the local AS teams were stored in PROAnet, a secure regional research platform previously used for research studies by the research team, for further analysis by the Johns Hopkins University coordinating team [8, 10]. Pharmacy verification refers to a process in which pharmacists assess prescriptions for drug interactions and allergies, duplication of therapy, dosing based on organ function, etc. Anti-methicillin-resistant *Staphylococcus aureus* (anti-MRSA) antibiotics include daptomycin, clindamycin, linezolid, ceftaroline, and intravenous (IV) vancomycin.

Statistical Analysis

The prevalence of AU was calculated as the proportion of patients on at least 1 antimicrobial divided by the number of patients on the unit of interest (MS-ICU or Gral-ward) on PPS days, with minimum and maximum ranges. AU patterns

Table 1. Characteristics of Patients Receiving Antimicrobials, Type of Antimicrobial, and Associated Indication Included in the Analysis

Patient Characteristics	Overall, n = 5067	MS-ICU, n = 3094 (61%)	Gral-Ward, n = 1973 (39%)
Age, median (IQR), y	58 (41–71)	58 (41–70)	59 (40–72)
Female sex, No. (%)	2084 (41)	1197 (39)	887 (45)
Country, No. (%)			
• Argentina	3328 (66)	1982 (64)	1346 (63)
• Colombia	788 (15)	474 (12)	314 (16)
• Ecuador	332 (7)	265 (9)	67 (3)
• Guatemala	224 (4)	61 (2)	163 (8)
• Panama	395 (8)	312 (10)	83 (4)
Antimicrobials per patient, mean (range)	1.5 (1–5)	1.6 (1–5)	1.3 (1–4)
Antimicrobial Characteristics	Overall, n = 7910	MS-ICU, n = 5208 (66%)	Gral-Ward, n = 2702 (34%)
Type of antimicrobial, No. (%)			
• Antibiotic	7392 (93)	4848 (94)	2544 (94)
• Antifungal	455 (58)	321 (6)	134 (5)
• Antimycobacterial	63 (1)	39 (1)	24 (1)
Indication, No. (%)			
• Medical prophylaxis	370 (5)	196 (4)	174 (6)
• Surgical prophylaxis	521 (7)	287 (5)	234 (9)
• Empiric treatment	4314 (54)	2811 (54)	1503 (56)
• Targeted treatment	2705 (34)	1914 (37)	791 (29)

Serial single-day point prevalence surveys were conducted in 41 hospitals from Guatemala, Panama, Ecuador, Colombia, and Argentina during March 2022–February 2022. Abbreviations: ICU, intensive care unit; IQR, interquartile range; Gral, general; MS, medical-surgical.

were further analyzed using descriptive statistics focusing on antibiotics used to treat infections (“treatment antibiotics”) and those used for surgical prophylaxis. Two-sided *P* values <.05 were considered statistically significant. Statistical analyses were performed using Stata, version 15.1 (StataCorp LLC, College Station, TX, USA).

RESULTS

Participating Hospital Characteristics and Overall AU Prevalence

The median bed size of the 41 participating hospitals (interquartile range [IQR]) was 179 (125–330) beds, 48% were for-profit, 57% were from Argentina, 17% from Colombia, 12% from Panama, 9% from Ecuador, and 5% from Guatemala. During the 12-month study period, 41 hospitals performed a median (IQR, range) of 11 (6.5–12, 2–10) PPS in the MS-ICUs. Additionally, 34 of these hospitals also performed a median (IQR, range) of 3 (2–3, 1–12) PPS on the Gral-wards during the same study time frame.

The overall AU prevalence was 53.5% (3094/5780) in the MS-ICUs and 25.5% (1973/7726) in the Gral-wards. Most antimicrobials evaluated were antibiotics (93%), 54% of which were prescribed for empiric therapy, 34% for targeted therapy, 7% for surgical prophylaxis, and 5% for medical prophylaxis. Characteristics of patients on antimicrobials and AU prevalence by indication type are presented in [Table 1](#).

Antibiotic Use Patterns

There were 4399 and 2186 antibiotics used to treat infections in the MS-ICUs and Gral-wards, respectively. The 3 most common indications for treatment antibiotics in the MS-ICUs were ventilator-associated pneumonia (n = 610, 14%), intra-abdominal infection (n = 601, 14%), and non-ventilator-associated pneumonia (n = 598, 14%), which includes community-acquired pneumonia (n = 381) and health care-associated pneumonia (n = 192). In the Gral-wards, the most common indications were skin and soft tissue infection (n = 404, 18%), urinary tract infection (n = 298, 14%), and intra-abdominal infection (n = 284, 13%) (a full list of indications by unit type is shown in [Supplementary Tables 1 and 2](#)). HAIs were responsible for 63% of MS-ICU and 38% of Gral-ward antibiotic prescriptions (see [Table 2](#) for types of infections driving antibiotic prescriptions for treatment of infections). The 5 most common antibiotics prescribed for treatment of infections in MS-ICUs and Gral-wards are shown in [Figure 1](#). The most common antibiotics prescribed for common community-acquired infections are summarized in [Figure 2](#).

Gral-wards had a higher proportion of empiric AU (66% vs 61%; *P* ≤ .001) and a higher proportion of empiric antibiotics without a microbiologic culture ordered (32% vs 15%; *P* < .001) than MS-ICUs ([Supplementary Tables 3 and 4](#)). Among antibiotics used for targeted therapy, 24% and 15% of MS-ICU and Gral-ward prescriptions, respectively,

Table 2. Type of Infections Driving Antibiotic Prescriptions for Treatment of Infections, by Unit Type (n = 6585)

	MS-ICU, n = 4399, No. (%)	Gral-Ward, n = 2186, No. (%)
Community-acquired infections	1476 (34)	1182 (54)
Hospital-acquired infections	2476 (56)	730 (33)
• Surgical site infection	399 (16)	210 (29)
• Hospital-onset <i>Clostridioides difficile</i> infection	49 (2)	44 (6)
• Device-associated hospital-acquired infection	897 (36)	96 (13)
o Catheter-associated urinary tract infection	89 (4)	37 (5)
o Catheter-related bloodstream infection	226 (9)	51 (7)
o Ventilator-associated pneumonia	582 (23)	8 (1)
• Nondevice hospital-acquired infection	1002 (40)	338 (46)
• Other	136 (5)	42 (6)
Unknown/other	447 (10)	274 (12)

Abbreviations: Gral, general; ICU, intensive care unit; MS, medical–surgical.

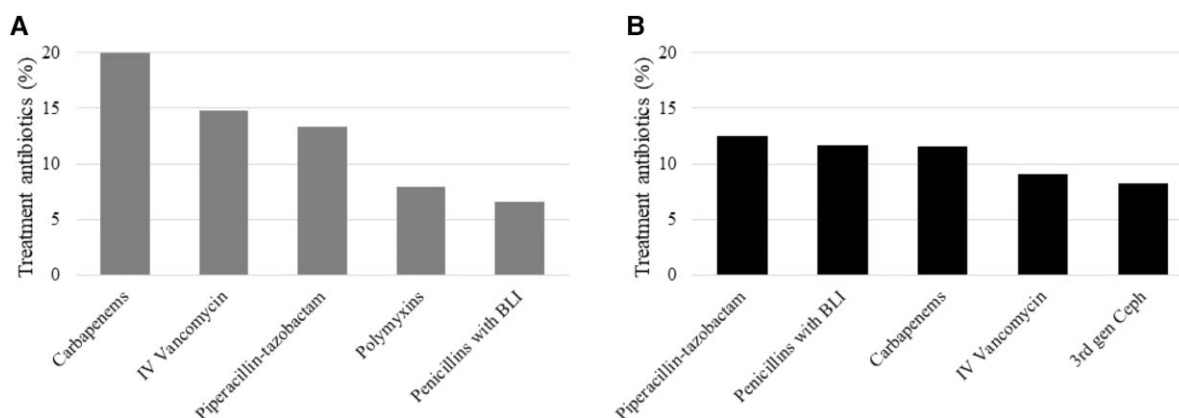


Figure 1. Count of top 5 antibiotic groups used for treatment of infections in MS-ICUs (A) and Gral-wards (B). Penicillins with BLI include ampicillin-sulbactam and amoxicillin-clavulanate. Serial single-day point prevalence surveys were conducted in 41 hospitals from Guatemala, Panama, Ecuador, Colombia, and Argentina during March 2022–February 2022. Abbreviations: BLI, β -lactamase inhibitor; Gral-wards, general wards; IV, intravenous; MS-ICUs, medical–surgical intensive care units.

represented escalation of therapy, while 17% in both units represented de-escalation (Table 3). A culture growing MRSA was present in 30% and 37% of anti-MRSA antibiotics prescribed for targeted therapy in the MS-ICUs and Gral-wards, respectively. The most common indications for which anti-MRSA antibiotics were prescribed without MRSA growing in culture included bacteremia (26%), ventilator-associated pneumonia (20%), and skin and soft tissue infection (17%). A documented infection due to an extended-spectrum β -lactamase (ESBL)-producing organism was associated with 54% of MS-ICU and 34% of Gral-ward carbapenem prescriptions.

Of 5407 antibiotics adjudicated for guideline compliance, 10% were deemed noncompliant based on indication. Most patients (84% in MS-ICUs and 73% in Gral-wards) had an infectious disease (ID) consult, and in most cases their recommendations were followed (92% in MS-ICUs and 88% in Gral-wards). Antibiotic verification by pharmacy occurred in 70% of treatment antibiotics, and renal adjustment was

performed in 28% of antibiotic prescriptions. Thirty-five percent of cefepime and 37% of piperacillin-tazobactam administrations in MS-ICUs were performed as prolonged infusions. Therapeutic drug monitoring was performed for 44% of MS-ICU and 31% of Gral-ward IV vancomycin used for targeted therapy, respectively, and for 22% of MS-ICU and 13% of Gral-ward aminoglycosides, respectively. Parenteral to oral switch was documented in 1.3% of MS-ICU and 4% of Gral-ward antibiotics used to treat infections.

Surgical Prophylaxis Antibiotic Use Patterns

Among surgical prophylaxis antibiotics (n = 517), first-generation cephalosporins were the most common (54%), followed by ampicillin-sulbactam (12%). Other antibiotics used for surgical prophylaxis included clindamycin (4%), fluoroquinolones (4%), metronidazole (4%), aminoglycosides (4%), vancomycin (2.5%), broad-spectrum penicillin with β -lactamase inhibitors (eg, piperacillin-tazobactam; 2%), and

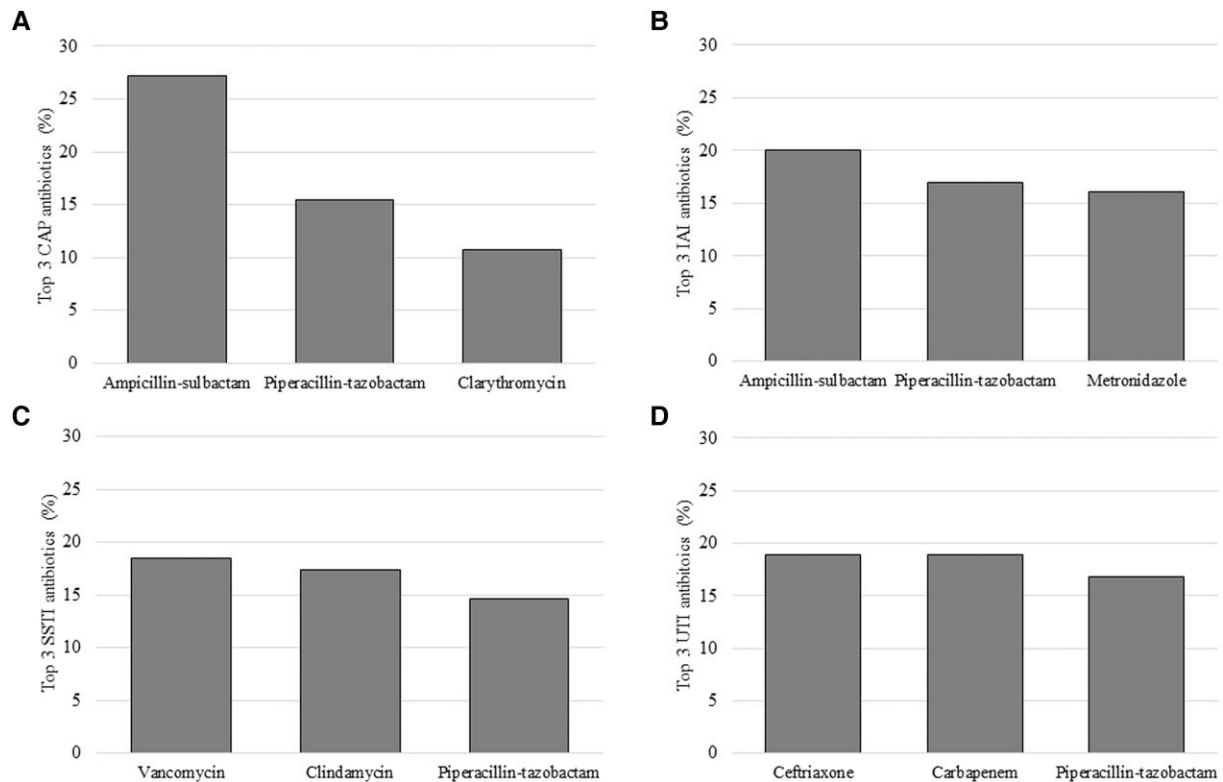


Figure 2. Top 3 antibiotics prescribed for treatment of common community-acquired infections including A) community-acquired pneumonia (CAP), B) intra-abdominal infections (IAI), C) skin and soft tissue infections (SSTI), and D) urinary tract infections (UTIs). The denominator is the total number of antibiotics for each indication presented in the figure (ie, CAP treatment antibiotics, n = 551; IAI treatment antibiotics, n = 492; SSTI treatment antibiotics, n = 369; UTI treatment antibiotics, n = 190). Serial single-day point prevalence surveys were conducted in 41 hospitals from Guatemala, Panama, Ecuador, Colombia, and Argentina during March 2022–February 2022.

Table 3. Proportion of Targeted Therapy Antibiotics Maintained as Initially Prescribed, Escalated, or De-escalated by Unit Type for the Study Period

	MS-ICU, n = 1735, No. (%)	Gral-Ward, n = 735, No. (%)
De-escalated	301 (17)	125 (17)
Escalated	412 (24)	107 (14)
Maintained	1022 (59)	503 (68)

Serial single-day point prevalence surveys were conducted in 41 hospitals from Guatemala, Panama, Ecuador, Colombia, and Argentina during March 2022–February 2022.

Abbreviations: Gral, general; ICU, intensive care unit; MS, medical–surgical.

carbapenems (1.5%). Antibiotics were stopped within 24 hours of surgery in 49% of cases. Certain types of surgery were more likely to have postoperative prophylaxis continued beyond 24 hours from surgery (~70% of neurosurgery, otolaryngology, and plastic surgeries) or use an alternative agent to first-generation cephalosporins or penicillin with β -lactamase inhibitors (~40% of abdominal, plastic, and neuro surgeries each had alternative agents compared with 0%–20% in other types).

DISCUSSION

We evaluated AU patterns in MS-ICUs and Gral-wards from 41 Latin American hospitals through serial cross-sectional PPS from March 2022 to February 2023. This multicenter evaluation revealed several potential opportunities for AS intervention, including optimization of antibiotic selection for empiric and targeted therapy for common infections, de-escalation, dosing strategies, and duration.

This study was carried out in a mix of private and public medium-sized hospitals from Argentina, Colombia, Ecuador, Guatemala, and Panama. The population analyzed was mostly middle-aged individuals hospitalized in MS-ICUs and Gral-wards. Several important findings were uncovered by this study. Although we observed a higher proportion of antibiotics prescribed for targeted therapy than previous PPS conducted in the region [6], empiric use still represented a large portion of treatment antibiotics, especially among Gral-wards where ~70% of treatment antibiotics were used as empiric therapy. Furthermore, 30% and 15% of Gral-ward and MS-ICU antibiotics, respectively, did not have an associated culture ordered; these are critical to guide subsequent antibiotic

management decisions such as de-escalation of therapy, conversion of IV to an oral option, and duration of treatment. We also found a limited number of anti-MRSA antibiotics associated with a positive MRSA culture. Most antibiotics prescribed for targeted therapy in both types of units were maintained (ie, not modified from initial therapy), and ~25% of MS-ICU antibiotics represented an escalation of therapy. These findings may suggest suboptimal selection of antibiotics for empiric use based on local pathogens and AMR prevalence and missed opportunities for de-escalation based on clinical response or microbiologic culture data. Notably, in a recent survey that explored Latin American health care workers' perceptions and attitudes toward AS, 22% of participants had not received education on how to select antibiotics based on culture/susceptibility results, 34% had limited access to health care facility treatment guidelines, and 51% did not have access to the hospital antibiogram [11]. These data indicate the need for more effective collaboration between the microbiology laboratory and ASPs; however, important barriers may need to be addressed first including improving staffing in the lab and resources to improve efficiency in extracting microbiology data [12].

Another notable finding was that for most antibiotic prescriptions in our study there was an ID consultation, and most of the ID recommendations were accepted by the primary teams. This highlights the opportunity to strengthen education on AS principles among ID consultants and the collaboration between the AS team and ID specialists. A study from Switzerland showed that ~40% of patients with an ID consult had at least 1 opportunity to improve AU [13]. We previously reported on the challenges related to daily AS interventions by ASPs in Latin America, mostly related to lack of protected time and insufficient personnel for AS activities (eg, in a cohort of 20 Latin American hospitals with a reported ASP, daily postprescription review with feedback was performed on a regular basis in only 45% of health care facilities) [12].

Another area for potential improvement relates to antibiotic dose and administration. Continuous or prolonged infusion of β -lactam antibiotics is recommended for critically ill patients, particularly those with gram-negative infections, as this method of administration has been associated with improved patient outcomes (reduced mortality and increase in clinical cure) [14]. In our study, a low proportion of cefepime or piperacillin-tazobactam was administered as continuous/prolonged infusion in MS-ICUs. Further research to understand the barriers to optimal antibiotic administration strategies is needed. Therapeutic drug monitoring of IV vancomycin was also infrequent in our study. Therapeutic drug monitoring of IV vancomycin is recommended due to vancomycin's narrow range for therapeutic effect and toxicity risk, especially for patients with abnormal or unstable renal function [15, 16]. Therapeutic drug

monitoring is not widely available throughout Latin America due to cost, lack of access to the technology needed to measure drug levels, and lack of trained personnel to perform or interpret results [17]. This highlights the need for AS to implement strategies to minimize unnecessary IV vancomycin use and for better integration of pharmacists in AS. Barriers to better integration of pharmacists in ASPs in Latin America include lack of pharmacist expertise in AS/clinical pharmacology, lack of protected time for clinical pharmacists to participate in AS activities, and cultural norms in which antibiotic decisions have traditionally been made exclusively by physicians [11, 12].

Up to ~40% of Gral-ward and ~60% of MS-ICU antibiotics were prescribed for treatment of HAIs. This is in agreement with prior reports [7, 8], and it is a reminder of the longstanding need to invest in both infection prevention and control and AS programs in Latin America [18]. Similar to other studies, we also observed a high rate of surgical prophylaxis extending beyond the first 24 hours postsurgery [6, 19]. Increasing the duration of antibiotic prophylaxis is associated with an increased risk of *Clostridioides difficile* colitis and acute kidney injury without a reduction in surgical site infection (SSI) and is not recommended by guidelines [20–22]. AS teams should collaborate with surgeons and anesthesiologists to ensure evidence-based best practices that have shown to reduce SSIs, such as optimal timing of antibiotic administration prior to incision, are implemented [23].

There are several limitations to this study. While serial PPS provided robustness to the data, this methodology remains suboptimal in assessing some important aspects of AU, such as parenteral to oral switch (conversion rates may be higher if evaluated upon discharge), duration of therapy, and temporal variations. However, the study significantly expanded the knowledge on key areas that would benefit from improvement. While we included a large number of hospitals, there was overrepresentation from Argentina, limiting generalizability of results. The timing of the study may have biased selection of participating hospitals (eg, those more affected by external factors such as coronavirus disease 2019 surges may have been less available to participate). We did not assess the availability of antibiotics at participating hospitals, which may have impacted antibiotic choices. However, the fact that antibiotic therapy was often escalated indicates that antibiotic availability may not have influenced antibiotic choice heavily. Finally, while the study team provided training to local teams regarding PPS methodology, there may have been inaccuracies introduced during data collection that could lead to under- or overestimation of findings.

In summary, serial PPS of AU in Latin American MS-ICUs and Gral-wards between March 2022 and February 2023 identified several potential areas for AS intervention, including processes related to antibiotic selection for empiric use, antibiotic

changes based on culture results, antibiotic dosing and administration, and duration of therapy. Improvements in these areas will likely require strengthening collaborations with microbiologists, pharmacists, and physicians, along with increasing resources to the ASP.

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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