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Original Article

Antimicrobial stewardship programs in adult intensive care units in Latin America: Implementation, assessments, and impact on outcomes

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Abstract

Objective: To assess the impact of antimicrobial stewardship programs (ASPs) in adult medical–surgical intensive care units (MS-ICUs) in Latin America.

Design: Quasi-experimental prospective with continuous time series.

Setting: The study included 77 MS-ICUs in 9 Latin American countries.

Patients: Adult patients admitted to an MS-ICU for at least 24 hours were included in the study.

Methods: This multicenter study was conducted over 12 months. To evaluate the ASPs, representatives from all MS-ICUs performed a self-assessment survey (0–100 scale) at the beginning and end of the study. The impact of each ASP was evaluated monthly using the following measures: antimicrobial consumption, appropriateness of antimicrobial treatments, crude mortality, and multidrug-resistant microorganisms in healthcare-associated infections (MDRO-HAIs). Using final stewardship program quality self-assessment scores, MS-ICUs were stratified and compared among 3 groups: ≤25th percentile, >25th to <75th percentile, and ≥75th percentile.

Results: In total, 77 MS-ICU from 9 Latin American countries completed the study. Twenty MS-ICUs reached at least the 75th percentile at the end of the study in comparison with the same number who remain within the 25th percentile (score, 76.1 ± 7.5 vs 28.0 ± 7.3; $P < .0001$). Several indicators performed better in the MS-ICUs in the 75th versus 25th percentiles: antimicrobial consumption (143.4 vs 159.4 DDD per 100 patient days; $P < .0001$), adherence to clinical guidelines (92.5% vs 59.3%; $P < .0001$), validation of prescription by pharmacist (72.0% vs 58.0%; $P < .0001$), crude mortality (15.9% vs 17.7%; $P < .0001$), and MDRO-HAIs (9.45 vs 10.96 cases per 1,000 patient days; $P = .004$).

Conclusion: MS-ICUs with more comprehensive ASPs showed significant improvement in antimicrobial utilization.
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The introduction of antimicrobials has transformed medical practice converting previously fatal infections into treatable diseases. Misuse and overuse of antimicrobials comprise a significant cause of emerging antimicrobial resistance (AMR).[1] Although early and appropriate treatment has been shown to reduce mortality[2] in patients with severe sepsis or septic shock, 20%–50% of antimicrobials prescribed in US hospitals are inappropriate or unnecessary.[3–5] Furthermore, antimicrobial exposure increases the risk of adverse events, drug interactions, superinfections, and the development of multidrug-resistant organisms (MDROs), fungal infections, *Clostridiodes difficile* infection (CDI), as well as healthcare costs.[6–9]

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Inappropriate use of antimicrobials has a negative impact not only on the patient but also on the broader patient population through increased rates of MDROs.[10]

Estimates indicate that >700,000 deaths occur worldwide each year from AMR, and this number is projected to reach 10 million in 2050.[11] The financial costs associated with treating these infections reach many billions of dollars.[1,12] The effective implementation of antimicrobial stewardship programs (ASPs) has allowed a cost-effective reduction in antimicrobial consumption, increasing patient safety and reducing AMR.[13,14] The implementation of strategies for appropriate use of antimicrobials is a cornerstone in reducing emergence and transmission of MDROs. Multiple guidelines have been published, proposing a framework to combat AMR based on the development of robust infection control programs, therapeutic committees, guidelines on antimicrobial management, and monitoring and feedback of prescription patterns.[15–18] This framework contributed to the development of ASPs, which focus on preprescription authorization and postprescription review and feedback, which have succeeded at curbing resistance, decreasing costs, and decreasing rates of CDI in US hospitals.[19–21] However, hospitals located in low- and middle-income countries (LMICs) have different sets of challenges.[22,23] Stories of modest success have been reported around the world, but robust data are lacking,[24] and data on AMR and ASPs in Latin America are especially scarce.

In this study, we aimed to implement ASPs in adult medical-surgical intensive care units (MS-ICUs) from Latin American countries and to assess impact on appropriateness of antimicrobial prescriptions, antimicrobial use, crude mortality, MDRO in healthcare-associated infections (MDRO-HAIs) and *Clostridioides difficile* infections (CDIs). We hypothesized that MS-ICUs with higher scores in the final self-assessment would show improved indicators of appropriate antimicrobial use and improved patient outcomes.

Methods

Study design

The study included a network of hospitals recruited from 9 Latin American countries. A nonrandom sample of 84 MS-ICUs from tertiary-care hospitals in Latin America were invited by infectious disease leaders from each country to voluntarily participate in the project. We included facilities with an ASP team composed of an infectious disease (ID) physician, a clinical pharmacist, and a microbiologist. All study data were deidentified, and patient consent was waived. Ethics approvals varied by country and were obtained by participating hospitals on an individual basis. A central ethics committee was enlisted at the coordinating center, the Global Health Initiative at Henry Ford Health System, Michigan. A data privacy document was made available for each participating hospital.

The study was built using methodology from a prior study.[25] The study was conducted over a 24-month period with a 6-month preintervention period, a 12-month intervention period, and a 6-month postintervention study period.

During the preintervention period, the members of the ASP teams were trained through an online course. During this period, each center completed a baseline self-assessment of their ASP through a previously validated instrument (Supplementary Material 1 online).[25]

During the 12-month intervention period and based on the results of the baseline self-assessment, each center implemented locally salient antimicrobial stewardship strategies in MS-ICUs as part of the ASP. During this period, monthly surveys were performed to measure the appropriateness of antimicrobial prescription, antimicrobial consumption, mortality, and incidence of MDRO-HAIs. The implementations of respective IPC strategies were registered monthly. At month 6 during the intervention period, an interim self-assessment using the same instrument was performed to respectively determine which ASP strategies had been implemented.

During the postintervention period, a final self-assessment was performed to summarize the level of development achieved by the ASP at each MS-ICU.

Data collection

All data were entered into a secured online database through a central website developed for this study. A help desk and supplementary documents were available there. The platform included the online training course, participating center characteristics, and standardized collection of study information. Data validation included several integrated verifications with error and warning messages to avoid duplicated and erroneous data entry and missing information. The system created monthly indicators and graphics comparing data from all participating MS-ICUs. Each investigator could monitor their own indicators in comparison with the rest of centers.

The following variables were collected from each participating hospital for analysis and comparison: affiliation type (public or private, teaching or nonteaching), number of MS-ICU beds, full-time equivalent for ASP team members, and the presence of an IPC committee and/or a pharmacy committee.

The instrument used to evaluate the ASPs was based on the CDC Core Elements checklist[26] and contained a total of 74 indicators, grouped into 33 standards, 15 components, and 4 domains (Supplementary Material 1 online). We evaluated the following domains: (1) leadership and coordination, (2) institutional intervention strategies, (3) monitoring, and (4) education. Partial scores for each domain and a global score were developed. The results of the self-assessment of ASPs were finalized on a scale from 0 to 100 points to allow institutional comparisons. The means of the self-assessment score were grouped by percentiles (≤25th, >25th to <75th, and ≥75th) for comparisons among the MS-ICUs.

A standardized surveillance methodology was used to collect data from antimicrobial prescriptions.[25,27] Monthly 1-day prevalence surveys, including all inpatients who were in an MS-ICU at 8:00 A.M. and who received at least 1 systemic antimicrobial, were collected. Survey information included characteristics of the patient (ie, age, gender, weight) and the antimicrobial prescription (ie, therapeutic indication, unit dose, number of daily doses, administration route, pharmacist validation, dose adjustments, and therapeutic drug monitoring). Prescriptions were categorized as treatment for community-acquired infections (CAIs), treatment for healthcare-associated infections (HAIs), medical prophylaxis, or surgical prophylaxis. Whether treatment was empirical or targeted was also recorded.

We analyzed the following indicators of appropriateness of the antimicrobial prescriptions: surgical prophylaxis <24 hours, validation of prescription by pharmacists, justification of prescription in the medical record, compliance with clinical guidelines, prospective audit and feedback, acceptance of ID physician recommendation, aminoglycosides in a 1-day dose, no redundant anaerobic therapy, de-escalation of therapy performed, and switch from intravenous to oral route.

Antimicrobial consumption was measured in defined daily doses per 100 patient days (DDD per 100 PD) per month for systemic antibacterials and antifungals (categories J01 and J02 from the Anatomical Therapeutic Chemical classification system).[28,29]

To determine the impacts of the respective ASPs, monthly CDI, MDRO-HAIs, and all-cause mortality in the MS-ICU were registered. Additionally, the respective implementations of the following IPC strategies were registered: hand hygiene program, periodic surveillance of MDRO-HAIs, policies for contact precautions and environmental cleaning, daily chlorhexidine bathing, surveillance, and bundles addressing device-associated infections.

Statistical analysis

The results of the self-assessment are shown as mean ± SD. The paired Student *t* test was used to compare the initial and final scores, and the Student *t* test was used to compare MS-ICUs. To identify institutional characteristics associated with the level of the ASP, a bivariate analysis was conducted using the final self-assessment score as the outcome. Statistically associated variables ($P < .10$) were introduced into a stepwise multiple linear regression model, and only those that were significantly associated ($P < .05$) remained in the model.

Indicators for appropriateness of antimicrobial prescriptions were presented as percentage of total prescriptions complying with each indicator. Overall, crude mortality was expressed as monthly death in the MS-ICU per 100 discharges. Cumulative compliance of IPC strategies was calculated as percentage of the 12 months each strategy was implemented. These variables were compared using the χ^2 statistic, and results are expressed as differences of the percentages and their respective 95% CIs.

The total DDD per 100 PD of targeted antimicrobials, MDRO-HAIs, and CDIs at the different MS-ICUs were compared as incidence densities using the Poisson test.

A *P* value <.05 (2-tailed) was considered statistically significant. For statistical analyses, we used SPSS version 22 software (IBM, Chicago, IL).

Results

Of the 84 MS-ICUs that initially agreed to participate in the project, 77 (91.7%) completed the study and 7 (8.3%) dropped out. Of the participating sites, 45 were from Argentina, 6 were from Ecuador, 5 were from Colombia, 5 were from Uruguay, 5 were from Brazil, 3 were from Chile, 3 were from Peru, 3 were from Panama, and 2 were from Bolivia. Overall, 233 members of ASP teams completed the online training course.

Self-assessment

The global scores of the initial and final self-assessments were 40.7 ± 17.3 and 52.1 ± 19.2, respectively (difference, 11.3; 95% CI, 8.1 to 14.6; $P < .0001$), and all 4 domains showed a significant improvement over the course of the study (Table 1).

The following components showed significant improvement in the final self-assessments: institutional support, staff commitment from other key departments, information technology assistance, institutional policies, interventions to optimize antimicrobial use, monitoring of antimicrobial use, appropriateness, impact indicators, and education and training for prescribers and for patients and relatives (Table 1).

Only Argentina, Colombia, Panama, and Uruguay showed a significant improvement in the global scores per country when the initial and final self-assessments were compared (Table 2).

The following institutional characteristics associated with a higher global score in the final self-assessment in the bivariate analysis: private versus public institution (56.2 vs 47.6; $P = .048$); at least 15 beds in the MS-ICU (58.7 vs 48.5; $P = .024$); full-time infection preventionist (53.1 vs 25.9; $P = .015$); at least 6 meetings per year of the IPC committee (55.4 vs 43.1; $P = .011$); and at least 6 meetings per year of the pharmacy committee (58.9 vs 47.4; $P = .009$). In the stepwise multiple linear regression, only facilities with at least 15 beds at the MS-ICU and at least 6 meetings per year of the pharmacy committee showed an independent significant statistical association ($P = .042$ and $P = .015$, respectively).

When institutions were stratified into 3 groups according to the global score of the final self-assessment (ie, ≤25th,>25th to <75th, ≥75th percentiles), only those centers in the >25th to <75th percentile and ≥75th percentile groups showed a significant improvement in their ASPs when the final and initial self-assessments were compared (52.1 vs 38.1 and 76.1 vs 59.2, respectively; both $P < .0001$). Centers within the 25th percentile did not show significant improvement in their ASPs (28.0 vs 27.1; $P = .7077$).

Antimicrobial prescriptions, antimicrobial consumption, and appropriateness indicators

Data from the point-prevalence surveys showed that of 10,058 MS-ICU inpatients, 6,019 inpatients (59.8%) received 10,523 antimicrobial prescriptions (1.75 antimicrobial per patient on antimicrobial treatment). Of these 10,523 prescriptions, 5,194 (49.4%) corresponded to HAIs treatment; 2,992 (28.4%) for CAIs; 590 (5.6%) surgical prophylaxis; 458 (4.4%) for medical prophylaxis; and 1,289 (12.2%) for indications not classified. Targeted treatments were significantly more common for HAIs than for CAIs (43.9% vs 25.1%; $P < .0001$).

Among all antibiotics prescribed for CAIs, the following were most frequently prescribed: 663 prescriptions (28.9%) were for penicillins with a β-lactamase inhibitor, 202 (8.8%) were for meropenem, 199 (8.7%) were for vancomycin, and 184 (8.0%) were for a third-generation cephalosporin (Fig. 1). Among the prescriptions for penicillins with a β-lactamase inhibitor, 314 prescriptions (13.7%) were for piperacillin with a β-lactamase inhibitor and 312 (13.6%) were for amoxicillin with a β-lactamase inhibitor. The following antibiotics were most commonly prescribed for HAIs: 1,242 prescriptions (23.9%) were for carbapenems, 840 (16.2%) were for glycopeptides, 758 (14.6%) were for penicillins with a β-lactamase inhibitor, and 597 (11.5%) were for polymyxins (Fig. 1).

Among the 426 systemic antifungal prescriptions, triazole drugs were the most frequently prescribed: 55 of 87 CAIs (2.4% of total prescriptions) and 177 of 339 HAIs (3.4% of total prescriptions) (Fig. 1).

Throughout the 12-month study period, 464,770 DDDs were consumed throughout 304,700 patient days in MS-ICUs (152.5 DDD per 100 PD). The following antimicrobial groups were most frequently consumed: penicillins with a β-lactamase inhibitor (34.0 DDD per 100 PD), followed by carbapemens (30.4 DDD per 100 PD), glycopeptides (13.2 DDD per 100 PD), and polymyxins (9.7 DDD per 100 PD).

The frequency distribution of antimicrobial consumption between MS-ICUs stratified by the final self-assessment into the 3 percentile groups are shown in Figure 2. Consumption of penicillin with a β-lactamase inhibitor, carbapenem, glycopeptide, third-generation cephalosporin, and aminoglycoside were lower in MS-ICUs in the ≥75th percentile.

The percentage of patients receiving at least 1 antimicrobial and the number of antimicrobials per patient on antimicrobial

Table 1. Comparison at the Domains Between Initial and Final Self-Assessment

	Initial						Final								
		Percentiles						Percentiles							
Domains/Components	Mean ± SD	10th	25th	50th	75th	90th	Mean ± SD	10th	25th	50th	75th	90th	Difference of Means	95% CI	*P* Value
Leadership and coordination	**56.5±21.2**	**30.0**	**41.2**	**57.6**	**69.8**	**85.6**	**62.7±21.2**	**36.6**	**45.2**	**63.8**	**83.1**	**92.0**	**6.2**	**1.8 to 10.5**	**.006**
Institutional support	38.3±28.5	0.0	16.7	33.3	66.7	73.3	48.1±31.4	0.0	16.7	50.0	66.7	100.0	9.7	3.4 to 16.1	.003
Accountability	62.3±30.2	25.0	50.0	50.0	100.0	100.0	69.5±27.7	25.0	50.0	75.0	100.0	100.0	7.1	−0.3 to 14.6	.060
Staff commitment from other key departments	55.6±25.4	30.0	40.0	50.0	80.0	90.0	62.7±25.4	30.0	40.0	60.0	90.0	100.0	7.1	0.8 to 13.5	.028
Information technology assistance	70.1±29.2	26.7	66.7	83.3	83.3	100.0	77.1±27.2	33.3	66.7	83.3	100.0	100.0	6.9	0.8 to 13.2	.026
Integration with other institutional committees	50.6±32.8	0.0	33.3	50.0	83.3	100.0	55.6±31.9	16.7	33.3	50.0	83.3	100.0	5.0	−1.2 to 11.2	.110
Integration with other institutional programs	56.5±32.5	0.0	25.0	50.0	75.0	100.0	61.0±31.8	25.0	50.0	50.0	100.0	100.0	4.5	−1.0 to 10.1	.109
Scope of the ASP	61.9±29.7	25.0	37.5	62.5	87.5	100.0	64.8±27.9	25.0	50.0	62.5	87.5	100.0	2.9	−3.6 to 9.4	.374
Institutional intervention strategies	**45.6±21.3**	**21.4**	**29.5**	**42.5**	**61.3**	**74.2**	**59.8±21.4**	**32.5**	**44.7**	**58.8**	**77.1**	**87.3**	**14.2**	**10.0 to 18.3**	**.000**
Institutional policies	47.1±29.6	10.0	19.2	46.2	65.4	93.9	65.3±26.8	38.5	46.2	61.5	92.3	100.0	18.3	12.8 to 23.8	.000
Interventions to optimize antimicrobial use	44.2±23.0	16.7	27.8	44.4	61.1	77.8	54.2±23.4	22.2	33.3	55.6	72.2	83.3	10.0	5.5 to 14.6	.000
Monitoring	**42±21.6**	**14.6**	**24.3**	**39.6**	**58.3**	**70.2**	**55.6±21.7**	**23.8**	**42.4**	**54.9**	**70.8**	**84.8**	**13.7**	**9.7 to 17.6**	**.000**
Antimicrobial use indicators	28.6±26.5	0.0	0.0	25.0	50.0	67.5	42.2±29.1	0.0	25.0	50.0	62.5	80.0	13.6	8.5 to 18.8	.000
Appropriateness indicators	28.3±25.0	0.0	8.3	16.7	50.0	66.7	39.0±28.4	8.3	16.7	33.3	58.3	78.3	10.6	4.9 to 16.3	.000
Impact indicators	63.1±32.5	22.2	33.3	61.1	94.4	100.0	79.1±25.1	50.0	61.1	88.9	100.0	100.0	16.0	9.2 to 22.7	.000
Institutional reporting	47.9±27.2	12.5	25.0	50.0	62.5	80.0	62.3±29.4	12.5	50.0	62.5	87.5	100.0	14.4	8.1 to 20.8	.000
Education	**18.8±17.2**	**0.0**	**0.0**	**15.0**	**30.0**	**40.0**	**30.1±25.8**	**0.0**	**5.0**	**25.0**	**50.0**	**62.0**	**11.4**	**6.1 to 16.6**	**.000**
Education and training to prescribers	31.0±27.0	0.0	0.0	30.0	40.0	80.0	44.0±33.7	0.0	10.0	50.0	70.0	90.0	13.0	6.3 to 19.7	.000
Education to patient and relatives	6.5±16.9	0.0	0.0	0.0	0.0	50.0	16.2±24.3	0.0	0.0	0.0	50.0	50.0	9.7	3.4 to 16.1	.003
Global score	**40.7±17.3**	**20.1**	**29.0**	**38.5**	**54.3**	**66.2**	**52.1±19.2**	**27.3**	**38.0**	**52.4**	**66.6**	**77.5**	**11.3**	**8.1 to 14.6**	**.000**

Note. SD, standard deviation; CI, confidence interval; ASP, antimicrobial stewardship program.

Table 2. Comparison of Global Scores per Country Between Initial and Final Self-Assessment

		Initial						Final								
			Percentiles						Percentile							
Country	No. of MS-ICUs	Mean±SD	10th	25th	50th	75th	90th	Mean±SD	10th	25th	50th	75th	90th	Difference of Means	95% CI	*P* Value
Argentina	45	42.1±15.9	26.3	29.2	36.1	54.3	66.8	50.6±15.7	30.1	39.8	49.8	64.0	69.7	8.5	4.7 to 12.2	.000
Bolivia	2	45.1±31.7						70.5±9.6						25.5	. . .	.351
Brazil	5	61.0±15.3	49.6	56.3	57.2	59.8	75.8	67.8±21.6	44.0	56.1	77.8	80.3	85.5	6.9	−9.6 to 23.3	.311
Chile	3	26.3±10.1	17.9	22.1	29.0	31.9	33.6	26.9±10.7	18.0	22.3	29.5	32.8	34.7	0.6	−0.9 to 2.1	.245
Colombia	5	52.2±11.8	39.3	42.4	55.7	62.5	62.9	77.3±13.7	61.9	65.3	86.4	87.0	87.6	25.0	0.9 to 49.2	.045
Ecuador	6	37.0±11.6	26.2	38.7	40.6	43.7	44.2	55.4±23.7	29.4	38.9	58.4	73.5	78.6	18.4	−0.8 to 37.7	.057
Panama	3	45.0±10.4	36.5	41.7	50.2	51.0	51.5	56.5±14.6	44.6	52.0	64.3	65.0	65.3	11.5	0.4 to 22.6	.047
Peru	3	23.6±9.2	16.0	20.3	27.4	28.9	29.7	41.1±22.2	23.0	34.3	53.0	53.9	54.4	17.5	−54.7 to 89.7	.407
Uruguay	5	15.1±7.2	8.7	12.7	14.0	16.9	22.3	31.7±7.0	26.9	27.9	30.1	30.4	38.5	16.6	13.3 to 19.9	.000

Note. MS-ICU, medical-surgical intensive care unit; SD, standard deviation; CI, confidence interval.

treatment were significantly lower in the MS-ICUs that reached the ≥75th percentile in comparison with those that remained within the 25th percentile at the final self-assessment (Table 3). The MS-ICUs that reached the ≥75th percentile had a significantly lower total antimicrobial consumption than those that remained in the 25th percentile (143.4 vs 159.4 DDD per 100 PD; $P <$ .0001) (Table 3).

The following appropriateness indicators performed better among MS-ICUs that reached the ≥75th percentile: validation of prescription by pharmacist, justification of prescription in the medical record, compliance with clinical guidelines, prospective audit with feedback, acceptance of ID physician recommendation, no redundant anaerobic therapy, de-escalation, and targeted treatments (Table 3). Surgical prophylaxis of <24 hours, therapeutic monitoring of vancomycin, aminoglycosides on 1-day dose, and switches from the intravenous to oral route did not show statistical difference.

Impact indicators

The cumulative impact indicators during the 12 months of the study showed that crude mortality and MDRO-HAIs were significantly lower in MS-ICUs in the ≥75th percentile than those in the 25th percentile. Only CDI was significantly higher in MS-ICUs in the ≥75th percentile (Table 3).

IPC strategies

MS-ICUs in the ≥75th percentile showed a significant higher frequency of IPC strategies implemented than those units within the 25th percentile (Table 4).

Discussion

This is the first multicenter study in Latin American MS-ICUs to evaluate antimicrobial prescription appropriateness, consumption and impact indicators in relation to the level of ASP development. Overall, 76.6% of the centers showed a significant improvement in their ASP scores. However, only 26.0% reached the 75th percentile in the final self-assessment, and 23.4% centers did not improve their global scores along the study.

The domain "leadership and coordination" scored highest at the final self-assessment, followed by "intervention strategies" and "monitoring." "Education" was the domain with the lowest score. The latter represents an opportunity to develop and implement new strategies to improve education and training to prescribers and to patient and relatives. These findings are consistent with a previous study analyzing 4,184 US acute-care hospitals through the 2014 National Healthcare Safety Network Annual Hospital Survey, which reported that only 39.2% of institutions have an ASP meeting all 7 core elements.[30] In addition, written support or salary funding were significantly associated with having a comprehensive ASP.[30] In a cross-sectional study including 103 hospitals in Central and South America, the lack of hospital administration, lack of information technology support, and opposition from prescribers were stated as main barriers to the development of ASPs.[31] More recently, in a survey conducted in 27 Latin American hospitals, 40.7% of respondent hospitals did not have a written statement supporting an ASP, and 51.9% reported no financial support for ASP practices. In addition, only 26% of laboratories agreed to perform testing for MDROs, and only 40.7% of hospitals included education to prescribers on improving antibiotic use.[32]

Our findings confirm that ASPs are often only partially implemented in Latin American hospitals. This issue represents a very important challenge because institutional support, interventions to optimizing antibiotic use, monitoring and reporting processes, as well as physician education, are necessary to implement an ASP effectively.[15]

The feasibility of doing a prevalence survey has been demonstrated in previous studies.[25,27] This methodology has allowed hospitals in LMICs to assess antibiotic prescribing patterns and to collect information about antibiotic resistance for the first time. In that sense, measurement of appropriateness of antimicrobial prescription is essential for monitoring and reporting ASPs.

We observed lower antimicrobial resistance in the higher percentile group, and this finding could be related to lower consumption of antibiotics in the MS-ICUs that have a more comprehensive ASP. As in a previous study, we found that targeted treatments were more common for HAIs than CAIs.[27] In addition, we observed a high rate of empiric use of carbapenems and vancomycin and a low rate of de-escalation. High rates of extended-spectrum β lactamase, methicillin-resistant *Staphylococcus aureus*, and carbapenem-resistant Enterobacteriaceae infections are leading to increased use of carbapenems, vancomycin, and

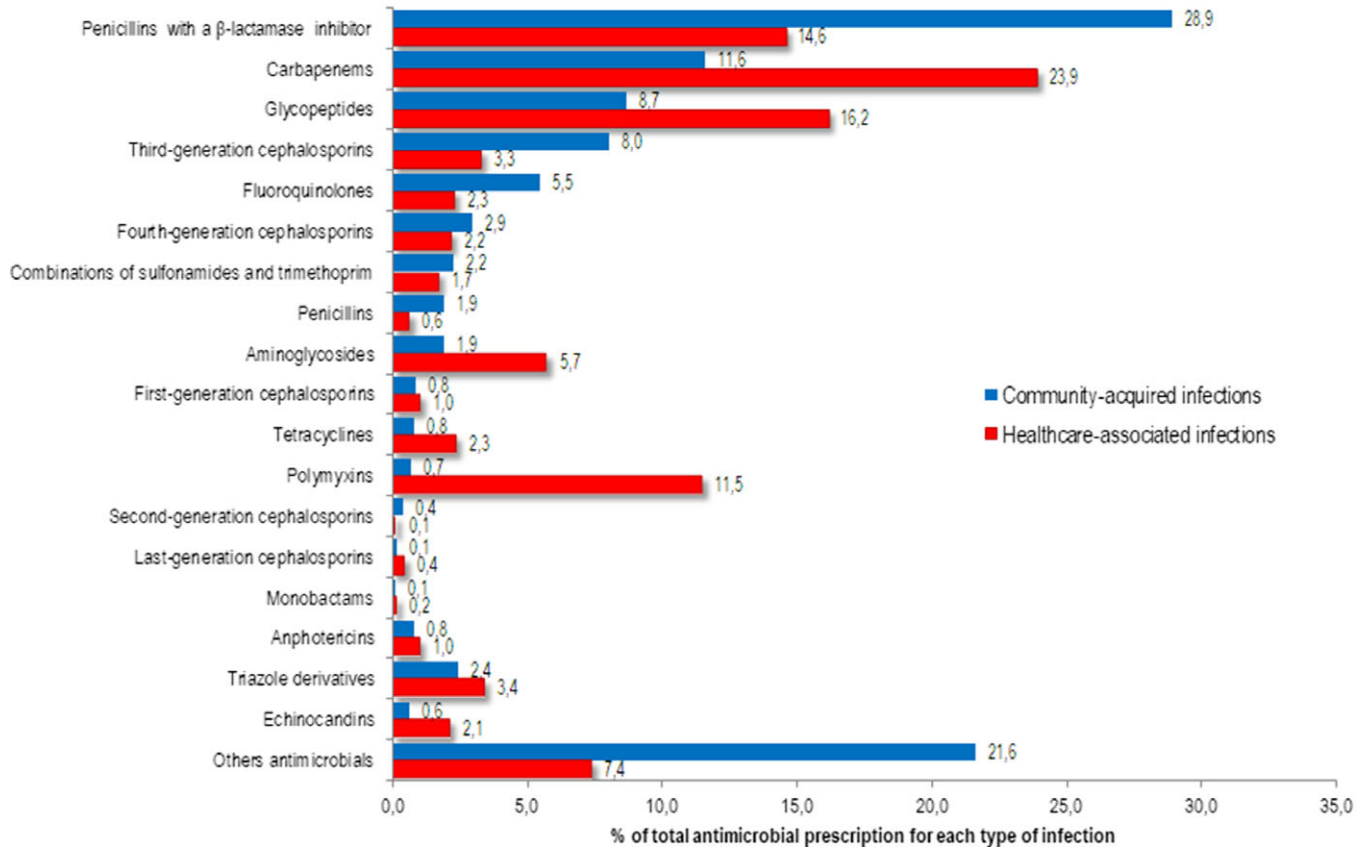

Fig. 1. Proportion of antimicrobials prescribed for systemic use in community-acquired (n=2292) and healthcare-associated (n=5194) infections among adult patients in medical-surgical ICU.

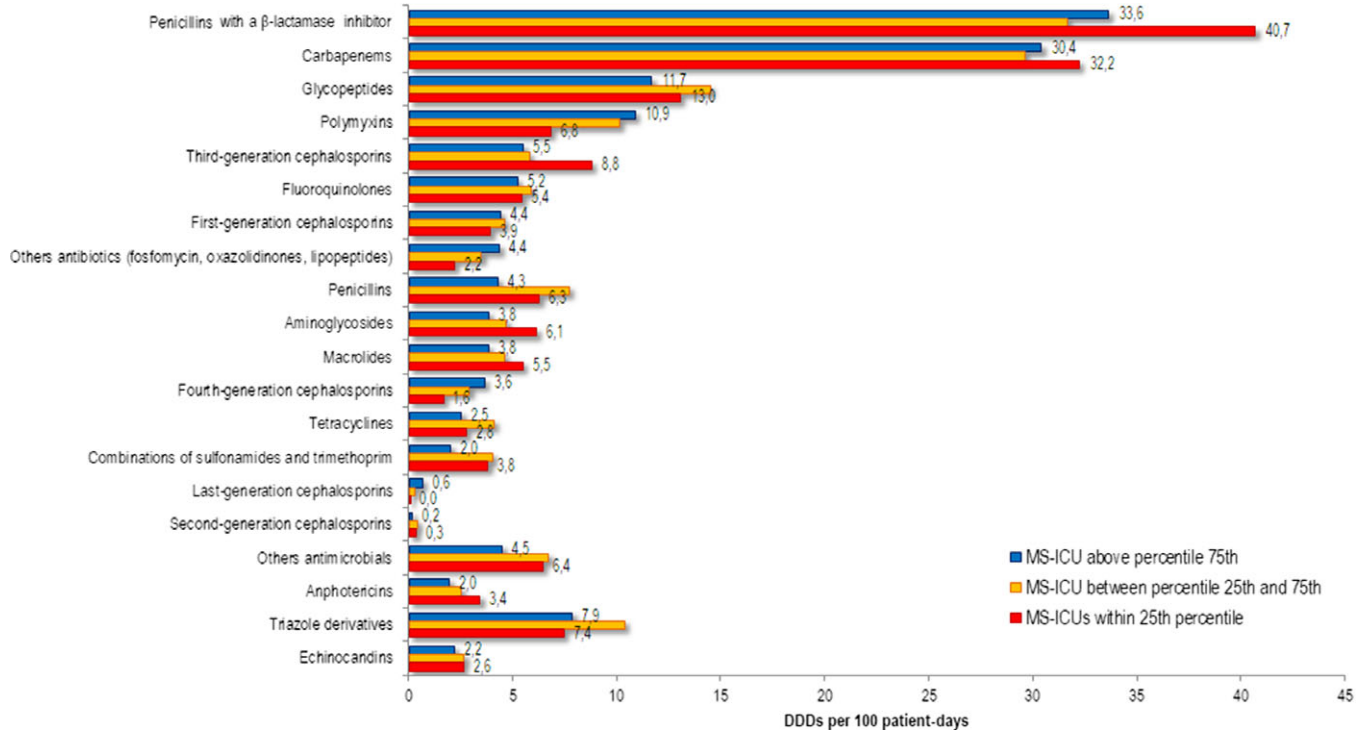

Fig. 2. Annual use of systemic antimicrobials in adult patients in medical-surgical ICU (MS-ICU) expressed as defined daily doses (DDDs) per 100 patient-days stratified by the global score of the final self-assessment.

Table 3. Indicators Comparison Between MS-ICU Stratified by the Global Score of the Final Self-Assessment

	Final Percentile Group, %[b]			Comparison Between ≥75th vs ≤25th Percentiles		
Indicators[a]	≤25th (n=20)	<75th >25th (n=37)	≥75th (n=20)	Differences	95% CI	*P* Value
Self-assessment final score (mean±SD)	28.0±7.3	52.1±8.6	76.1±7.5	48.1	43.4 to 52.8	.000
Antimicrobial prescription						
% of patients receiving at least 1 antimicrobial	62.6	61.0	56.7	−5.9	−8.6 to −3.1	.000
No. of antimicrobials per patient on antimicrobial treatment	1.74	1.82	1.64	−0.10	−0.19 to −0.05	.004
Appropriateness indicators						
Surgical prophylaxis <24 h[c]	46.2	59.0	51.5	5.4	−4.8 to 15.5	.352
Validation of prescription by pharmacists[c]	58.0	58.6	72.0	14.0	11.4 to 16.6	.000
Justification of prescription in the medical record[c]	94.7	97.2	97.6	2.9	1.8 to 4.0	.000
Compliance with clinical guidelines[c]	59.3	72.2	92.5	33.2	30.9 to 35.5	.000
Prospective audit with feedback[c]	76.2	87.9	86.1	9.9	7.7 to 12.1	.000
Acceptance of (ID) physician recommendation[c]	72.3	89.6	94.8	22.5	19.7 to 25.2	.000
Therapeutic monitoring of vancomycin[c]	24.4	33.5	25.0	0.6	−15.6 to 16.9	.882
Aminoglycosides on 1-day dose[c]	91.6	85.5	93.2	1.6	5.3 to 8.5	.839
No redundant anaerobic therapy[c]	0.96	0.80	0.26	−0.70	−0.03 to −0.75	.039
De-escalation[c]	3.8	5.2	8.2	4.4	3.0 to 5.7	.000
Switch from intravenous to oral route	37.9	35.8	35.2	−2.8	−18.6 to 13.1	.867
Targeted treatments[c]	27.6	35.9	39.5	12.0	9.2 to 14.7	.000
Antimicrobial use (DDDs per 100 patient days[d])	159.4	156.5	143.4	−16.0	−17.2 to −14.7	.000
Impact indicators						
MDRO in healthcare-associated infections (cases per 1,000 patient days[e])	10.96	13.53	9.45	−1.52	−2.56 to −0.48	.004
CDIs (cases per 1,000 patient days)	0.19	0.25	0.57	0.37	0.19 to 0.56	.000
Crude mortality (events per 100 discharges)	17.7	16.0	15.9	−1.8	−2.8 to −0.8	.000

Note. MS-ICU, medical-surgical intensive care unit; CI, confidence interval; SD, standard deviation; ID, infectious diseases; DDD, defined daily dose; MDRO, multidrug-resistant organism; CDI, *Clostridioides difficile* infection.
[a]Cumulative indicators from July 2018 to June 2019.
[b]Percent unless otherwise indicated.
[c]Appropriateness rate: no. of prescriptions complying with the indicator × 100/total prescriptions of this category.
[d]Antimicrobial categories J01 and J02.
[e]MDROs: methicillin-resistant *S. aureus*; vancomycin-resistant *Enterococcus*; extended-spectrum β-lactamase Enterobacteriacea; carbapenem-resistant Enterobacteriacea; carbapenem-resistant *P. aeruginosa* and *Acinetobacter* spp.

polymyxins.[27,33–35] These findings represent an opportunity to promote new and rapid diagnostic tests to improve empiric treatments.[36]

In our study, MS-ICUs that reached the 75th percentile showed improvements in antimicrobial prescription appropriateness, antimicrobial consumption, and impact indicators compared to those that remained within the 25th percentile. Only CDI rates were significantly higher at MS-ICUs above the 75th percentile, likely related to better detection, as well as other risk factors such as consumption of proton pump inhibitors, which were not evaluated in this study.[37] In addition, higher compliance with IPC strategies was associated with ASPs that are more comprehensive.

This study has several limitations. Participation was voluntary, which may have biased participation to hospitals with an interest in antibiotic stewardship. The restriction of the study to MS-ICU may limit the generalizability of the results, and overrepresentation of Argentinean hospitals may limit more generalizable conclusions. The strengths of the project include the prospective study design, findings of improved antibiotic use, better outcomes, and description of a model that is practical for the LMIC setting.

Based on previous experience, we limited our project to adult inpatients admitted to MS-ICUs. We restricted the study to adult patients because of difficulties in performing data collection using days of therapy as the measure of antimicrobial consumption in many Latin American institutions. Although, DDD is a useful indicator in the adult population, it is not useful for pediatric patients.[25,29] Another reason to constrain the study to MS-ICUs was to enhance feasibility and sustainability because a limited number of human resources are involved in development, implementation, and monitoring ASPs in many hospitals located in low- and middle- and lower-income countries.[31] In addition, AMR and the challenges of appropriateness of antimicrobial use are more frequent in ICUs than in general wards.[38,39]

In summary, our results suggest that MS-ICUs with ASPs with higher global scores in the final-self assessment showed improved appropriateness and impact indicators and lower antimicrobial

Table 4. Infection Prevention and Control Strategies Implemented at MS-ICUs Stratified by the Global Score of the Final Self-Assessment

	Final Percentile Group, %			Comparison Between the ≥75th vs ≤25th Percentiles		
Indicators[a]	≤ 25th (n=20)	<75th to >25th (n=37)	≥75th (n=20)	Difference, %	95% CI	*P* Value
Hand hygiene program	82.9	95.0	100.0	17.1	12.3 to 21.8	.000
Surveillance of hand hygiene adherence	68.8	69.9	88.8	19.9	12.3 to 27.5	.000
Surveillance of MDRO-HAI	61.7	82.0	88.3	26.7	19.3 to 34.0	.000
Policy for contact precautions	97.1	99.3	100.0	2.9	0.8 to 5.1	.022
Contact precautions for CRE	98.7	98.0	100.0	1.3	−0.1 to 2.7	.236
Contact precautions for CDI	92.7	83.9	96.3	3.5	−0.6 to 7.7	.136
Policy for environmental cleaning	93.3	98.0	100.0	6.7	3.5 to 9.8	.000
Measurement of environmental cleaning effectiveness	34.4	62.8	68.8	34.4	25.8 to 42.9	.000
Policy for daily chlorhexidine bathing	83.3	89.9	95.4	12.1	6.7 to 17.5	.000
Use of cloths impregnated with chlorhexidine for daily bathing	55.0	74.2	76.9	21.9	13.1 to 30.7	.000
Bundle for CLABSI	67.5	75.9	95.0	27.5	21.0 to 34.0	.000
Surveillance of CLABSI	81.5	89.9	100.0	18.5	12.5 to 24.5	.000
Bundle for CAUTI	65.8	72.1	91.3	25.4	18.4 to 32.4	.000
Surveillance of CAUTI	81.6	90.6	98.6	17.0	10.8 to 23.2	.000
Bundle for VAP	80.8	78.2	100.0	19.2	14.2 to 24.1	.000
Surveillance of VAP	87.1	91.1	99.2	12.1	7.2 to 16.9	.000

Note. MS-ICU, medical-surgical intensive care unit; CI, confidence interval; MDRO multidrug-resistant organisms: methicillin-resistant *Staphylococcus aureus*; vancomycin-resistant *Enterococcus*; extended-spectrum β-lactamase *Enterobacteriacea*; carbapenem-resistant *Enterobacteriacea*; carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter* spp.; CDI, *Clostridioides difficile* infection. CLABSI, catheter-associated bloodstream infection; CAUTI, catheter-associated urinary tract infection; VAP, ventilator-associated pneumonia; HAI, healthcare-associated infection.
[a]Cumulative compliance from July 2018 to June 2019.

consumption than those with lower scores. MS-ICUs with more comprehensive ASPs showed significant improvement in antimicrobial utilization.

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